Electronic Supplementary Material (ESI) for Green Chemistry.

Controlled photo-flow oxidative reaction (UV-FOR) platform for ultra-fast phthalide and API synthesis

Dnyaneshwar Aand, Sanjeev Karekar, Bhushan Mahajan, Amit B. Pawar, Ajay K Singh*

Organic synthesis and Process Chemistry, CSIR-Indian Institute of Chemical Technology, Hyderabad-500007, India.

Table of Contents

1. General

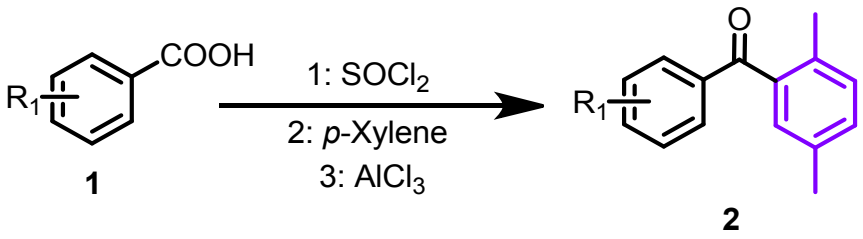
1.1. Materials: Most of the reagents and chemicals bought from sigma-aldrich as used as such without any further purification. Common organic chemicals and salts were purchased from Avra chemicals, India. Deionized water (18.2 mS conductivity) was used in all experiments. All work-up and purification procedures were carried out with reagent-grade solvents in air. Analytical thin-layer chromatography (TLC) was performed using analytical chromatography silica gel 60 F254 precoated plates (0.25 mm). The developed chromatogram was analysed by UV lamp (254 nm). PTFE (id = 500 μm) tubing, T-junction, high-purity PFA tubing was purchased from Upchurch IDEX HEALTH &SCIENCE. Asia syringe pump, heating system, back pressure controller (BPR), valve, catalytic reactor, Asia Manager PC software system bought from Syrris Asia System. For hydrogenation reaction used high-pressure Kauner-pump. H-cube and mass-flow controller (MFC) bought from thales-nano. High-pressure gas regulator bought from Amar-Equipment Mumbai. Homemade photo- batch reactor bought from lelesil Mumbai, India and slightly modified for the continuous flow reaction.

1.2. Analysis: High-resolution mass spectra (HRMS) were obtained from a JMS-T100TD instrument (DART) and Thermo Fisher Scientific Exactive (APCI). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker 600, 500, 400 or 300 MHz in CDCl3 or DMSO-d6 solvent. Chemical shifts for 1H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for 13C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, quin = quintet, sext = sextet, m = multiplet), coupling constant (Hz), and integration.GC/MS analysis was

conducted on an Simadzu technology GCMS-QP2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard) and inbuilt MS 5975C VL MSD system with triple axis detector.

2. General reaction procedure and characterization of products in details.

2.1. Preparation of starting materials 2b-2l:

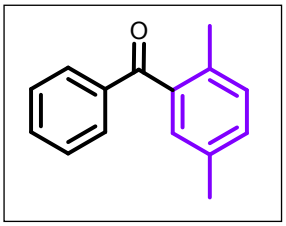


1 **2**

Reported method has been applied to synthesis of starting materials. At first, substituted aromatic acid (2.0 mmol) and then slowly $SOCl_2$ (8 mmol) was added to the reaction mixture and then refluxed until a clear solution had formed (ca. 2 h). Excess $SOCl_2$ was removed in vacuo (under nitrogen), and the resulting acid chloride (2.0 mmol) was slowly mixed with substituted benzene (4mmol) and $AlCl_3$ (3 mmol) at 0 ^{0}C and then stirred at RT for 10-12h. After the reaction completion, 40 ml ice cold water was added to reaction mixture and then then quenched with 1M HCl (1 ml). Organic product was extracted with DCM (3 x 40 mL). Further to remove unused aromatic acid, we have added saturated $NaHCO_3$ (20 mL). The combined organic layers were washed with brine solution (20 mL), dried over Na_2SO_4, and the solvent removed *in vacuo* to yield the crude product. The title compound was obtained after silica gel flash chromatography (Hexane/Ethyl acetate (95:05, v/v) as a followed phase product.

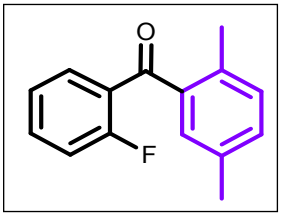
Phenyl (o-tolyl) methanone (2a): Directly purchased form sigma-aldrich and used as such.

(2, 5-Dimethylphenyl) (phenyl) methanone (2b).[1]



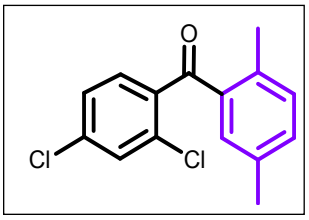
Starting material **2b** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a colorless liquid (344.4 mg, 82%); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 (d, *J* = 7.6 Hz, 2H), 7.51 (s, 1H), 7.39 (t, *J* = 7.0 Hz, 2H), 7.18 – 7.08 (m, 3H), 2.28 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.7, 138.6, 137.8, 134.8, 133.5, 133.1, 131.0, 130.9, 130.1, 128.9, 128.5, 20.9, 19.5; **IR (ν_{max}):** 2921, 1660, 1593, 1447, 1289, 1265, 1210, 949, 819, 692, 649 cm^{-1}; **HRMS (ESI):** m/z calcd. for $C_{15}H_{14}O$ $[M+H]^+$: 211.1123, found: 211.1121.

(2, 5-Dimethylphenyl) (2-fluorophenyl) methanone (2c).



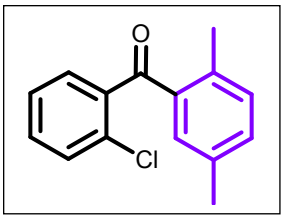
Starting material **2c** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a yellow color liquid (392.2 mg, 86%); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 (d, *J* = 4.3 Hz, 1H), 7.43 (s, 1H), 7.21 – 7.09 (m, 4H), 7.04 (d, *J* = 7.8 Hz, 1H), 2.40 (s, 3H), 2.23 (d, *J* = 3.2 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 194.8 (s), 160.3 (d, *J* = 254.3 Hz), 138.0, 134.5, 134.3, 133.3 (d, *J* = 8.2 Hz), 131.7, 131.0, 130.7, 129.8, 127.5 (d, *J* = 11.8 Hz), 123.8 (d, *J* = 3.6 Hz), 116.13, 116.0 (d, *J* = 21.8 Hz), 20.2, 19.6; **IR (ν_{max}):** 3019, 1663, 1213, 1016, 948, 743, 660 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{13}FO$ $[M+H]^+$: 229.1029, found: 229.1026.

(2-Chlorophenyl) (2, 5-dimethylphenyl) methanone (2d):



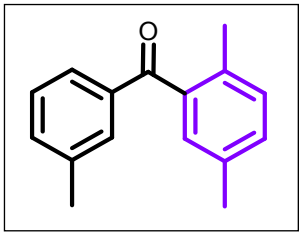
Starting material **2d** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a brown colour liquid (405 mg, 83%); The spectra data matched with values reported in the literature.[2] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.37 (m, 3H), 7.34 – 7.30 (m, 1H), 7.19 (q, *J* = 7.6 Hz, 2H), 7.12 (s, 1H), 2.50 (s, 3H), 2.26 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 197.4, 139.6, 136.8, 136.2, 135.0, 132.7, 131.7, 131.7, 131.6, 131.3, 130.2, 129.86, 126.6, 20.7, 20.6; **IR (ν_{max}):** 3059**,** 2924, 1668, 1565, 1420, 1297, 1265, 1198, 1075, 957, 901, 811, 757, 676 cm^{-}1; **HRMS (ESI):** m/z calcd for $C_{15}H_{13}ClO$ $[M+H]^+$: 245.0733, found: 245.0733.

(2, 4-dichlorophenyl) (2, 5-dimethylphenyl) methanone (2e):



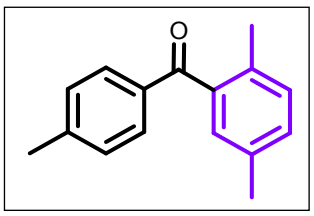
Starting material **2e** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a pale brown solid (483.8 mg, 87%); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41 (d, J = 1.8 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.28 (dd, J = 8.3 Hz, 1.9 Hz, 1H), 7.18 (dd, J = 18.5 Hz, 7.7 Hz, 2H), 7.10 (s, 1H), 2.48 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 196.0, 137.8, 136.7, 136.3, 136.2, 135.0, 132.85, 132.7, 131.7, 131.3, 130.8, 130.0, 126.9, 20.6, 20.5; **IR (ν_{max}):** 2971, 2861, 1667, 1580, 1451, 1376, 1297, 1206, 1103, 1052, 945, 858, 819, 775, 661 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{12}Cl_2O$ $[M+H]^+$: 279.0343, found : 279.0345.

(2, 5-dimethylphenyl) (m-tolyl) methanone (2f):



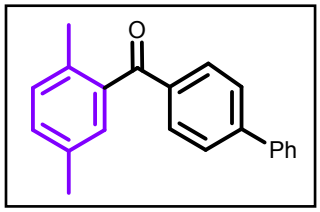
Starting material **2f** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a colourless liquid (385.3 mg, 86%); The spectra data matched with values reported in the literature.[3] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (s, 1H), 7.55 (d, *J*=7.6 Hz, 1H), 7.35 (d, *J*=7.6 Hz, 1H), 7.29 (t, *J*=7.6 Hz, 1H), 7.18 – 7.07 (m, 3H), 2.36 (s, 3H), 2.30 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.80, 138.64, 138.08, 137.66, 134.52, 133.70, 133.17, 130.68, 130.63, 130.09, 128.62, 128.11, 127.35, 21.09, 20.66, 19.28; **IR (ν_{max}):** 3016, 2994, 2917, 2885, 1657, 1605, 1494, 1451, 1380, 1297, 1269, 1178, 1040, 961, 840, 811, 757, 704, 649 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{16}H_{16}O$ $[M+H]^+$: 225.1279, found: 225.1276.

(2, 5-dimethylphenyl) (p-tolyl) methanone (2g):



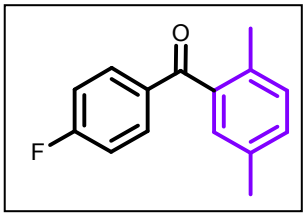
Starting material **2g** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a white solid (398.7 mg, 89%); The spectra data matched with values reported in the literature.[4] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 4.3 Hz, 2H), 7.09 (s, 1H), 2.40 (s, 3H), 2.31 (s, 3H), 2.24 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 198.42, 143.86, 138.84, 135.12, 134.61, 133.09, 130.66, 130.62, 130.15, 129.06, 128.55, 21.57, 20.76, 19.30; **IR (ν_{max}):** 3027, 2929, 2858, 1660, 1605, 1455, 1403, 1297, 1265, 1183, 1040, 953, 846, 815, 767, 684cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{16}H_{16}O$ $[M+H]^+$: 1279, found: 225.1271.

(2, 5-dimethylphenyl) [1, 1'-biphenyl]-4-yl) methanone (2h):



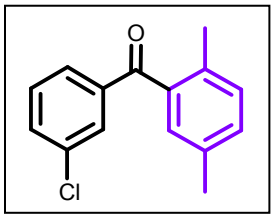
Starting material **2h** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a white solid (520.5 mg, 81%); **m.p:** 112ºC; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.91 – 7.87 (m, 2H), 7.69 – 7.63 (m, 4H), 7.50 – 7.46 (m, 2H), 7.44 – 7.38 (m, 1H), 7.24 – 7.11 (m, 3H), 2.35 (s, 3H), 2.30 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 198.48, 145.80, 139.91, 138.70, 136.44, 134.82, 133.38, 130.90, 130.85, 130.70, 128.94, 128.78, 128.23, 127.29, 127.11, 20.88, 19.48; **IR (ν_{max}):** 2924, 2865, 1664, 1597, 1447, 1265, 1206, 948, 818, 692, 652 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{21}H_{18}O$ $[M+H]^+$: 287.1438, found: 287.1436.

(2, 5-dimethylphenyl) (4-fluorophenyl) methanone (2i):



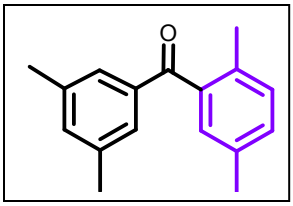
Starting material **2i** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a yellow colour liquid (396.7 mg, 86%); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.87 – 7.77 (m, 2H), 7.22 – 7.08 (m, 5H), 2.33 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 197.29, 167.03, 164.49, 138.32, 134.88, 134.12 (d, *J*=2.9 Hz), 133.29, 132.69 (d, *J*=8.8 Hz), 130.95 (d, *J*=11.7 Hz), 128.63, 115.68, 115.46, 20.84, 19.39; **IR (ν_{max}):** 2930, 1662, 1598, 1501, 1411, 1269, 1223, 1159, 952, 849, 785, 675; **HRMS (ESI):** m/z calcd for $C_{15}H_{13}OF$ $[M+H]^+$: 229.1029, found: 229.1026.

(3-chlorophenyl) (2, 5-dimethylphenyl) methanone (2j):



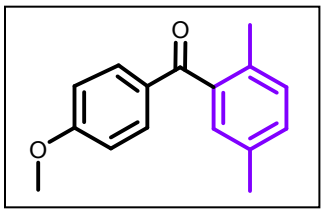
Starting material **2j** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a yellow colour liquid (410.0 mg, 86%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 – 7.77 (m, 1H), 7.65 – 7.58 (m, 1H), 7.45 (ddd, *J* = 7.9, 2.0, 0.9 Hz, 1H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.17 – 7.07 (m, 3H), 2.28 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.32, 139.13, 137.31, 134.38, 134.26, 133.26, 132.37, 130.97, 130.66, 129.35, 129.18, 128.56, 127.82, 20.35, 19.07; **IR (ν_{max}):** 2961, 1662, 1552, 1423, 1262, 1203, 1074, 965, 894, 809, 752, 674 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{13}OCl$ $[M+H]^+$: 245.0733, found : 245.0733.

(2, 5-dimethylphenyl) (3, 5 dimethyl phenyl) methanone (2k):



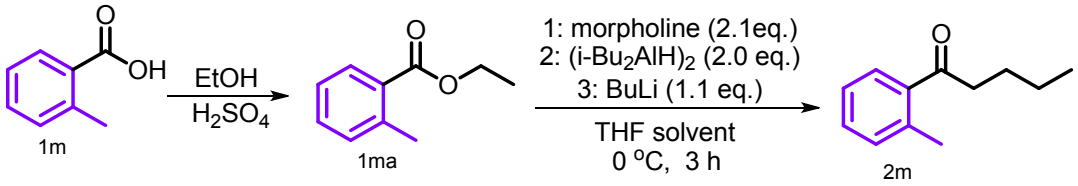
Starting material **2k** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a colourless liquid (395.0 mg, 83%); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (s, 2H), 7.22 – 7.14 (m, 3H), 7.10 (s, 1H), 2.35 (s, 6H), 2.33 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 199.4, 139.0, 138.1, 137.9, 134.8, 134.7, 133.3, 130.7, 130.7, 128.7, 127.8, 21.2, 20.9, 19.5; **IR (ν_{max}):** 2929, 1662, 1605, 1450, 1308, 1243, 1178, 1043, 862, 785, 675 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{17}H_{18}O$ $[M+H]^+$: 239.1436, found: 239.1433.

(4-methoxyphenyl) (2, 5-dimethylphenyl) methanone (2l):



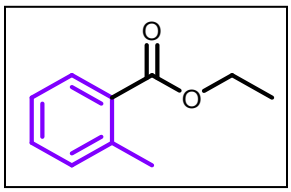
Starting material **2l** was prepared according to general procedure 2.1. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a white solid (379.2 mg, 79%); The spectra data matched with values reported in the literature.[5] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 – 7.75 (m, 2H), 7.20 – 7.12 (m, 2H), 7.09 (s, 1H), 6.96 – 6.89 (m, 2H), 3.87 (s, 3H), 2.33 (s, 3H), 2.23 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 197.61, 163.63, 139.15, 134.72, 132.87, 132.45, 130.65, 130.58, 130.47, 128.33, 113.66, 55.47, 29.68, 20.86, 19.27; **IR (ν_{max}):** 2971, 1656, 1597, 1507, 1300, 1262, 1165, 1029, 951, 842, 737, 687 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{16}H_{16}O_2$ $[M+H]^+$: 241.1229, found: 241.1229.

2.2. Preparation of starting materials 2m:



First ethyl 2-methylbenzoate was prepared by using same method which already reported elsewhere.[6] To make starting materials by using ethyl 2-methylbenzoate slightly modified method was used.[7] A dry and argon-flushed flask, equipped with a magnetic stirring bar and a septum, was charged with morpholine (0.90 mL, 5.5 mmol) and 50 mL THF. After cooling to 0°C, (i-$Bu_2AlH)_2$ (10.0 mL, 1.0 M in hexane, 10.0 mmol) was added dropwise and stirred for 3h at same temperature. To a reaction mixture was slowly added ethyl benzoate (0.82g, 1.0 mmol) and stirred for 10min. Then, n-BuLi (6.25 mL, 1.6M in hexane, 2.0mmol) was added and the mixture was stirred for 10 min again. The reaction was stopped by the aqueous 1N HCl (50 mL) and extracted with diethyl ether (2 × 50mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel yielded 1-(o-tolyl) pentan-1-one (748 mg, 85%).

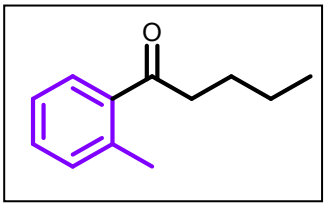
Ethyl 2-methylbenzoate:



Colorless liquid (149 mg, 91% yield); The spectra data matched with values reported in the literature.[8] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.92 (dd, *J*=8.1 Hz, 1.5, 1H), 7.37 (t, *J*=7.5, 1H), 7.23 (t, *J*=7.0, 2H), 4.36 (d, *J*=7.2, 2H), 2.61 (s, 3H), 1.39 (t, *J*=7.1, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ

167.51, 139.85, 131.66, 131.49, 130.35, 129.82, 125.51, 60.51, 21.56, 14.19; **IR (ν_{max}):** 2979, 1719, 1455, 1368, 1293, 1253, 1135, 1079, 1028, 858, 736 cm^{-1};

1-(o-tolyl) pentan-1-one (2m):



Starting material **2m** was prepared according to general procedure 2.2. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 98:02) to provide a pale yellow colored liquid (748 mg, 85%); Hexane/Ethyl acetate (95:05); The spectra data matched with values reported in the literature.[9] **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.60 (d, *J*=7.8 Hz, 1H), 7.39 – 7.32 (m, 1H), 7.28 – 7.19 (m, 2H), 2.87 (t, *J*=7.4 Hz, 2H), 2.48 (s, 3H), 1.68 (dt, *J*=20.6 Hz, 7.5 Hz, 2H), 1.45 – 1.32 (m, 2H), 0.94 (t, *J*=7.4 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 204.59, 138.20, 137.58, 131.68, 130.80, 128.09, 125.44, 41.19, 26.38, 22.31, 21.00, 13.88, 13.78; **IR (ν_{max}):** 3075, 2960, 2980, 1688, 1569, 1455, 1253, 1210, 1016, 969, 744 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{12}H_{16}O$ $[M+H]^+$: 176.1229, found: 176.1229.

2.3. Procedure for synthesis of phthalide: A 0.0125M solution of phenyl (o-tolyl) methanone was taken in bottle and oxygen cylinder was connected with mass-flow controller (MFC) (Figure S1). Two reactants were introduced through T-mixer (T1) in a flow rate molar ratio of 1:35 to maintain the stoichiometry (Table S1), and then passed through a PFA tubing (id = 1000 μm, length = varied) for the generation of phthalides. As mentioned in Table S1 various reaction parameters (retention time, temperature, bulb power, pressure) were regulated to optimize reaction performance. Eventually, 145 psi back pressure regulator (BPR), medium pressure lamp (250 W, max. 365 nm light), 12.1 min retention time at RT generated the best yield 92% of phthalides production (Table S1, Entry 11).

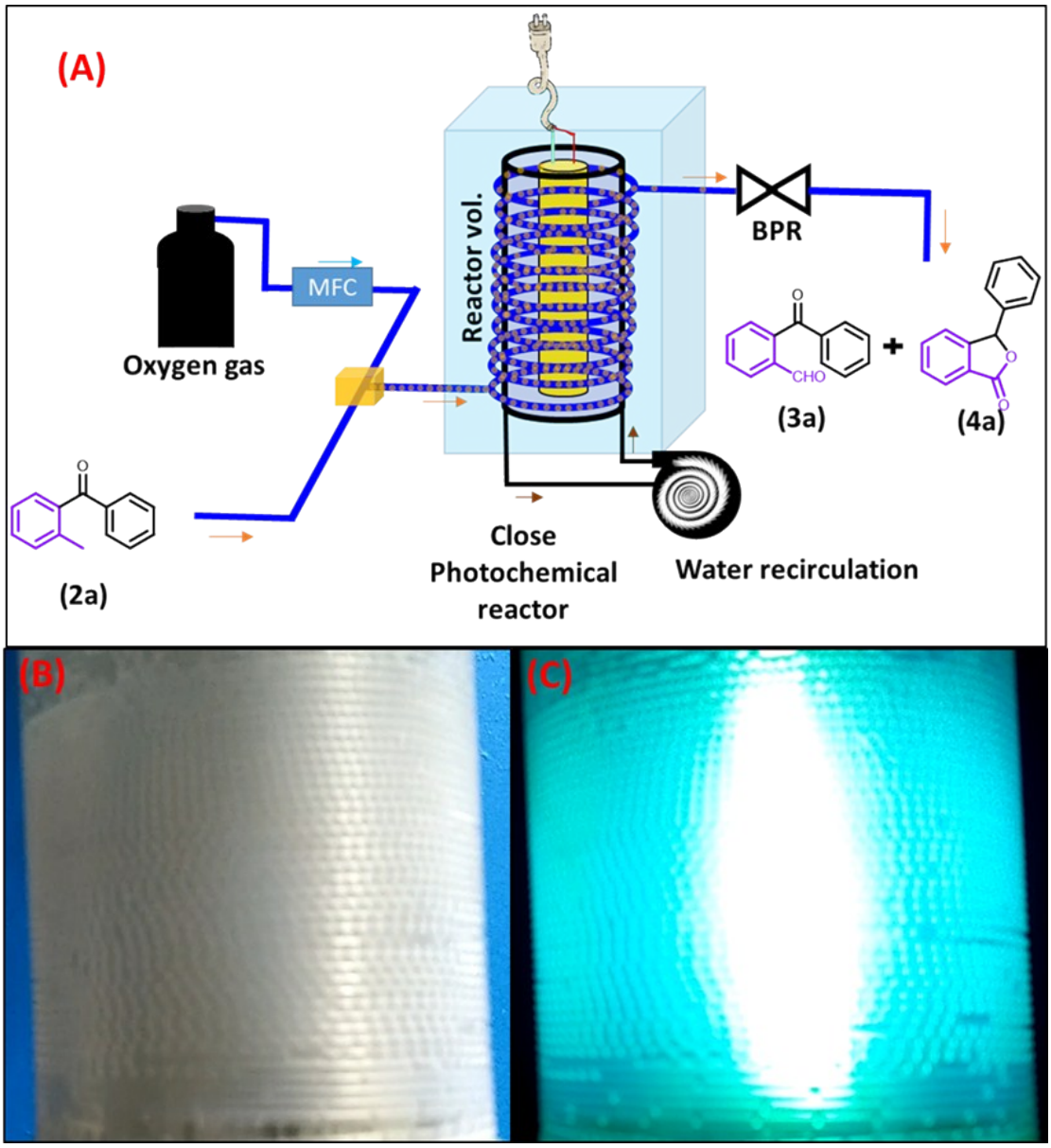
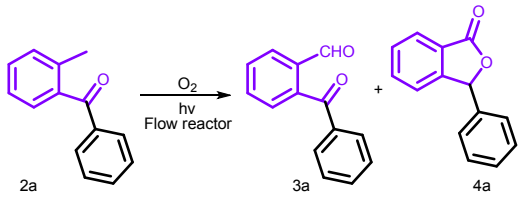


Figure S1: (A) Schematic diagram of continuous photo-enolization oxidation reaction; (B) oxygen gas-liquid droplets under visible light; (C) oxygen gas-liquid droplets under ultra-violet light.

Table S1: Optimization of O_2 segmental flow reaction to synthesize phthalide (3) in catalyst free methods.



Entry	Flow rate µL/min		Molar ratio (2a:O_2)	Retention time (Min.)	Conversion (%)	% Yield[j]	
	2a	O_2				3a	4a
1[a]	95	70	1:1.24	12.3	11	5	3
2[a]	60	300	1:8.75	5.6	52	38	10
3[a]	20	200	1:17.5	9.1	50	31	18
4[a]	20	100	1:8.75	16.7	100	49	41
5[a]	10	300	1:52.5	6.5	40	19	NA
6[a]	10	200	1:35	9.5	100	58	24
7[a]	10	100	1:17.5	18.5	100	21	65
8[b]	40	200	1:17.5	8.5	100	25	71
9[b]	20	200	1:35	9.2	100	15	82
10[c]	100	1000	1:35	12.1	100	5	89
11[d]	100	1000	1:35	12.1	100	3	92 (85)
12[c]	100	1000[e]	1:7.33	12.1	43	11	32
13 [c&f]	100	1000	1:35	12.1	NA	NA	NA
14 [c&g]	100	1000	1:35	12.1	NA	NA	NA
15[h]	100	1000	1:35	12.1	NA	NA	NA
16[i]	batch	-	-	4320	83	42	12

Reaction condition: (a) medium pressure lamp (250 W), 2a: 0.025 M in DMSO, reactor volume 2 mL; BPR 40 psi; (b) medium pressure lamp (250 W), 2a: 0.0125 M in DMSO, reactor volume 2 mL, BPR 40 psi; (c) medium pressure lamp (250 W), 2a: 0.0125 M in DMSO; reactor volume 13.3 mL; [d] medium pressure lamp (250 W), 2a: 0.0125 M in DMSO; reactor volume 13.3 mL; BPR (145 psi); [e] air; [f] medium pressure lamp replaced with 254 nm lamp (4 W); [g] medium pressure lamp replaced with green led 550 nm (15 W); [h] medium pressure lamp replaced with red led 630 nm (15 W); [i] batch reactor (medium pressure lamp (250 W), 2a: 0.025 M in DMSO (total volume 20 mL), reactor volume 50 mL; O_2 gas balloon; [j] yield are determined by GC-MS analysis with dodecane as internal standard, at least three measurements were taken to obtain an average yield; yield in parenthesis indicated isolated yield.

Table S2: Solvent screening.

Entry	Solvent	Dipole moment	Light cut-off	Relative dielectric constant	Conversion %	Yield % 3a	Yield % 4a
1[a]	DMF	245	268	31.47	100	12	83
2[a]	DMSO	3.96	268	46.45	100	3	92
3[a]	Chlorobenzene	1.54	287	5.69	100	8	90
4[a]	ACN	3.92	190	35.94	90	7	81
5[a]	1, 4- dioxane	0.45	215	2.21	18	18	NA
6[a]	Toluene	0.36	284	2.38	68	26	41
7[a]	DCM	1.6	233	8.93	05	5	NA
8[a]	Ethyl acetate	1.78	256	6.02	09	9	NA
9[a]	Methanol	1.7	205	32.66	06	6	NA
10[a]	Acetone	2.88	330	20.56	02	2	NA
11[a]	Hexane	0.08	195	01.88	19	19	NA

Reaction condition: UV medium pressure lamp 250 W (a) 2a: 0.0125 M in DMSO; reactor volume 13.3 mL; BPR (145 psi) Yield are determined by GC-MS analysis with dodecane as internal standard, at least three measurements were taken to obtain an average yield.

3. Typical procedure to extract and to separate the product in a UV-FOR platform:

3.1. Micro-separator design and work: To switch the solvent containing the product from DMSO to DCM, the additional PTFE membrane embedded phase separator was connected to outlet of the photo-reactor as shown in Fig S1. The homemade microseparator was fabricated as following: to protect the metal corrosion, firstly, we were place the laser cutted polyethylene grooves kit (60 mm x 60 mm x 240 μm thickness) as shown in Figure S2, with metal holder. Secondly, laser cutted HDPE plastic (60 mm x 60 mm x 2 mm thickness) single groove with rectangular shape (1 mm x 35.5 mm). The 4-corners of two PE film were holed (1 mm diameter) to align the film patterns. Polytetrafluoroethylene (PTFE) membrane (Whatmann, 0.45 μm pore, 37 mm dia.) was sandwiched by two HDPE plastic and PE sheets with identical dimension of groove channels, and aligned to each other by inserting metal pins through the holes at the film corners. Finally, the metal holder was tightly pressed by screw to seal the device with no leak. A serial process of droplet formation, extraction and separation for purification of the phthalide was conducted in droplet microfluidics equipped with the PTFE membrane microseparator, as explained in a step-wise manner at the below.

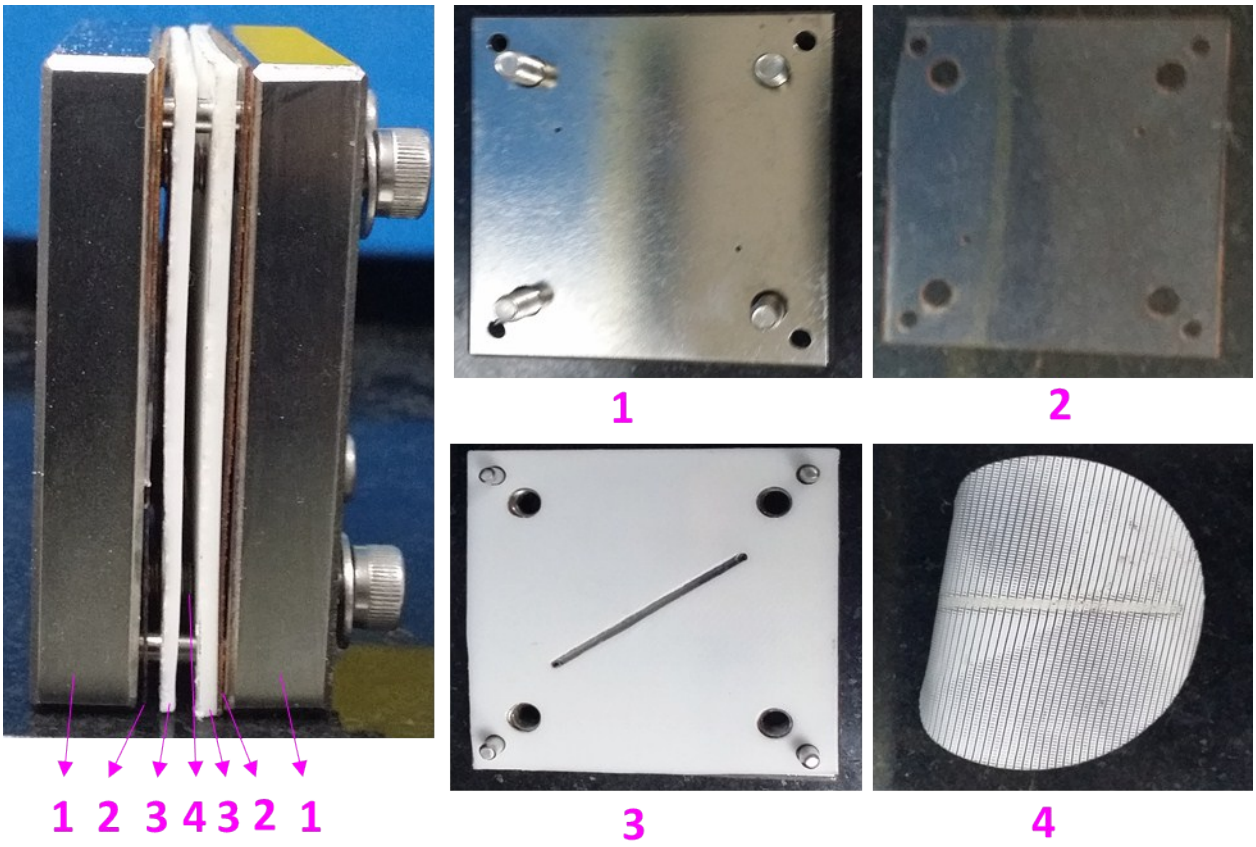


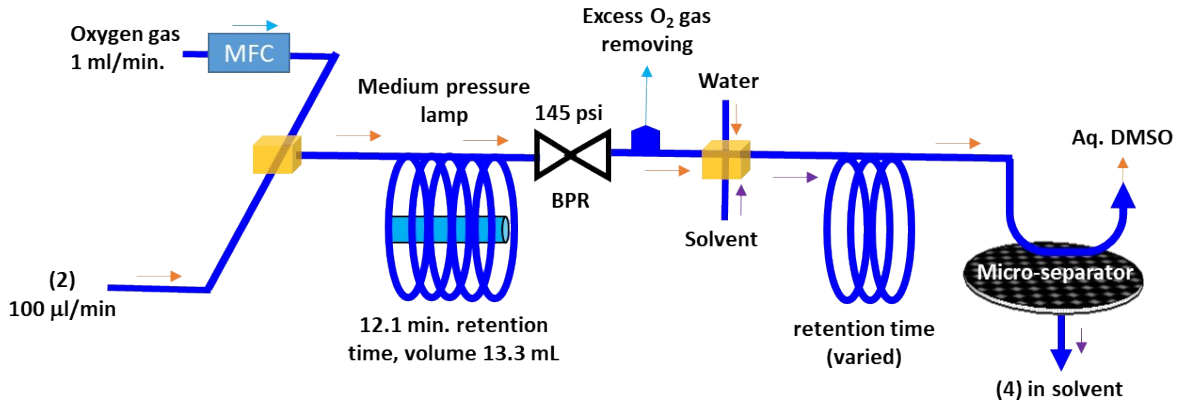
Figure S2. Illustration of a fluoropolymer PTFE membrane microseparationsandwiched between two polyethylene films with laser cutted channel; (1) original image of metal holder; (2) original image of laser cutted polyethylene grooves kit (60 mm x 60 mm x 240 µm thickness); (3) original image of laser cutted HDPE plastic (60 mm x 60 mm x 2mm thickness) grooves (single groove with rectangular shape (1 mm x 35.5 mm,); (4) original image of polytetrafluoroethylene (PTFE) membrane (Whatmann, 0.45 µm pore, 37 mm diameter).

Step 1: Formation of alternating organic-aqueous droplets: Water was introduced into the product mixture in DCM through X-junction.

Step 2: Extraction: The DMSO solvent in the reaction mixture were gradually moved to aqueous droplet phase and real time extraction through a PTFE capillary (id = 1000 µm, length = 2.6 m, vol. = 2 mL):

Step 3: Complete separation: The organic phase containing product could wet thin PFPE membrane and permeated to the opposite channel of the separator, whereas the waste containing aqueous phase did not wet the membrane and maintained at the original stream. The obtained product dissolved in DCM was analyzed by GC-MS, which showed a no DMSO and as confirmed by absence of the corresponded peaks in NMR analysis (^{1}H and ^{13}C NMR spectra of 4a). Note that there was no workup such as washing the product with aq. NH_4Cl, there was no need to be dried with Na_2SO_4. The reaction mixture was purified by column chromatography (hexane/ethyl acetate) to give the product 4a (44.7 mg, 85%).

Table S3. Optimization of product extraction parameters in a solvent switching work-up step.



Entry	Water (Flow rate: µl/min)	Solvent (Flow rate: µl/min)	%Yields (4)
1[a]	100	100	12
2[a]	200	200	10
3[a]	200	100	34
4[a]	500	100	73
5[a]	800	100	81
6[a]	1000	100	85
7[b]	1000	100	85
8[c]	1000	100	NA
9[d]	1000	100	72
10[e]	1000	100	64
11[f]	1000	100	79

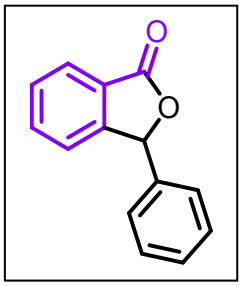
Yield is based on isolated yields; (a) DCM; (b) diethyl ether; (c) ethyl acetate; (d) hexane; (e) toluene; (f) chloroform.

3.2. Procedure for synthesis, extraction and separation of phthalides: A 0.0125 M solution of phenyl (o-tolyl) methanone was taken in bottle and oxygen cylinder was connected with mass-flow controller (MFC) (Figure S1). Two reactants were introduced through T-mixer (T1) in a flow rate molar ratio of 1:35 to maintain the stoichiometry (Table

S1), and then passed through a PFA tubing (id = 1000 μm, length = 17 meter, medium pressure lamp 250W) for the synthesis of phthalides during 12.1 min of residence time and 145 psi pressure. Next the excess amount of oxygen gas was removed by collecting reaction mixture in open flask. Next reaction mixture was quenched and solvent exchange (from high boiling solvent DMSO to low boiling solvent DCM, diethyl ether, ethyl acetate, hexane, toluene, chloroform) by introducing water and low boiling solvent through additional X-mixer to form organic-aqueous droplets (table S3). Complete extraction between the organic-aqueous segments was occurred for 1.7 min retention time by flowing through a PTFE capillary (id = 1000 μm, length = 2.6 m, vol. = 2 mL). Further, organic-aqueous segment was separated by passing through the above designed homemade microseparator and complete separation (Table S3, entry 6) was achieving by regulating the back pressures and retention time (0.1 min) and flow rate of water (1000 μl/min) and DCM (100 μl/min). Extracted waste water layer was further extracted with diethyl ether and analyzed by GC-MS, which showed a no product and again confirmed by absence of the corresponded peaks in crude NMR analysis (^{1}H and ^{13}C NMR spectra). Under similar condition, several solvent system was used during replacement of DCM to diethyl ether, ethyl acetate, hexane, toluene, chloroform solvent. The reaction mixture was purified by column chromatography (hexane/ethyl acetate) to give the product **4a-4m**.

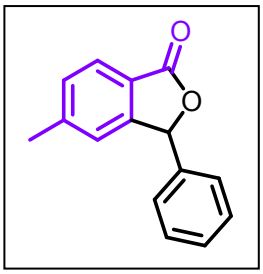
Note: Distribution ratio is very important parameter for the liquid-liquid membrane based extraction of the product.[10] In optimized solvent distribution ration we need to use 1:10:1 ratio of DMSO: Water: DCM.

3-phenylisobenzofuran-1-(*3H*)-one (4a):



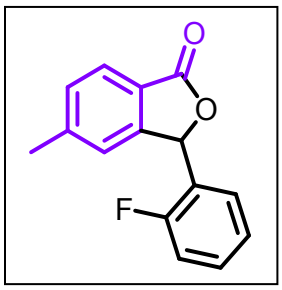
Compound **4a** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 44.7 mg (85% Yield); The spectra data matched with values reported in the literature.[11] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96 (d, *J*=7.6 Hz, 1H), 7.65 (td, *J*=7.5 Hz, 1.0 Hz, 1H), 7.55 (t, *J*=7.5 Hz, 1H), 7.40 – 7.36 (m, 3H), 7.33 (dd, *J*=7.6 Hz, 0.8 Hz, 1H), 7.29 – 7.25 (m, 2H), 6.40 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.49, 149.67, 136.40, 134.29, 129.35, 129.29, 128.96, 126.96, 125.65, 122.84, 82.71; **IR (ν_{max}):** 2884, 1751, 1613, 1451, 1285, 1107, 1060, 973, 839, 767, 696 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{14}H_{10}O_2$ $[M+H]^+$: 211.0759, found: 211.0756.

5-methyl 3-phenylisobenzofuran-1-(3*H*)-one (4b):



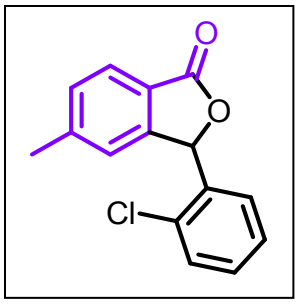
Compound **4b** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 50.83 mg (89% Yield); the spectra data matched with values reported in the literature.[12] **^{1}H NMR (400 MHz, $CDCl_3$)** 7.84 (d, *J*=7.8 Hz, 1H), 7.41 – 7.33 (m, 4H), 7.28 (dt, *J*=5.5 Hz, 2.0 Hz, 2H), 7.11 (d, *J*=0.6 Hz, 1H), 6.34 (s, 1H), 2.43 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.56, 150.26, 145.60, 136.64, 130.52, 129.18, 128.92, 126.91, 125.37, 123.05, 122.99, 82.43, 22.04; **IR (ν_{max}):** 3058, 2967, 2916, 1766, 1612, 1458, 1288, 1209, 1063, 1016, 798, 747, 700 cm-1; **HRMS (ESI):** m/z calcd for $C_{15}H_{12}O_2$ $[M+H]^+$: 225.0916, found: 225.0919.

3-(2-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (4c):



Compound **4c** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 42.37mg (75% Yield); melting point: 112 ºC; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 (d, *J*=7.8 Hz, 1H), 7.31 – 7.25 (m, 2H), 7.14 (s, 1H), 7.06 (dtd, *J*=8.7 Hz, 7.9 Hz, 0.9 Hz, 3H), 6.62 (s, 1H), 2.37 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.42, 161.67, 159.20, 149.84, 145.83, 130.68 (d, *J*=7.3 Hz), 127.64, 125.49, 124.63 (d, *J*=2.9 Hz), 124.30 (d, *J*=13.2 Hz), 122.92 (d, *J*=18.3 Hz), 115.99, 115.78, 76.34 (d, *J*=3.7 Hz), 22.06; **IR (ν_{max}):** 3016, 2937, 1755, 1711, 1605, 1486, 1387, 1289, 1229, 1135, 1008, 941, 811, 760, 688 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{11}FO_2$ $[M+H]^+$: 243.0821, found: 243.0825.

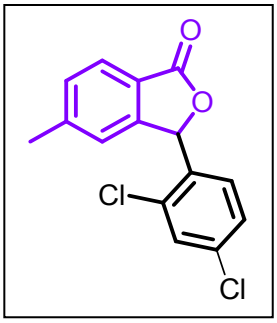
3-(2-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (4d):



Compound **4d** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 52.25 mg (81% yield); melting point: 108 ºC; the spectra data matched with values reported in the literature.[13] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J*=7.9, 1H), 7.47 (dd, *J*=7.9 Hz, 1.2 Hz, 1H), 7.35 (d, *J*=7.8 Hz, 1H), 7.29 (dt, *J*=5.0 Hz, 3.7 Hz, 2H), 7.24 – 7.19 (m, 1H), 7.10 (dd, *J*=7.8 Hz, 1.7 Hz, 1H), 6.89 (s, 1H), 2.43 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.54 150.01, 145.85, 134.69, 132.73, 130.68, 130.68, 130.03 (d, *J=8.8)*, 127.51, 127.42, 125.52, 123.09, 122.71, 78.70, 22.07; **IR (ν_{max}):** 2929, 2858, 1771, 1617, 1443, 1281, 1214, 1115, 1048, 1008,

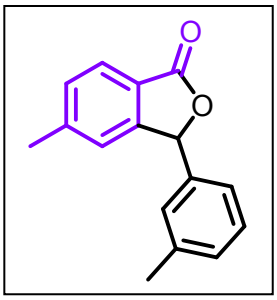
834, 763, 681 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{11}ClO_2$ $[M+H]^+$: 259.0526, found: 259.0526.

3-(2, 4-dichlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (4e):



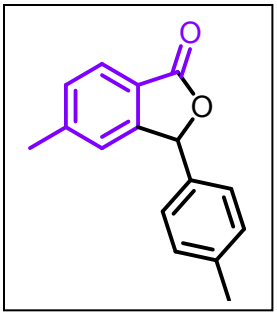
Compound **4e** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 57.67mg (79% Yield); melting point:148 ºC; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J*=7.8 Hz, 1H), 7.50 (d, *J*=2.1 Hz, 1H), 7.36 (d, *J*=7.8 Hz, 1H), 7.26 (s, 1H), 7.21 (dd, *J*=8.4 Hz, 2.1 Hz, 1H), 7.03 (d, *J*=8.4 Hz, 1H), 6.83 (s, 1H), 2.44 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.28, 149.58, 146.04, 135.42, 133.45, 133.41, 130.88, 129.83, 128.52, 127.87, 125.67, 123.00, 122.66, 78.10, 22.09; **IR (ν_{max}):** 2921, 2858, 1771, 1617, 1589, 1466, 1384, 1277, 1214, 1107, 1044, 831, 779, 681 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{11}Cl_2O_2$ $[M+H]^+$: 293.0136, found: 293.0135.

5-methyl-3-(m-tolyl) isobenzofuran-1-(3*H*)-one (4f):



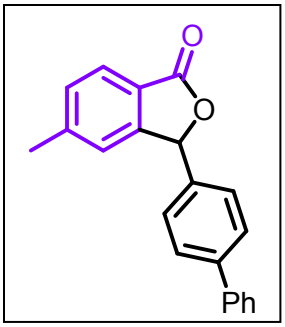
Compound **4f** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 52.36 mg (88% yield); melting point: 119 ºC; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J*=7.8 Hz, 1H), 7.34 (d, *J*=7.8 Hz, 1H), 7.27 (t, *J*=7.5 Hz, 1H), 7.18 (d, *J*=7.6 Hz, 1H), 7.12 – 7.05 (m, 3H), 6.30 (s, 1H), 2.43 (s, 3H), 2.34 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.64, 150.39, 145.56, 138.78, 136.55, 130.46, 129.94, 128.78, 127.40, 125.34, 123.99, 123.04, 122.96, 82.52, 22.04, 21.35; **IR (ν_{max}):** 3027, 2964, 2924, 2853, 1767, 7696, 1605, 1494, 1459, 1376, 1231, 1186, 1135, 1087, 973, 842, 763, 732, 676, 641 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{16}H_{14}O_2$ $[M+H]^+$: 239.1072, found 239.1071.

5-methyl-3-(p-tolyl) isobenzofuran-1-(3*H*)-one (4g):[13]



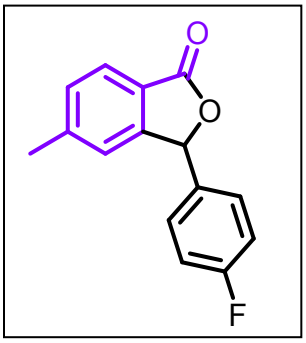
Compound **4g** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 49.39 mg (83% yield); melting point: 125 ºC; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J*=7.8 Hz, 1H), 7.34 (d, *J*=7.8 Hz, 1H), 7.23 – 7.12 (m, 4H), 7.09 (s, 1H), 6.31 (s, 1H), 2.43 (s, 3H), 2.36 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 170.64, 150.40, 145.52, 139.21, 133.62, 130.44, 129.59, 126.98, 125.32, 123.06, 82.47, 22.03, 21.22; **IR (ν_{max}):** 2913, 1767, 1613, 1459, 1289, 1060, 1000, 834, 755, 692 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{16}H_{14}O_2$ $[M+H]^+$: 239.1436, found 239.1436.

3-([1, 1'-biphenyl]-4-yl)-5-methylisobenzofuran-1-(3*H*)-one (4h):



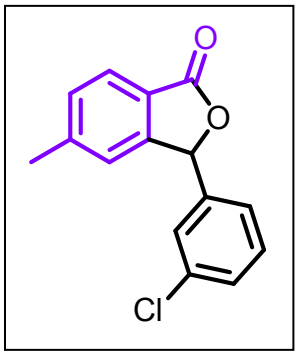
Compound **4h** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide white solid; 68.25 mg (91% Yield); melting point: 207 ºC; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.86 (d, *J*=7.9, 1H), 7.62 – 7.56 (m, 4H), 7.46 – 7.42 (m, 2H), 7.39 – 7.33 (m, 4H), 7.16 (s, 1H), 6.39 (s, 1H), 2.45 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 170.59, 150.24, 145.70, 142.26, 140.33, 135.58, 130.63, 128.88, 127.72, 127.45, 127.16, 125.49, 123.15, 82.28, 22.12; **IR (ν_{max}):** 2898, 1760, 1656, 1612, 1489, 1297, 1060, 982, 850, 763, 763, 693 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{21}H_{16}O_2$ $[M+H]^+$: 323.1047, found 323.1043.

3-(4-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (4i):



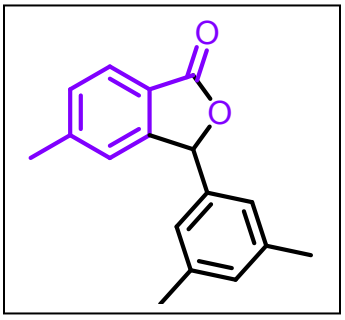
Compound **4i** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a White solid; 47.19 mg (78% yield); melting point: 162 ºC; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, *J*=7.8 Hz, 1H), 7.36 (d, *J*=7.8 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.07 (dd, *J*=12.0 Hz, 5.4 Hz, 3H), 6.33 (s, 1H), 2.45 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.29, 164.37, 161.91, 149.97, 145.74, 132.47, 130.66, 128.97 (d, *J*=8.1 Hz), 125.43, 123.03, 116.12, 115.95 (d, *J*=22.0 Hz), 81.70, 22.02; **IR (ν_{max}):** 3019, 2960, 2921, 853, 1763, 1696, 1597, 1506, 1407, 1262, 1218, 1155, 1099, 1012, 961, 846, 803, 752, 665 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{11}FO_2$ $[M+H]^+$: 243.0821, found 243.0825.

3-(3-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (4j):



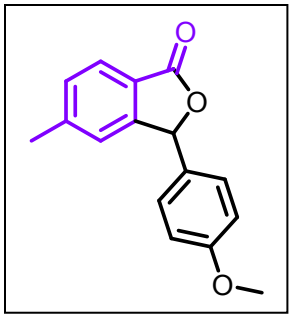
Compound **4j** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 51.6 mg (80% Yield); melting point: 129 ºC; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, *J*=7.8 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.26 (s, 1H), 7.19 (dt, *J*=6.6 Hz, 1.8 Hz, 1H), 7.11 (d, *J*=0.6 Hz, 1H), 6.30 (s, 1H), 2.45 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** 170.21, 149.64, 145.89, 138.71, 134.92, 130.81, 130.27, 129.39, 126.93, 125.59, 125.01, 122.97, 122.80, 81.42, 22.08; **IR (ν_{max}):** 2893, 1767, 1609, 1477, 1431, 1285, 1210, 1115, 1052, 981, 874, 826, 779, 712 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{15}H_{11}ClO_2$ $[M+H]^+$: 259.0256, found 259.0257.

3-(3, 5-dimethylphenyl)-5-methylisobenzofuran-1-(3*H*)-one (4k):



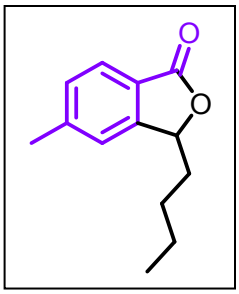
Compound **4k** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 49.77 mg (79% yield); melting point**:** 158 ºC; (hexane/ethyl acetate; 90: 10); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J*=7.8 Hz, 1H), 7.33 (dd, *J*=9.5 Hz, 5.3 Hz, 1H), 7.11 (d, *J*=0.5 Hz, 1H), 6.99 (s, 1H), 6.87 (s, 2H), 6.26 (s, 1H), 2.43 (s, 3H), 2.30 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 170.69, 150.46, 145.51, 138.57, 136.45, 130.79, 130.38, 125.25, 124.50, 123.00, 122.89, 82.58, 22.00, 21.19; **IR (ν_{max}):** 2923, 2854, 1769, 1612, 1463, 1229, 1113, 1060, 982, 860, 781, 711 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{17}H_{16}O_2$ $[M+H]^+$: 253.1229, found 253.1224.

3-(4-methoxyphenyl)-5-methylisobenzofuran-1-(3*H*)-one (4l):



Compound **4l** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a white solid; 53.54 mg (83% Yield); melting point**:** 137 ºC; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.82 (d, *J*=7.8, 1H), 7.34 (d, *J*=7.8, 1H), 7.19 – 7.15 (m, 2H), 7.09 (d, *J*=0.6, 1H), 6.92 – 6.87 (m, 2H), 6.30 (s, 1H), 3.80 (s, 3H), 2.43 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** 170.54, 160.29, 150.33, 145.49, 130.42, 128.66, 128.49, 125.23, 123.27, 123.11, 114.25, 82.40, 55.28, 22.00; **IR (ν_{max}):** 2921, 2850, 1752, 1617, 1513, 1455, 1307, 1248, 1171, 1120, 1068, 1029, 965, 835,752, 680 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{16}H_{14}O_2$ $[M+H]^+$: 255.1021, found 255.1025.

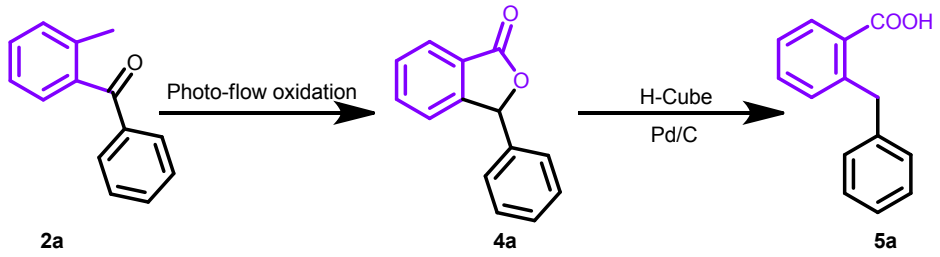
3-butylisobenzofuran-1(3H)-one (4m):



Compound **4m** was prepared according to general procedure 2.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 95: 05) to provide a light yellow liquid; 35.7 mg (70% yield). The ^{1}H NMR spectra data matched with values reported in the literature.[14] **^{1}H NMR (400 MHz, $CDCl_3$):** δ = 7.89 (d, *J*=7.6 Hz, 1H), 7.66 (td, *J*=7.6 Hz, 1.0 Hz, 1H), 7.52 (t, *J*=7.5 Hz, 1H), 7.43 (dd, *J*=7.6 Hz, 0.7, 1H), 5.47 (dd, *J*=7.9 Hz, 4.1 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.77 (tdd, *J*=9.3 Hz, 6.4 Hz, 3.7 Hz, 1H), 1.48 – 1.34 (m, 4H), 0.90 (t, *J*=7.1 Hz, 3H).

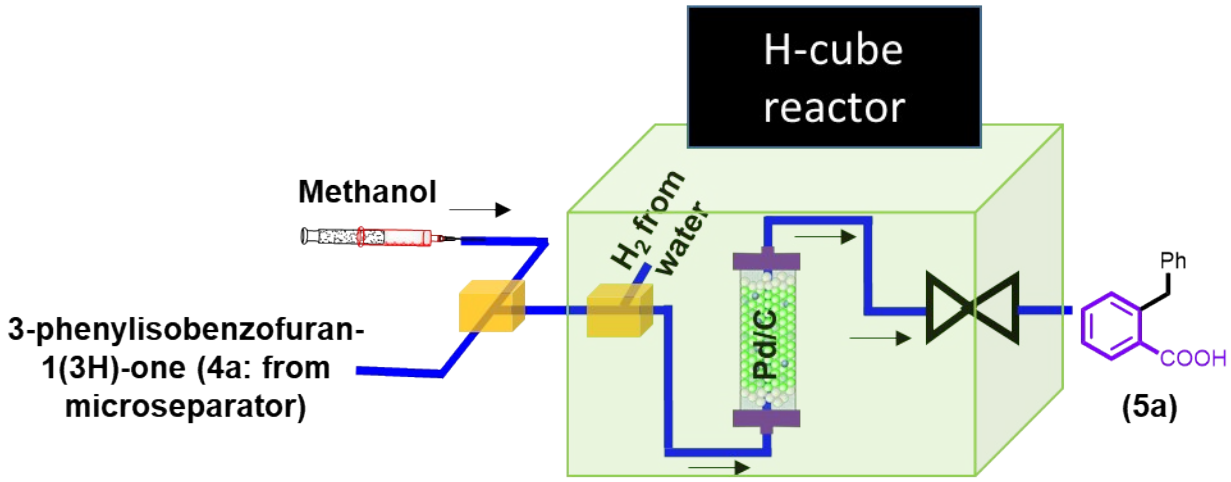
Gram–scale 4m synthesis: To synthesize gram scale of ischemic stroke relevant active pharmaceutical ingredient, **4m** was prepared according to general procedure mentioned in section 2.3. To check the durability of platform we have successfully run for four days (96 h) and crude material was purified by silica gel column chromatography to provide isolated gram scale (1.04 g) light yellow color product.

3.3. Typical procedure to make UV-FOR platform for one flow multi-step 2-benzylbenzoic acid synthesis:



Solution of 2-methylbenzophenone **2a** (0.0125 M) in dimethyl sulfoxide (DMSO) as a model compound of o-alkylphenyl ketones and oxygen mass-flow controller (MFC)into homemade photo-flow reactor to synthesize 3-phenylisobenzofuran-1(3H)-one. Next, switch the solvent containing the product from high boiling DMSO to low boiling DCM, the additional PTFE membrane embedded phase separator was connected to outlet of the photo-reactor as mentioned above. Finally, out-flowing 3-phenylisobenzofuran-1(3H)-one (**4a**) solution in DCM (100 μlmin^{-1}) directly pump through the H-cube in the presence of 10% Pd/C with applied 10 bar pressure and 4.2 retention time gave 70% yield of 2-benzylbenzoic acid (Table S4, Entry 1). To enhance the productivity, we have change several reaction condition but when we have flowed addition protic solvent methanol (100 μlmin^{-1}) then it's gave excellent 81% yield (Table S4, Entry 2).

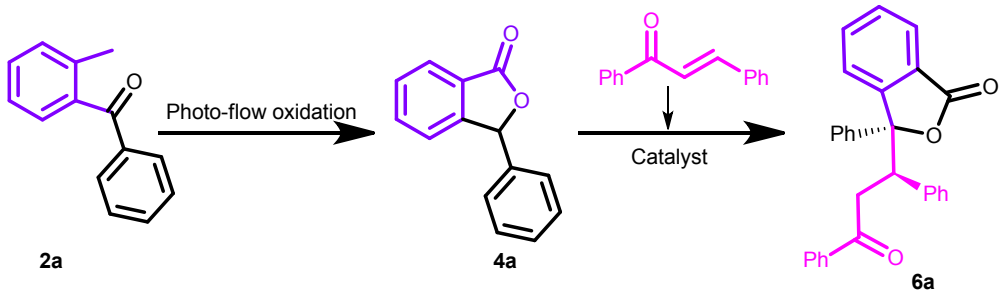
Table S4: Optimization of one flow multi-step synthesis of 2-benzylbenzoic acid by using H-cube.



Entry	Flow rate (μL/min.)		Retention time (min.)	Conversion	% Yield (5a)
	(4a)	Methanol			
1[a]	100	0	4.2	100	70
2[a]	100	100	2.1	100	81
3[a]	100	200	1.4	95	73
4[a]	100	50	2.8	100	78
5[b]	100	100	2.1	92	64
6[c]	100	100	2.1	74	51
7[d]	100	100	2.1	69	42

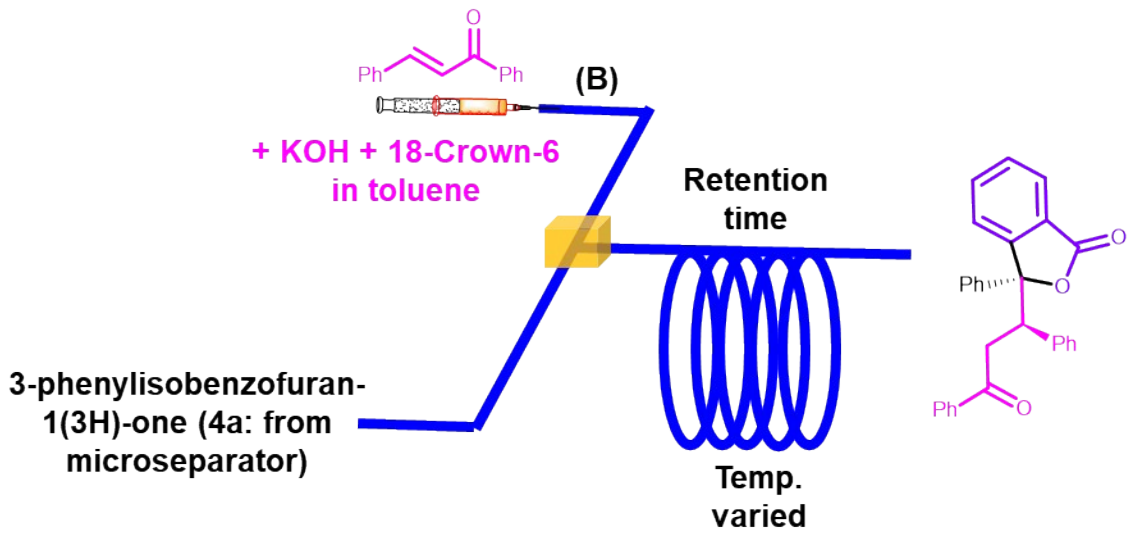
Reaction condition: cylindrical shape cartridge (6 Cm length X 0.3 Cm diameter), temperature (RT); Pressure 10 bar; 10% Pd/C; (a) 4a: 0.0115 M in DCM; (b) 4a: 0.0115 M in diethylether; (c) 4a: 0.0115 M in toluene; (d) 4a: 0.0115 M in hexane; yields are based on isolated yield.

3.4. Typical procedure to make UV-FOR platform for one flow multi-step arylogous Michael addition reactions:



The solution of 2-methylbenzophenone 2a (0.0125 M) in Dimethyl sulfoxide (DMSO) as a model compound of o-akylphenyl ketones (100 $\mu lmin^{-1}$) and oxygen mass-flow controller (MFC, 1 $mlmin^{-1}$) into homemade photo-flow reactor to synthesize 3-phenylisobenzofuran-1(3H)-one. Next, switch the solvent containing the product from high boiling DMSO to low boiling DCM, the additional PTFE membrane embedded phase separator was connected to outlet of the photo-reactor as mentioned above. Properly mixed chalcone (0.0115 M in toluene), KOH (10 mol%), and crown ether (10 mol%) solution was connected by another T-mixer and directly to outlet of the microseparator. Out-flowing 3-phenylisobenzofuran-1(3H)-one (100 $\mu Lmin^{-1}$) and the substrate were controlled to become molar ratio 1:1. (chalcone: 3-phenylisobenzofuran-1(3H)-one). The three components (chalcone, 3-phenylisobenzofuran-1(3H)-one, catalyst) were mixed through T-junction (Table S5) and infused to PTFE tubing (id = 1mm, length = 13 m) for 51 min. Note that the tube length was varied with different retention times. Under the stable condition the product was collected and diluted with DCM and finally washed with sat. NH_4Cl solution to remove impurities. Collected product was analyzed by ^{1}H and ^{13}C NMR and GC-MS (data mentioned in below).

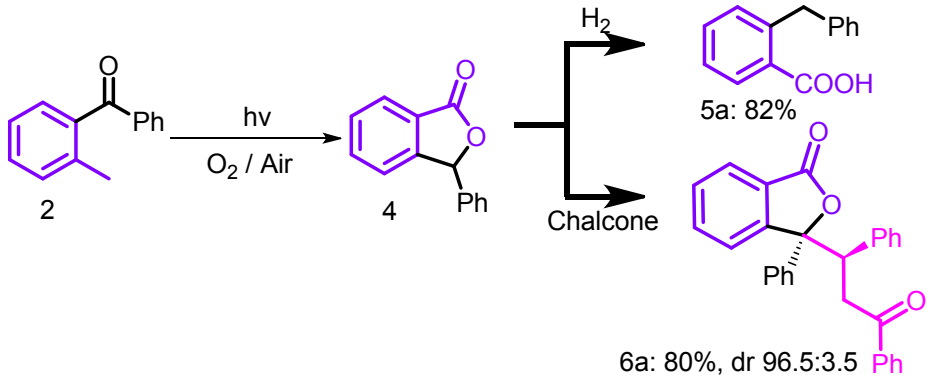
Table S5: Optimization of one flow multi-step synthesis of arylogous Michael addition product.



Entry	Flow rate B (μL/min.)	Retention time (min.)	Temp. (°C)	% Yield[b] 5a (dr)
1	100	51.0	0	80 (96:3.5)
2	110	48.6	0	79
3	100	51.0	10	78
4	100	51.0	20	81 (90:9.5)
5[a]	100	5	0	12

Reaction condition: 4a stock solution: 0.0115 M in DCM; **B** stock solution: [chalcone (0.0115 M in toluene) + KOH (10 mol%) + crown ether (10 mol%)]; pfa tubing (id: 1 mm and length 13 meter); (a) pfa tubing replace with 1 ml glass micro-fluidic chip (width 1 mm × depth 1 mm × length 1 meter); yields are based on isolated yield and diastereomeric ratio based on HPLC analysis.

3.5. Typical procedure to make fully integrated UV-FOR platform for one flow multi-step reactions:



The solution of 2-methylbenzophenone **2a** (0.0125 M) in dimethyl sulfoxide (DMSO) as a model compound of o-akylphenyl ketones (100 μlmin^{-1}) and oxygen mass-flow controller (MFC, 1 mlmin^{-1}) into homemade photo-flow reactor to synthesize 3-phenylisobenzofuran-1(3H)-one. Next, switch the solvent containing the product from high boiling DMSO to low boiling DCM, the additional PTFE membrane embedded phase separator was connected to outlet of the photo-reactor as mentioned above. Next, outflowing phthalide solution again connect with manual multi-valve (Figure S3). The manual-valve outlet connected with H-cube reactor and arylogous Michael addition reactor. As per our requirements, we were diverting the phthalide solution flow and make the product. Under the stable condition the product was collected and diluted with DCM and finally washed with sat. NH_4Cl solution to remove impurities. Collected product was analyzed by ^{1}H and ^{13}C NMR and GC-MS/LC-MS/HPLC (data mentioned in below).

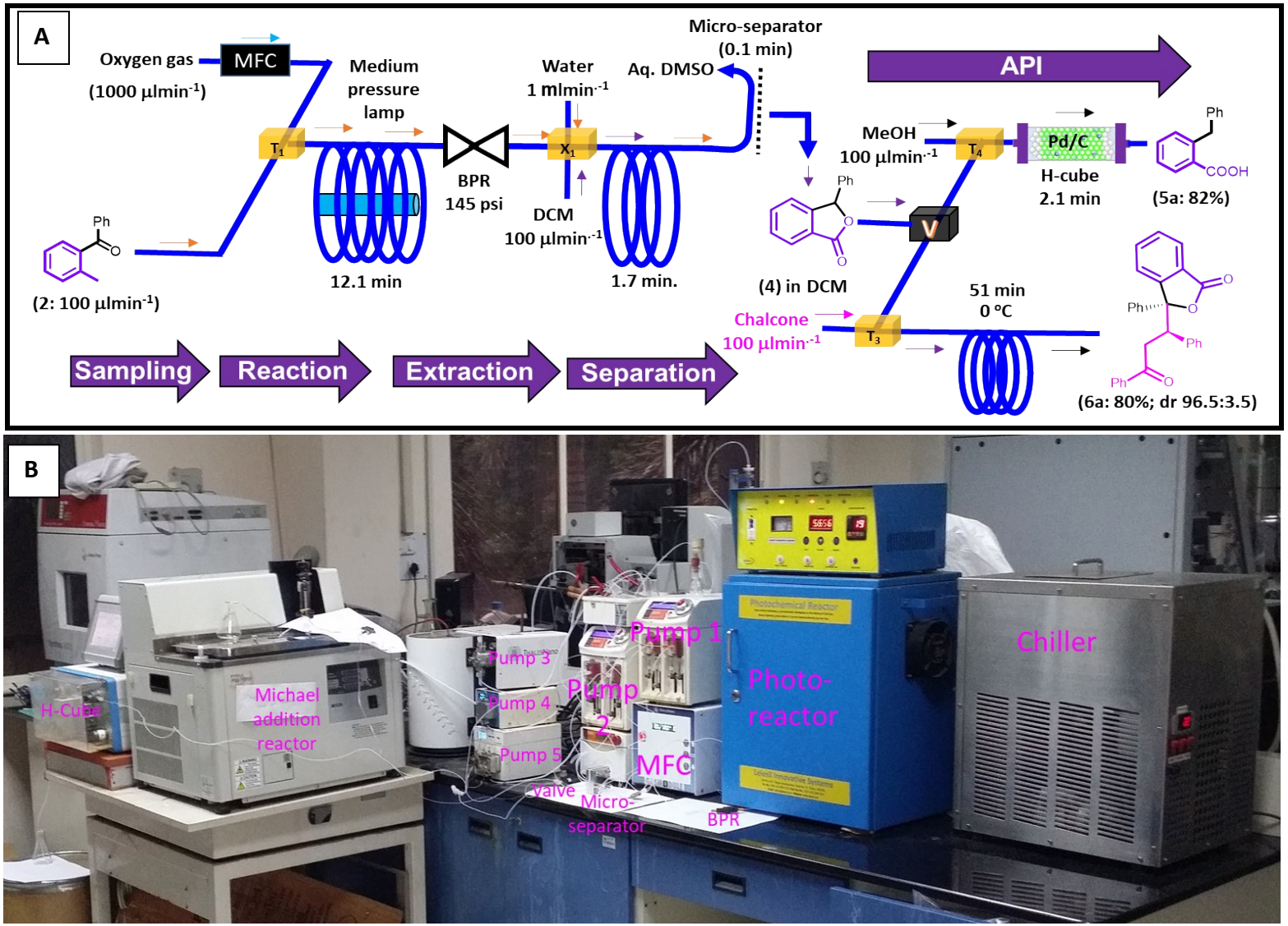
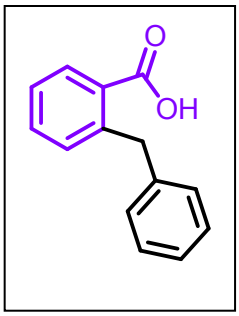


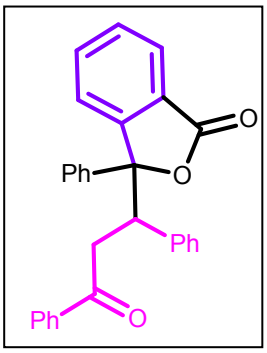
Figure S3: (A) Blue-print for fully integrated UV-FOR platform; (**B**) Snapshot picture of reactor set-up for one flow multi-step reactions.

2-Benzylbenzoic acid (5a):



Compound **5a** was prepared according to general procedure 3.3. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 90:10) to provide a white solid; 43.54 mg (81% yield); the spectra data matched with values reported in the literature.[15] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.09 – 8.04 (m, 1H), 7.48 (td, *J*=7.5 Hz, 1.4 Hz, 1H), 7.32 (td, *J*=7.8 Hz, 1.2 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.23 (d, *J*=7.8 Hz, 1H), 7.21 – 7.15 (m, 3H), 4.46 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.37, 143.45, 140.67, 132.97, 131.72, 131.68, 129.03, 128.94, 128.42, 128.31, 126.31, 125.95, 39.58; **IR (ν_{max}):** 3070, 3022, 2923, 2858, 2835, 2652, 1734, 1685, 1572, 1450, 1409, 1265, 1043, 928, 794, 734, 699 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{14}H_{10}O_2$ $[M+H]^+$: 211.0759, found 211.0764.

3-(3-oxo-1,3-diphenylpropyl)-3-phenylisobenzofuran-1(3H)-one (6a):



Compound **6a** was prepared according to general procedure 3.4. The crude material was purified by silica gel column chromatography (hexane/ethyl acetate; 90: 10) to provide a white solid; 83.60 mg (83% Yield); the spectra data matched with values reported in the literature. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 – 7.75 (m, 4H), 7.64 (d, *J*=7.8 Hz, 1H), 7.54 – 7.46 (m, 3H), 7.39 (dt, *J*=15.7 Hz, 7.6 Hz, 4H), 7.30 (t, *J*=7.4 Hz, 1H), 7.24 (t, *J*=7.5 Hz, 1H), 7.18 (d, *J*=7.3 Hz, 2H), 7.00 (t, *J*=7.3 Hz, 2H), 6.95 (t, *J*=7.2 Hz, 1H), 4.69 (dd, *J*=10.4 Hz, 2.6 Hz, 1H), 4.01 (dd, *J*=17.9 Hz, 10.5 Hz, 1H), 3.20 (dd, *J*=18.0 Hz, 2.6 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 197.60, 170.02, 152.39, 139.83, 137.32, 136.65, 133.93, 133.14, 129.30, 129.20, 128.74, 128.47, 128.32, 127.96, 127.04,

125.32, 124.87, 124.62, 122.23, 91.84, 48.87, 39.80; **IR (ν_{max}):** 3057**,** 2923, 2856, 1765, 1683, 1600, 1454, 1366, 1277, 1245, 1081, 1041, 958,755, 695 cm^{-1}; **HRMS (ESI):** m/z calcd for $C_{14}H_{10}O_2$ $[M+Na]^+$: 441.1467, found 441.1467.

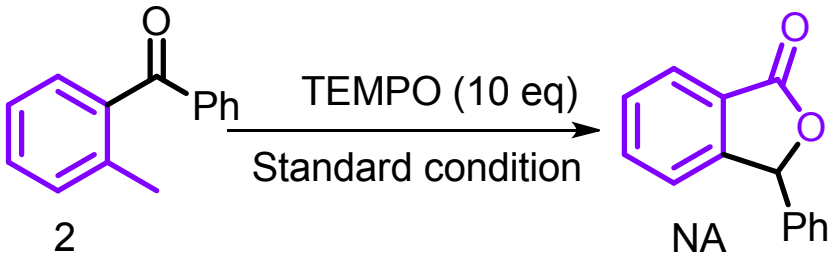
Control experiments for step 1

First, A 0.0125M solution of phenyl (o-tolyl) methanone in DMSO was mix with 10 eq. of (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO) and taken in bottle and oxygen cylinder was connected with mass-flow controller (MFC) (Figure S1). Two reactants were introduced through T-mixer (T1) with a flow rate molar ratio of 1:35 to maintain the stoichiometry (Table S1), and then passed through a PFA tubing (id = 1000 µm, volume 13.3 ml) for light exposure and end point connected with 145 psi back pressure regulator (BPR). Under the stable condition the product was collected and diluted with DCM and finally washed with sat. NH_4Cl solution to remove impurities. Collected product was analyzed by ^1H and ^{13}C NMR and GC-MS/LC-MS.

Control experiments for step 2:

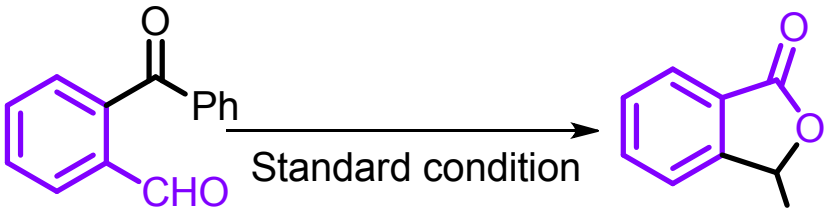
A 0.0125M solution of 2-benzoylbenzaldehyde in DMSO was taken in bottle and oxygen cylinder was connected with mass-flow controller (MFC) (Figure S1). Two reactants were introduced through T-mixer (T1) with a flow rate molar ratio of 1:35 to maintain the stoichiometry (Table S1), and then passed through a PFA tubing (id = 1000 µm, volume 13.3 ml) for light exposure and end point connected with 145 psi back pressure regulator (BPR). Under the stable condition the product was collected and diluted with DCM and finally washed with sat. NH_4Cl solution to remove impurities. Collected product was analyzed by ^1H and ^{13}C NMR and GC-MS/LC-MS.

Step 1: Quenching with radical scavenger.



2 NA

Step 2: Intermediate confimation experiments.



3a 4a 94%

4. References:

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5. Spectra:

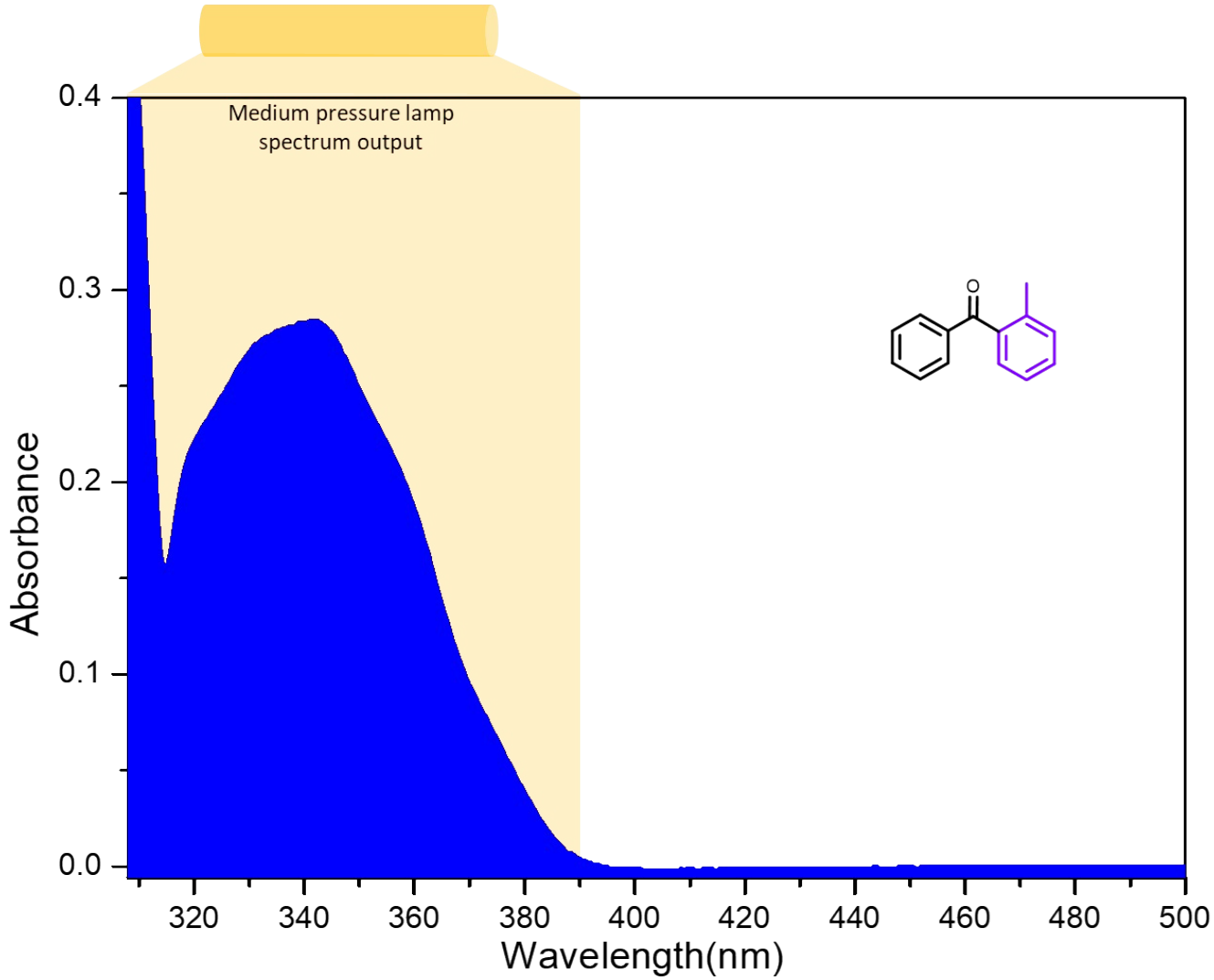


Figure S4. UV-Visible spctra of (2, 5-dimethylphenyl) (phenyl) methanone (2b) in 0.0022 M DMSO.

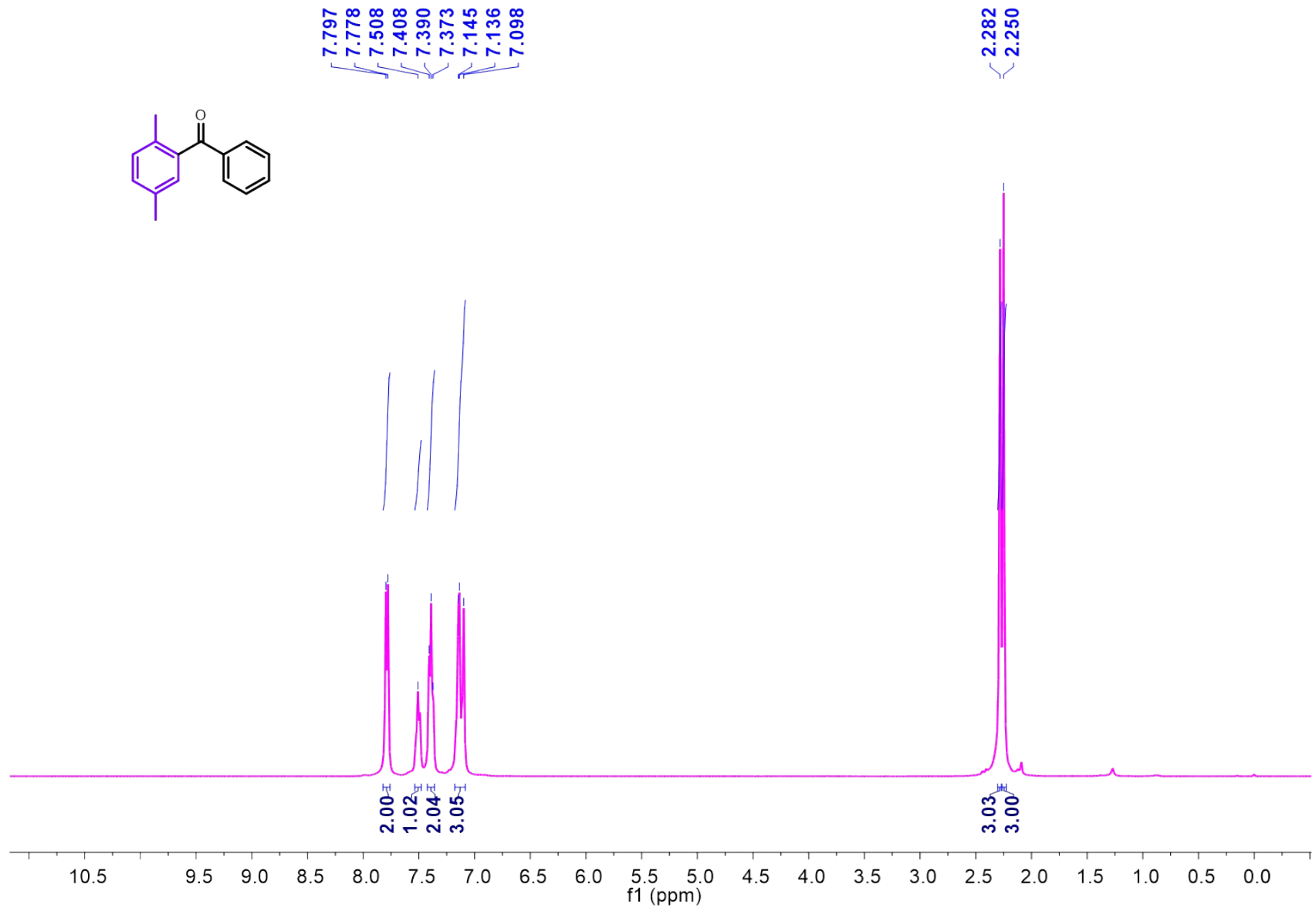


Figure S5. ^{1}H NMR spectra of (2, 5-dimethylphenyl) (phenyl)methanone (**2b**) in $CDCl_3$.

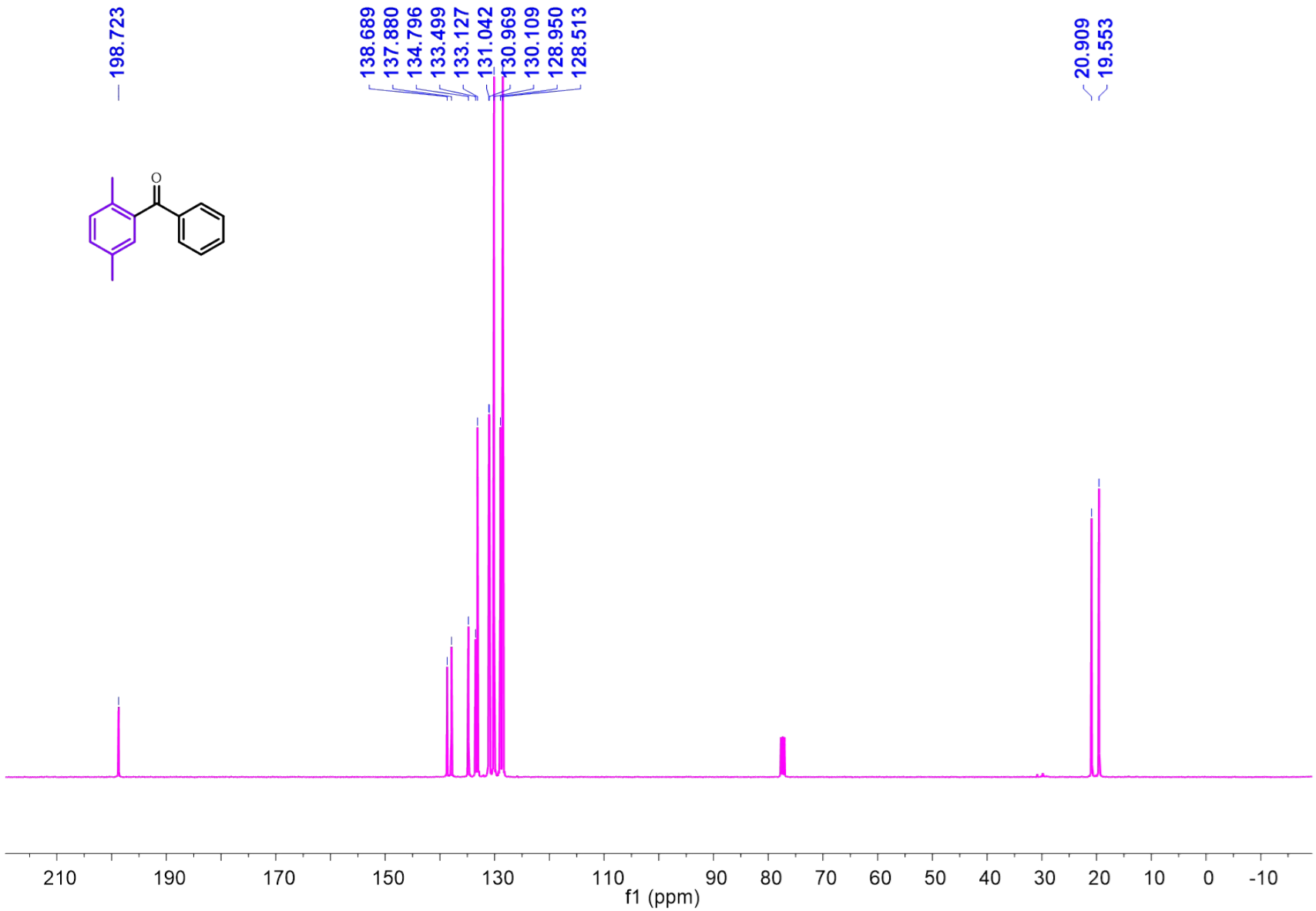


Figure S6. ^{13}C NMR spectra of (2, 5-dimethylphenyl) (phenyl) methanone (2b) in $CDCl_3$.

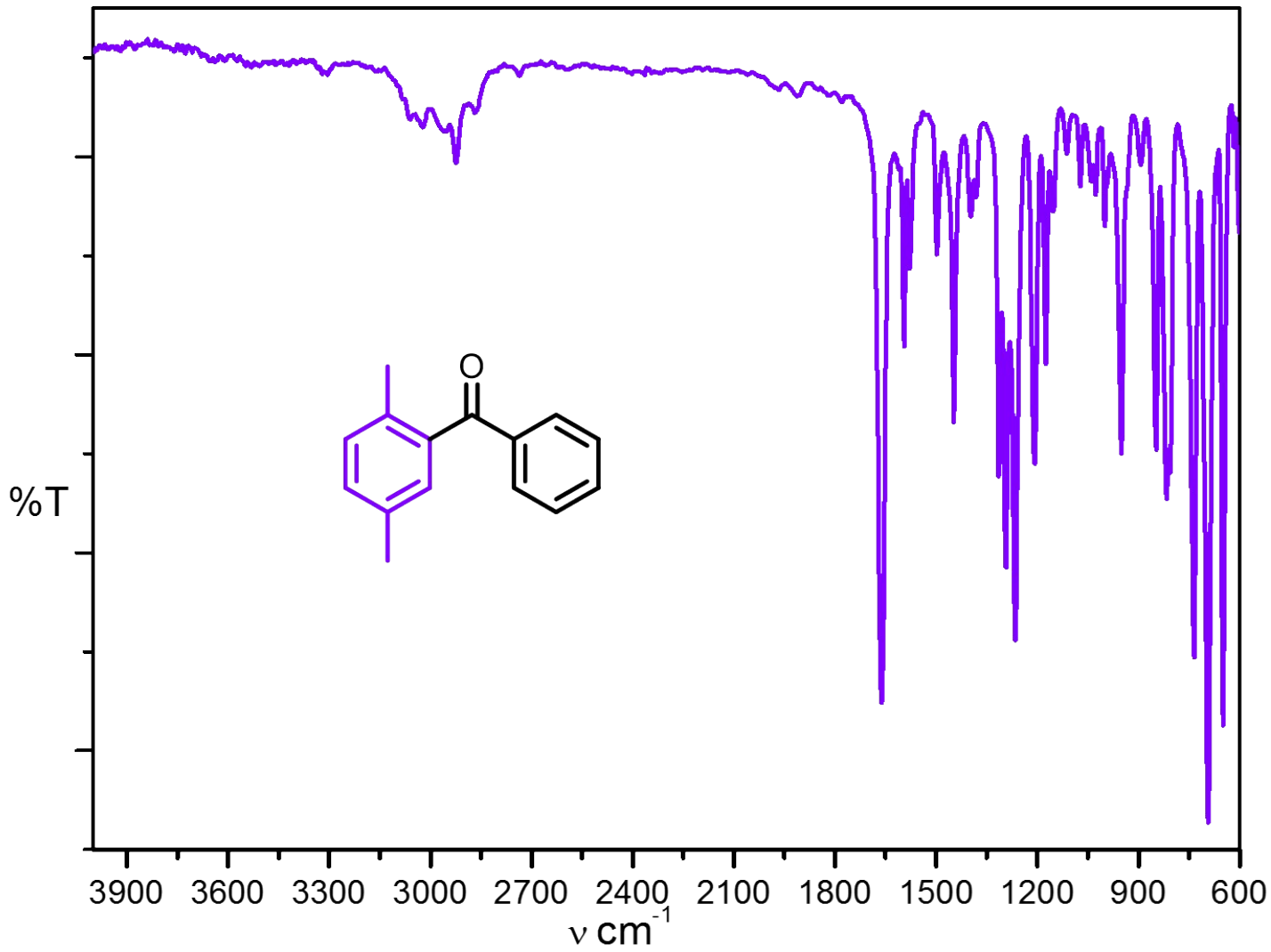


Figure S7. IR spectra of (2, 5-dimethylphenyl) (Phenyl) methanone (2b).

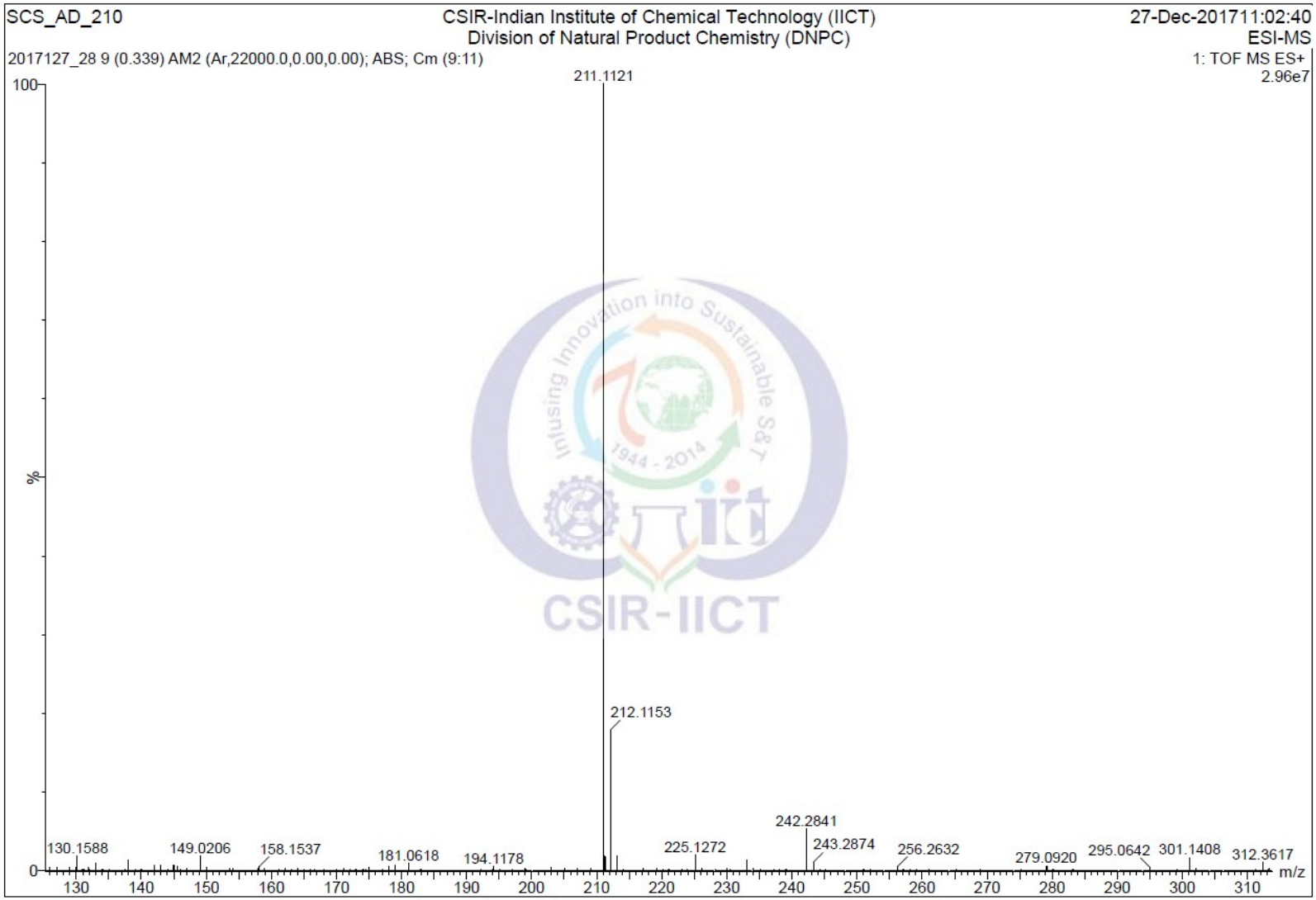


Figure S8. HRMS spctra of (2, 5-dimethylphenyl) (phenyl) methanone (2b).

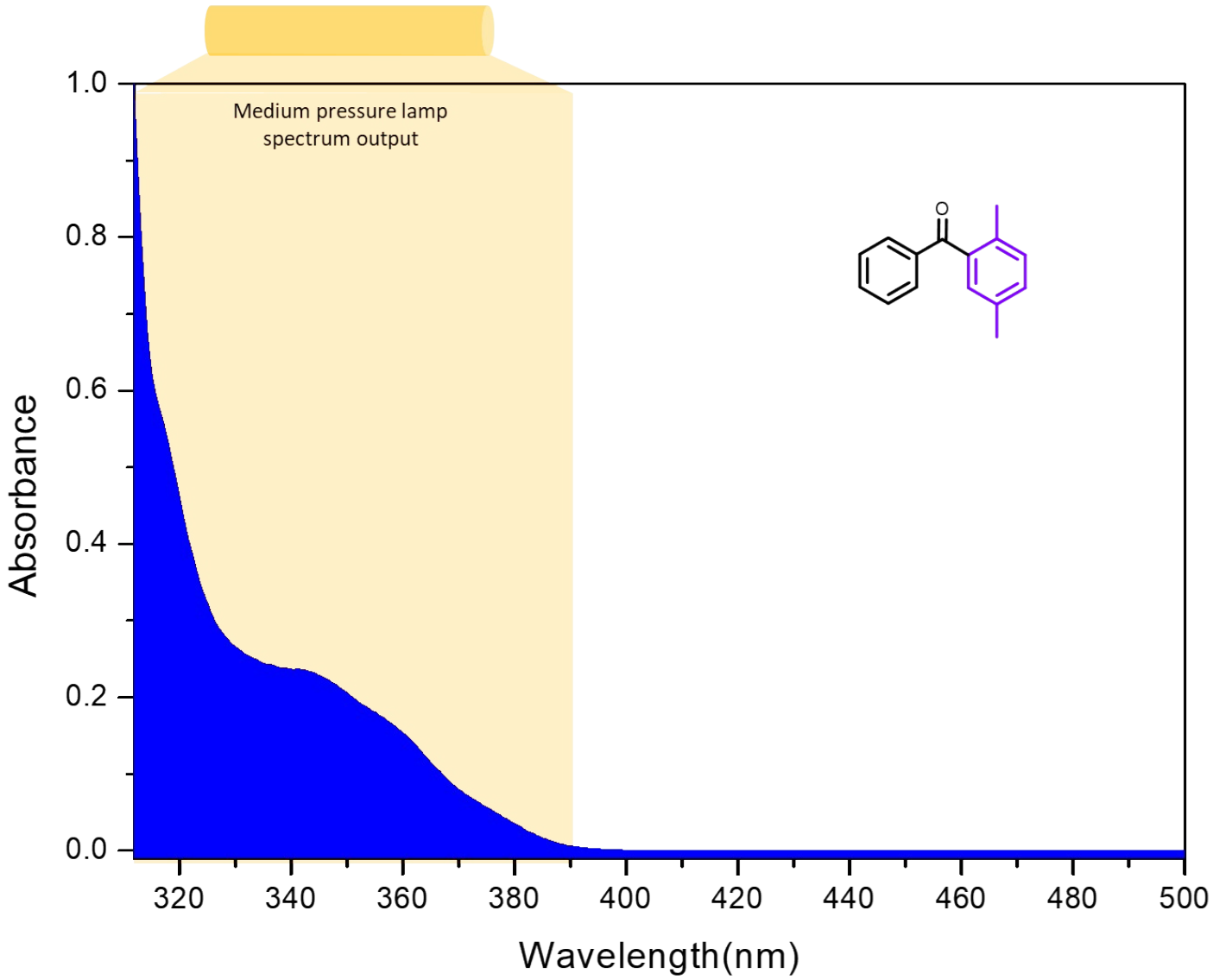


Figure S9. UV-Visible spctra of (2, 5-dimethylphenyl) (phenyl) methanone (2b) in 0.0022 M DMSO.

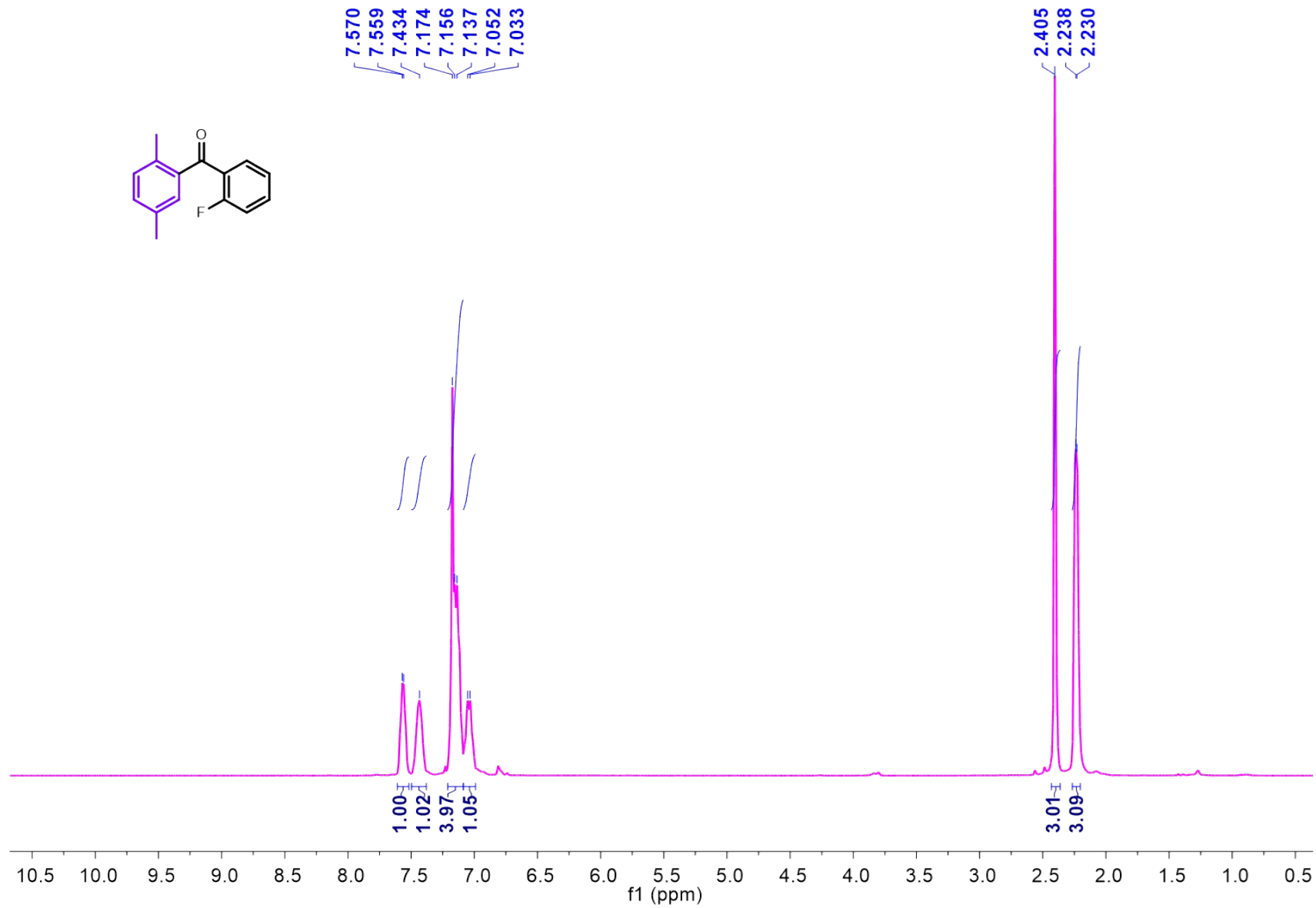


Figure S10. ^{1}H NMR spectra of (2, 5-dimethylphenyl) (2-fluorophenyl) methanone (2c) in $CDCl_3$.

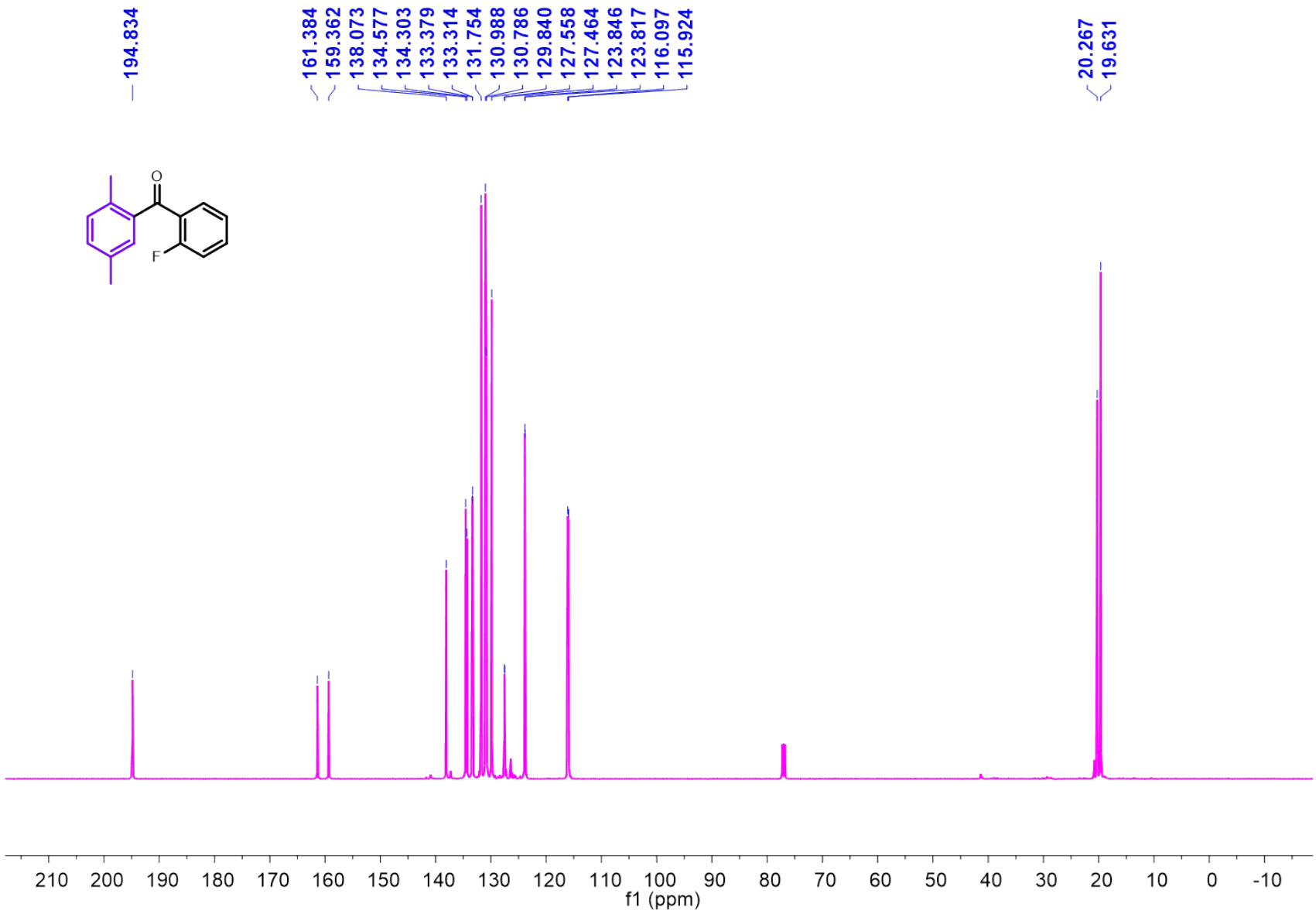


Figure S11.^{13}C NMR spectra of (2, 5-dimethylphenyl) (2-fluorophenyl) methanone (2c) in $CDCl_3$.

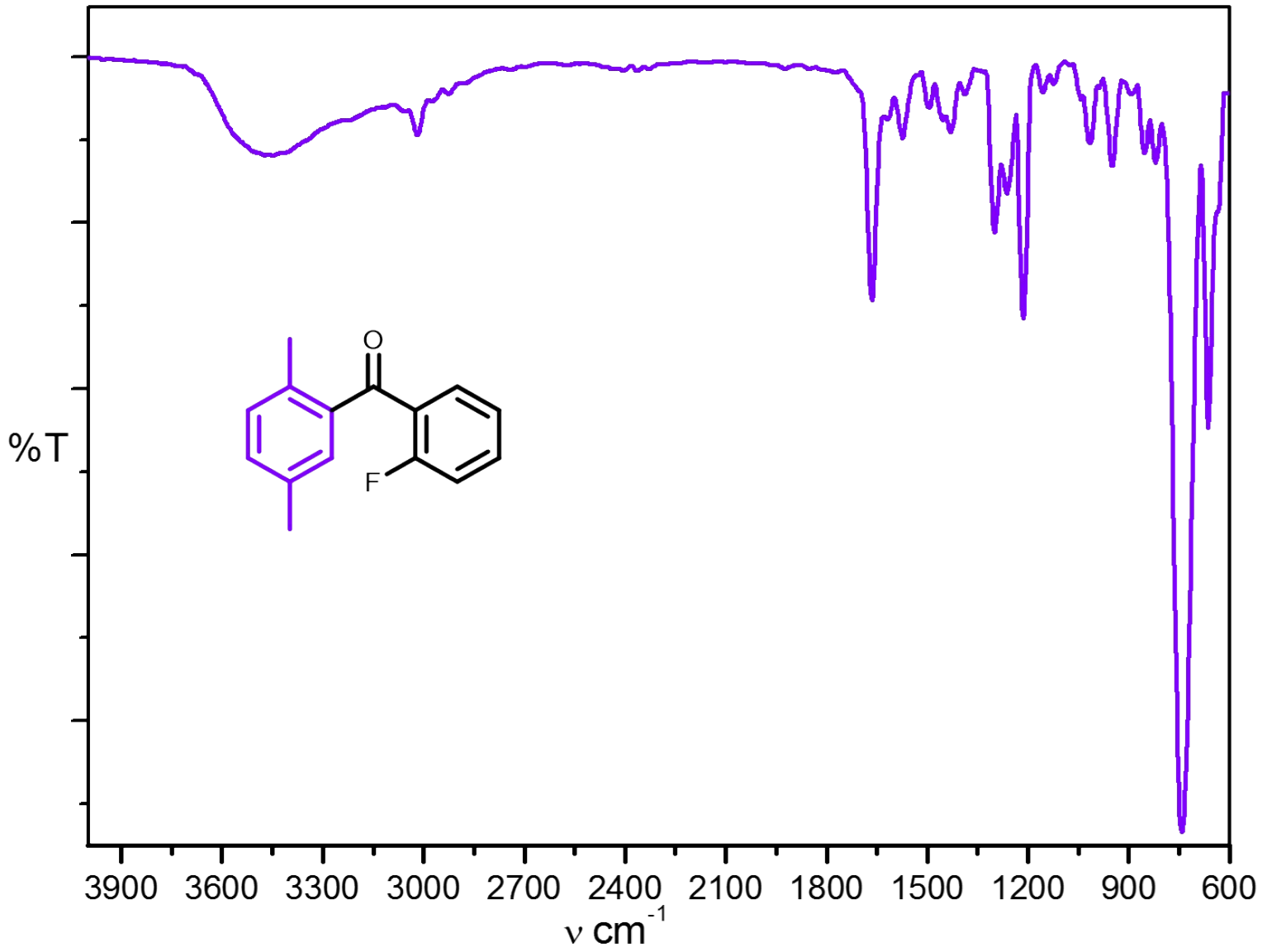


Figure S12. IR spectra of (2-Chlorophenyl) (2, 5-dimethylphenyl) methanone (2d).

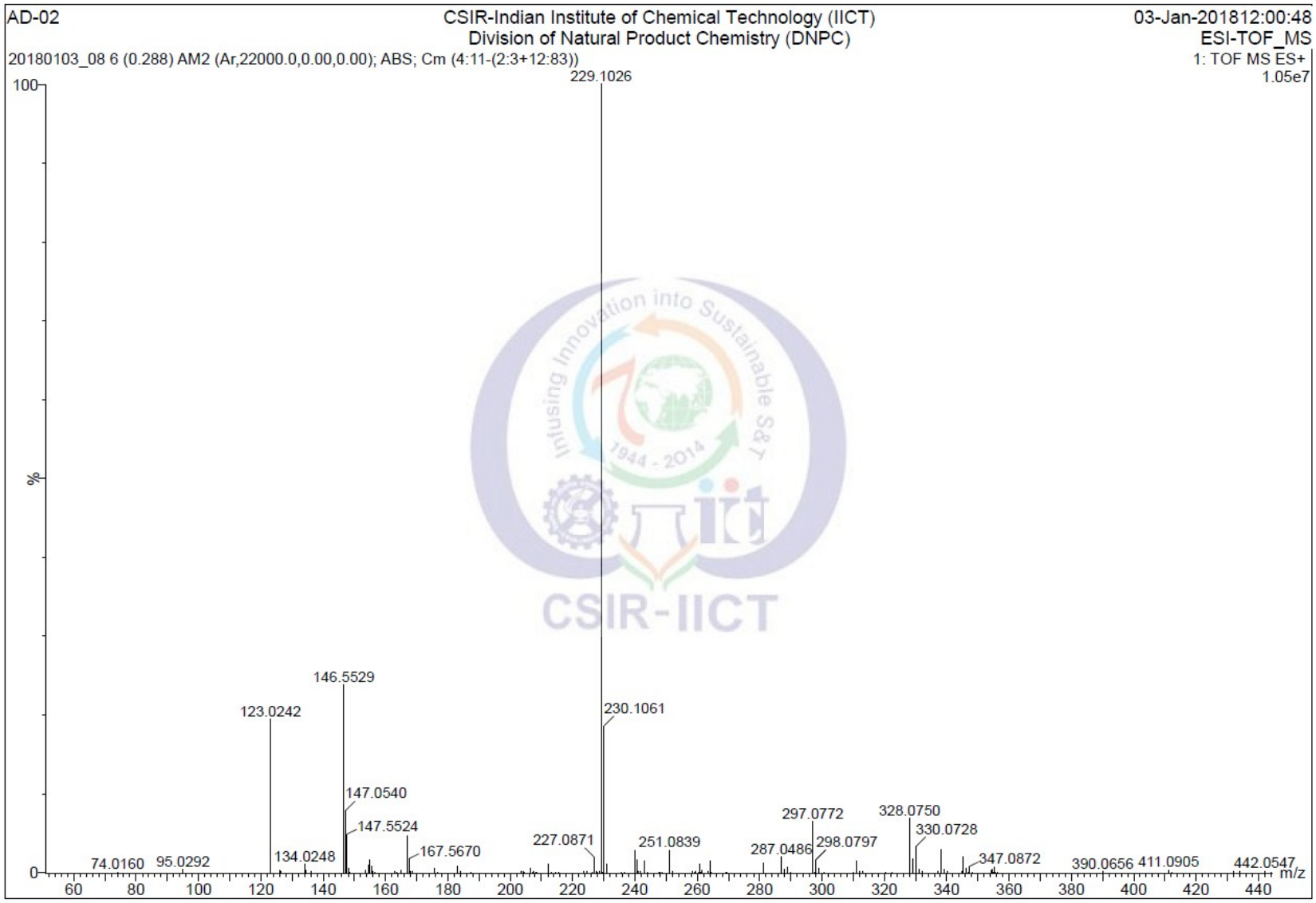


Figure S13. HRMS spctra of (2, 5-dimethylphenyl) (2-fluorophenyl) methanone (2c).

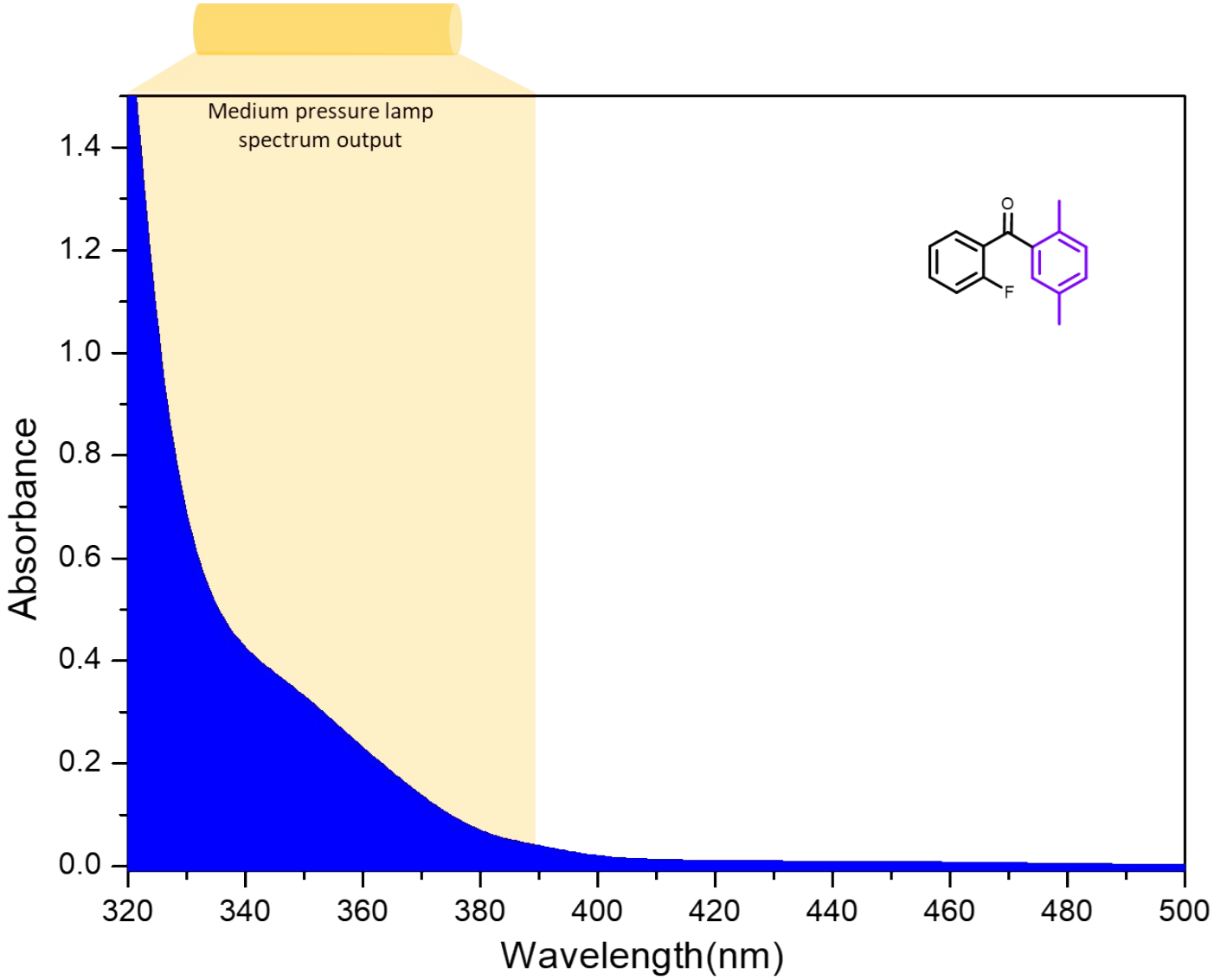


Figure S14. UV-Visible spctra of (2, 5-dimethylphenyl) (2-fluorophenyl) methanone (2c) in 0.0022 M DMSO.

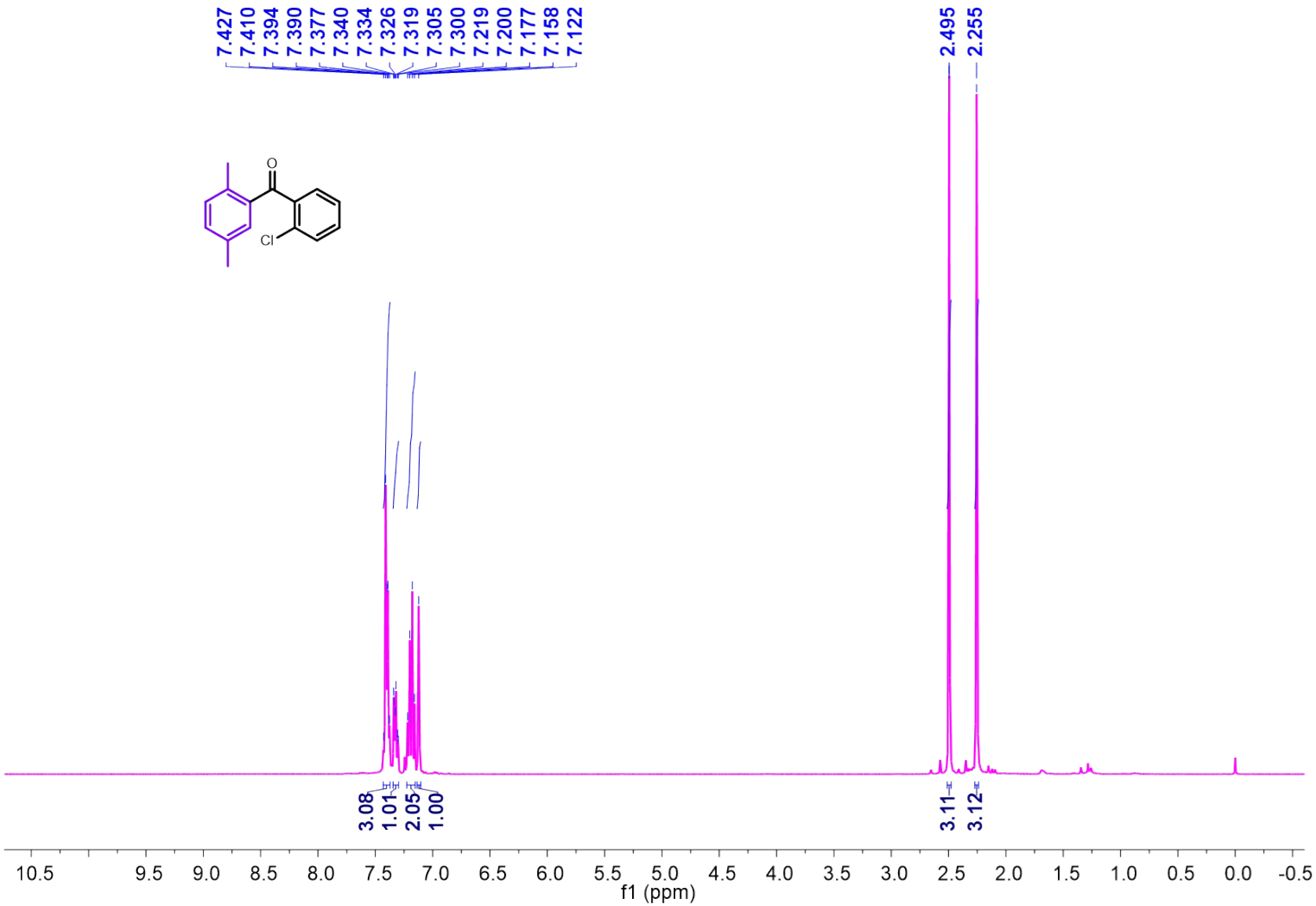


Figure S15. ^{1}H NMR spectra of (2-chlorophenyl) (2, 5-dimethylphenyl) methanone (2d) in $CDCl_3$.

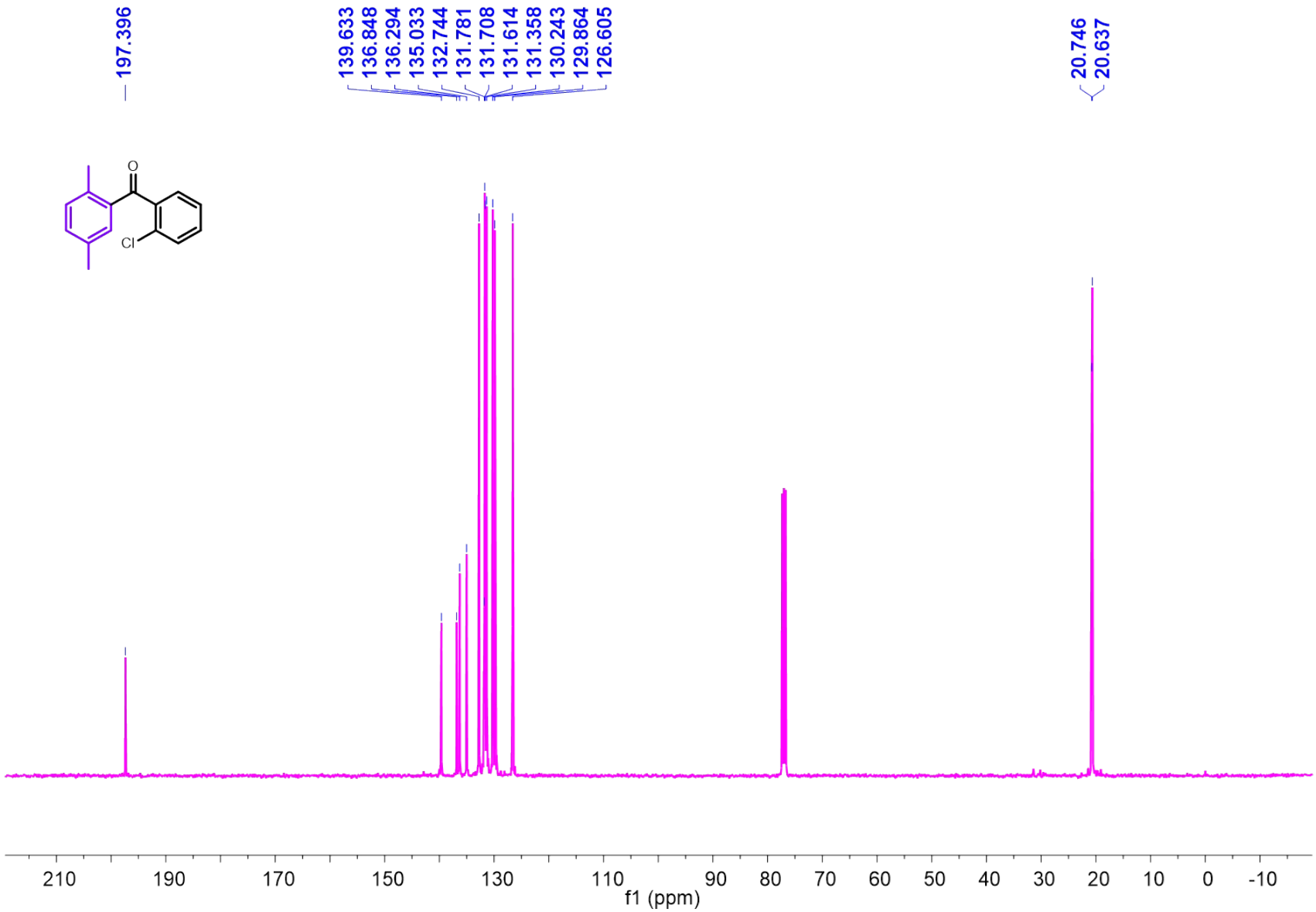


Figure S16. ^{13}C NMR spectra of (2-chlorophenyl) (2, 5-dimethylphenyl) methanone (2d) in $CDCl_3$.

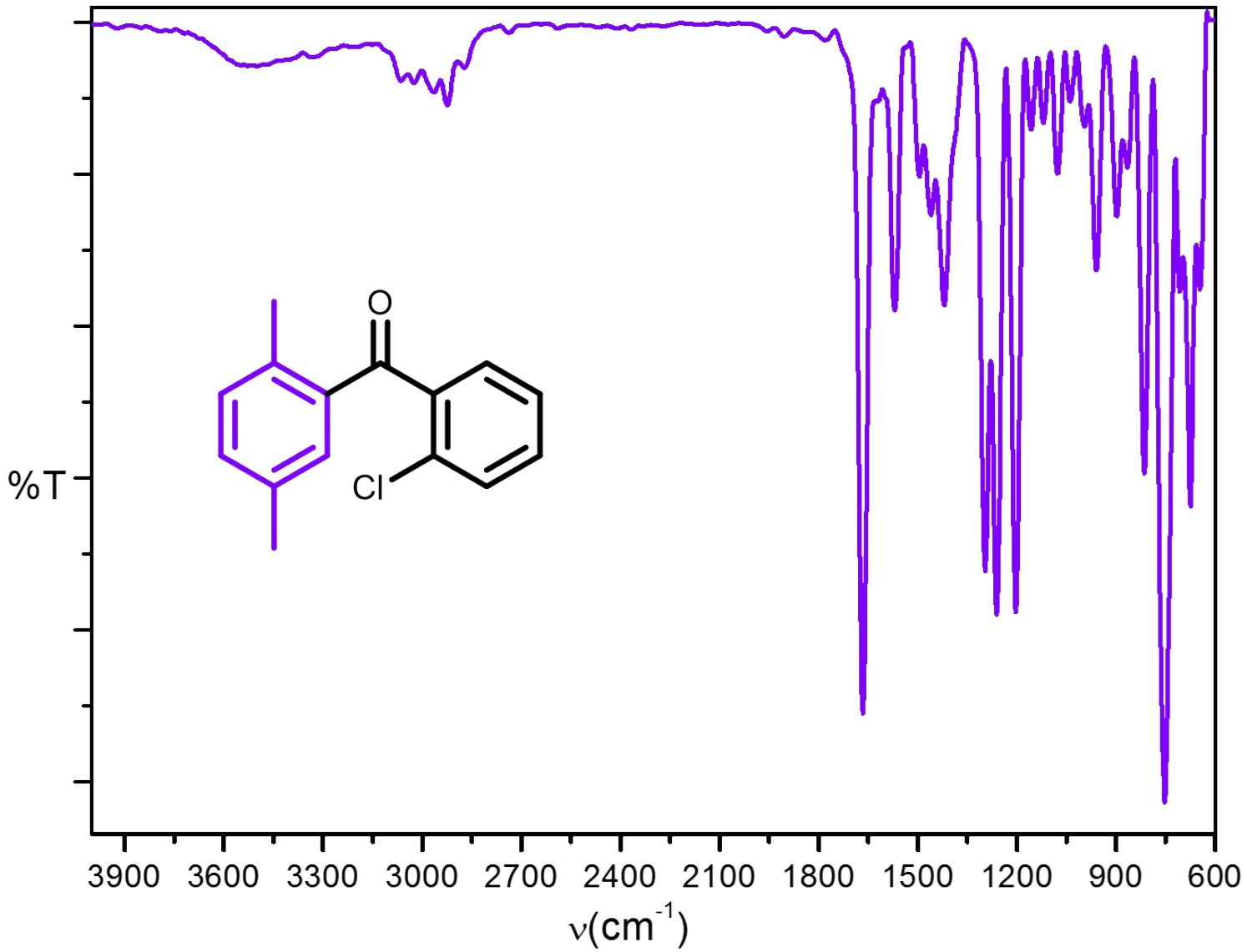


Figure S17. IR spectra of (2-Chlorophenyl) (2, 5-dimethylphenyl) methanone (2d).

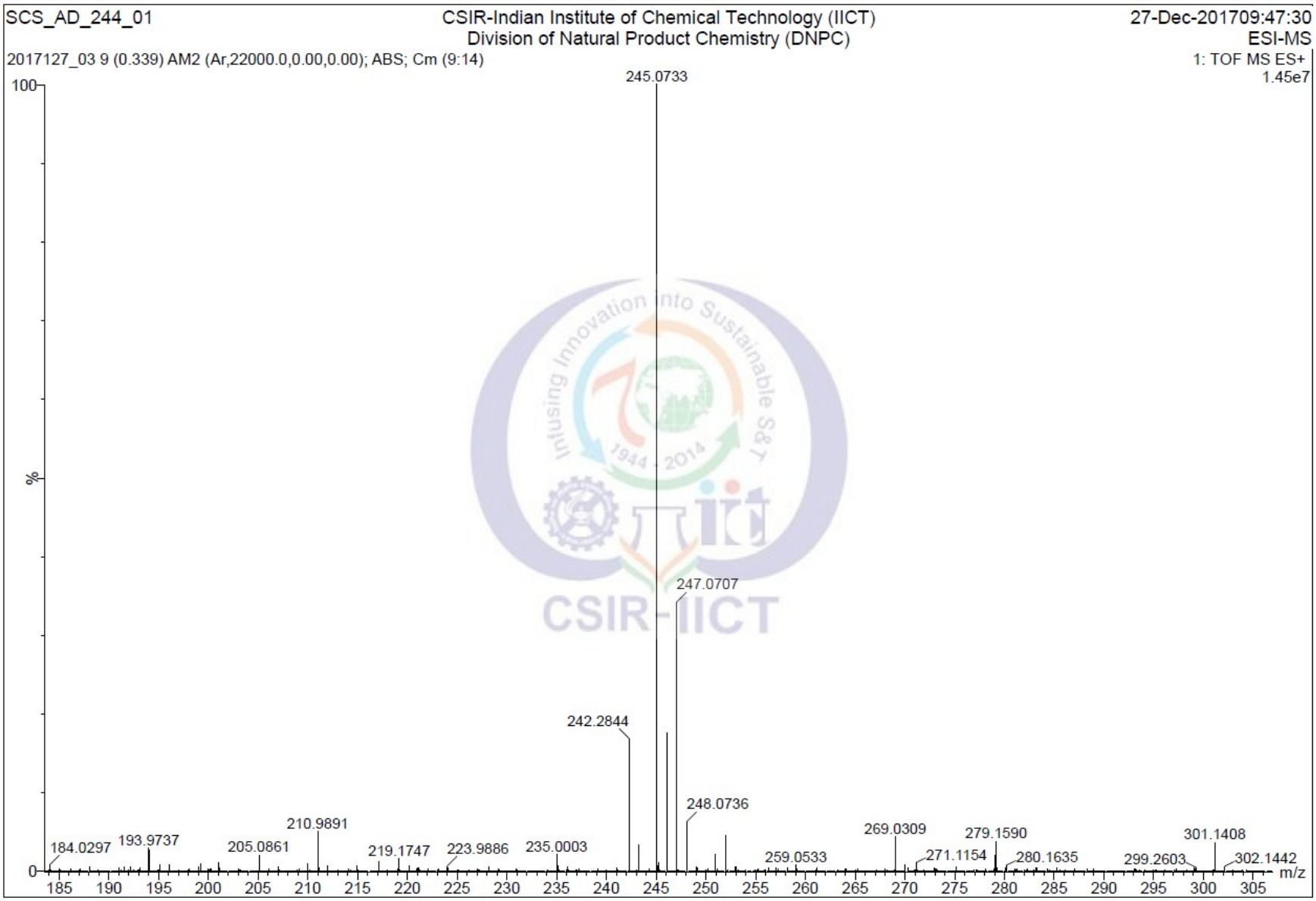


Figure S18. HRMS spctra of (2-Chlorophenyl) (2, 5-dimethylphenyl) methanone (**2d**).

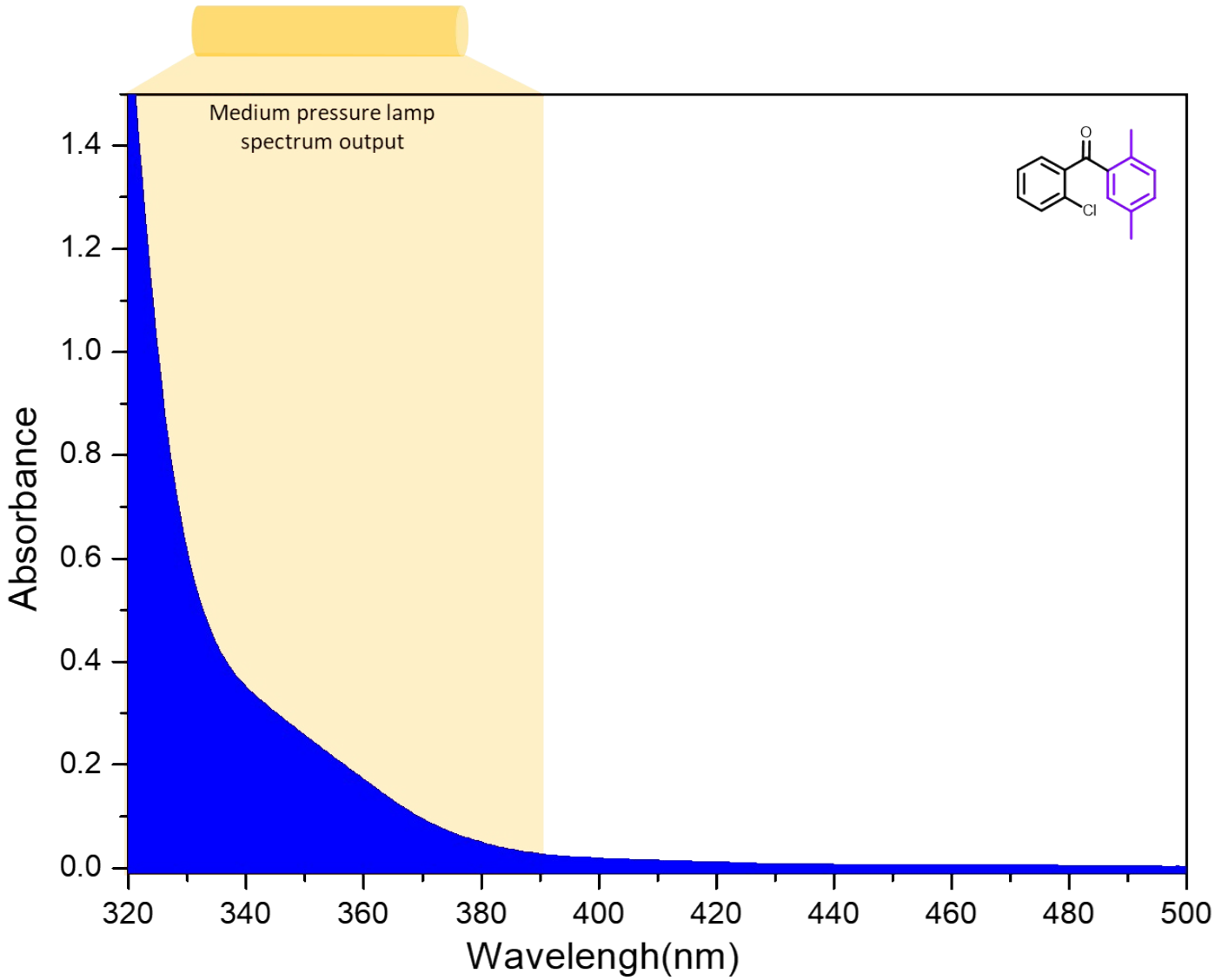


Figure S19. UV-Visible spectra of (2-chlorophenyl) (2, 5-dimethylphenyl) methanone (**2d**) in 0.0022 M DMSO.

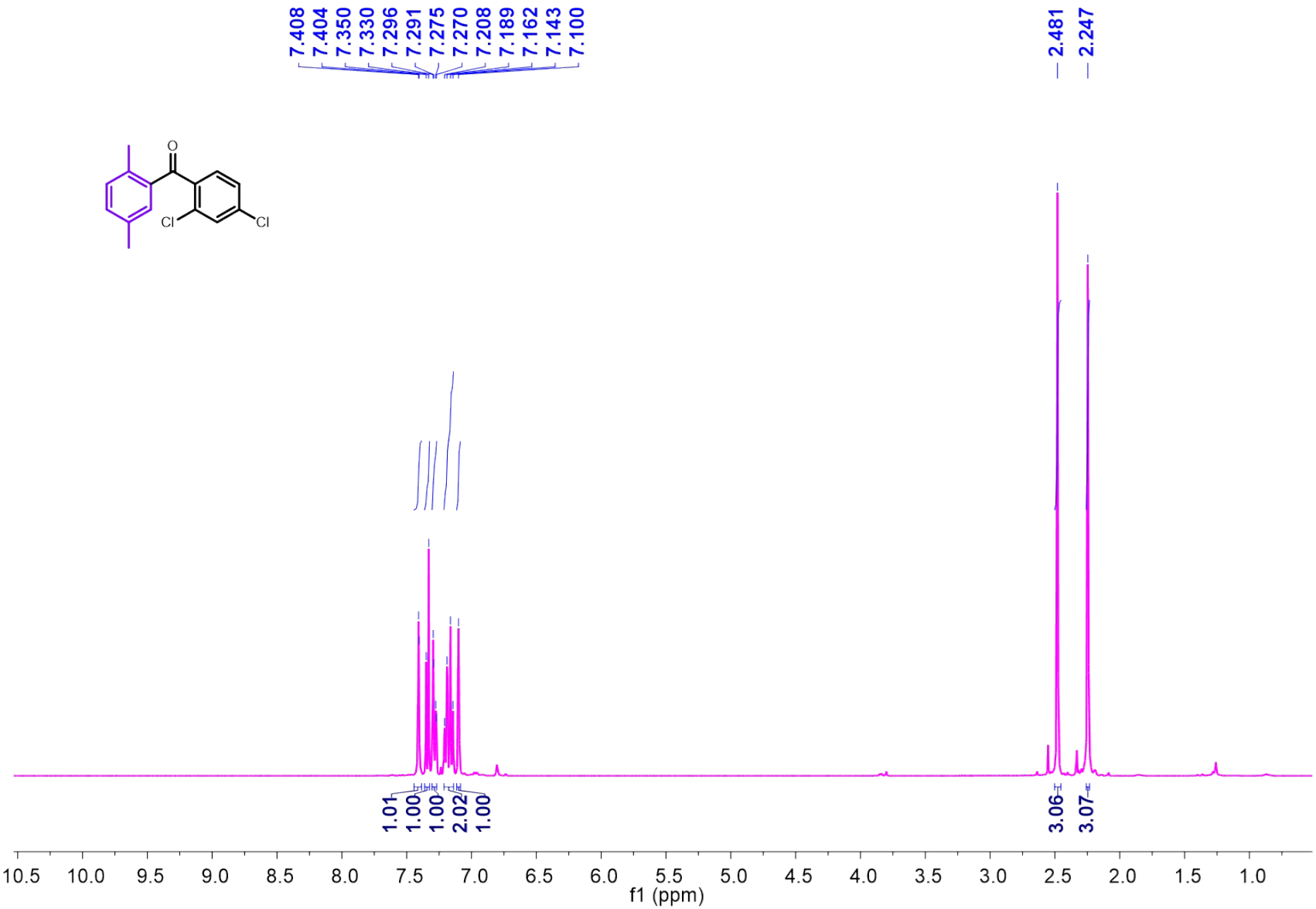


Figure S20. ^{1}H NMR spectra of (2, 4-dichlorophenyl) (2, 5-dimethylphenyl) methanone (**2e**) in $CDCl_3$.

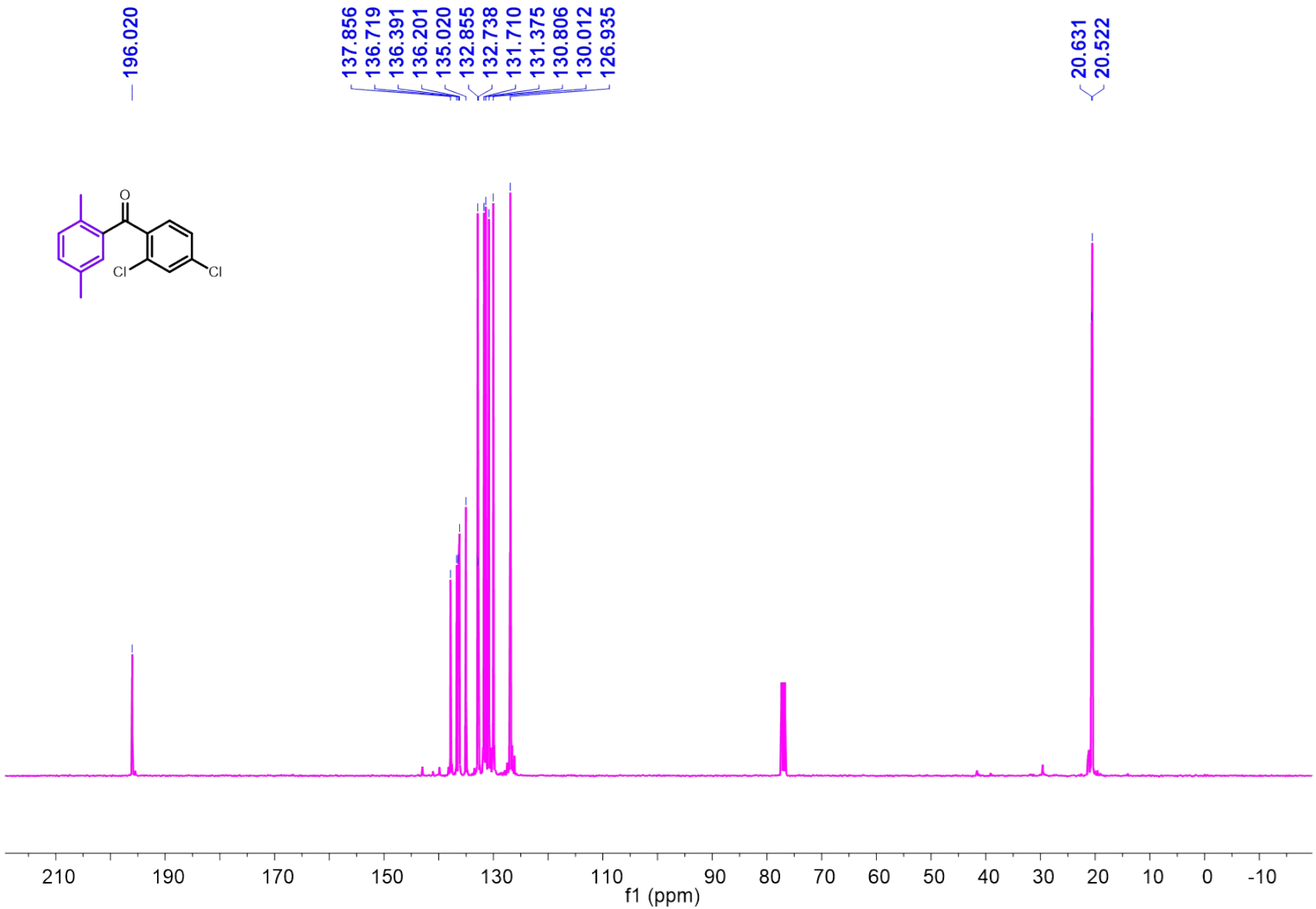


Figure S21. ^{13}C NMR spectra of (2, 4-dichlorophenyl) (2, 5-dimethylphenyl) methanone (**2e**) in $CDCl_3$.

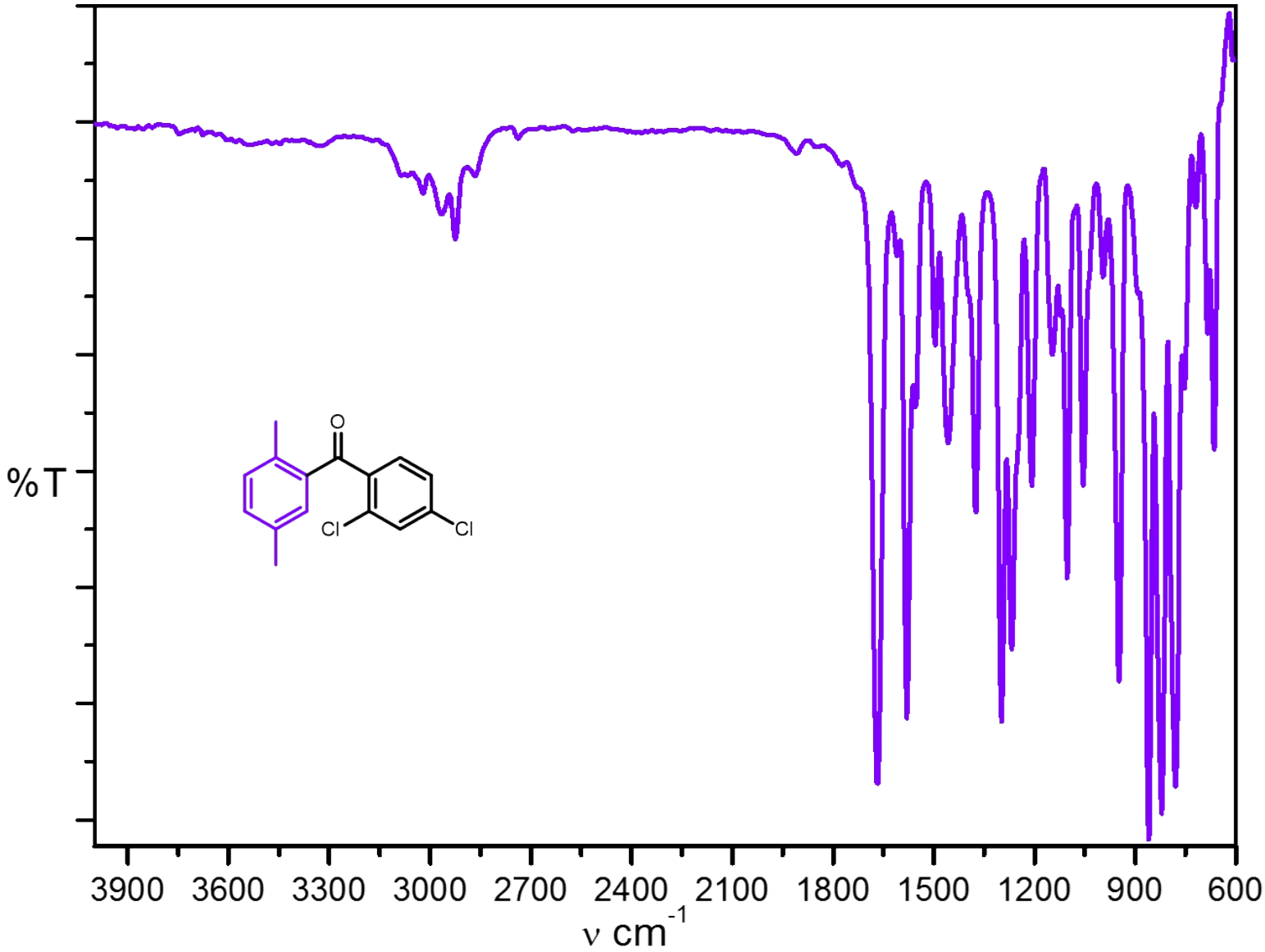


Figure S22. IR spectra of (2, 4-dichloroPhenyl) (2, 5-dimethylphenyl) methanone (**2e**).

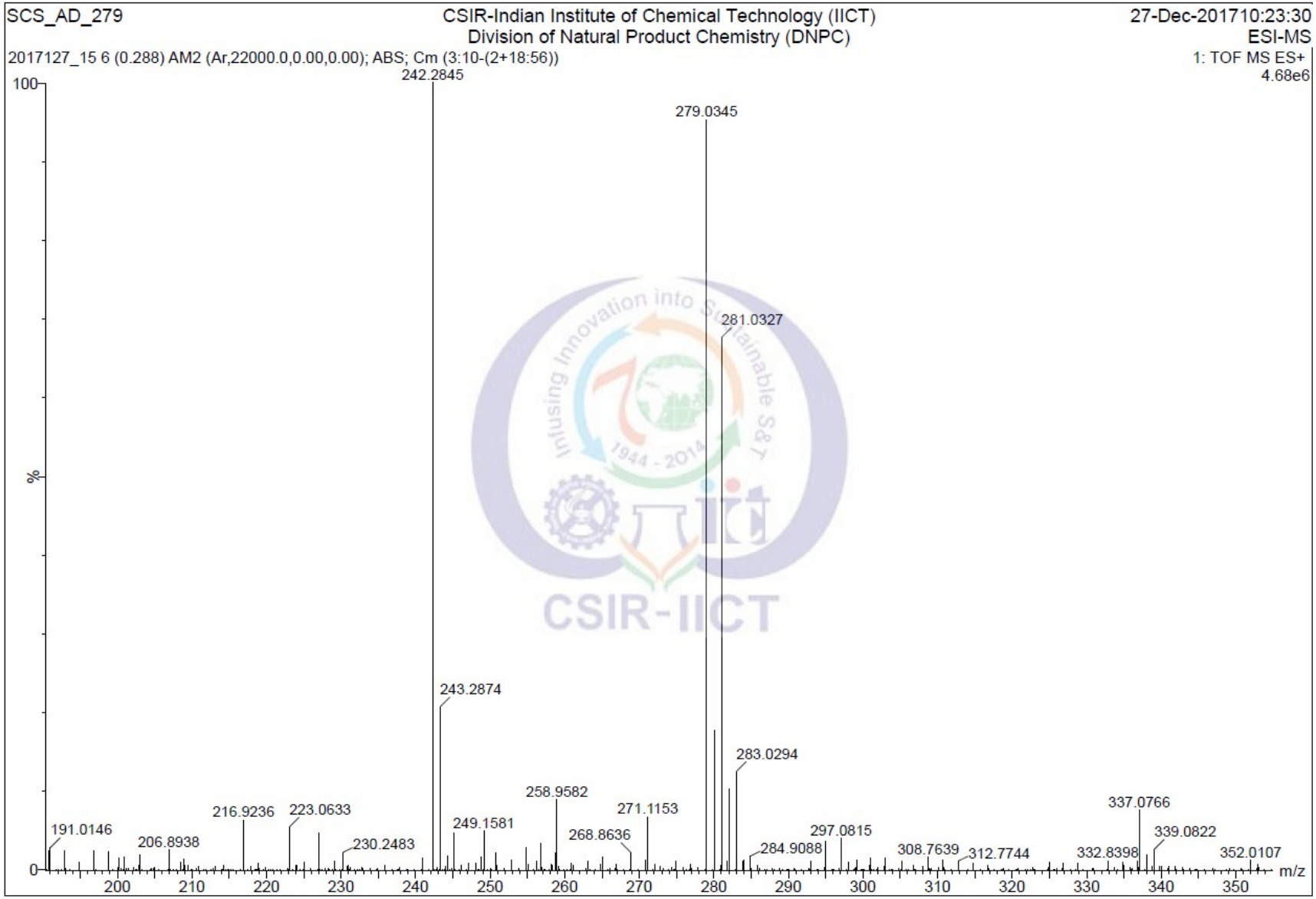


Figure S23. HRMS spctra of (2, 4-dichlorophenyl) (2, 5-dimethylphenyl) methanone (**2e**).

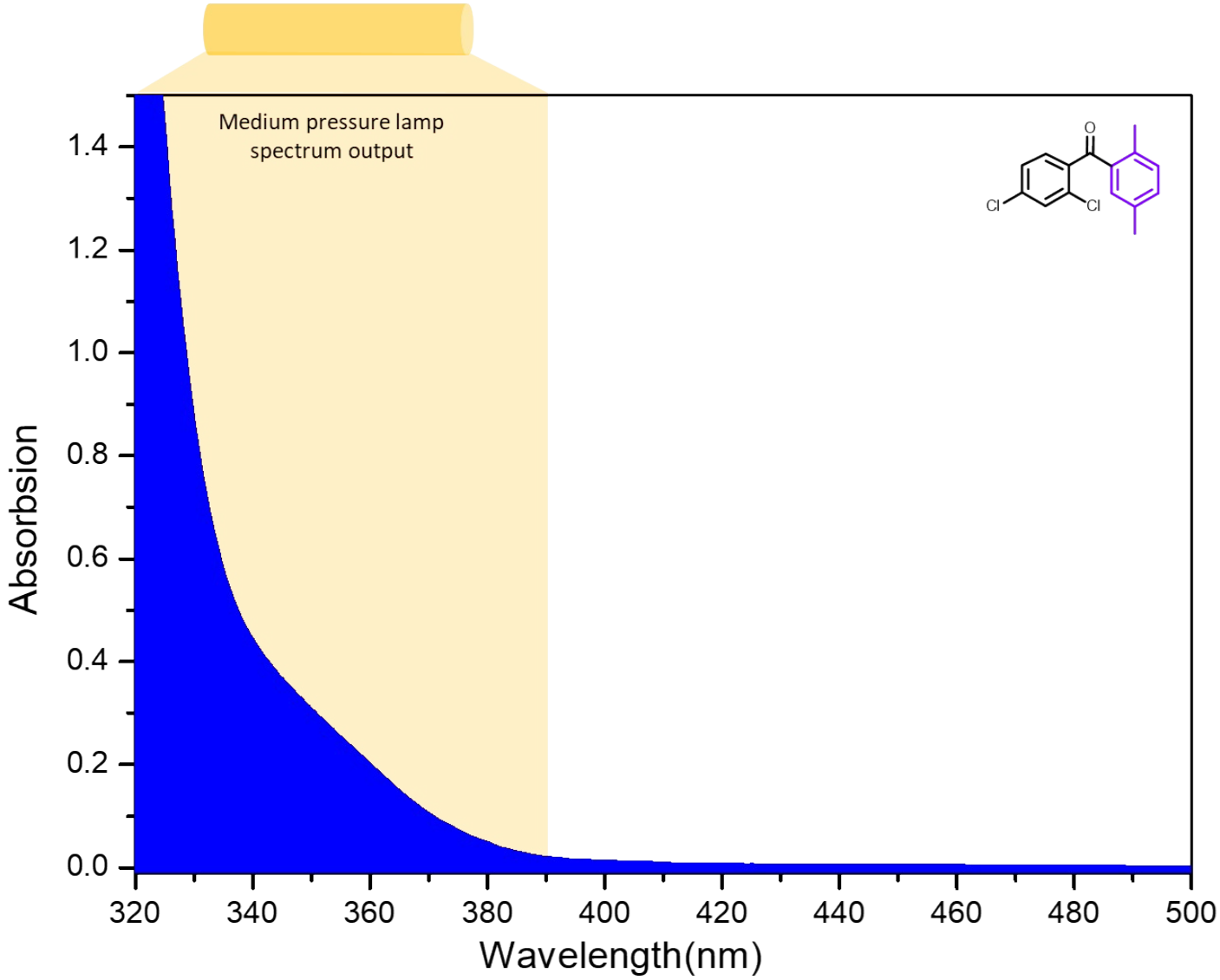


Figure S24. UV-Vis spctra of (2, 4-dichlorophenyl) (2, 5-dimethylphenyl) methanone (**2e**) in 0.0022 M DMSO.

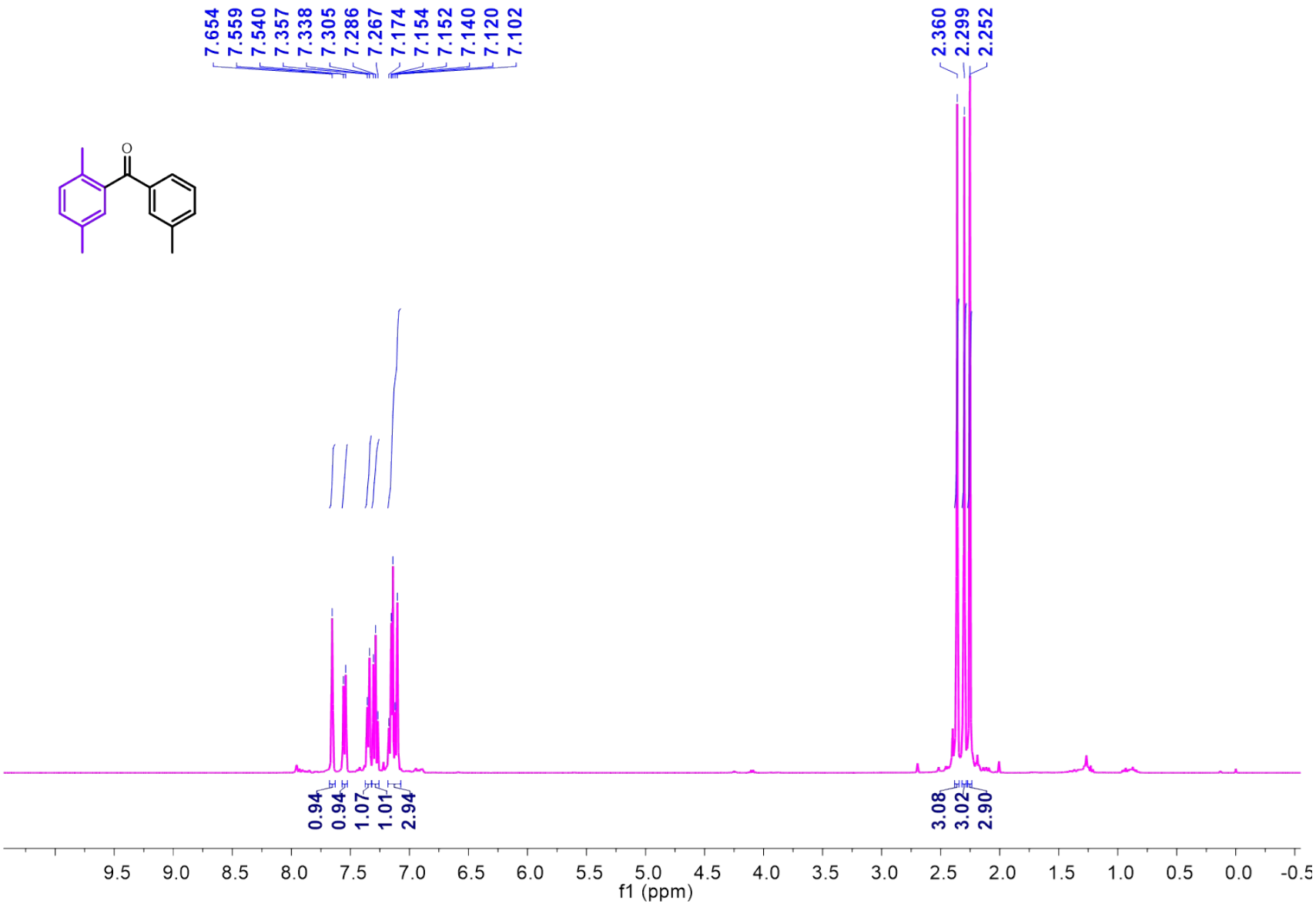


Figure S25. ^{1}H NMR spectra of (2, 5-dimethylphenyl) (m-tolyl) methadone (**2f**) in $CDCl_3$.

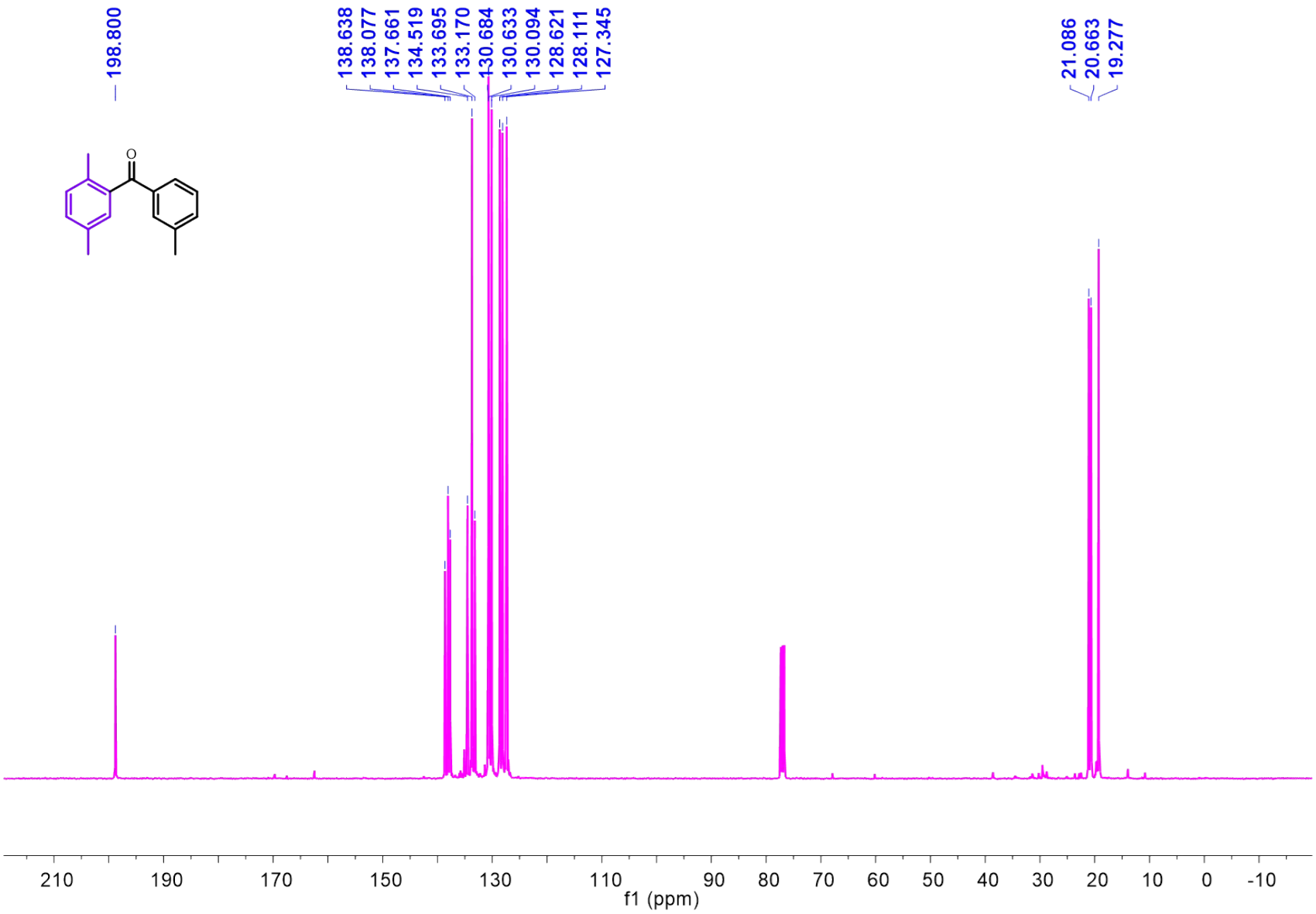


Figure S26. ^{13}C NMR spectra of (2, 5-dimethylphenyl) (m-tolyl) methanone (**2f**) in $CDCl_3$.

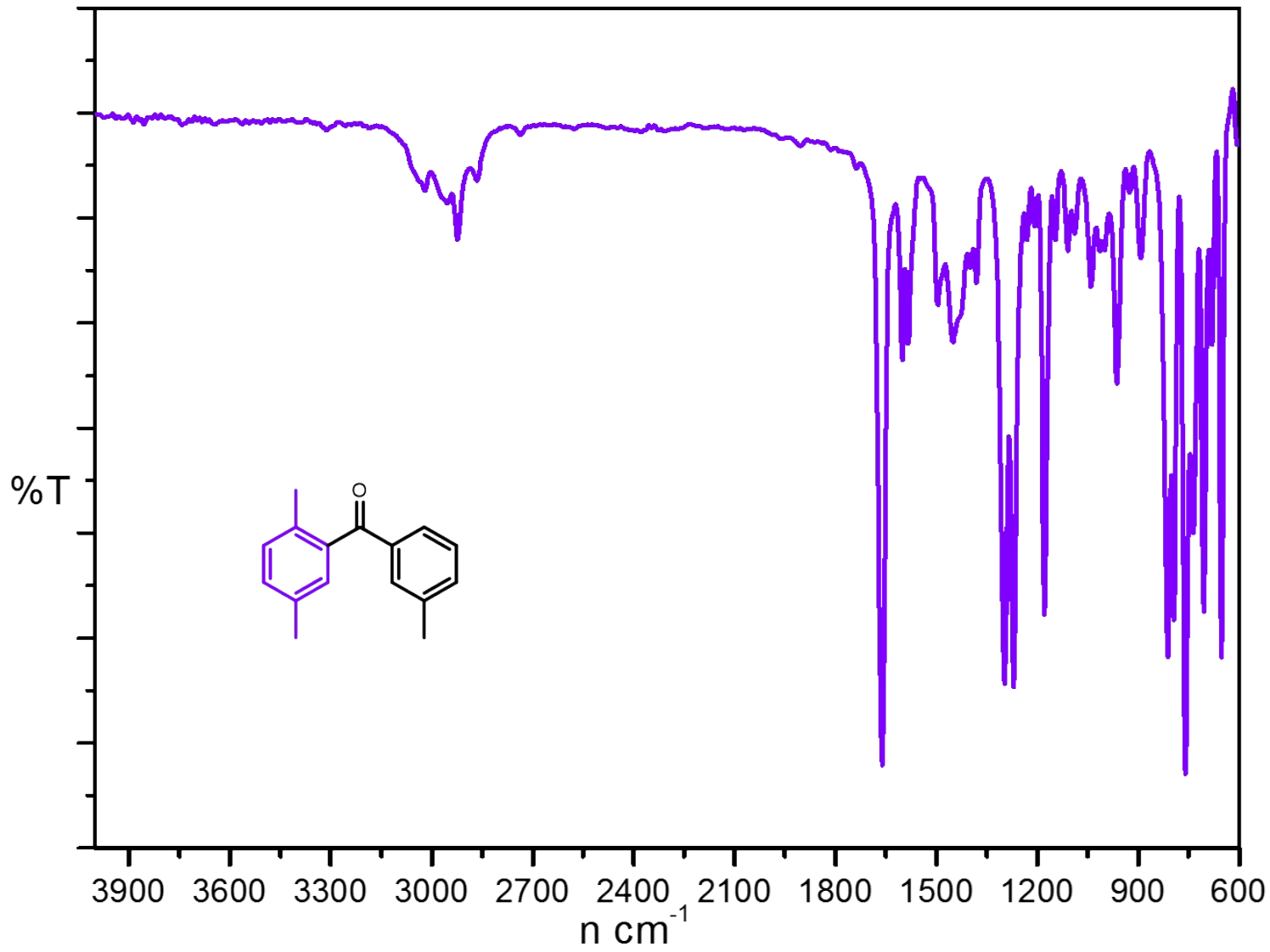


Figure S27. IR spectra of (2, 5-dimethylphenyl) (m-tolyl) methanone) (**2f**).

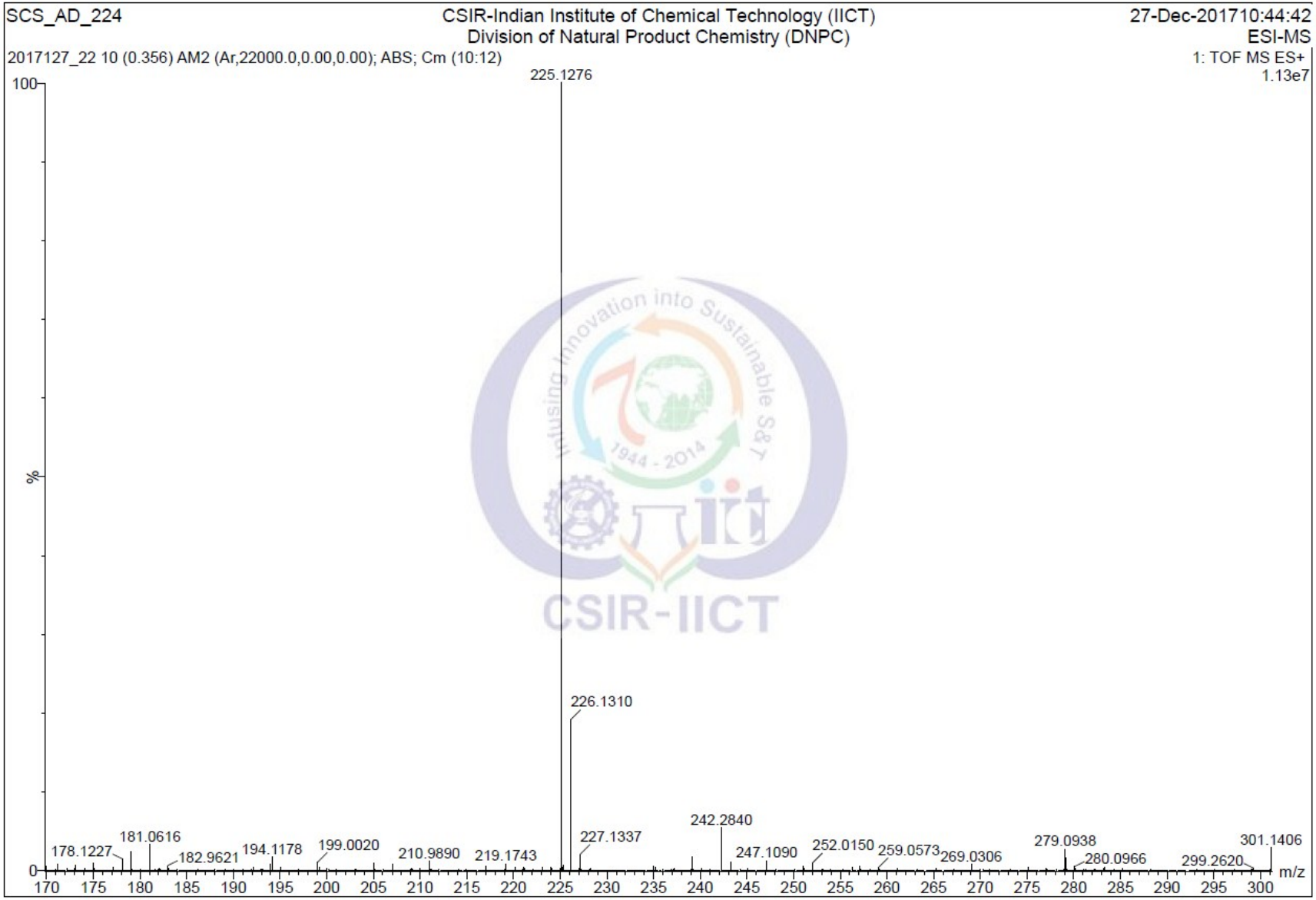


Figure S28. HRMS spctra of (2, 5-dimethylphenyl) (m-tollyl) methanone (**2f**).

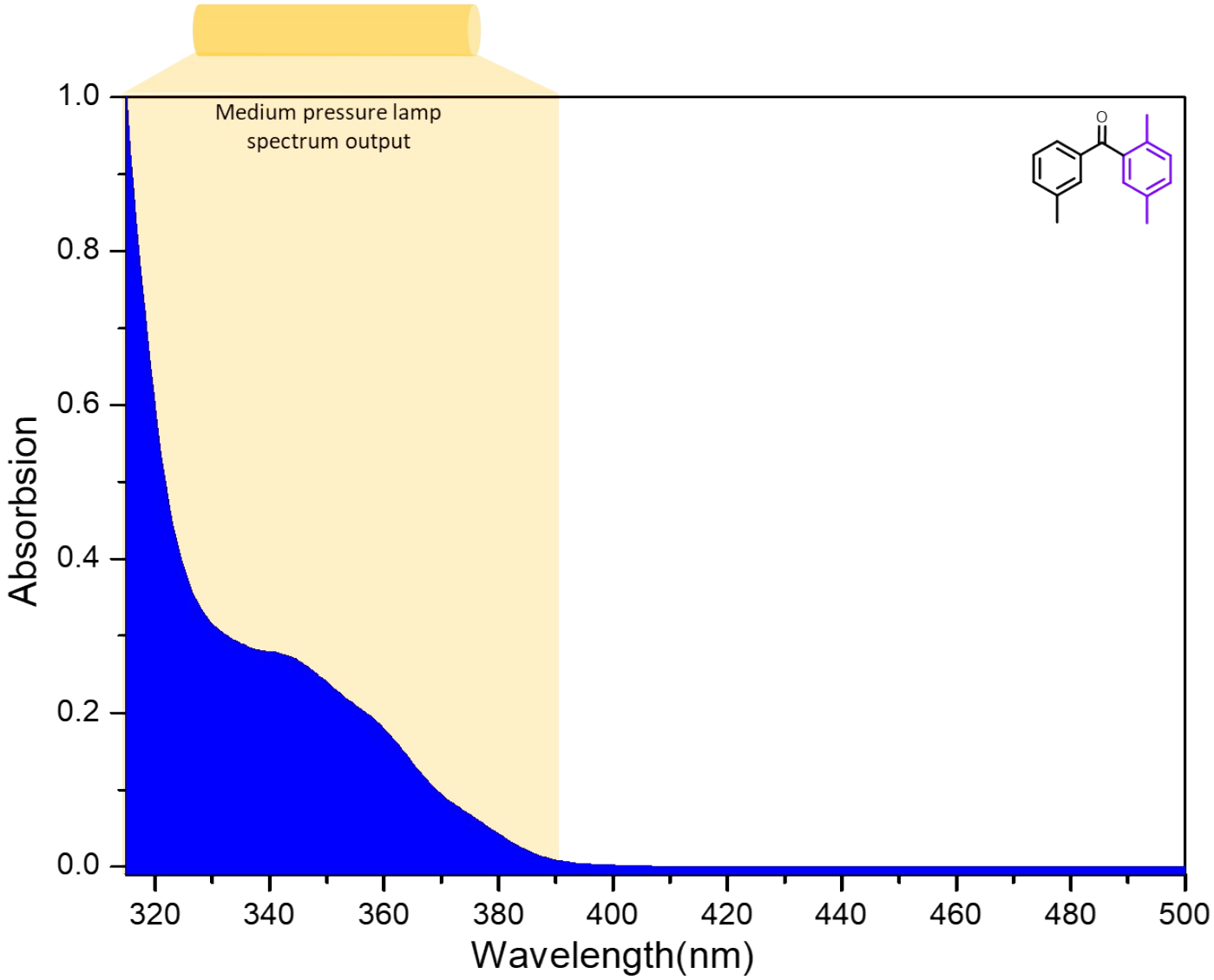


Figure S29. UV-Visible spctra of (2, 5-dimethylphenyl) (m-tollyl) methanone (**2f**) in 0.0022 M DMSO.

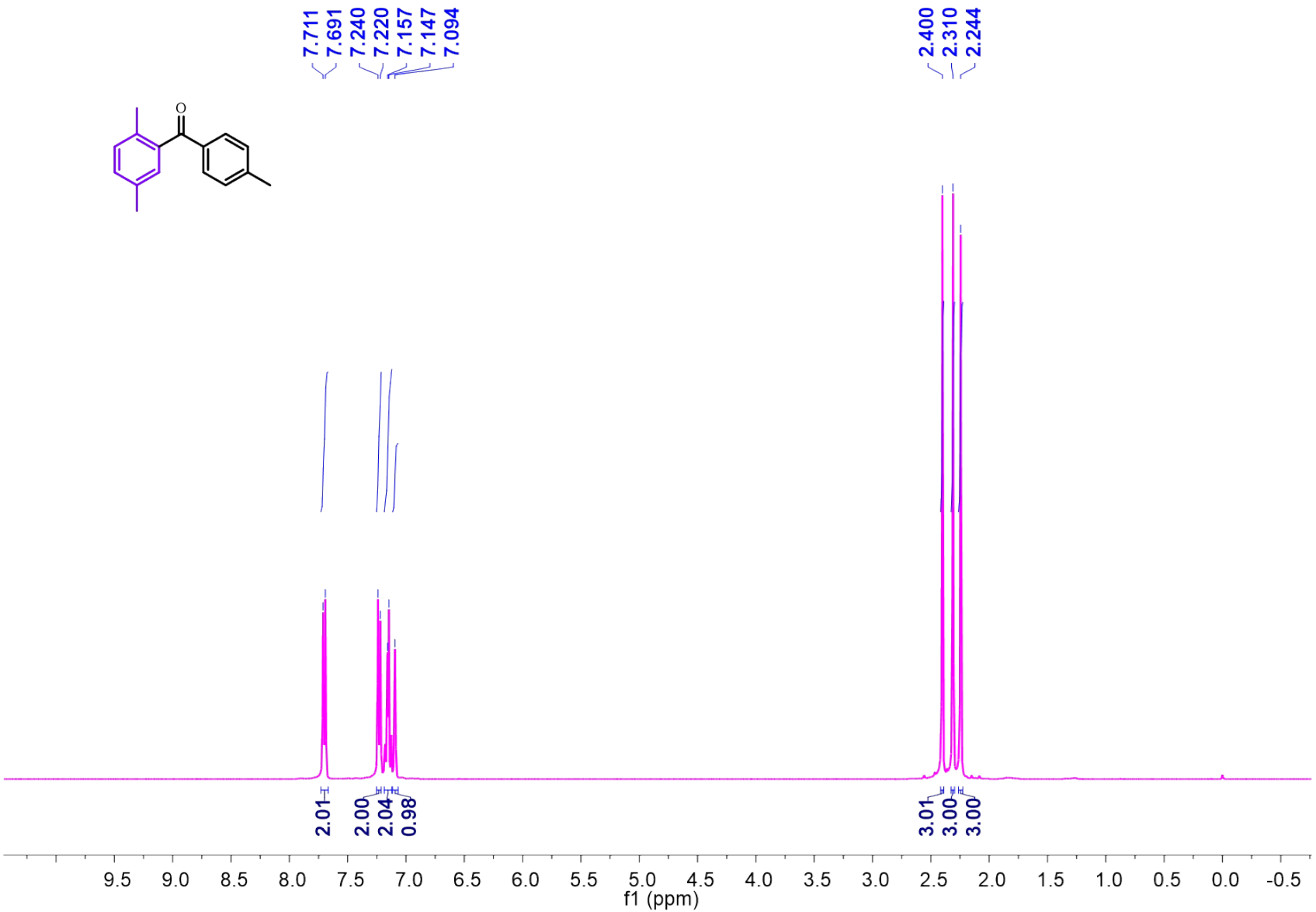


Figure S30. ^{1}H NMR spectra of (2, 5-dimethylphenyl) (p-tolyl) methanone (**2g**) in $CDCl_3$.

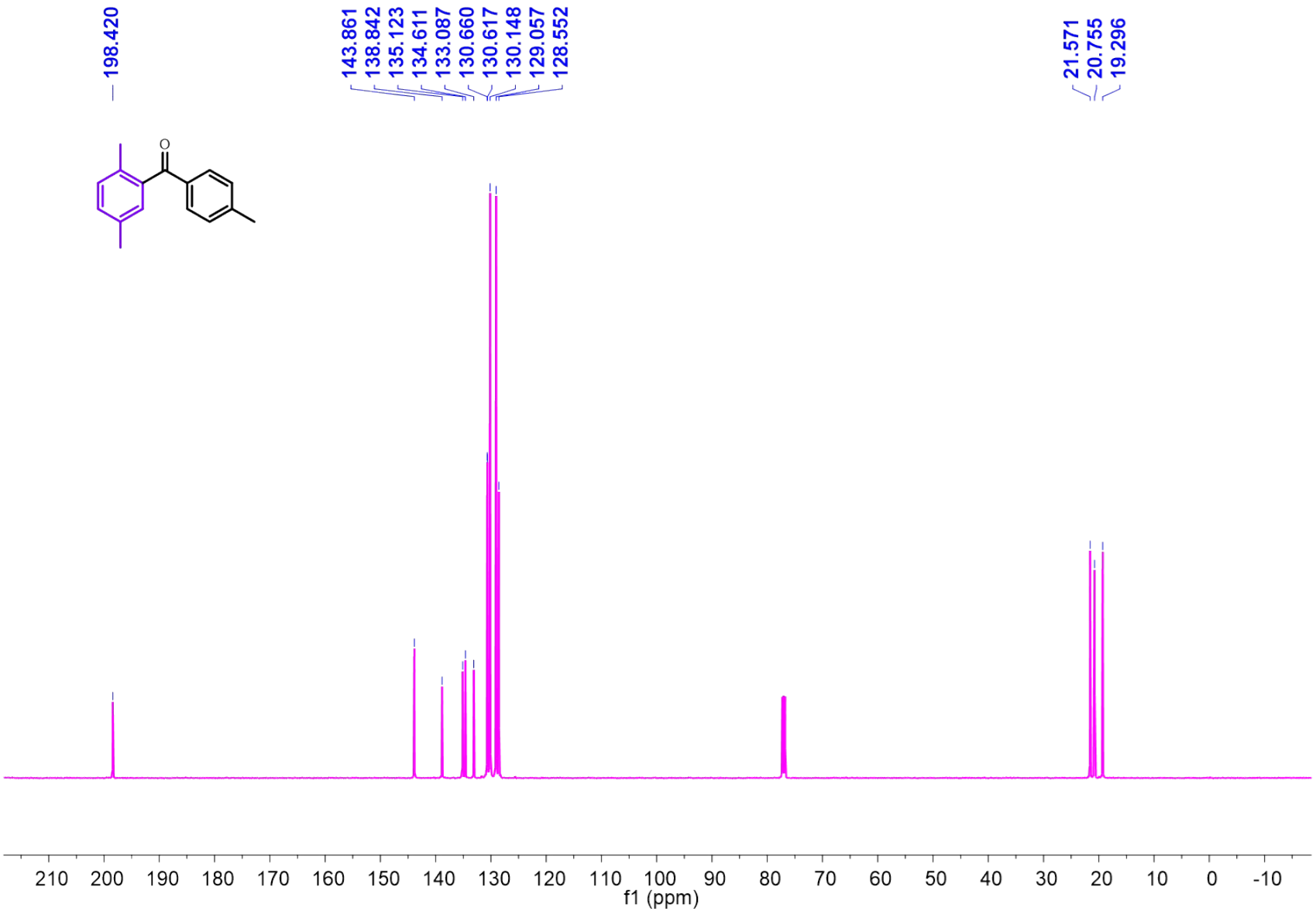


Figure S31. ^{13}C NMR spectra of (2, 5-dimethylphenyl) (p-tolyl) methanone (**2g**) in $CDCl_3$.

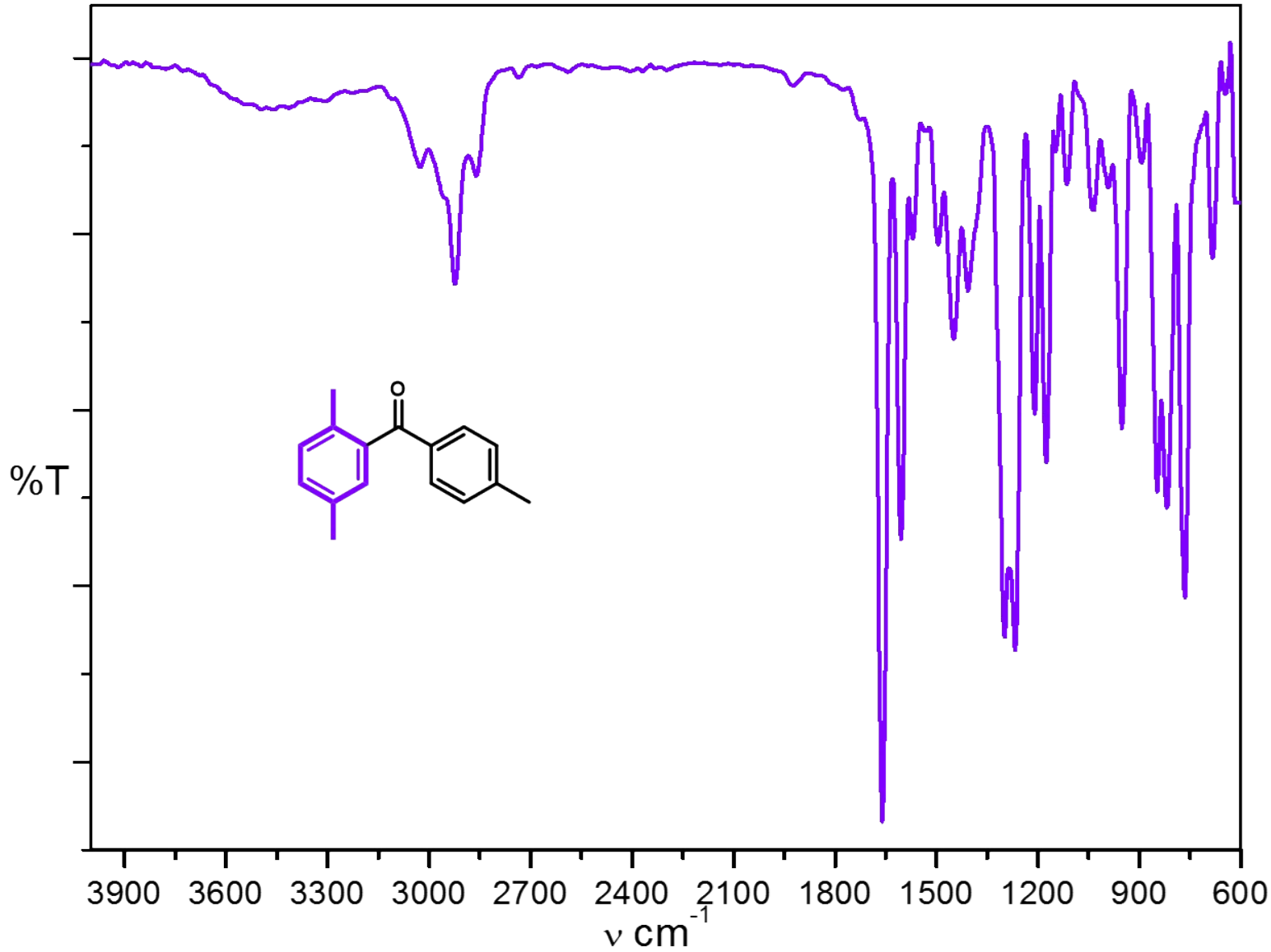


Figure S32. IR spectra of (2, 5-dimethylphenyl) (p-tolyl) methanone (**2g**).

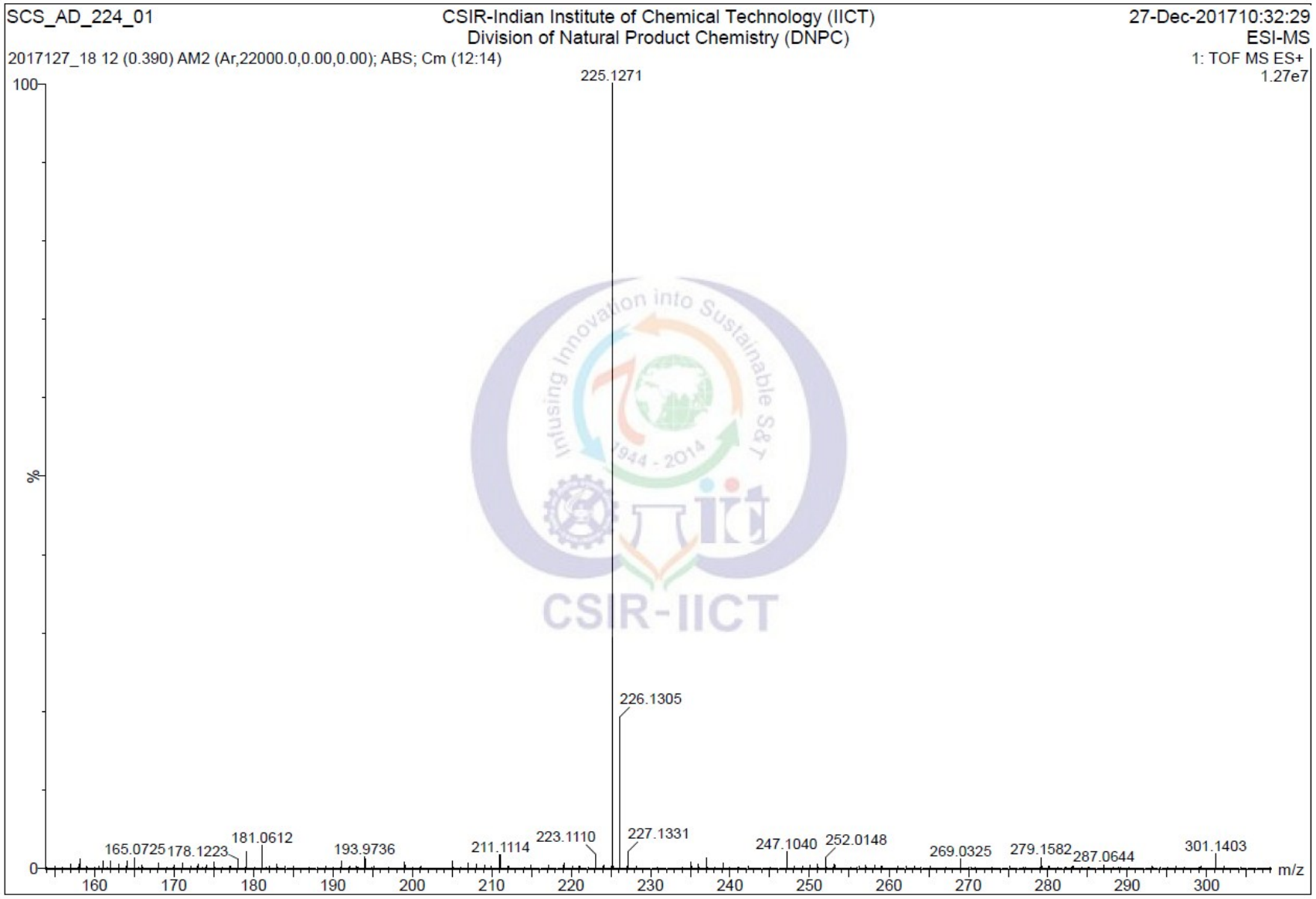


Figure S33. HRMS spctra of (2, 5-dimethylphenyl) (p-tolyl) methanone (**2g**).

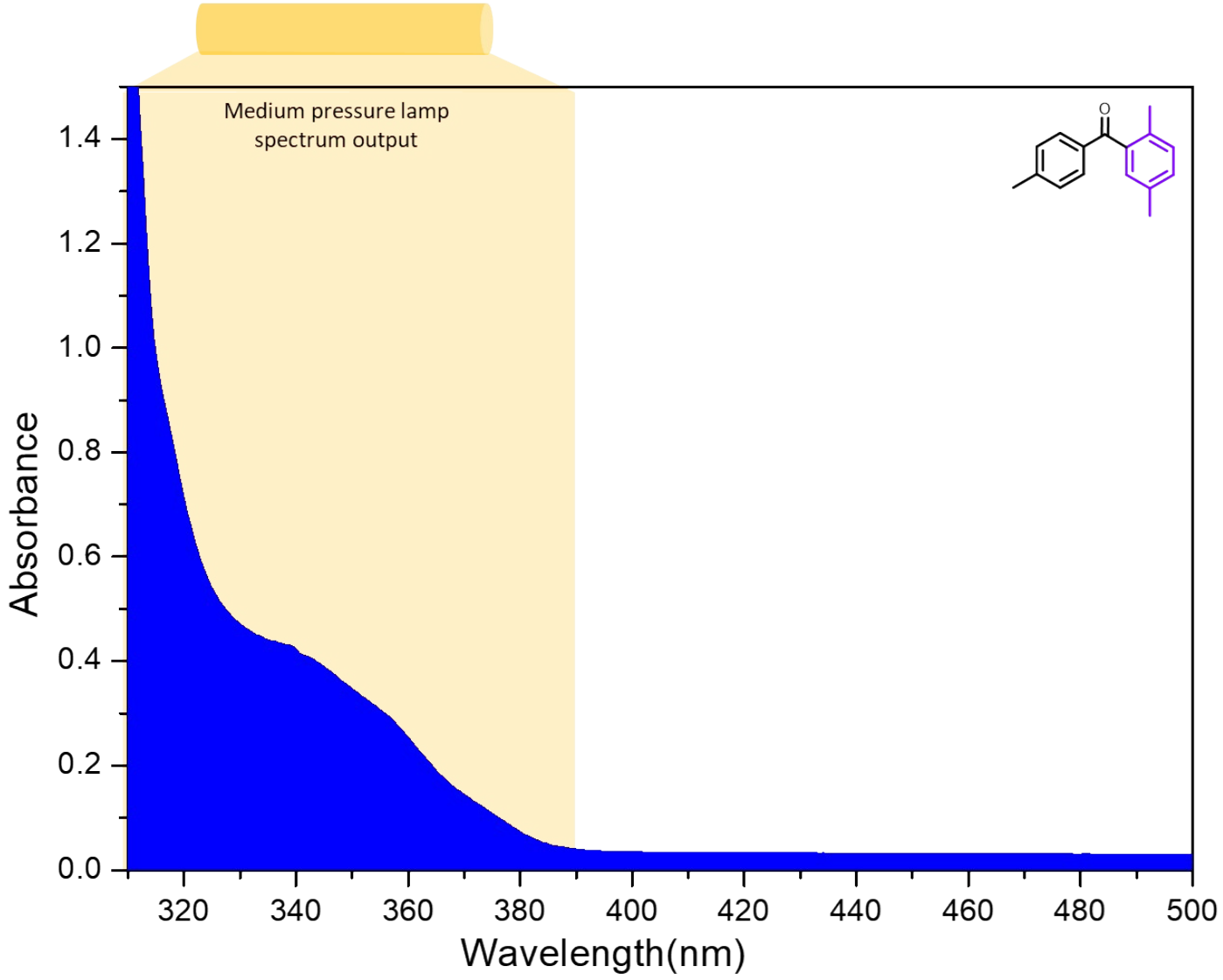


Figure S34. UV-Visible spctra of (2, 5-dimethylphenyl) (p-tolyl) methanone (**2g**) in 0.0022 M DMSO.

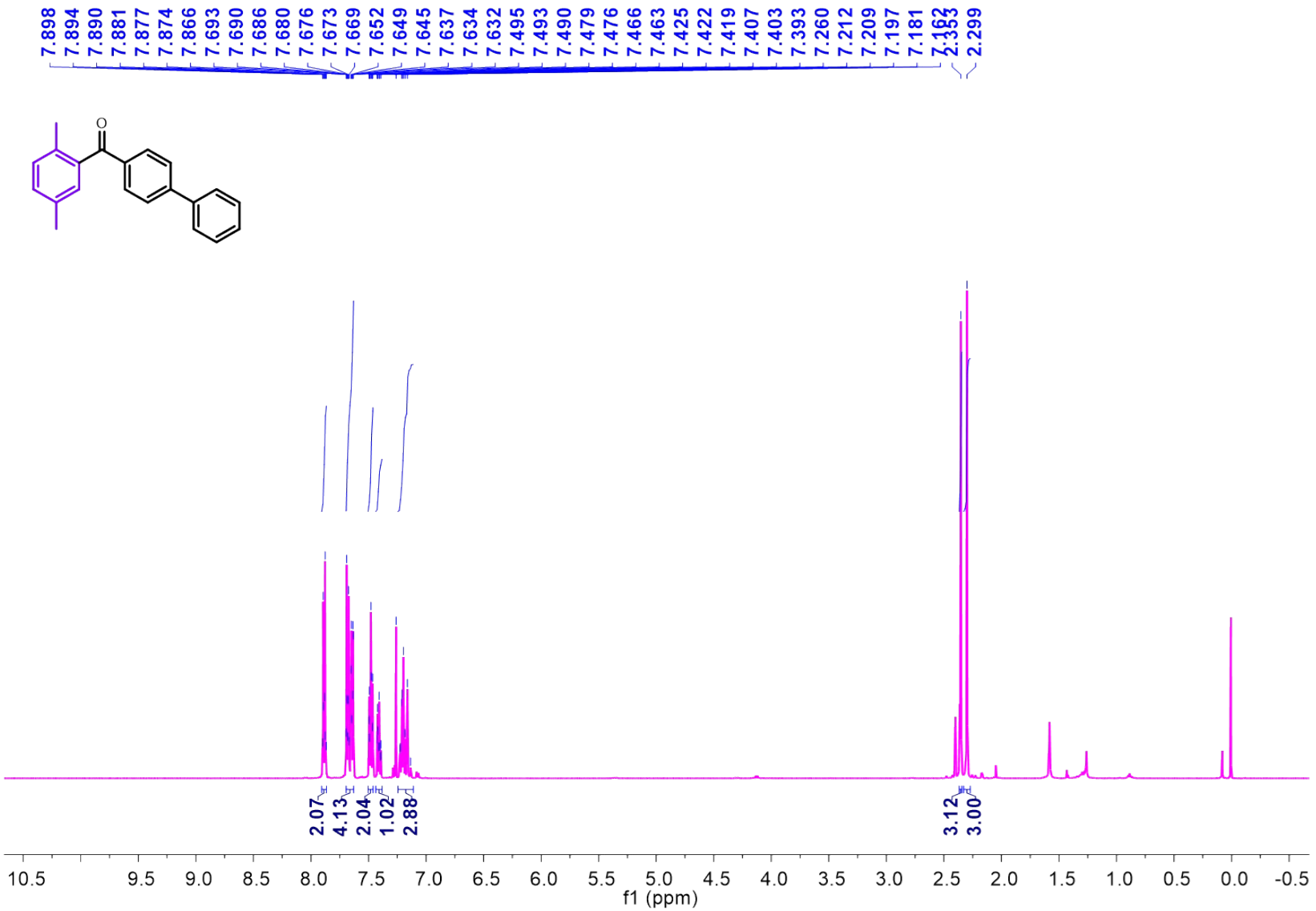


Figure S35. ^{1}H NMR spectra of (2, 5-dimethylphenyl) [1, 1'-biphenyl]-4-yl) methanone (**2h**) in $CDCl_3$.

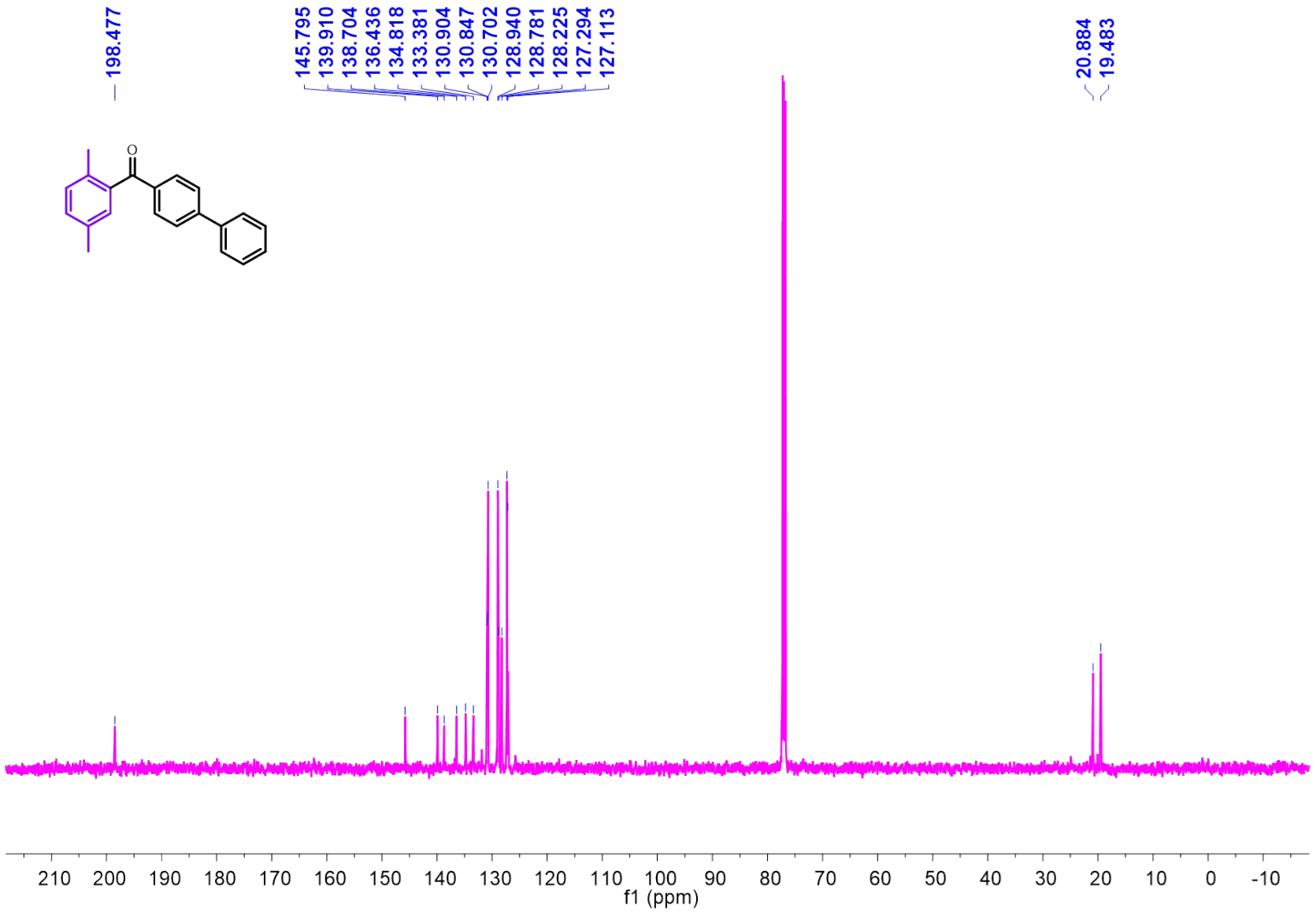


Figure S36. ^{13}C NMR spectra of (2, 5-dimethylphenyl) [1, 1'-biphenyl]-4-yl) methanone (**2h**) in $CDCl_3$.

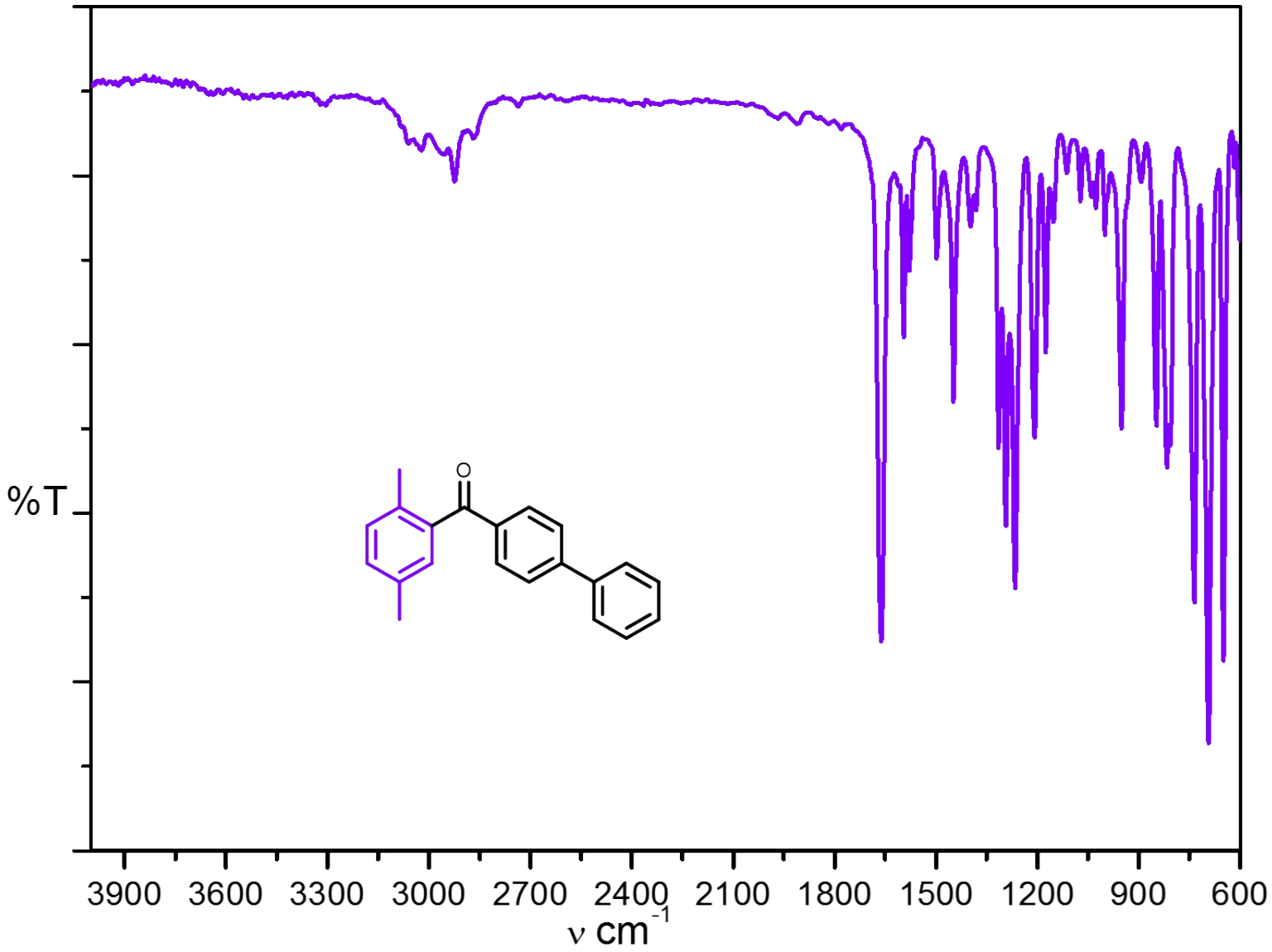


Figure S37. IR spectra of (2, 5-dimethylphenyl) [1, 1'-biphenyl]-4-yl) methanone (**2h**).

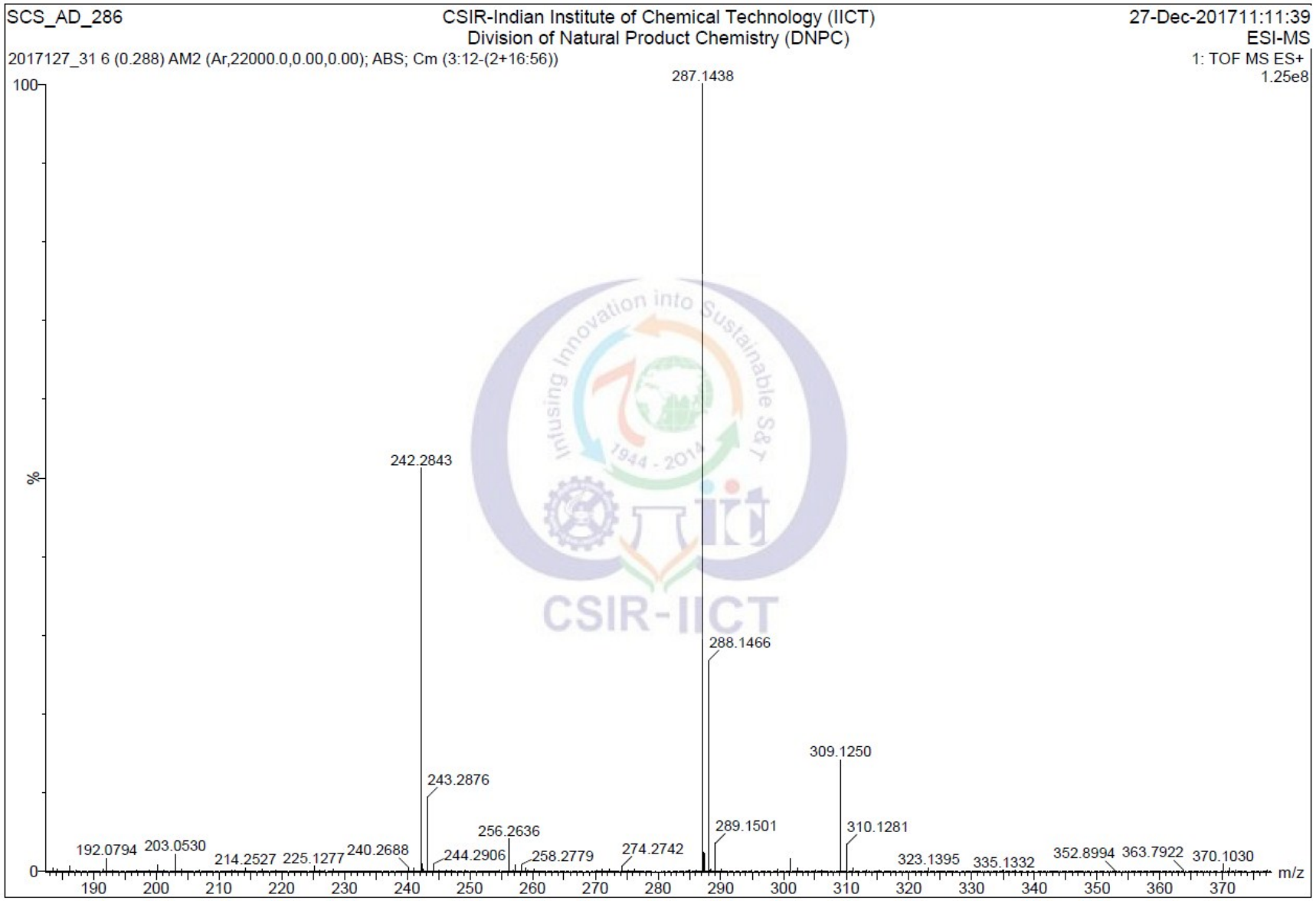


Figure S38. HRMS spectra of 2, 5-(dimethylphenyl) [1,1'-biphenyl]-4-yl) methanone (**2h**).

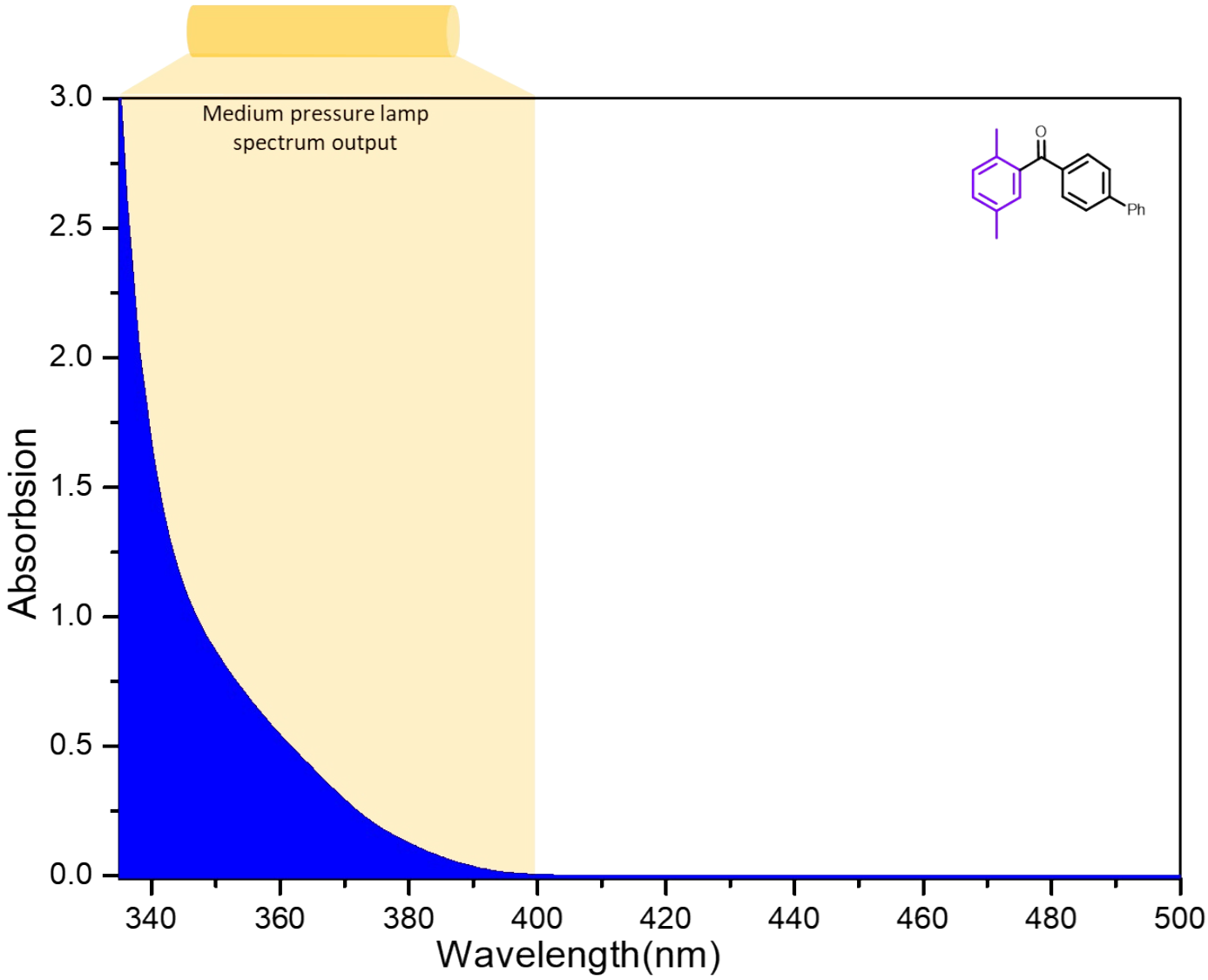


Figure S39. UV-Visible spectra of 2, 5-(dimethylphenyl) [1,1'-biphenyl]-4-yl) methanone (**2h**) in 0.0022 M DMSO.

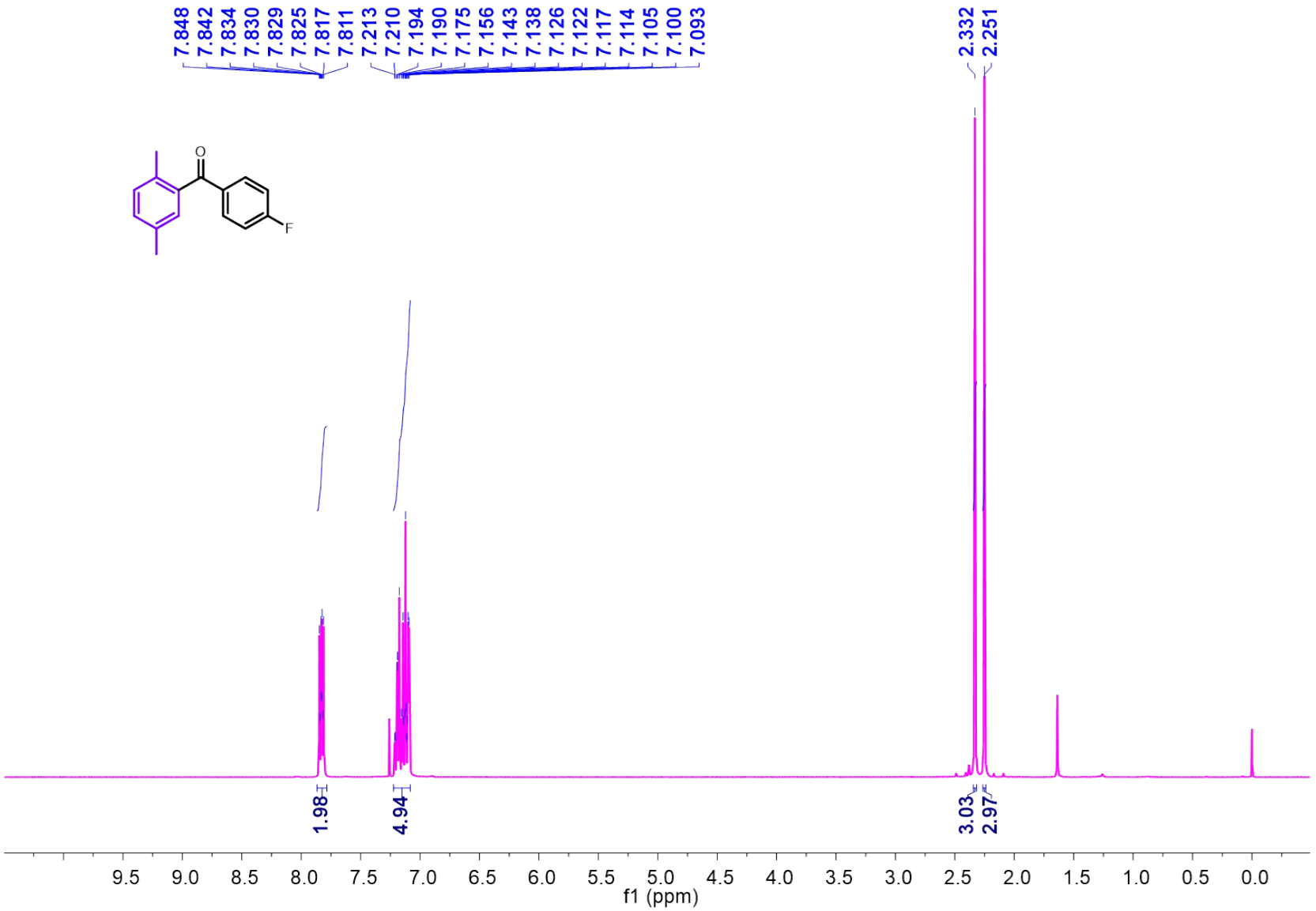


Figure S40. ^{1}H NMR spectra of (2, 5-dimethylphenyl) (4-fluorophenyl) methanone (**2i**) in $CDCl_3$.

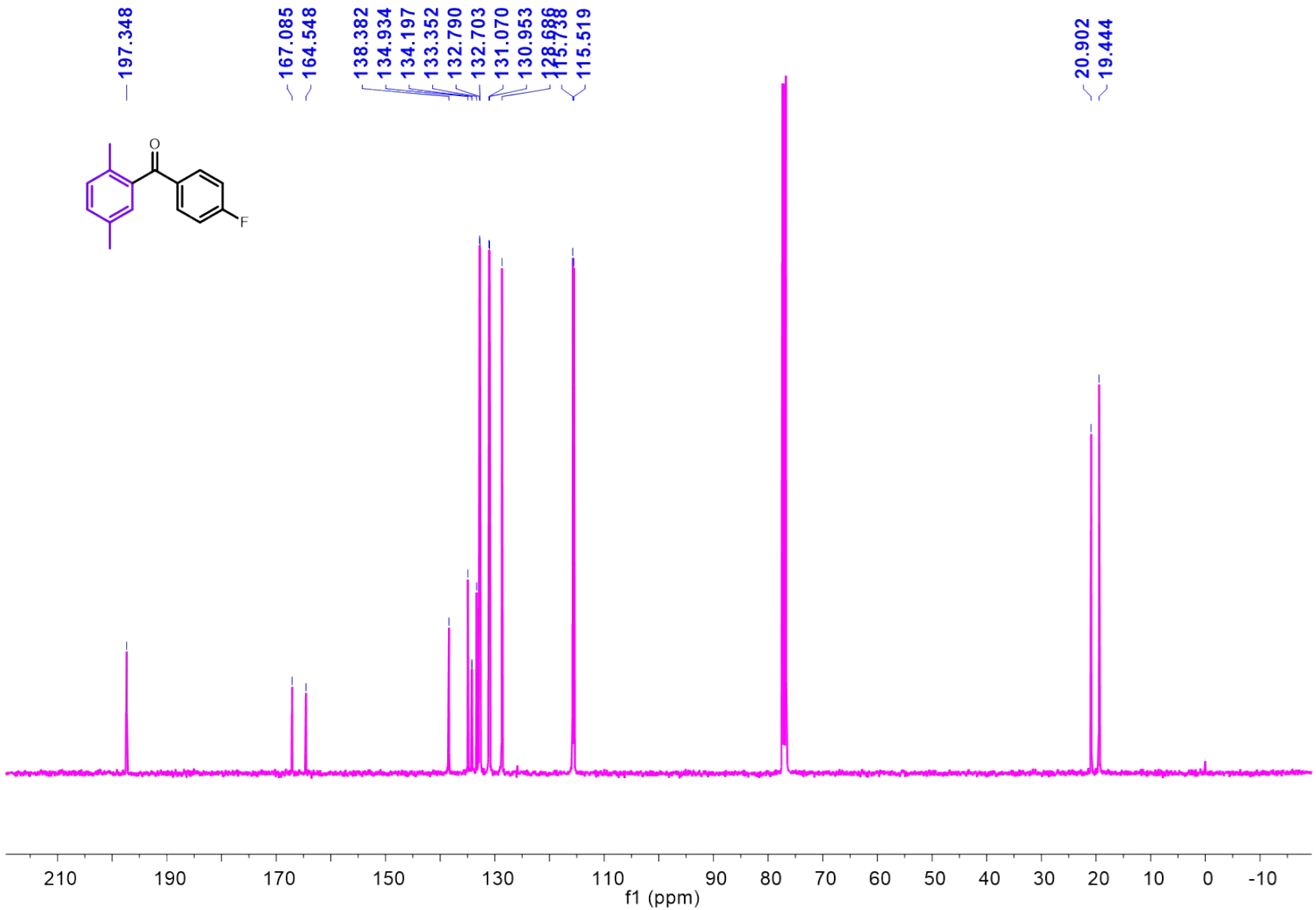


Figure S41. ^{13}C NMR spectra of (2, 5-dimethylphenyl) (4-fluorophenyl) methanone (**2i**) in $CDCl_3$.

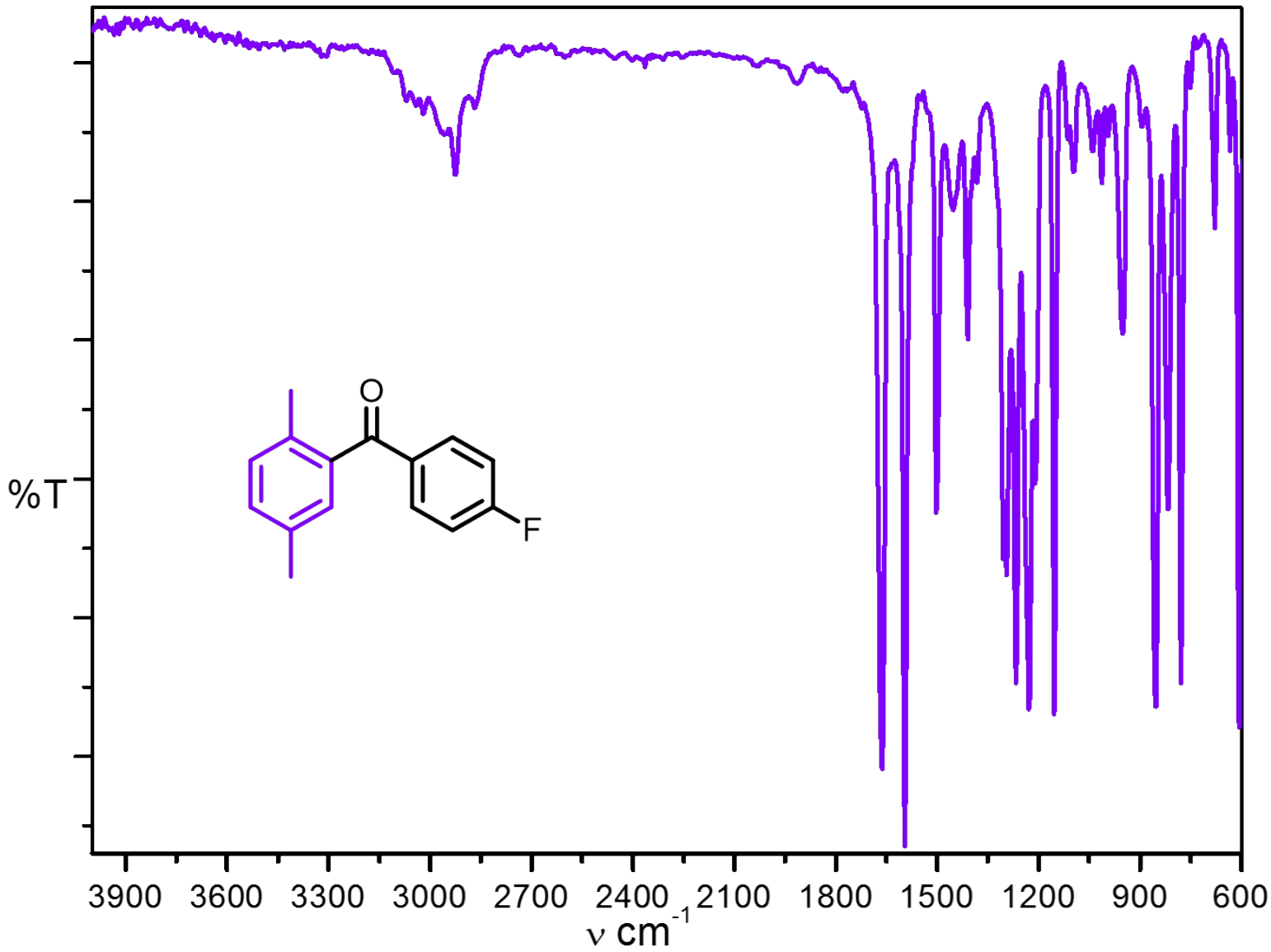


Figure S42. IR spectra of (2, 5-dimethylphenyl) (4-fluroPhenyl) methanone (**2i**).

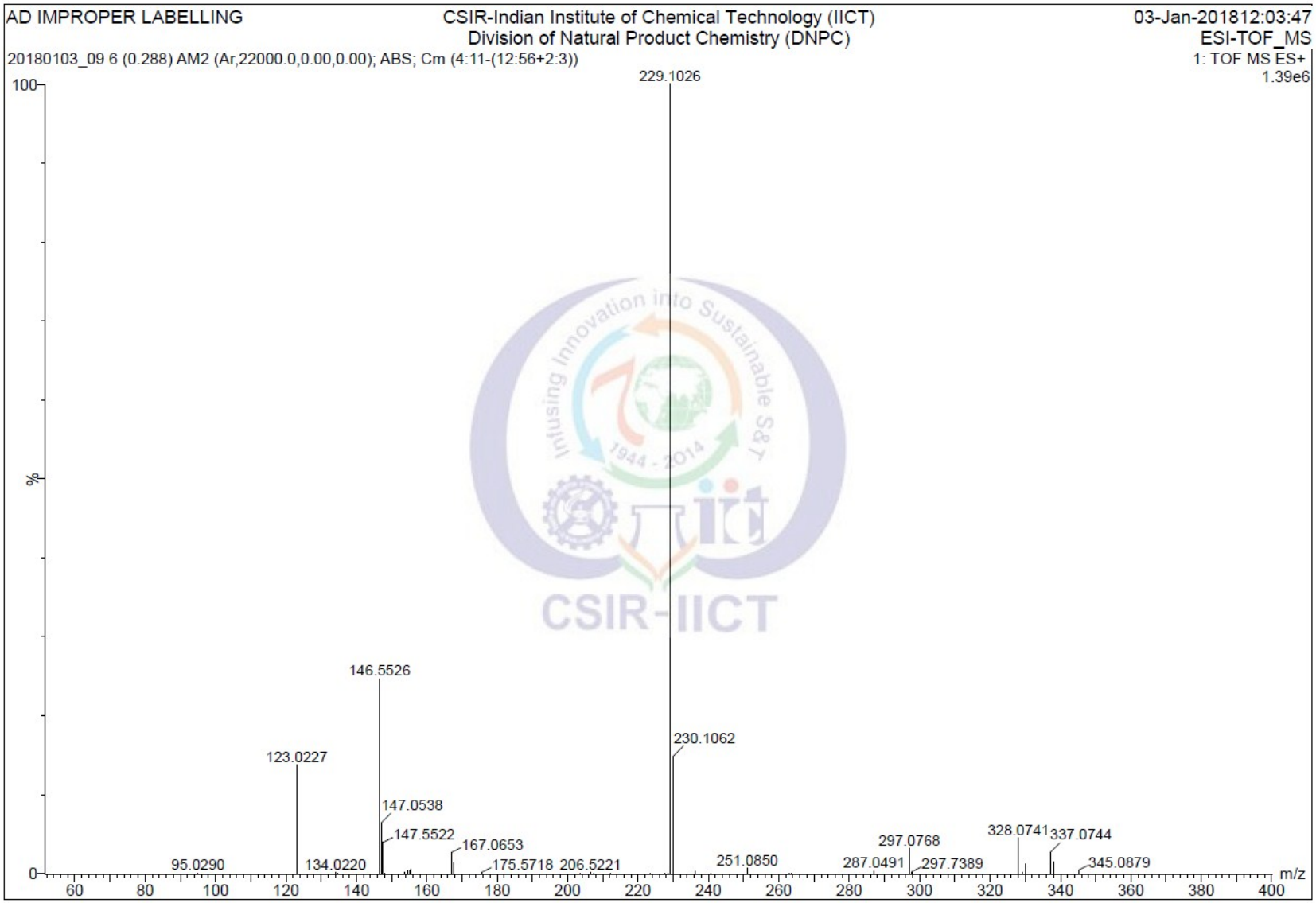


Figure S43. HRMS spectra of (2, 5-dimethylphenyl) (4-fluorophenyl) methanone (**2i**).

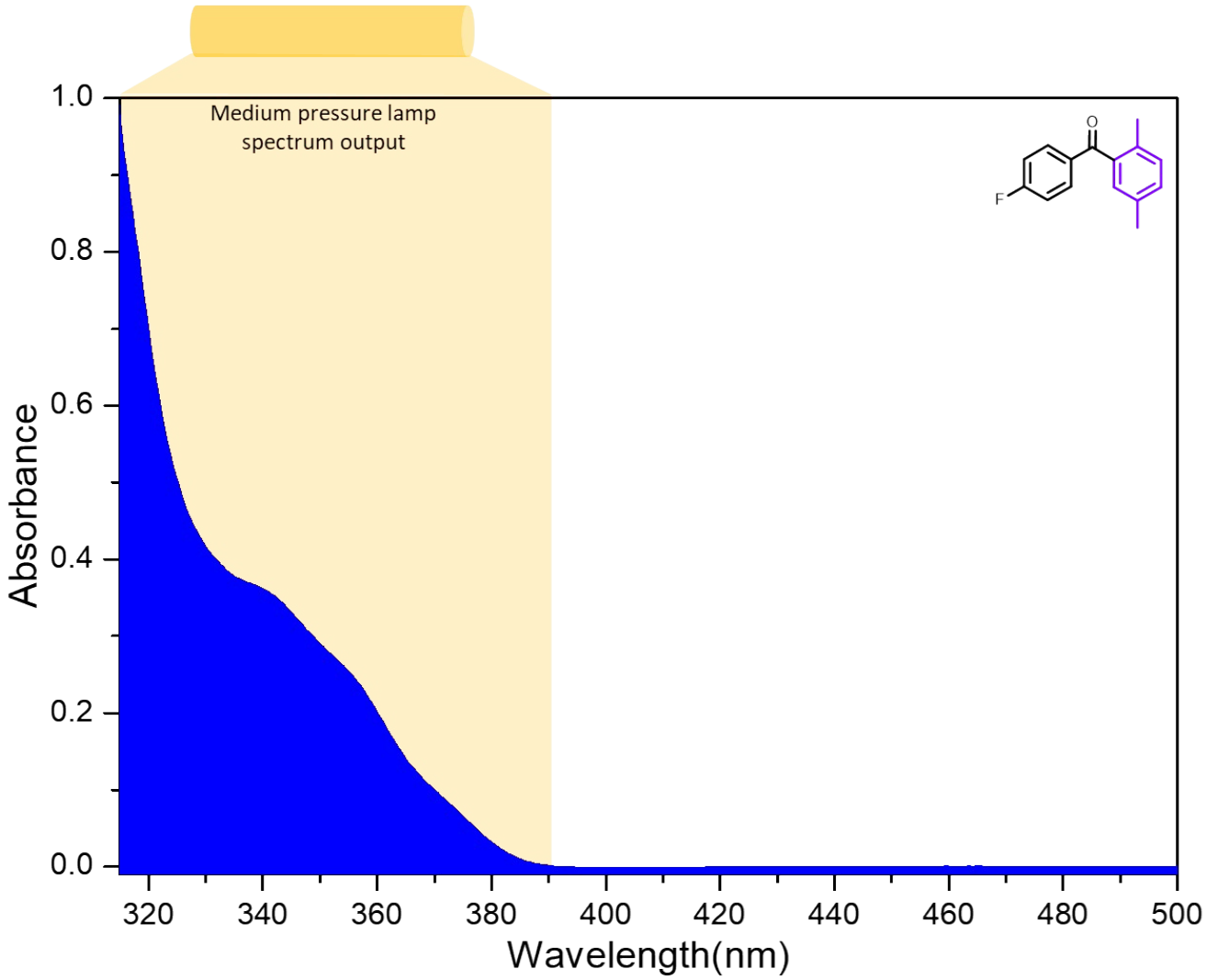


Figure S44. UV-Visible spectra of (2, 5-dimethylphenyl) (4-fluorophenyl) methanone (**2i**) in 0.0022 M DMSO.

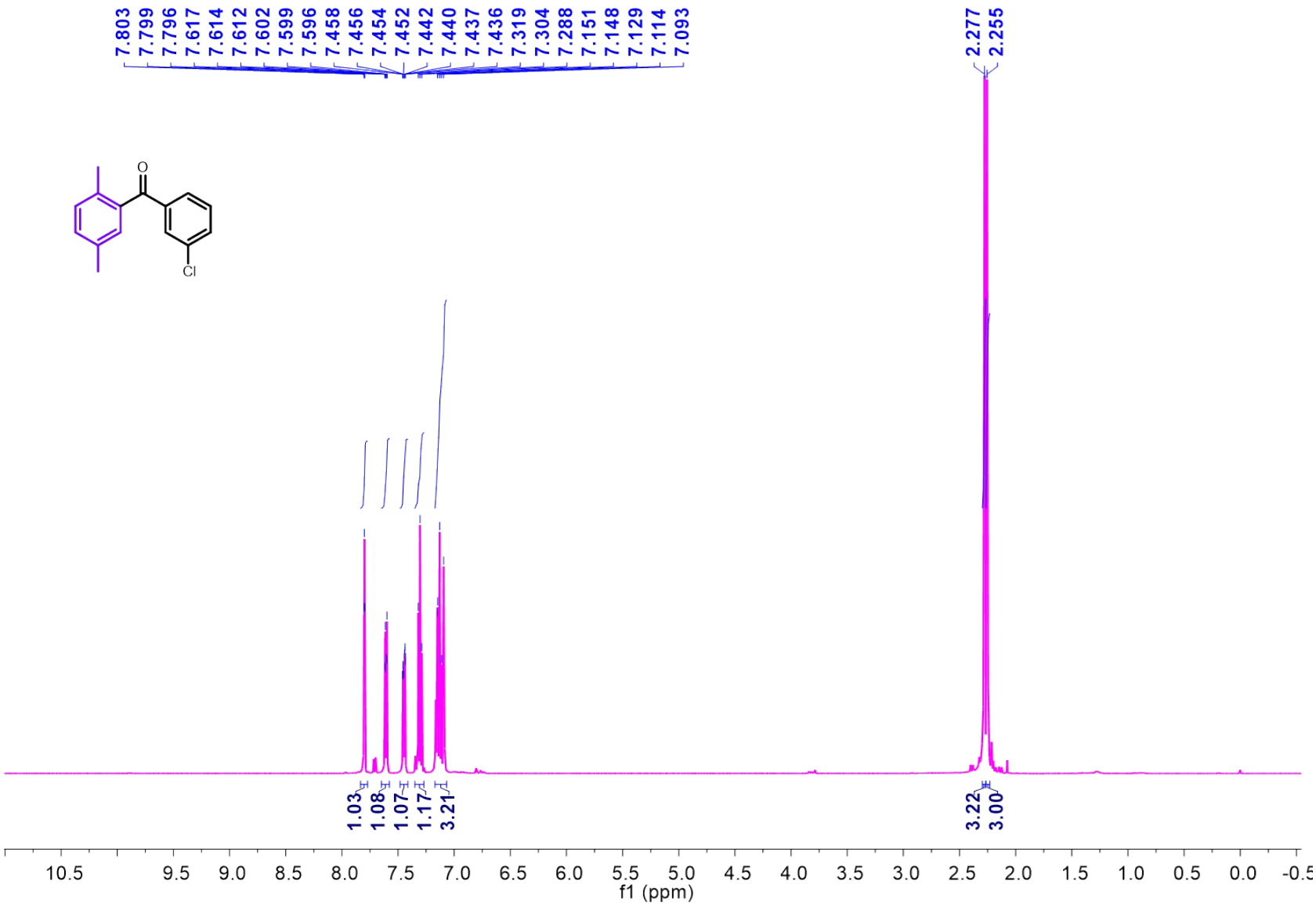


Figure S45. ^{1}H NMR spectra of (3-chlorophenyl) (2, 5-dimethylphenyl) methanone (**2j**) in $CDCl_3$.

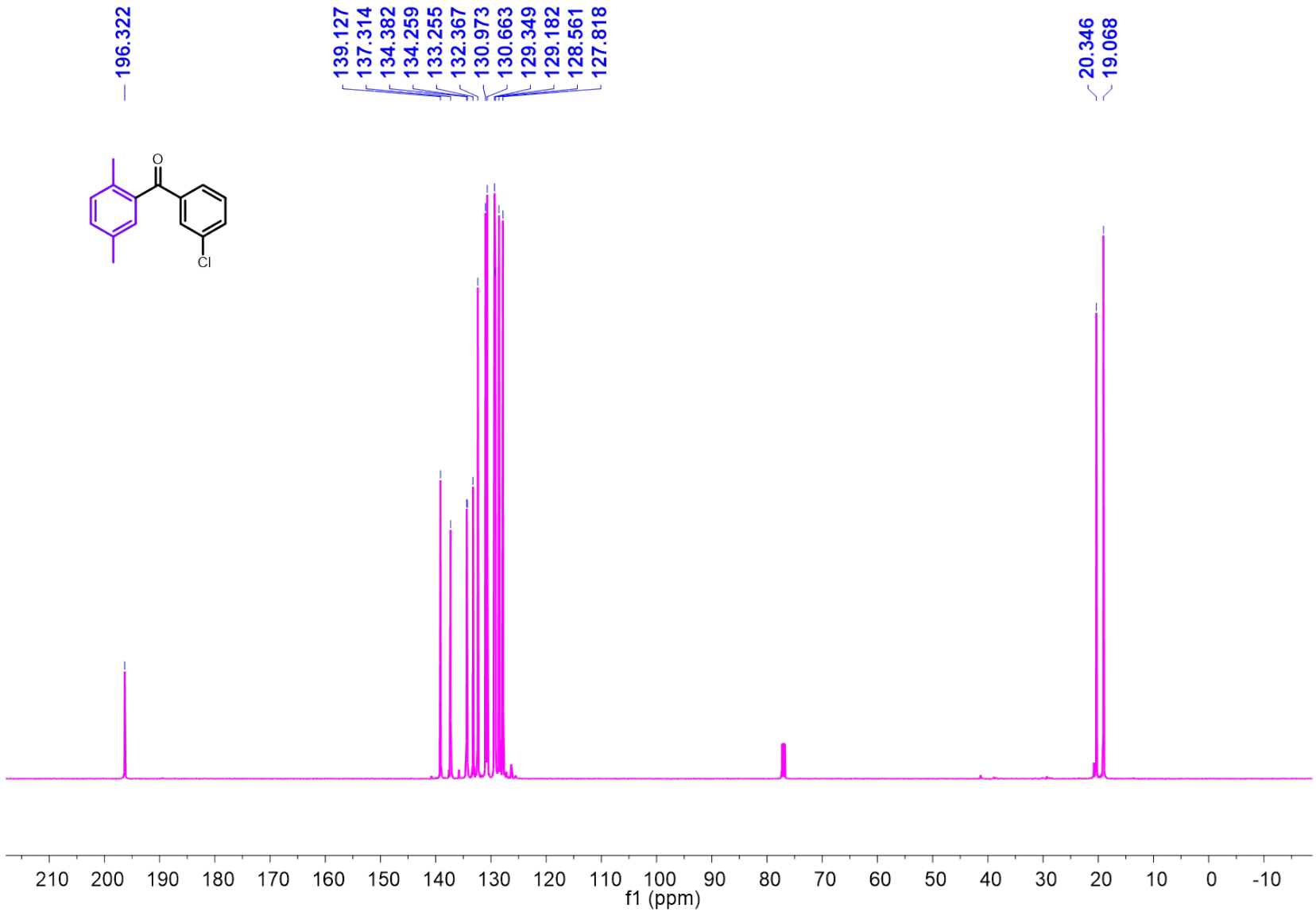


Figure S46. ^{13}C NMR spectra of (3-chlorophenyl) (2, 5-dimethylphenyl) methanone (**2j**) in $CDCl_3$.

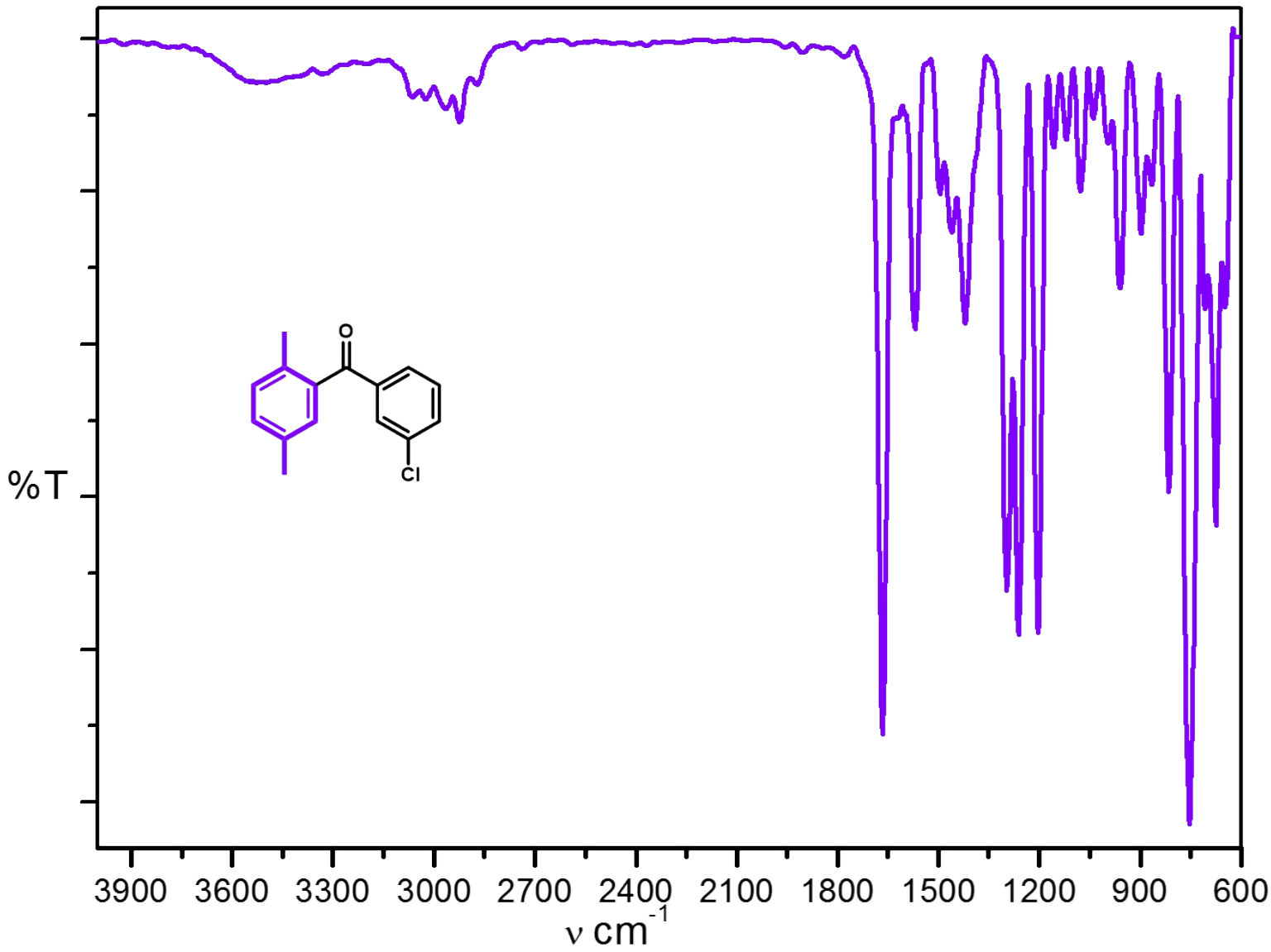


Figure S47. IR spectra of (3-chlorophenyl) (2, 5-dimethylphenyl) methanone (**2j**).

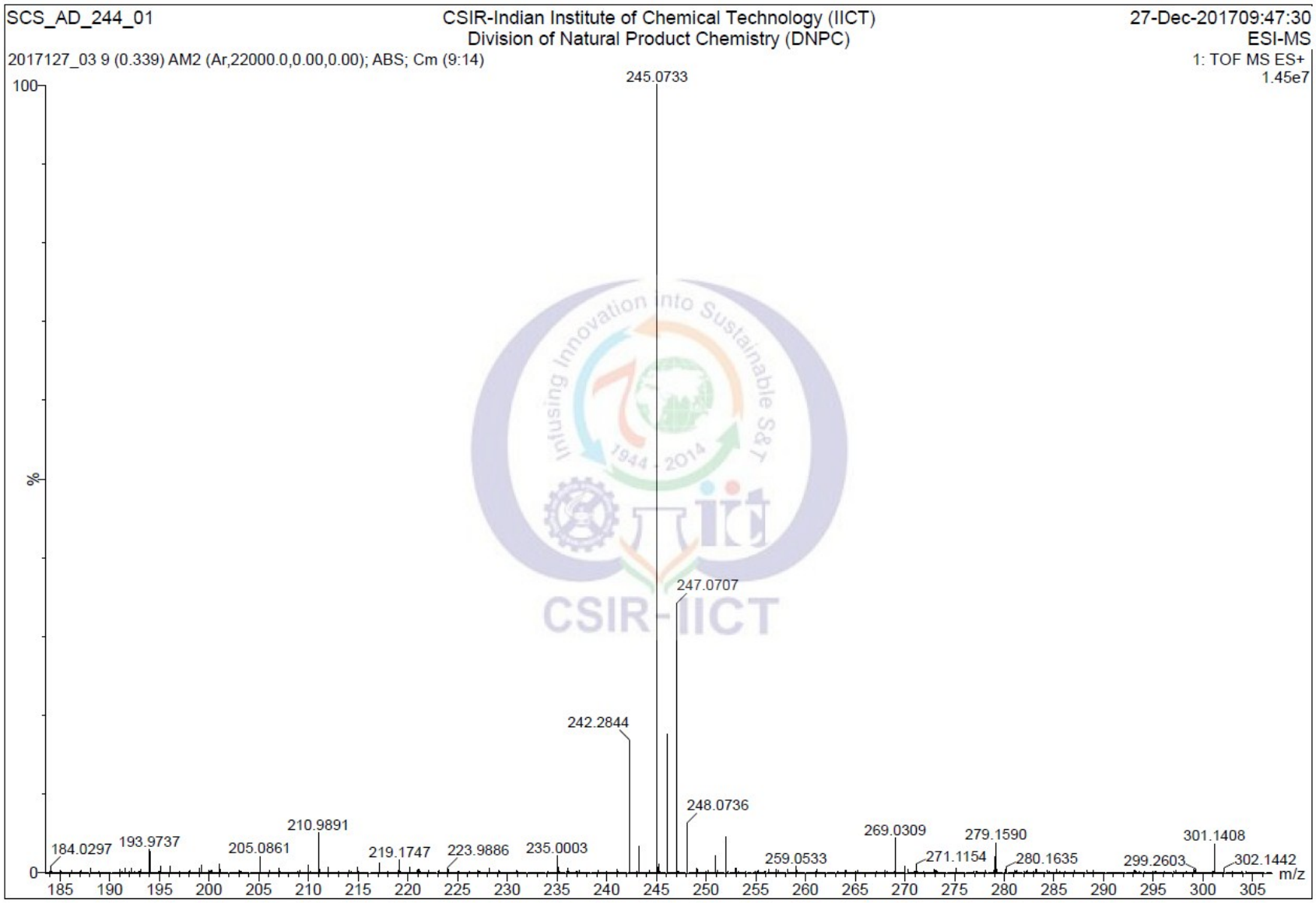


Figure S48. HRMS spectra of (3-chlorophenyl) (2, 5-dimethylphenyl) methanone (**2j**).

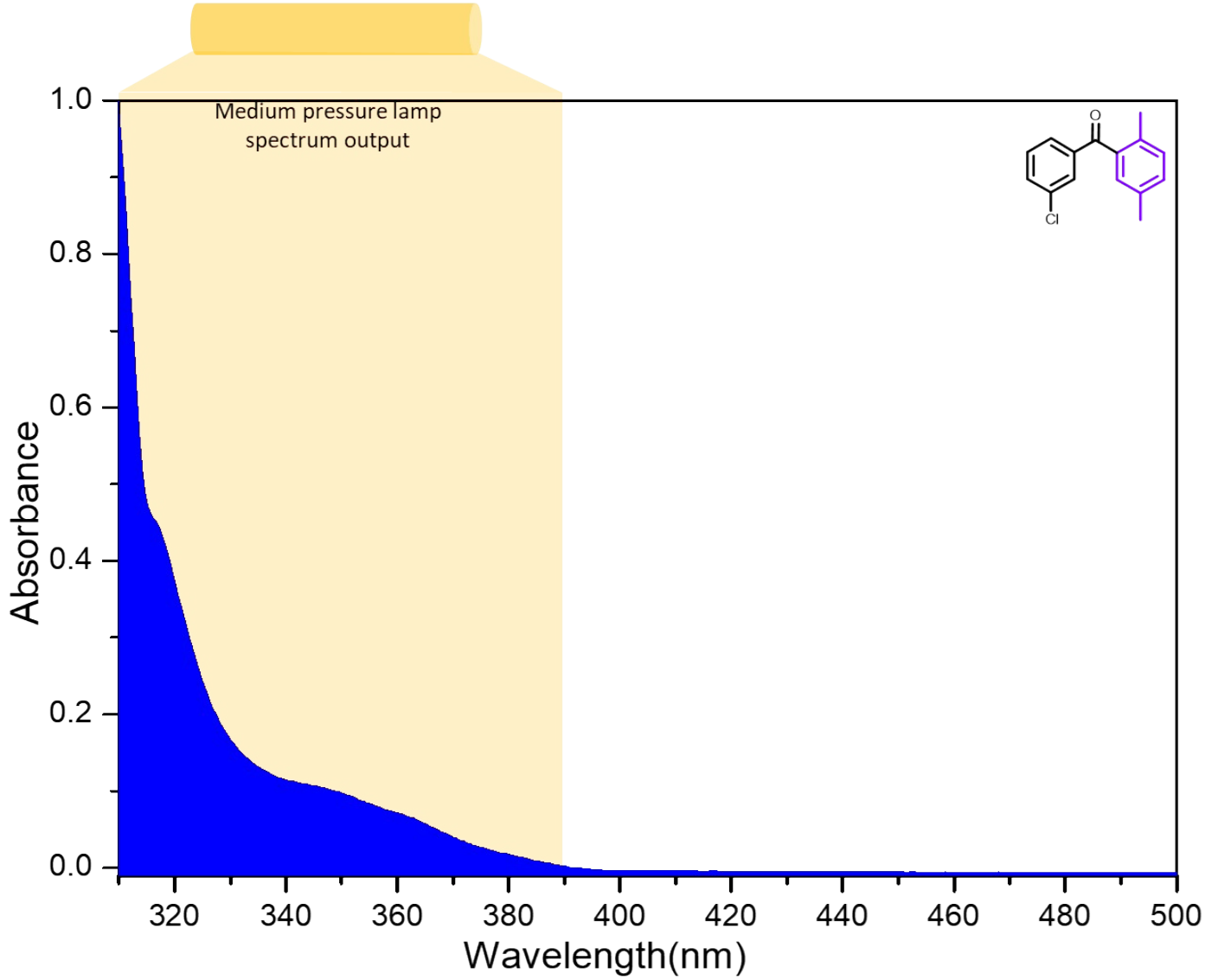


Figure S49. UV-Visible spectra of (3-chlorophenyl) (2, 5-dimethylphenyl) methanone (**2j**) in 0.0022 M DMSO.

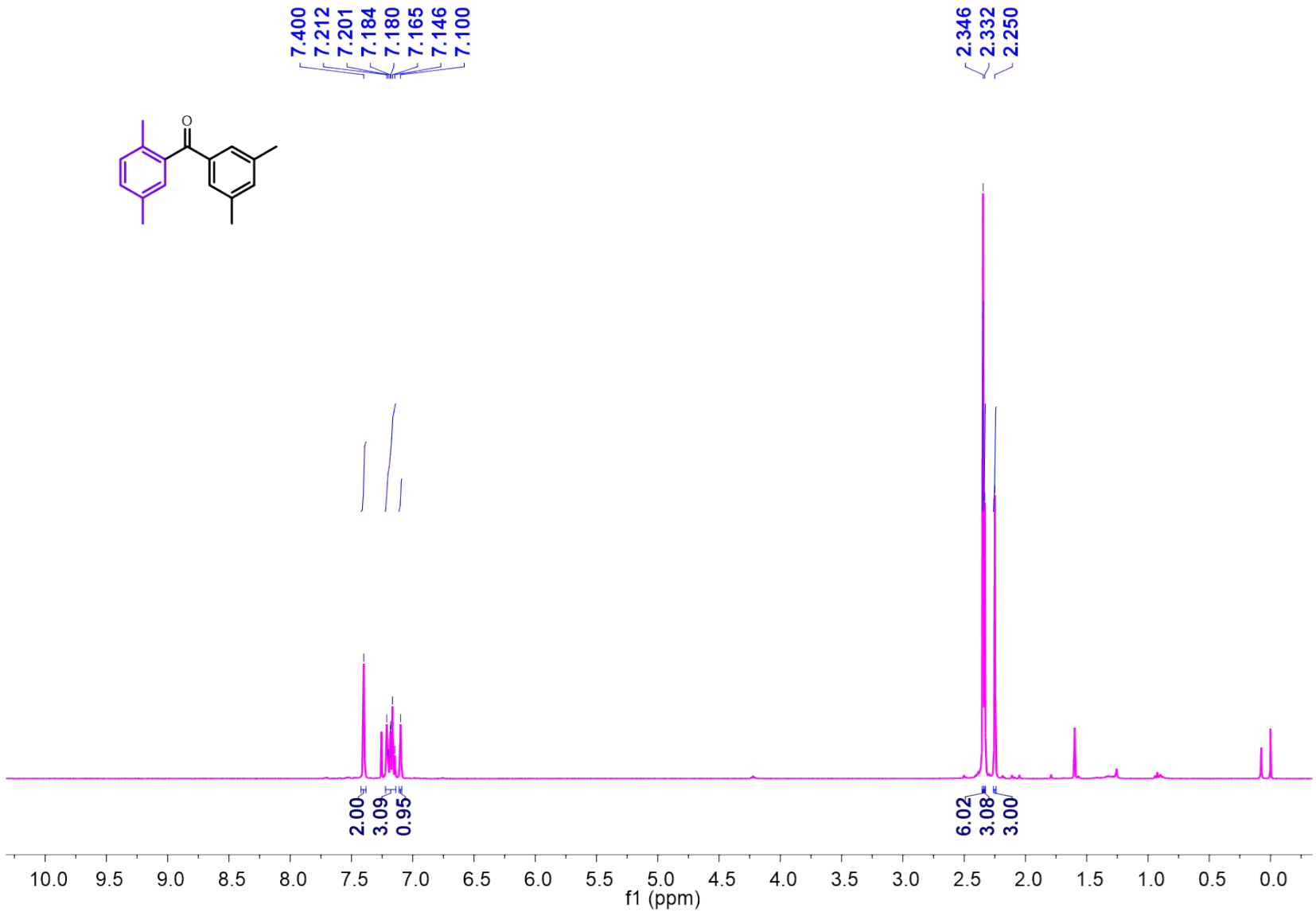


Figure S50. ^{1}H NMR spectra of (2, 5-dimethylphenyl) (3, 5 dimethyl phenyl) methanone (**2k**) in $CDCl_3$.

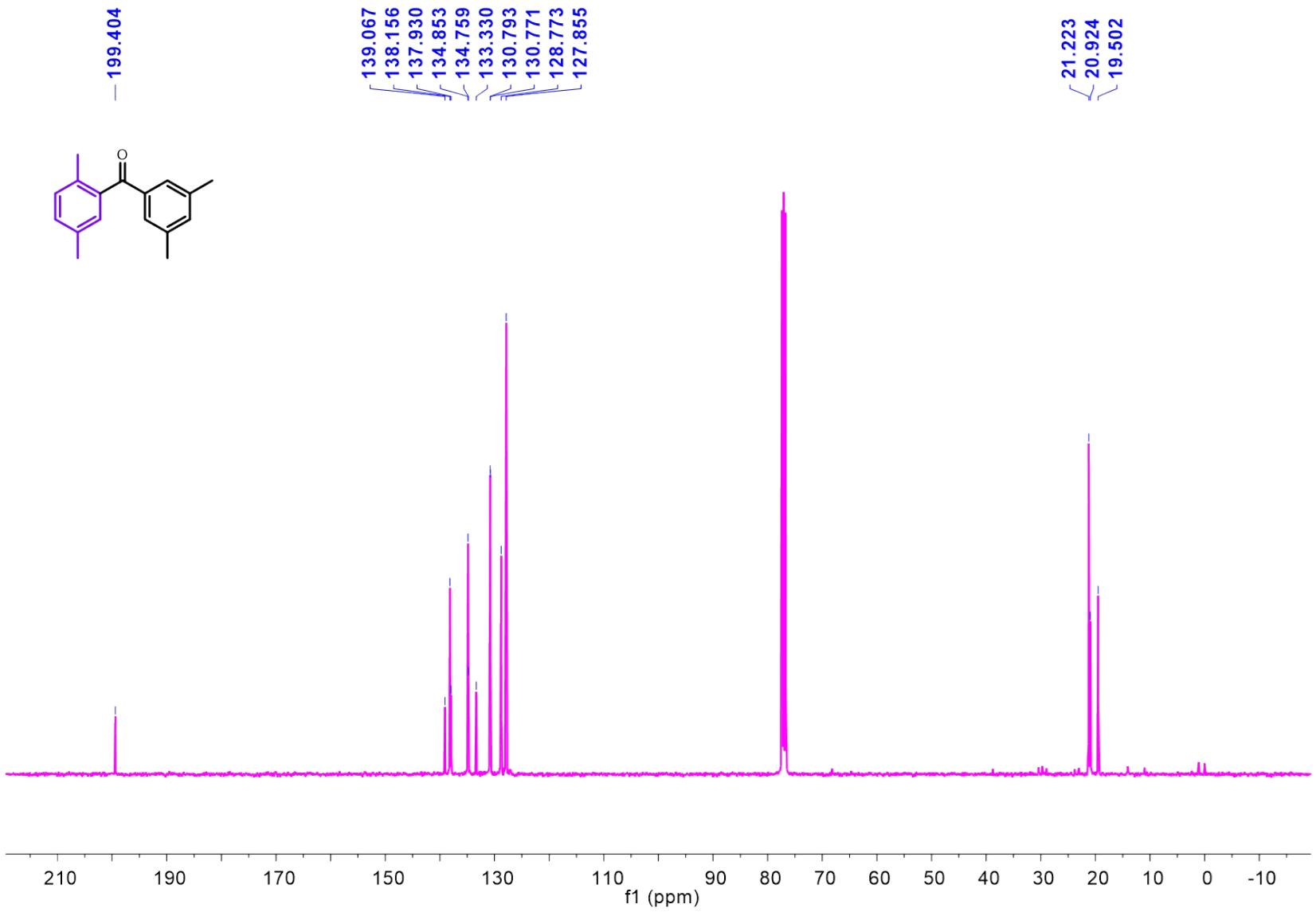


Figure S51. ^{13}C NMR spectra of (2, 5-dimethylphenyl) (3, 5 dimethyl phenyl) methanone (**2k**) in $CDCl_3$.

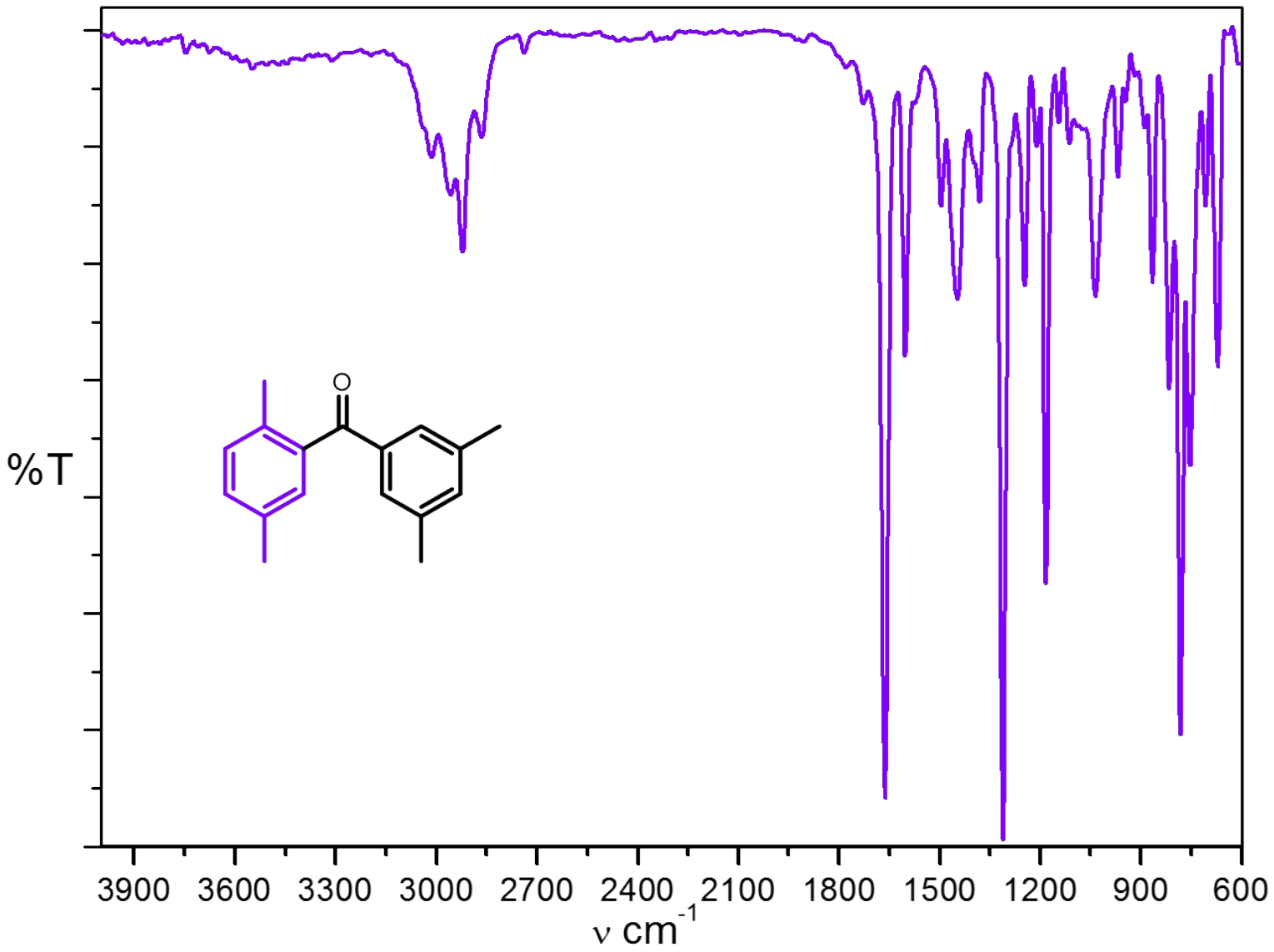


Figure S52. IR spectra of (2, 5-dimethylphenyl) (3, 5-dimethylphenyl) methanone (**2k**).

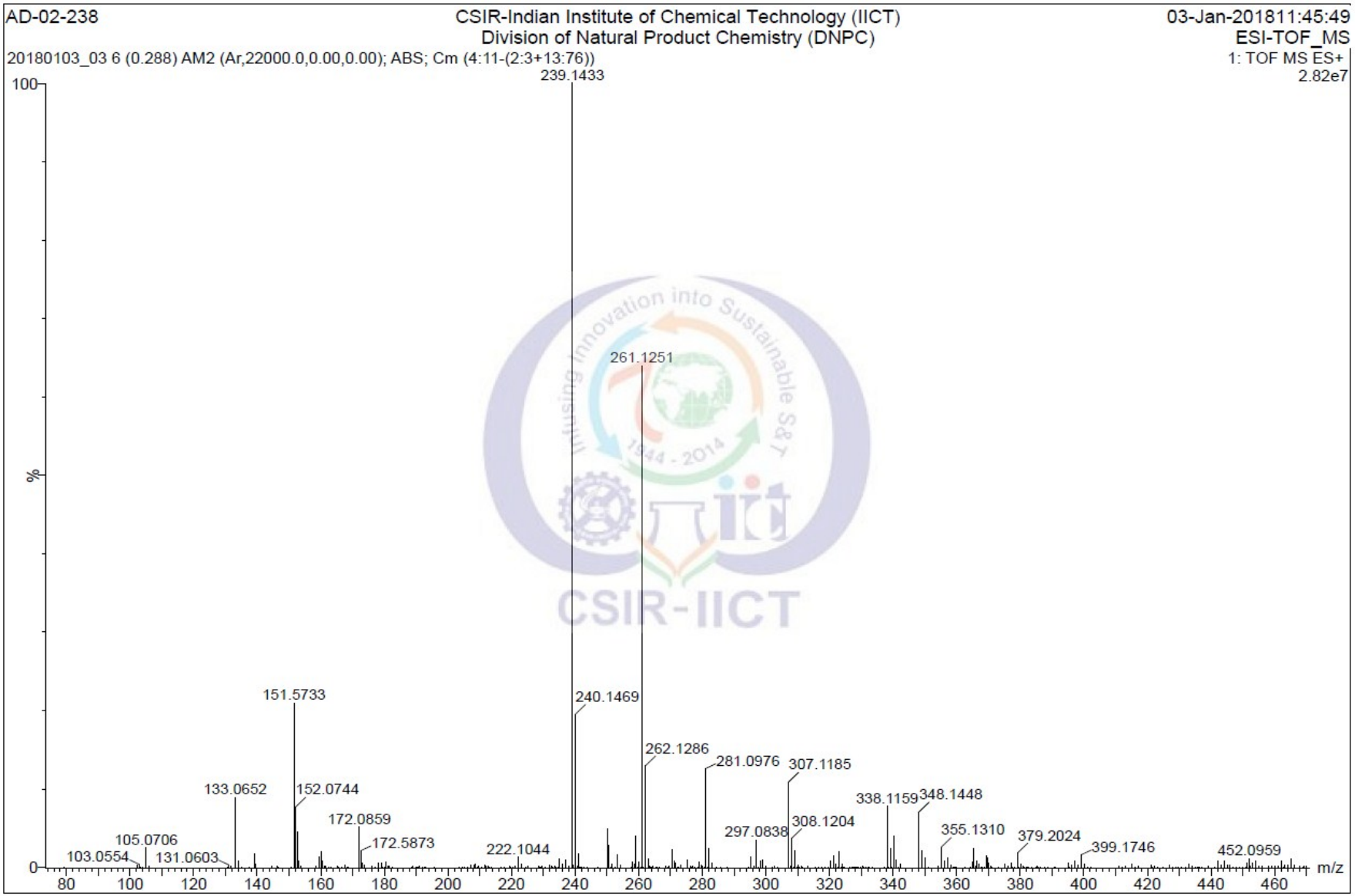


Figure S53. HRMS spectra of (2, 5-dimethylphenyl) (3, 5dimethyl phenyl) methanone (**2k**).

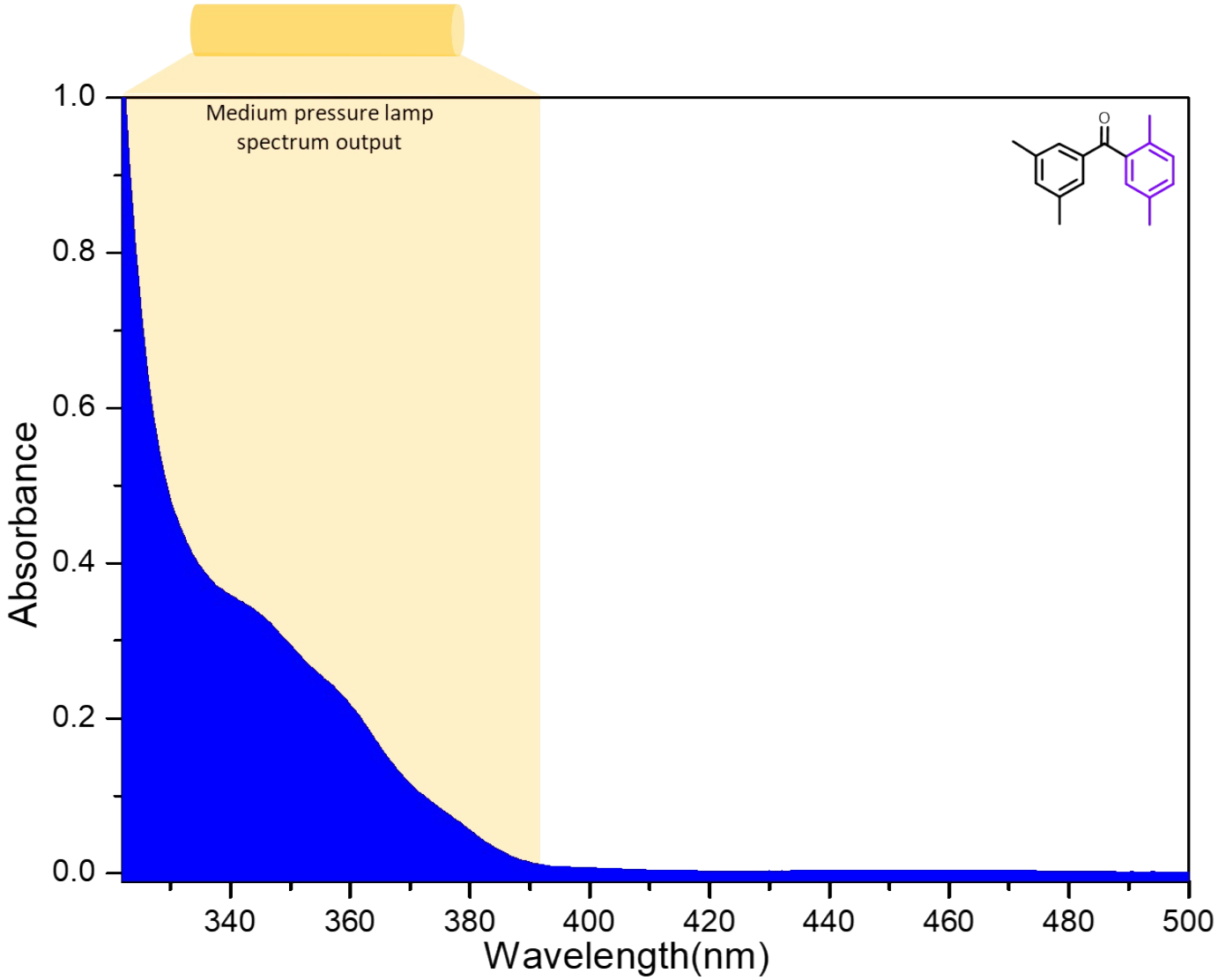


Figure S54. UV-Visible spectra of (2, 5-dimethylphenyl) (3, 5dimethyl phenyl) methanone (**2k**) in 0.0022 M DMSO.

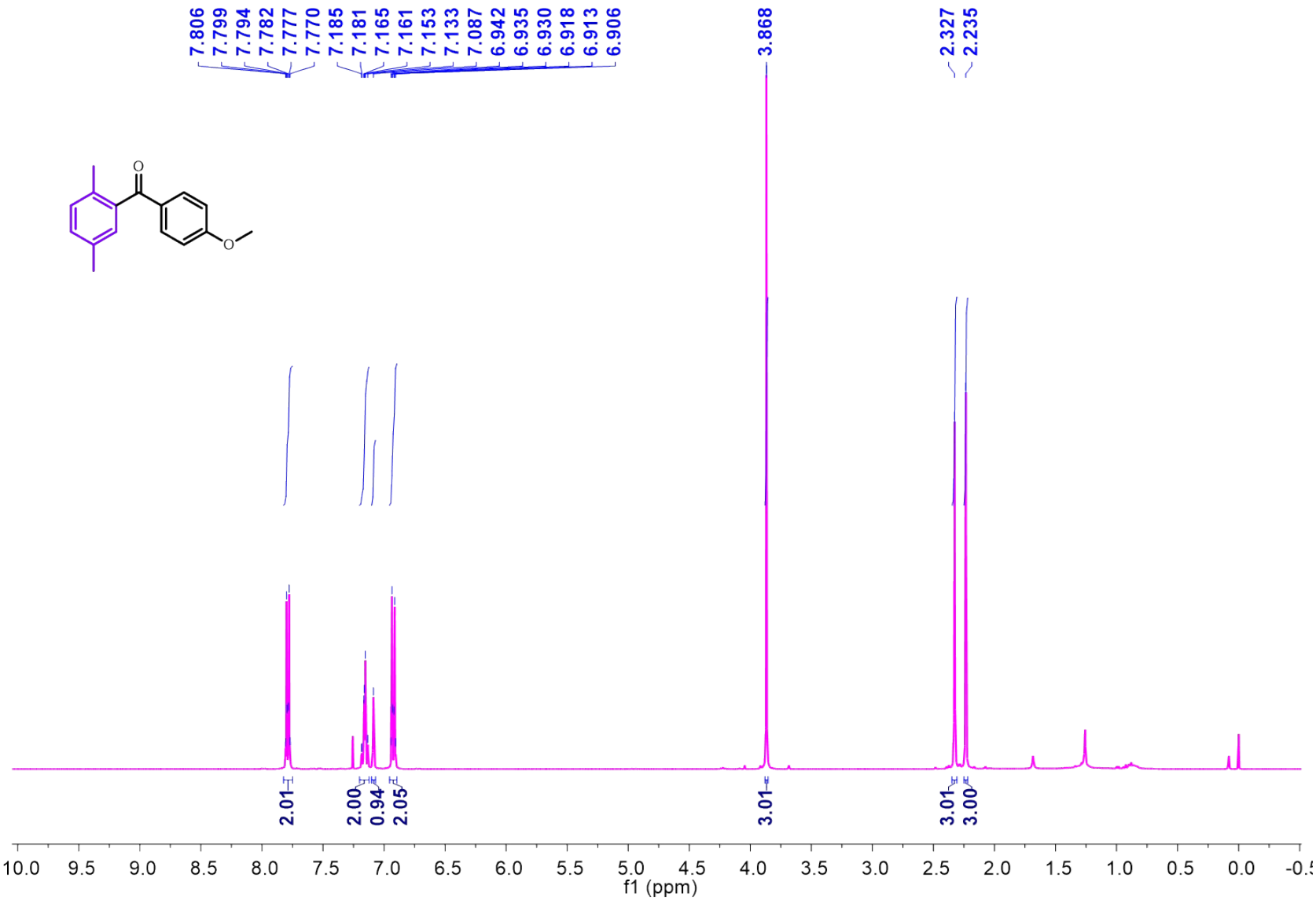


Figure S55. ^{1}H NMR spectra of (4-methoxyphenyl) (2, 5-dimethylphenyl) methanone (**2l**) in $CDCl_3$.

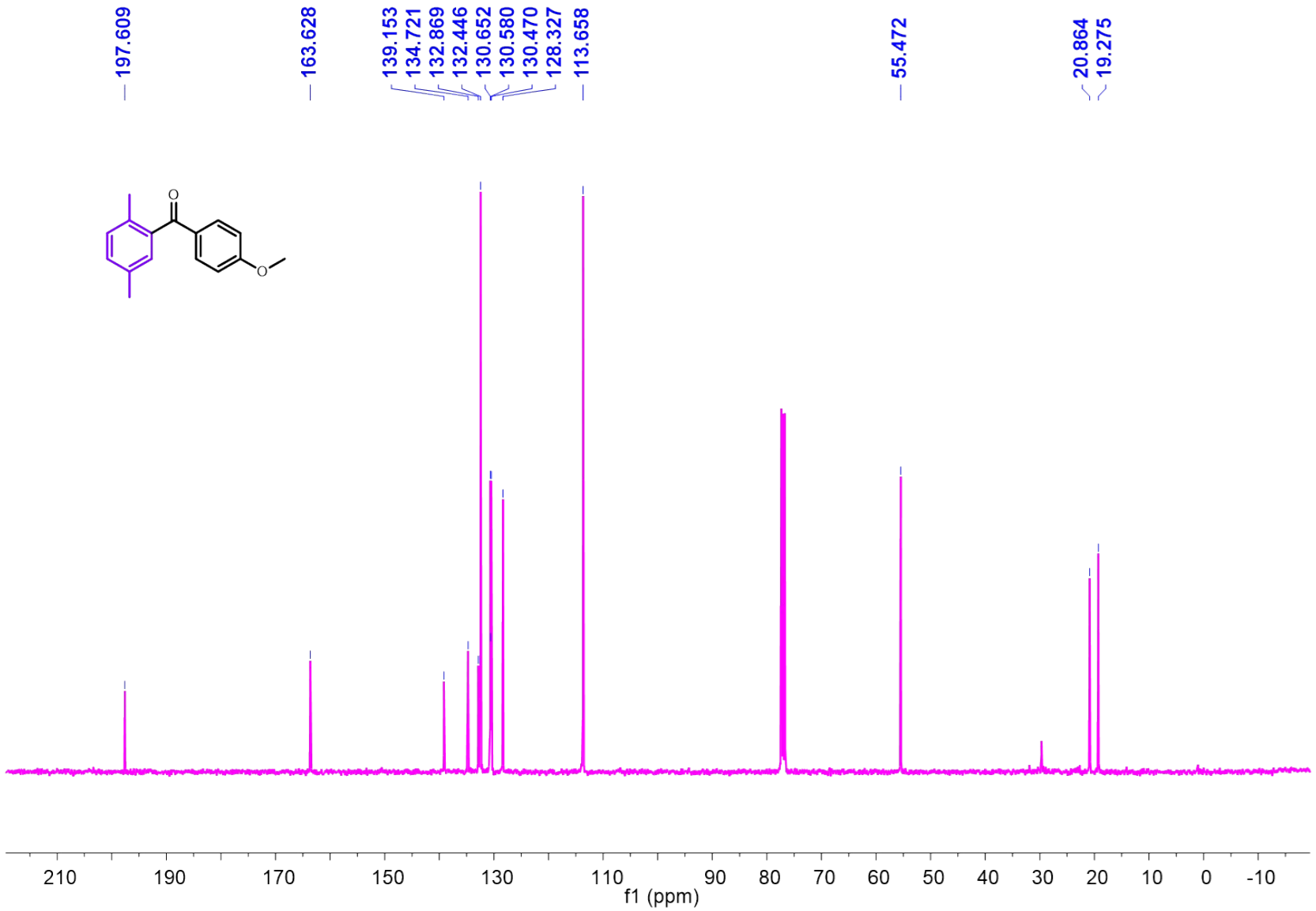


Figure S56. ^{13}C NMR spectra of (4-methoxyphenyl) (2, 5-dimethylphenyl) methanone (**2l**) in $CDCl_3$.

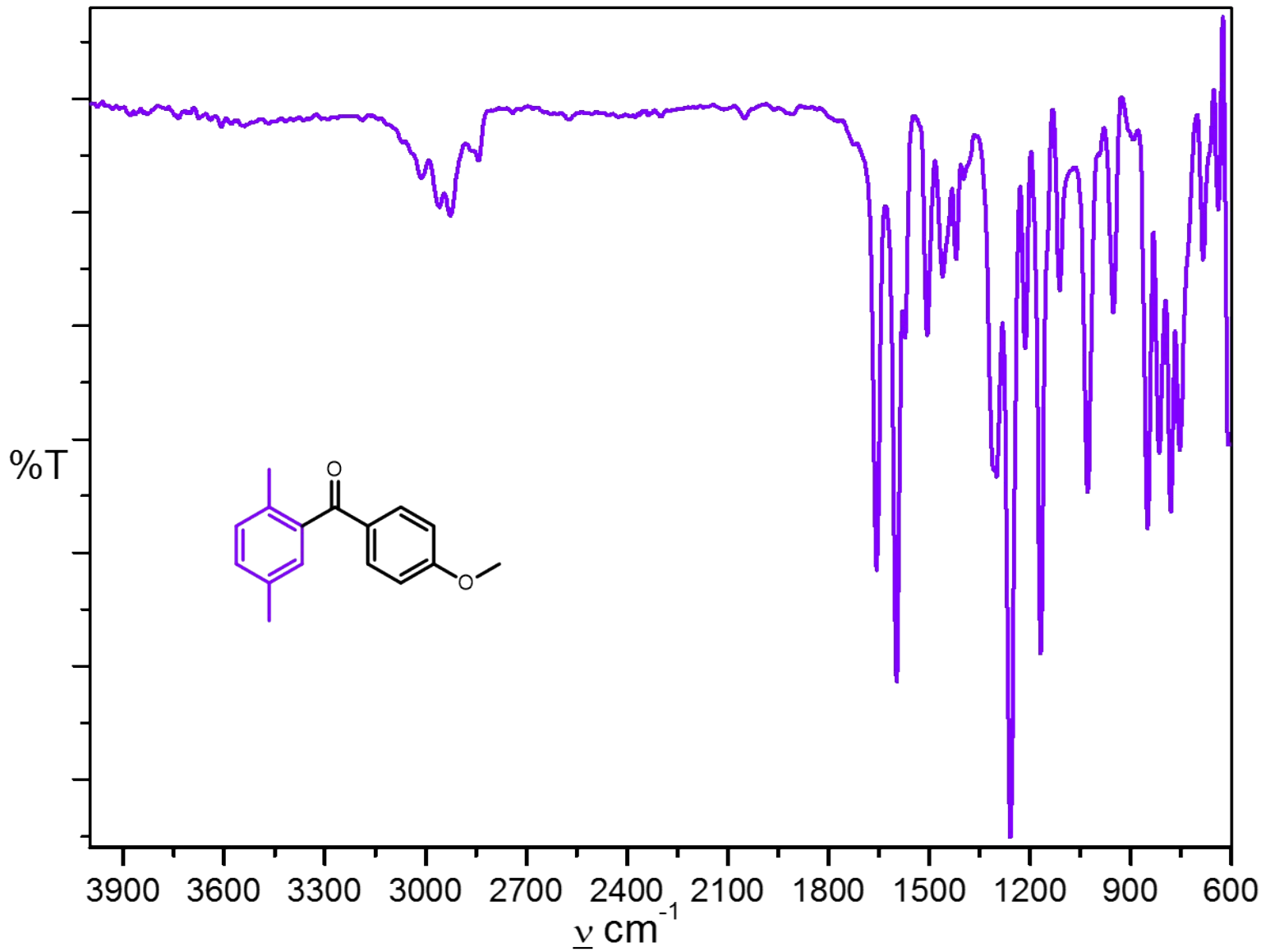


Figure S57. IR spectra of (4-methoxyphenyl) (2, 5-dimethylphenyl) methanone (**2k**).

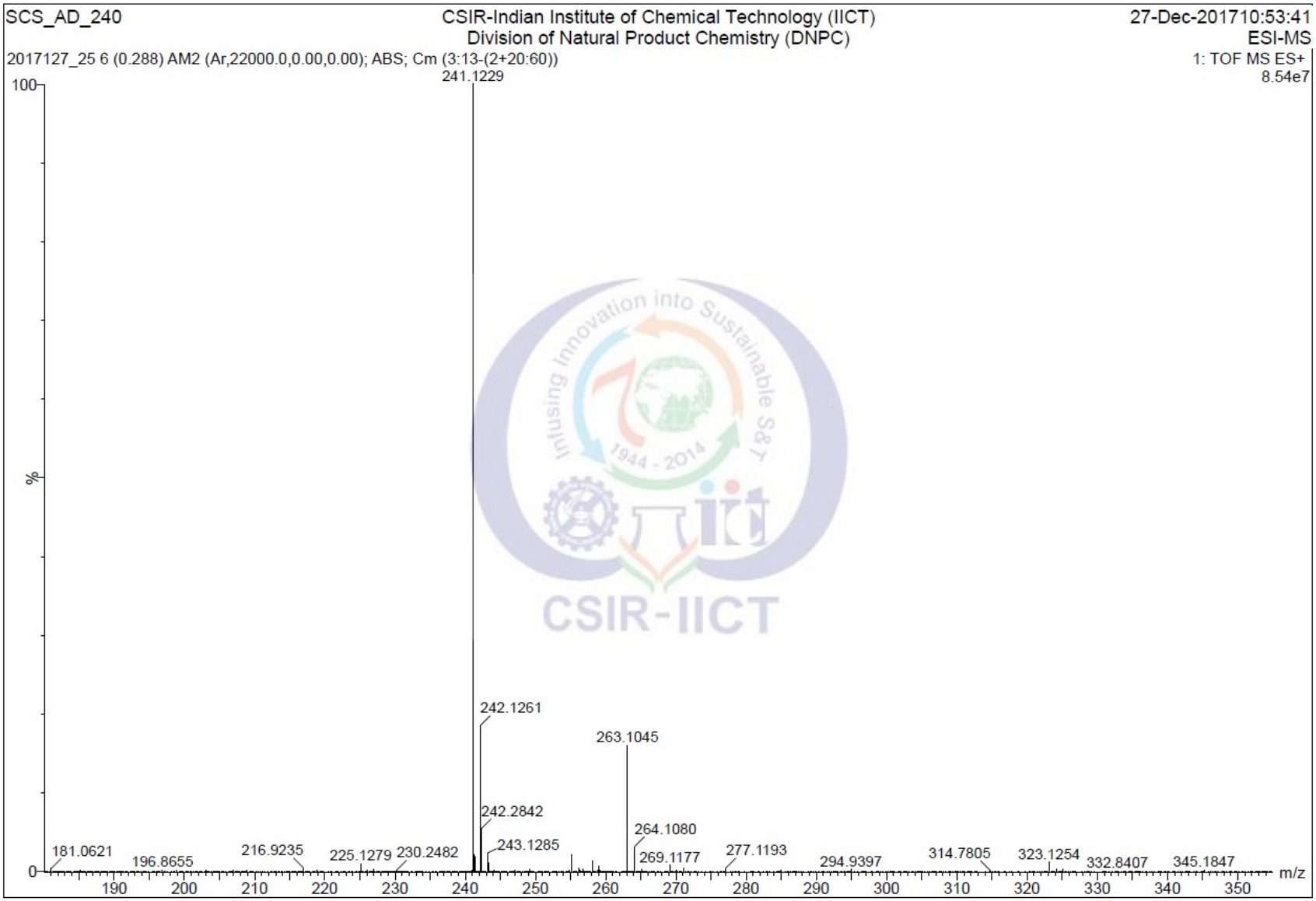


Figure S58. HRMS spctra of (4-methoxyphenyl) (2, 5-dimethylphenyl) methanone (**2l**).

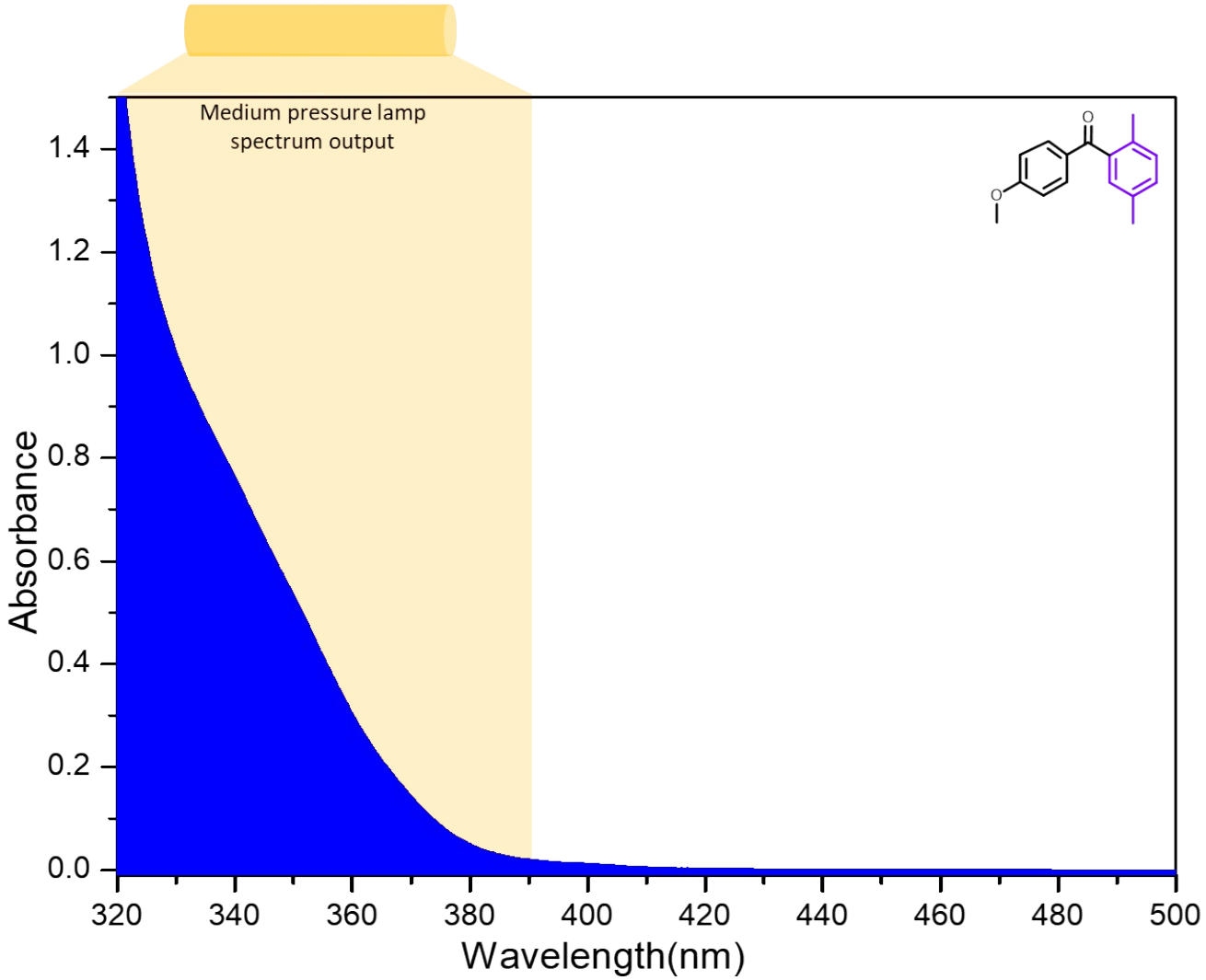


Figure S59. UV-Visible spctra of (4-methoxyphenyl) (2, 5-dimethylphenyl) methanone (**2l**) in 0.0022 M DMSO.

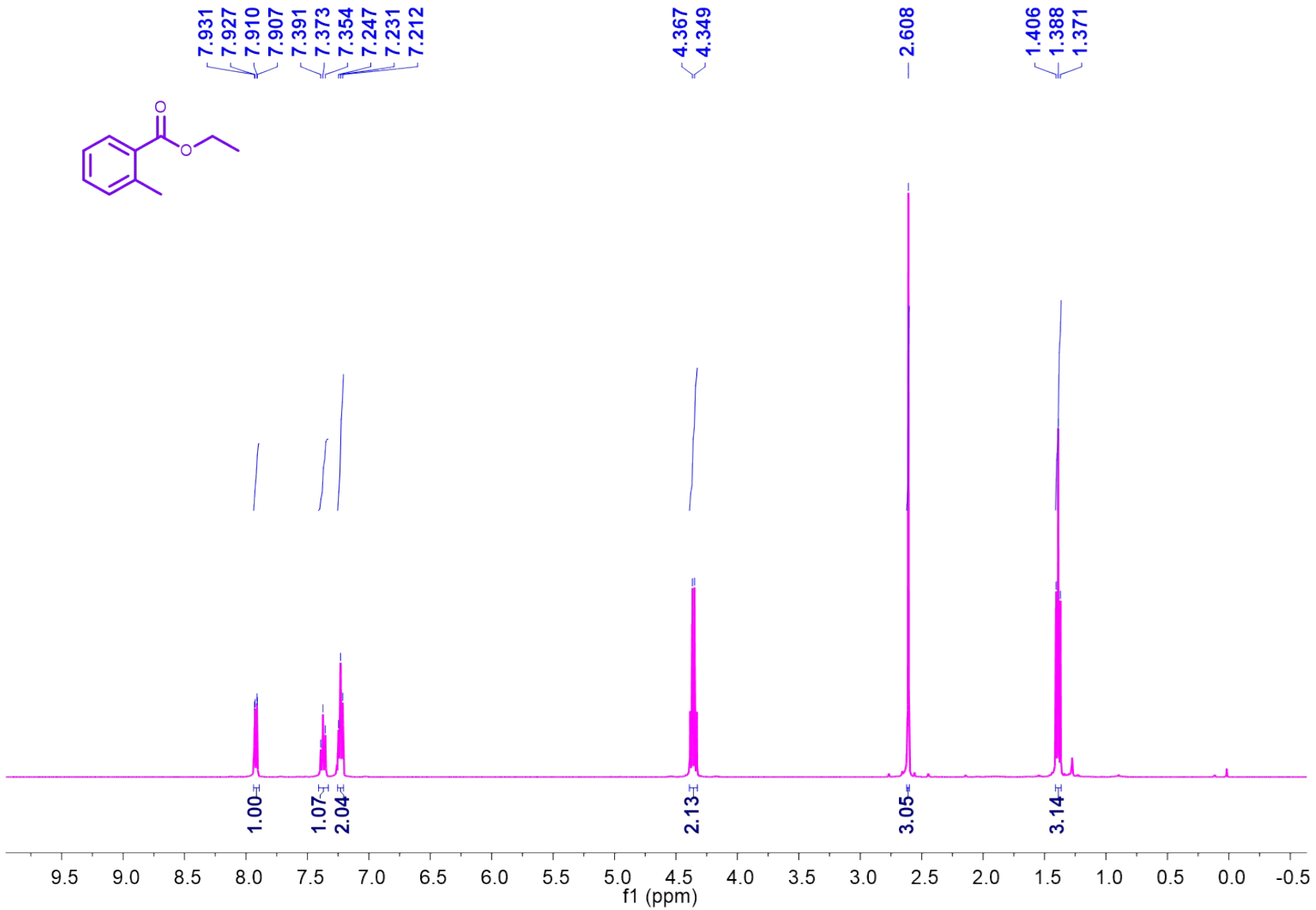


Figure S60. ^{1}H NMR spectra of ethyl 2-methylbenzoate in $CDCl_3$.

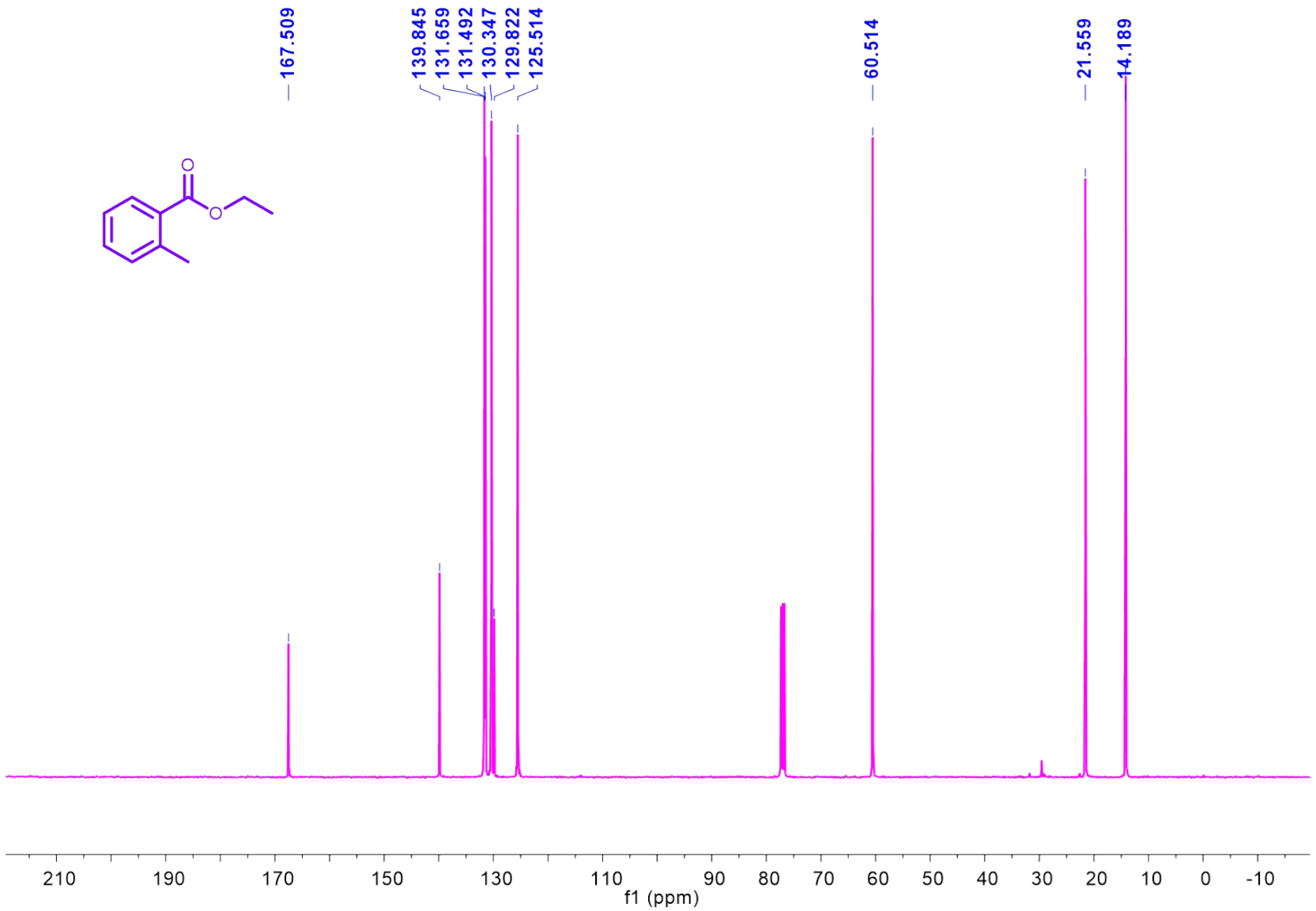


Figure S61. ^{13}C NMR spectra of ethyl 2-methylbenzoate in $CDCl_3$.

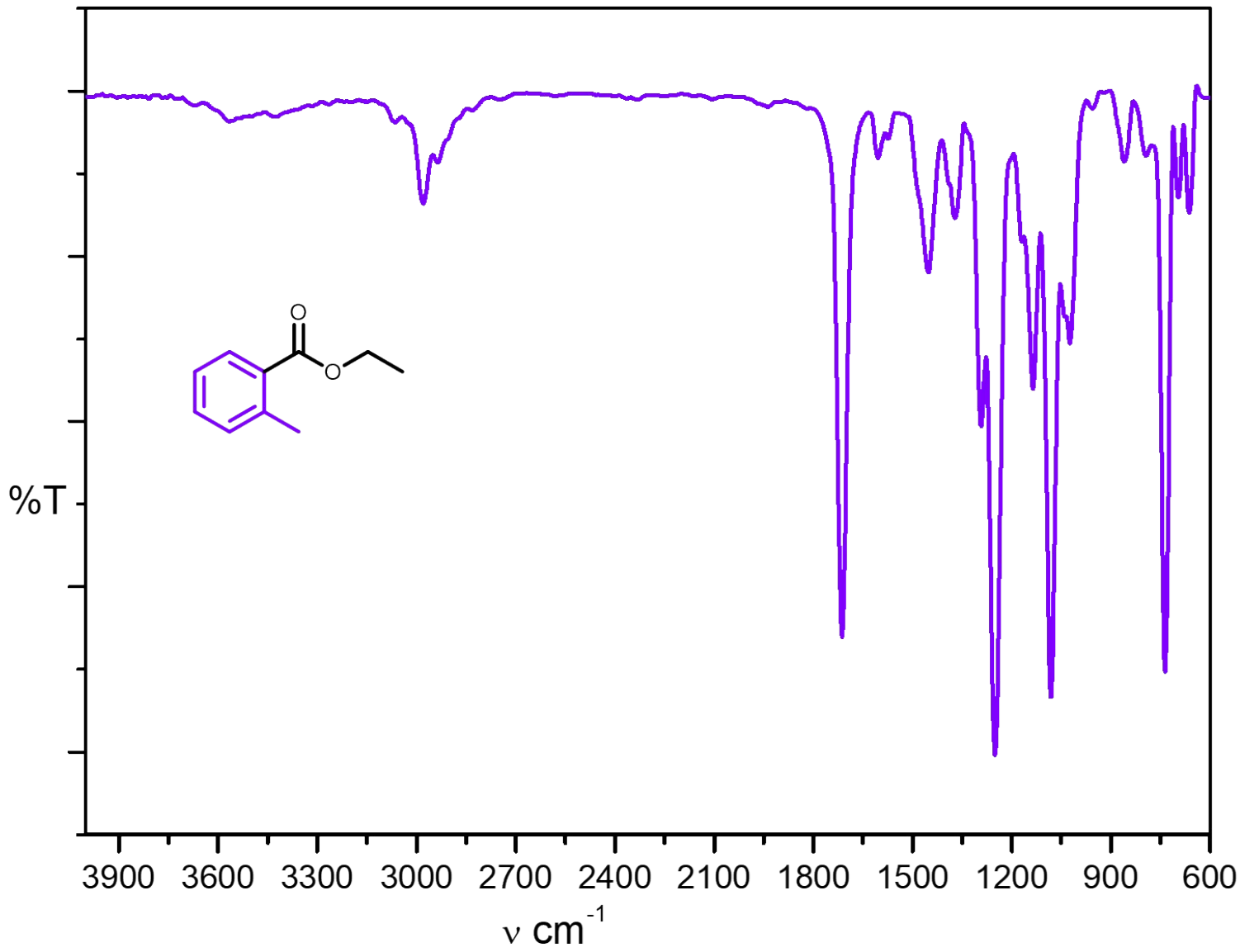


Figure S62. IR spectra of ethyl 2-methylbenzoate.

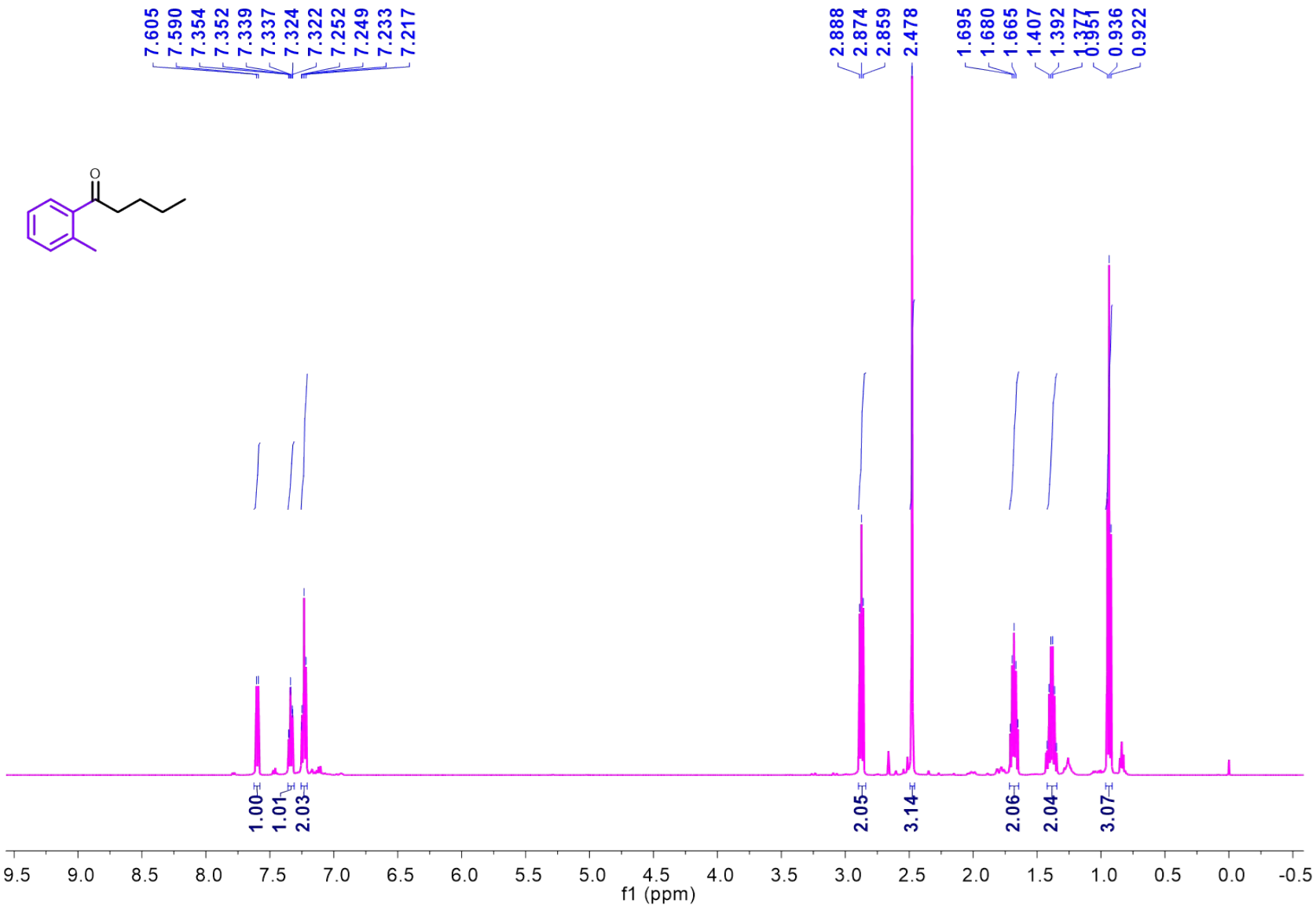


Figure S63. ^{1}H NMR spectra of 1-(o-tolyl) pentan-1-one (**2m**) in $CDCl_3$.

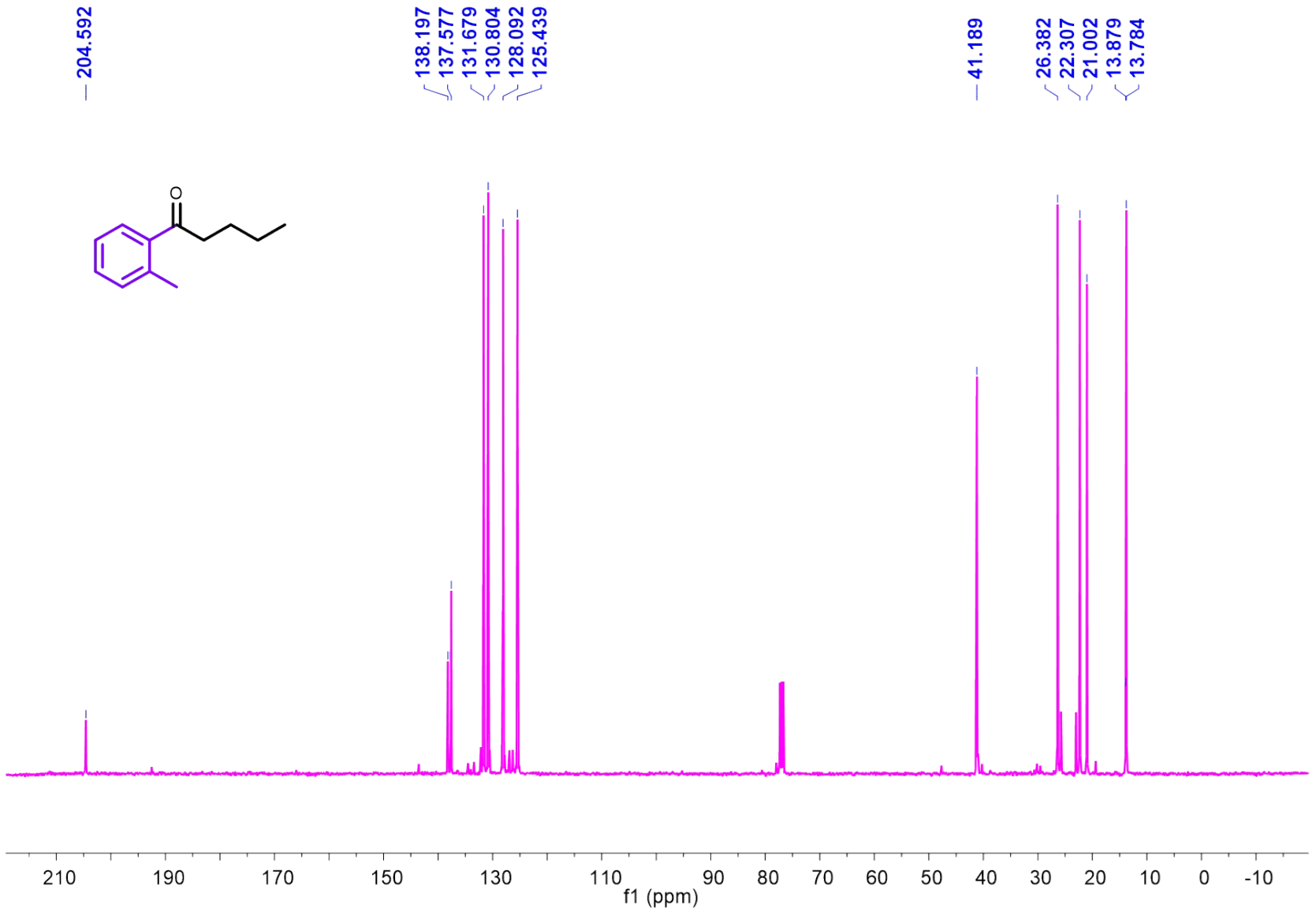


Figure S64. ^{13}C NMR spectra of 1-(o-tolyl) pentan-1-one (**2m**) in $CDCl_3$.

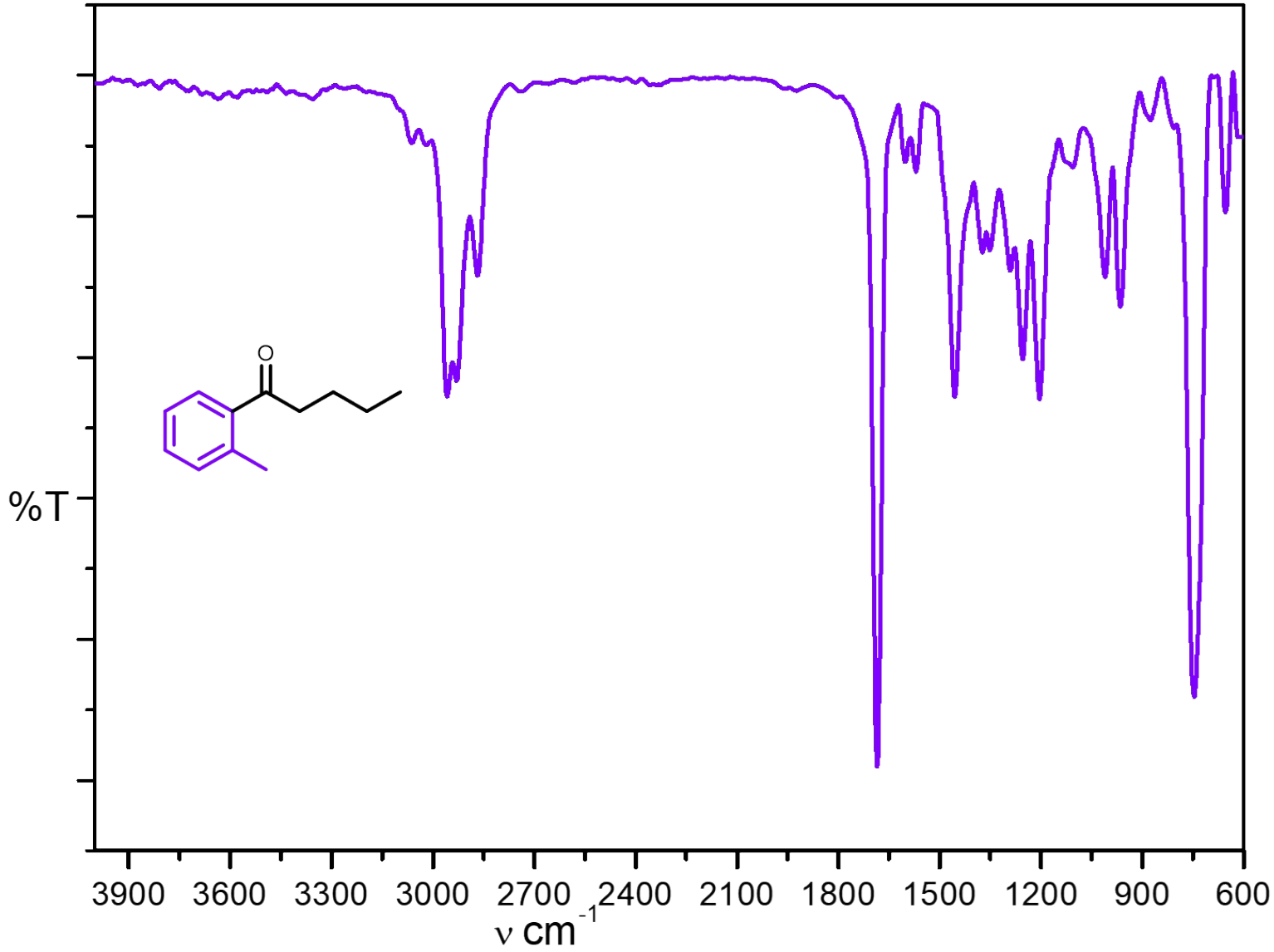


Figure S65. ^{13}C NMR spectra of 1-(o-tolyl) pentan-1-one (**2m**).

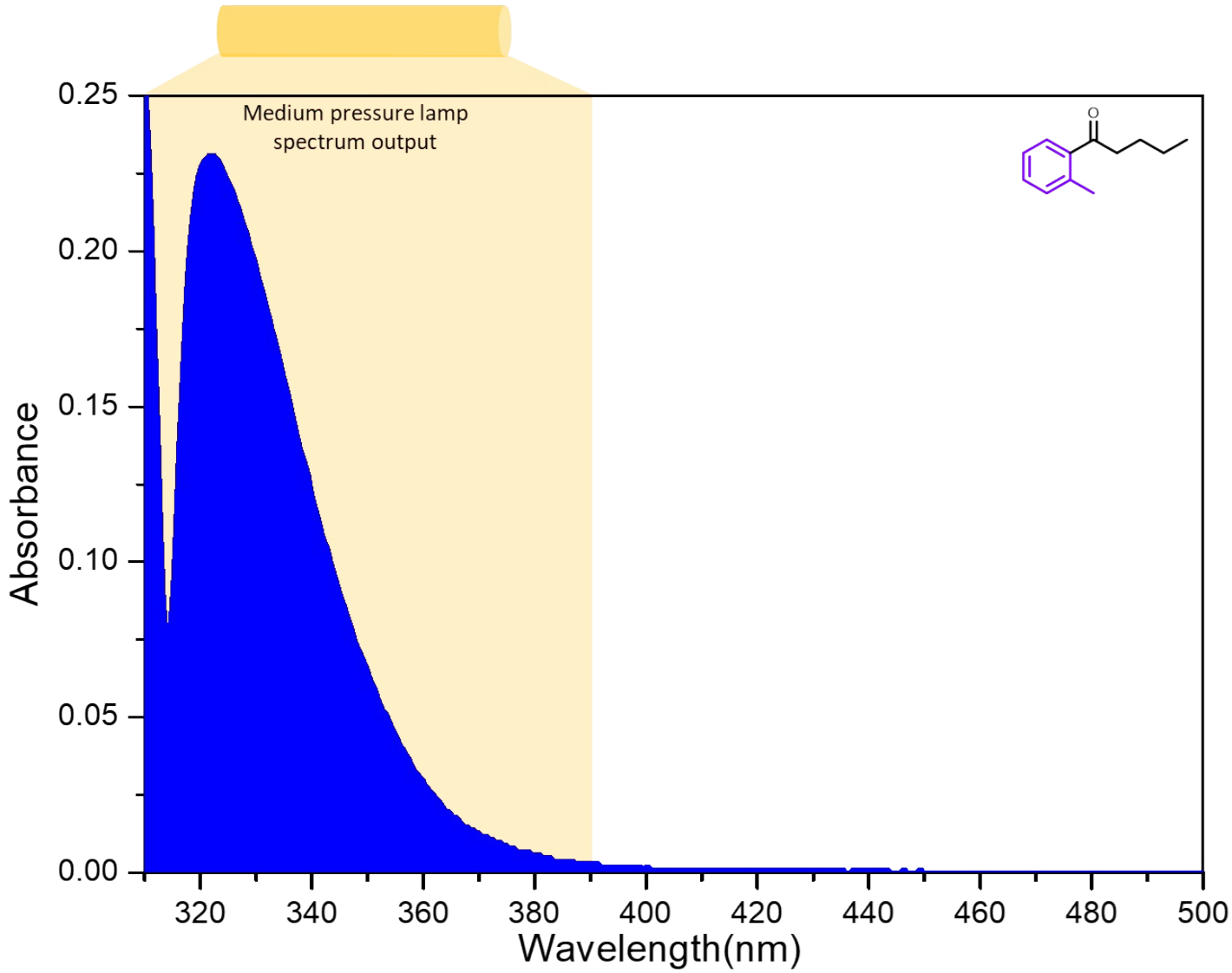


Figure S66. UV-Visible spectra of 1-(o-tolyl) pentan-1-one (**2m**) in DMSO in 0.0022 M DMSO.

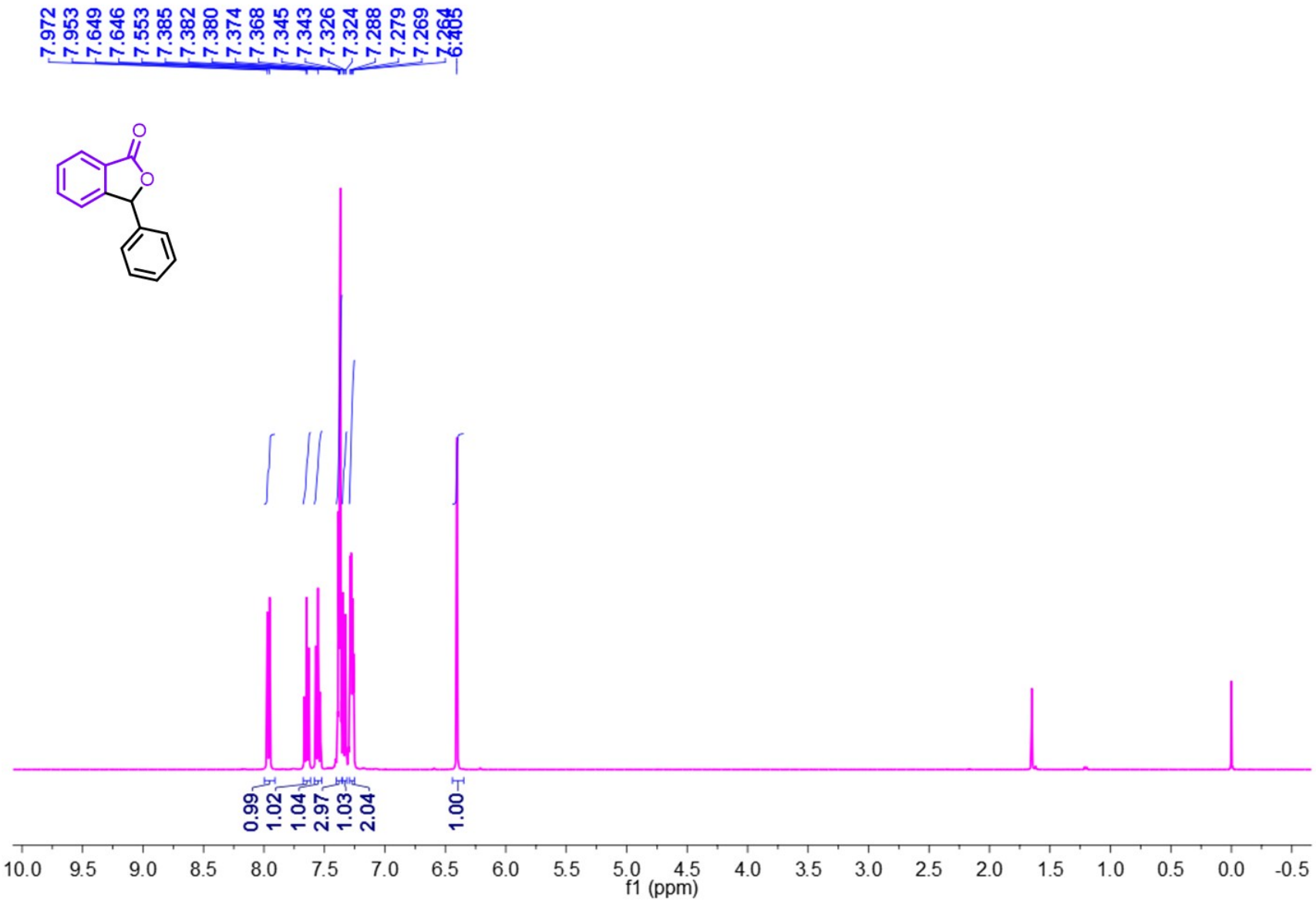


Figure S67. ^{1}H NMR spectra of 3-phenyliso-benzofuran-1-(3*H*)-one (**3a**) in $CDCl_3$.

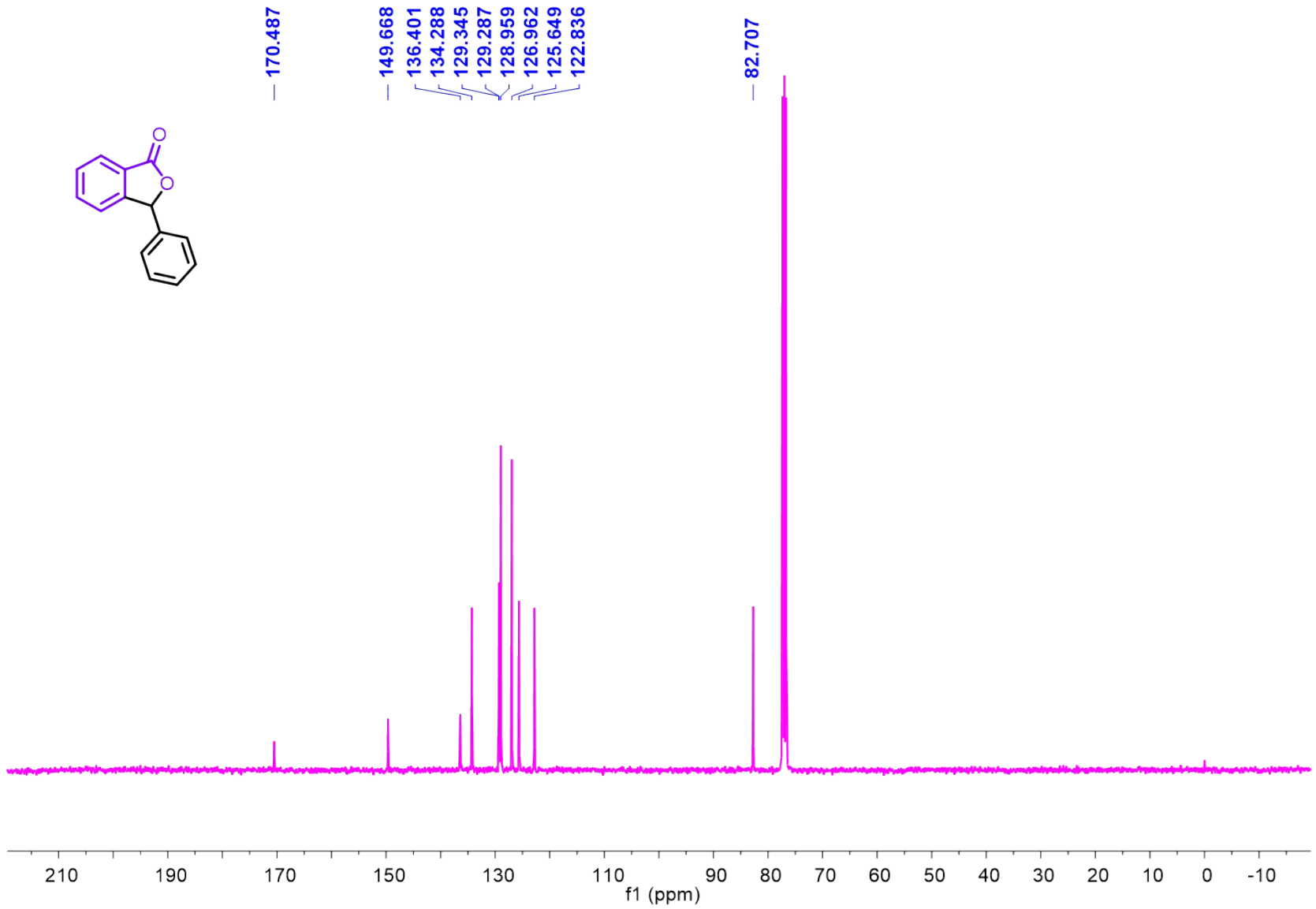


Figure S68. ^{13}C NMR spectra of 3-phenyliso-benzofuran-1-(3*H*)-one (**3a**) in $CDCl_3$.

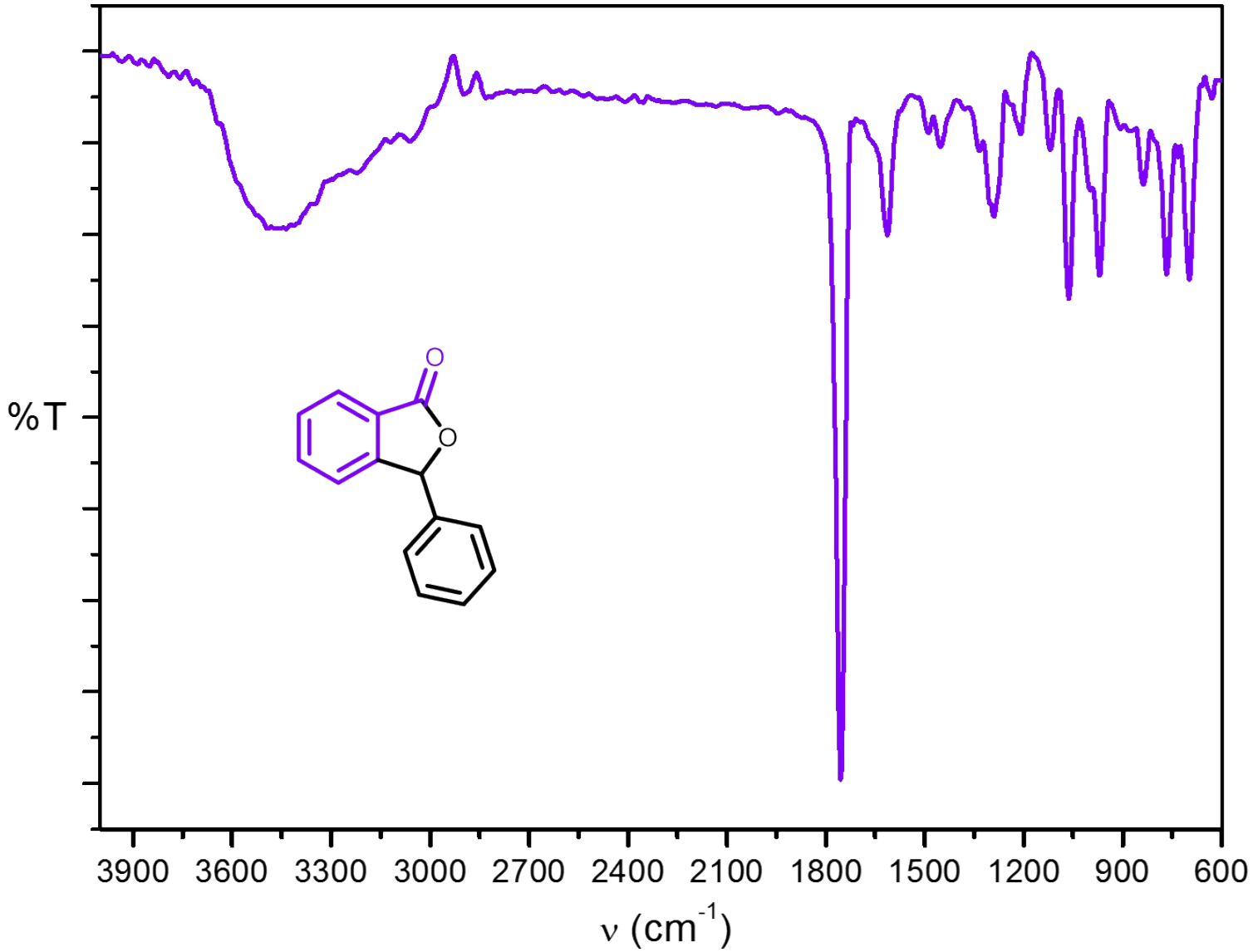


Figure S69. IR spectra of 3-phenylisobenzofuran-1-(*3H*)-one (**3a**).

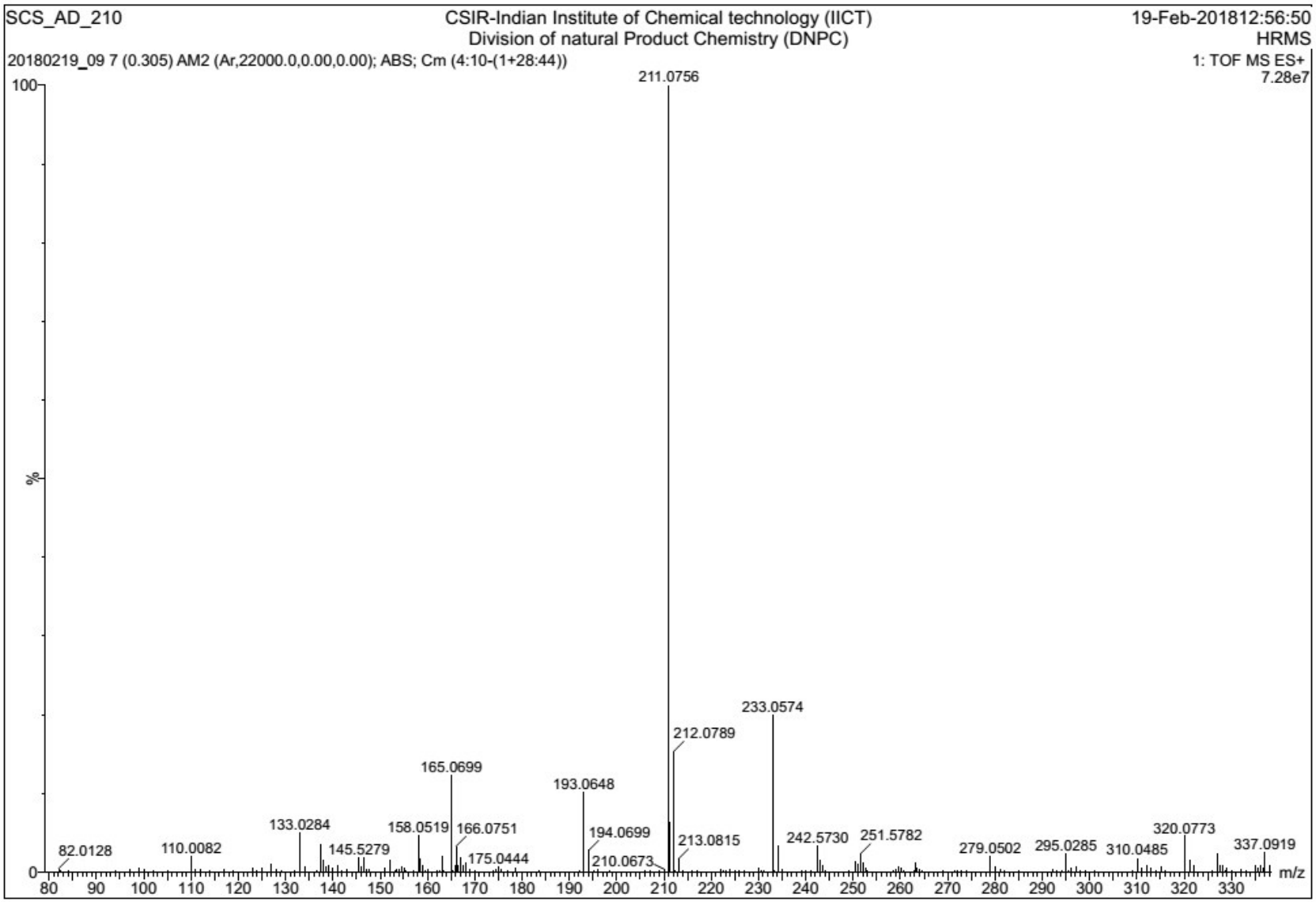
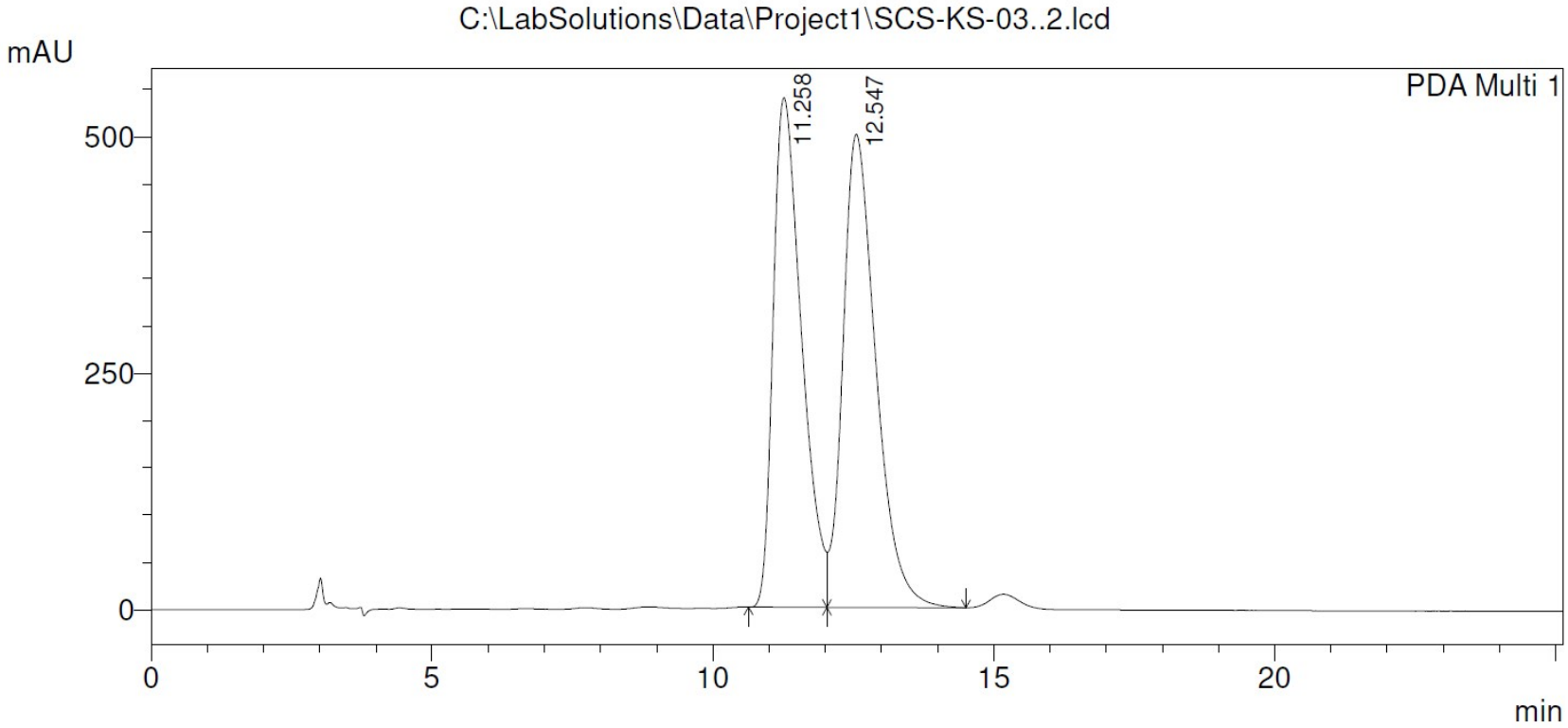


Figure S70. HRMS spctra of 3-phenylisobenzofuran-1-(*3H*)-one (**3a**).

<Chromatogram>



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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2	12.547	20453124	500487	51.856	48.149
Total		39441997	1039452	100.000	100.000

Figure S71. HPLC spctra of 3-phenylisobenzofuran-1-(*3H*)-one (**3a**).

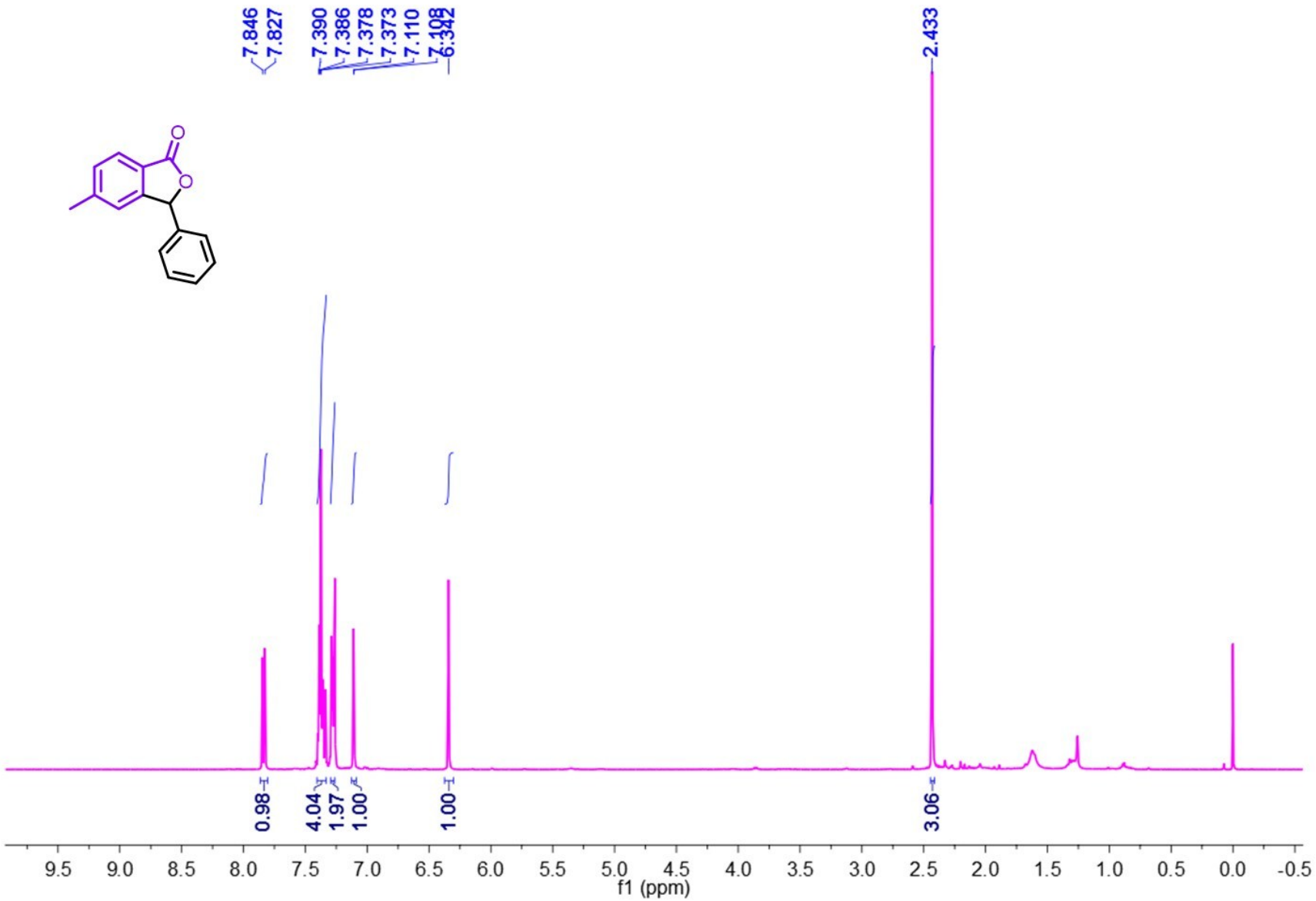


Figure S72. ^{1}H NMR spectra of 5-methyl 3-phenyliso-benzofuran-1-(3*H*)-one (**3b**) in $CDCl_3$.

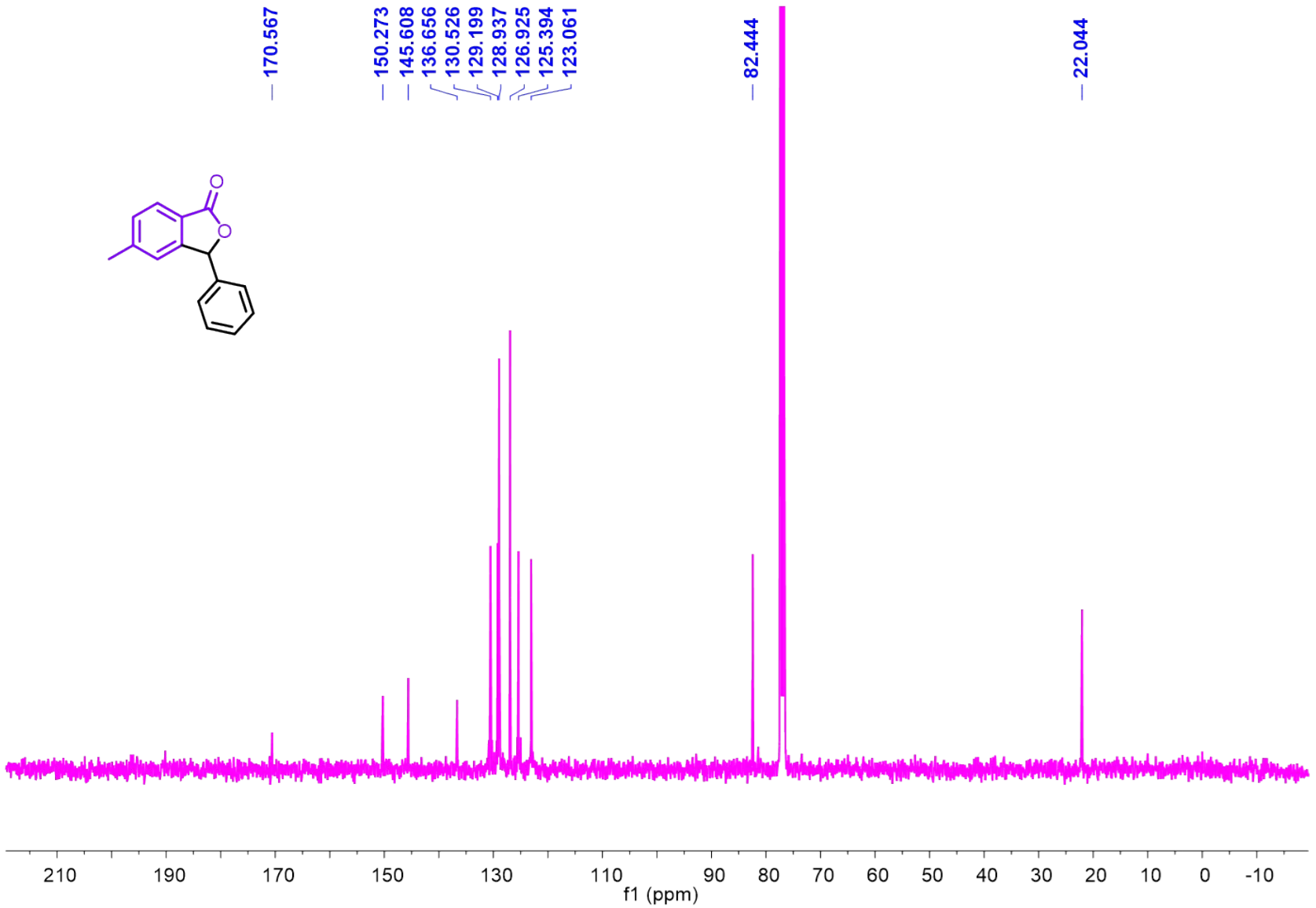


Figure S73. ^{13}C NMR spectra of 5-methyl 3-phenyliso-benzofuran-1-(3*H*)-one (**3b**) in $CDCl_3$.

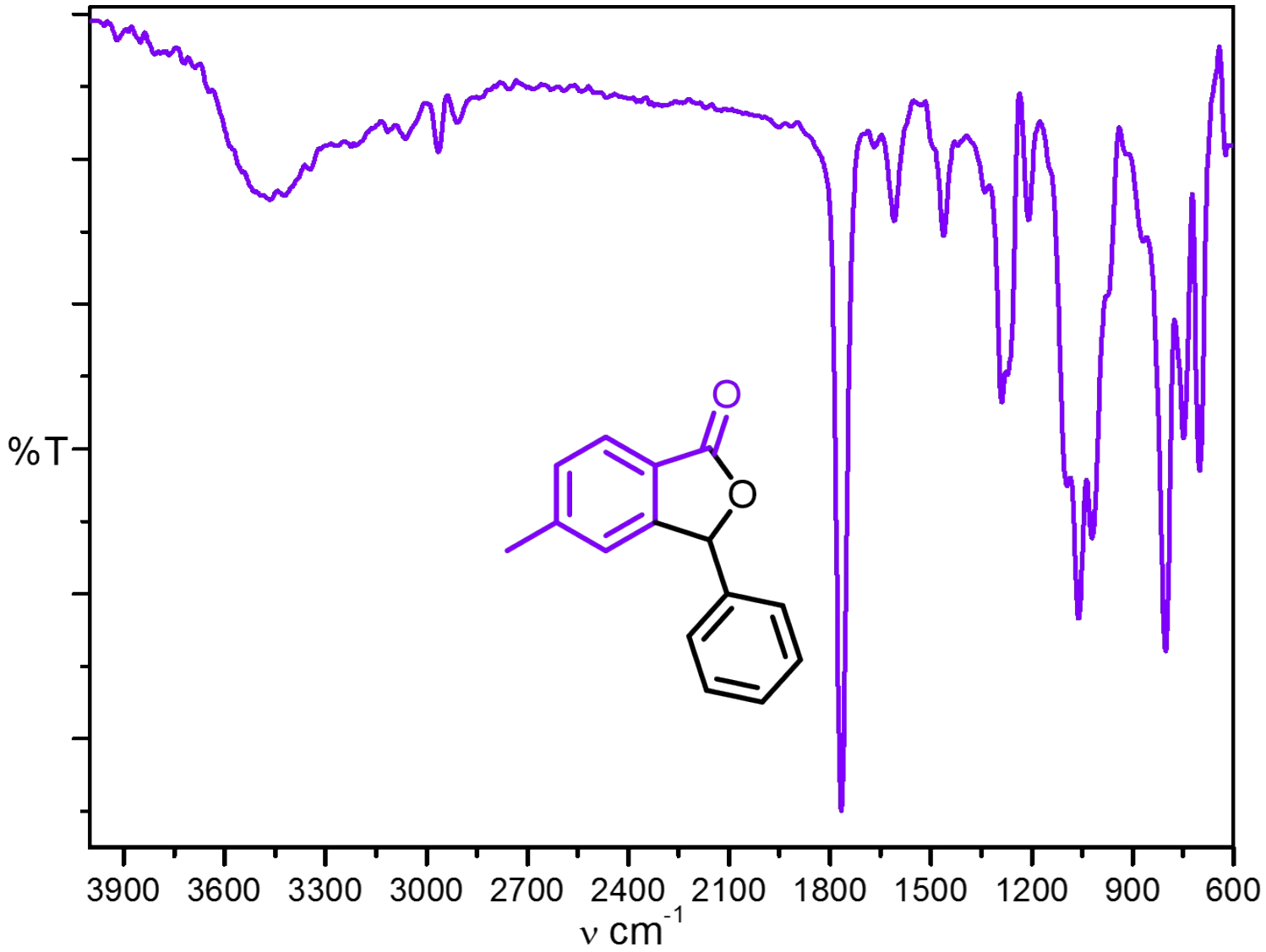


Figure S74. IR spectra of 5-methyl 3-phenylisobenzofuran-1-(3*H*)-one (**3b**).

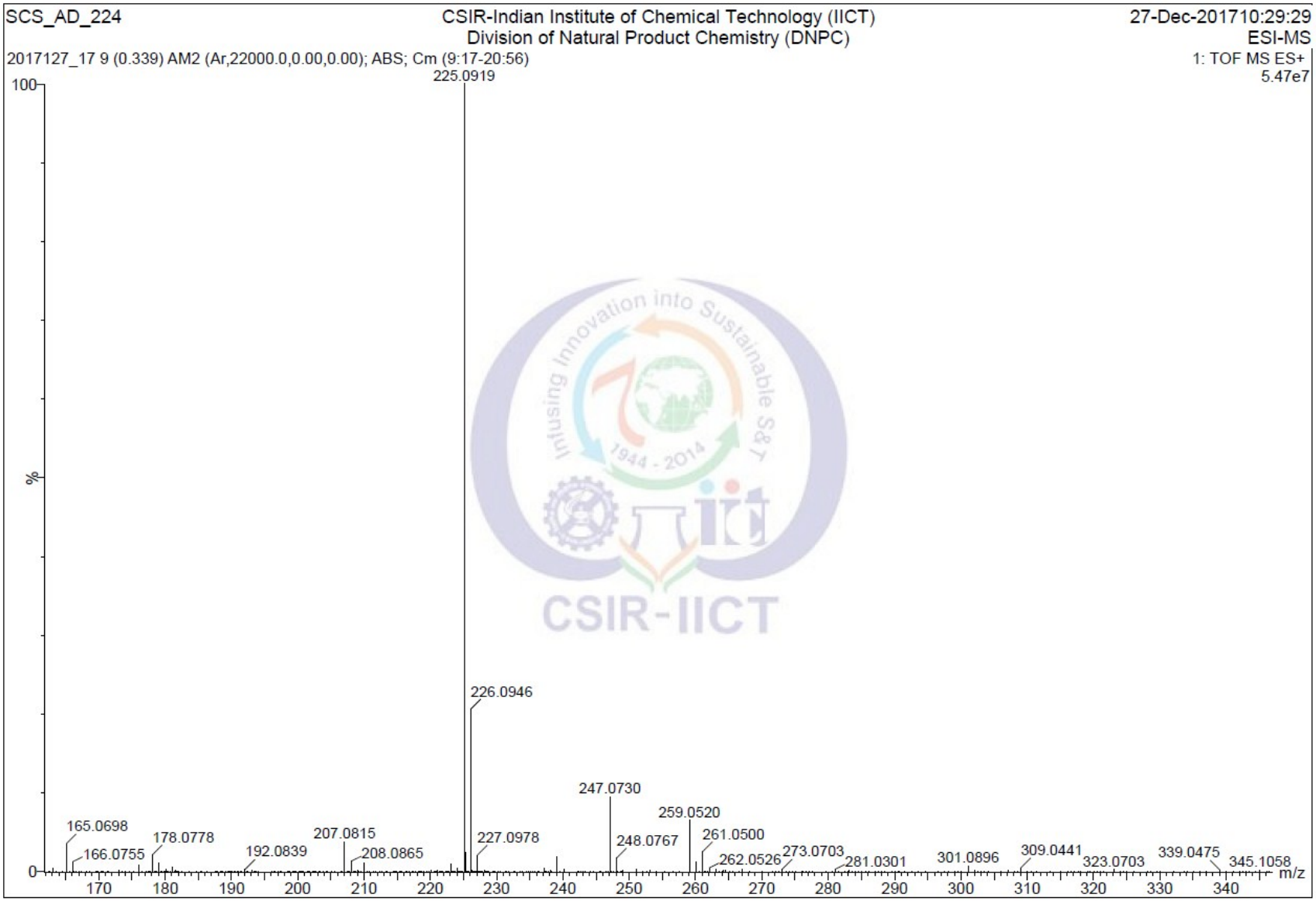


Figure S75. HRMS spctra of 5-methyl 3-phenylisobenzofuran-1-(3*H*)-one (**3b**).

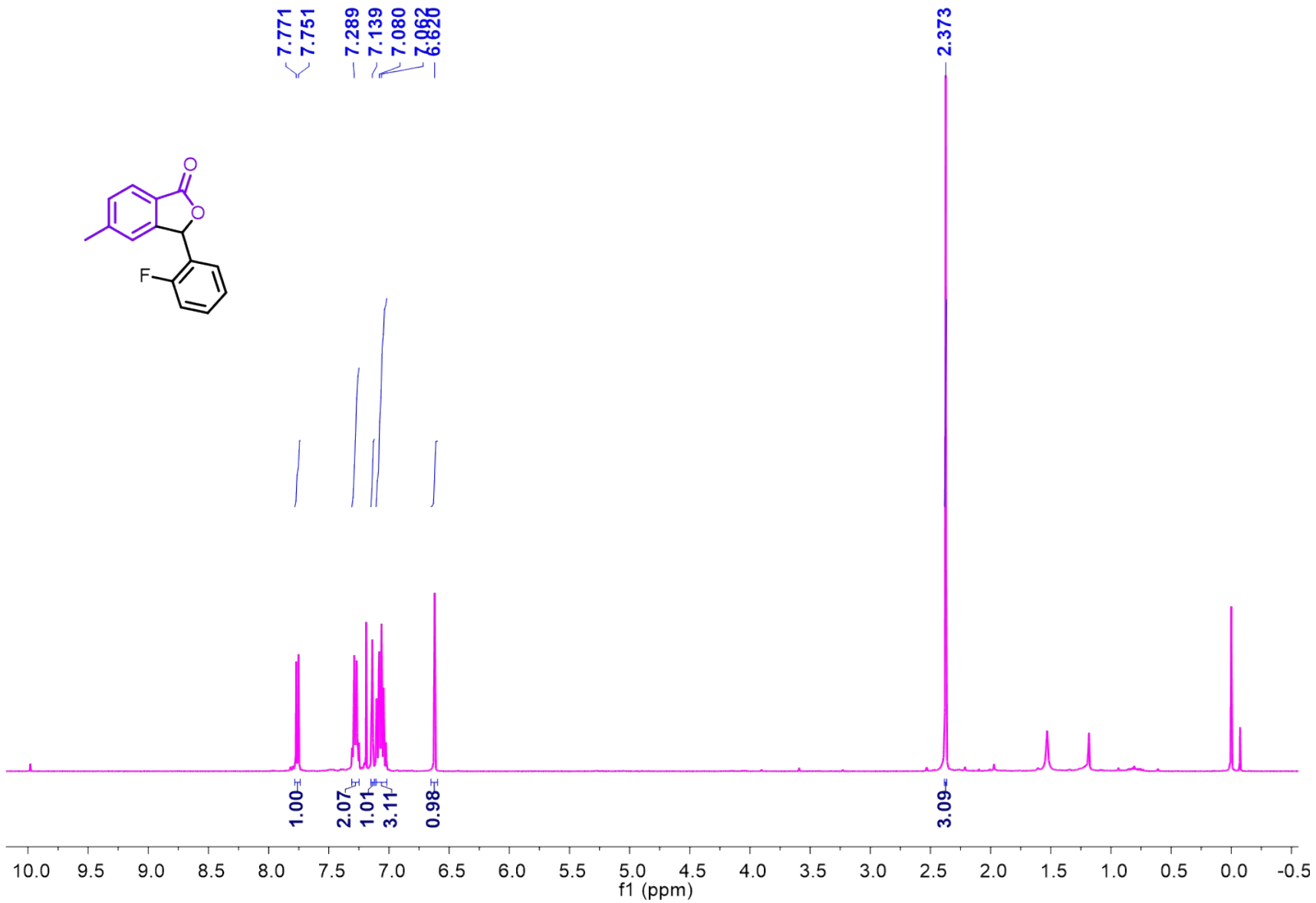
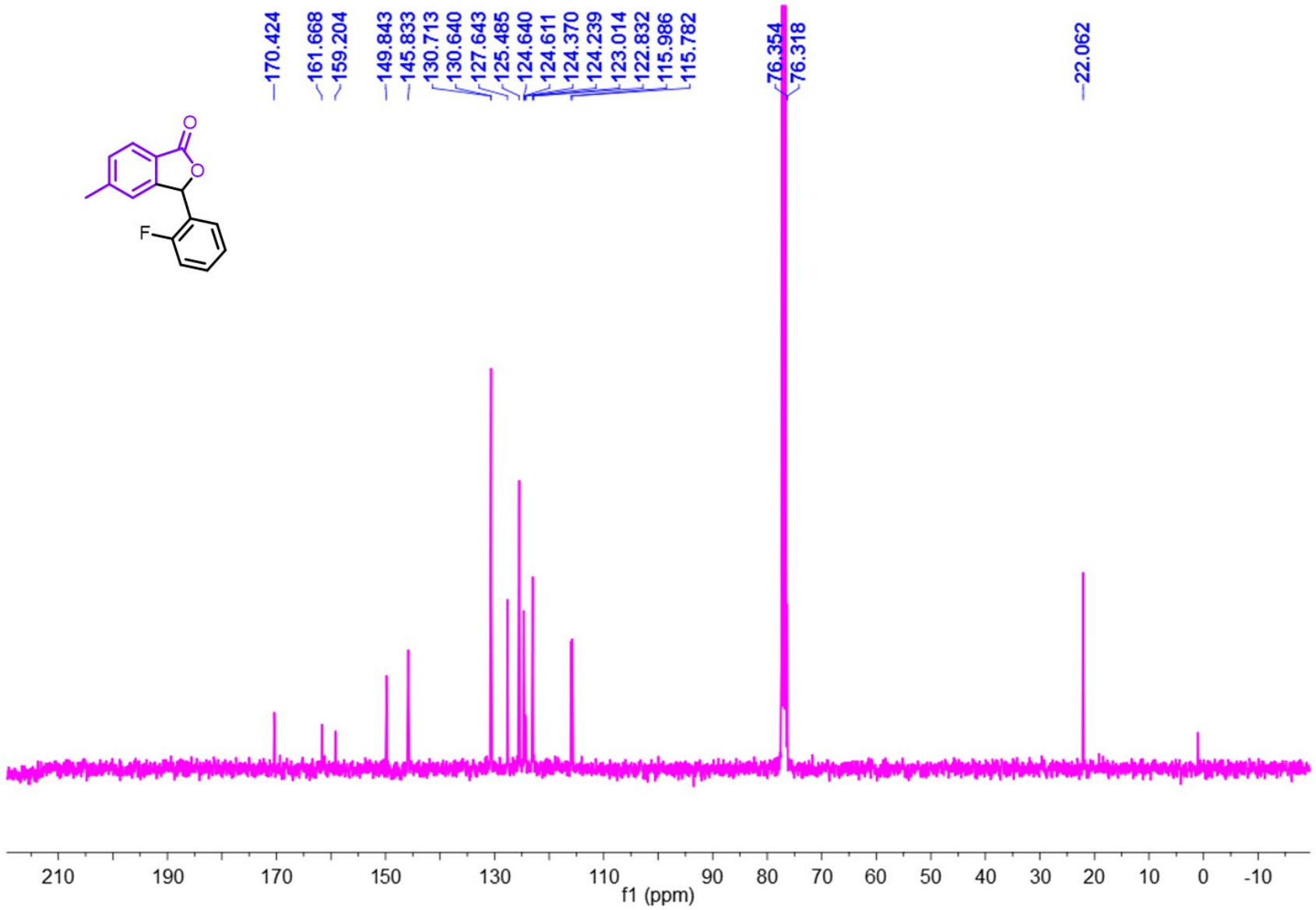


Figure S76. ^{1}H NMR spectra of 3-(2-flurophenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3c**) in $CDCl_3$.


170.424
161.668
159.204
149.843
145.833
130.713
130.640
127.643
125.485
124.640
124.611
124.370
124.239
123.014
122.832
115.986
115.782
76.354
76.318
22.062
O
O
F
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Figur

e S77. ^{13}C NMR spectra of 3-(2-flurophenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3c**) in $CDCl_3$.

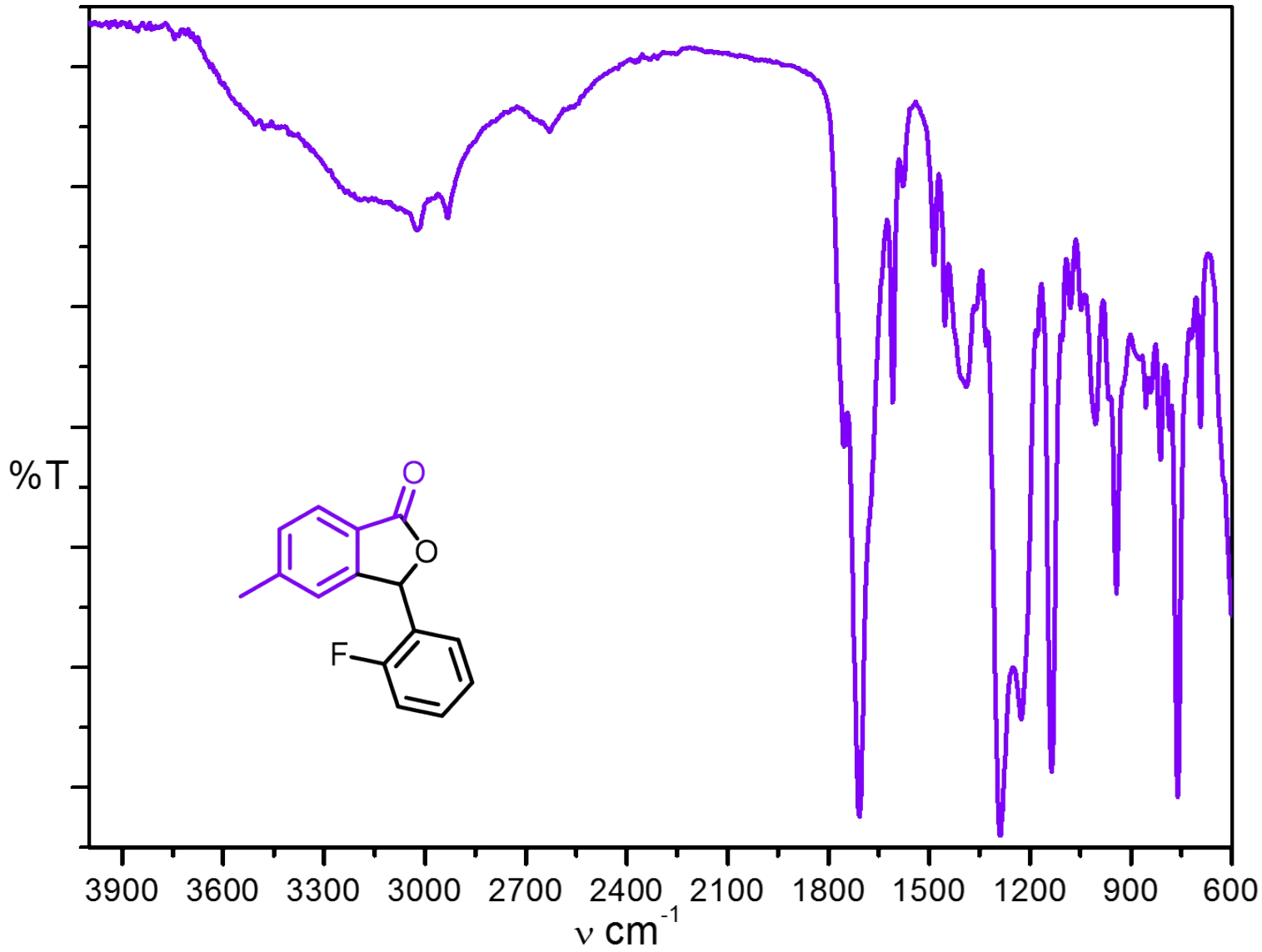


Figure S78. IR spectra of 3-(2-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3c**).

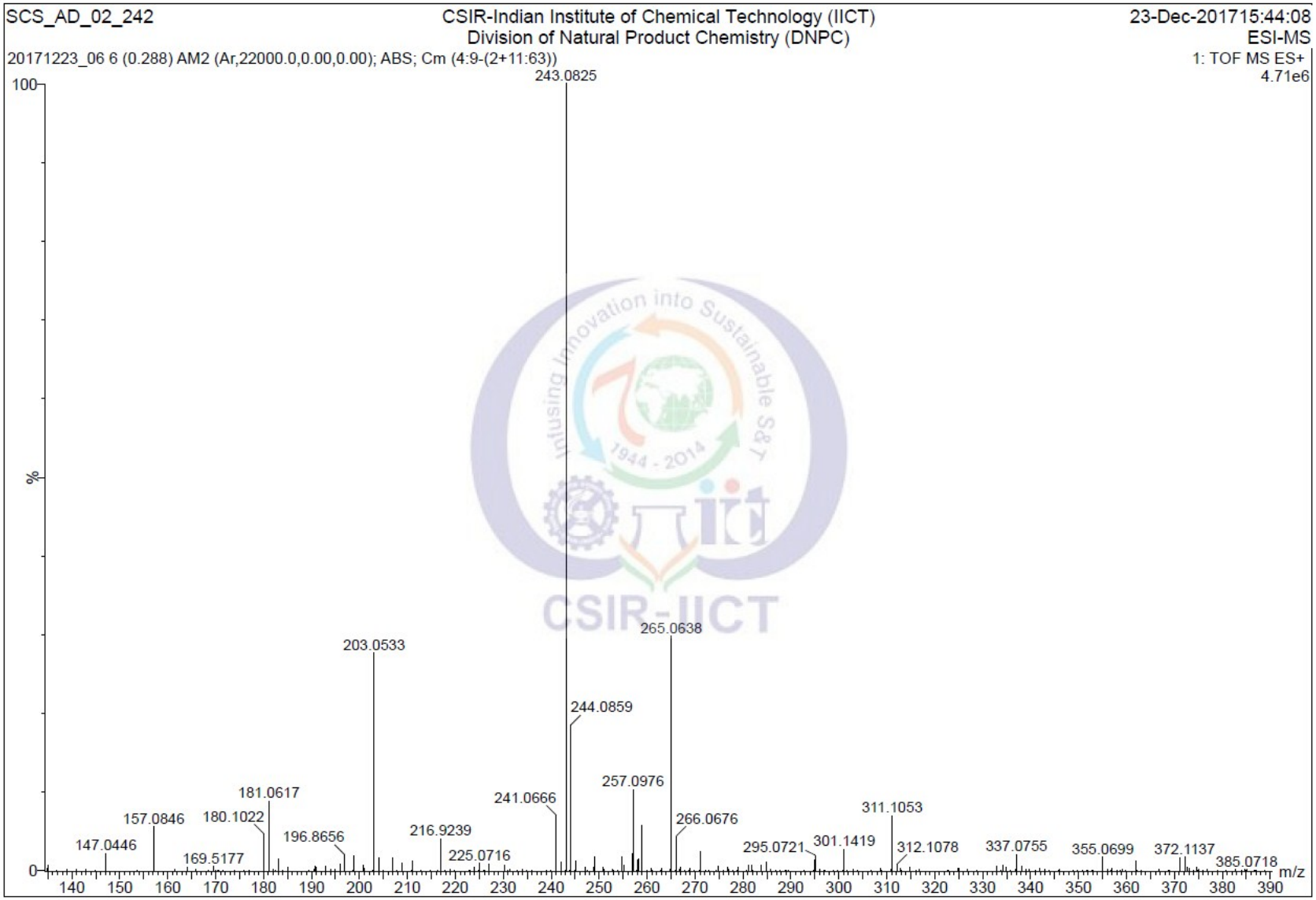


Figure S79. HRMS spctra of 3-(2-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3c**).

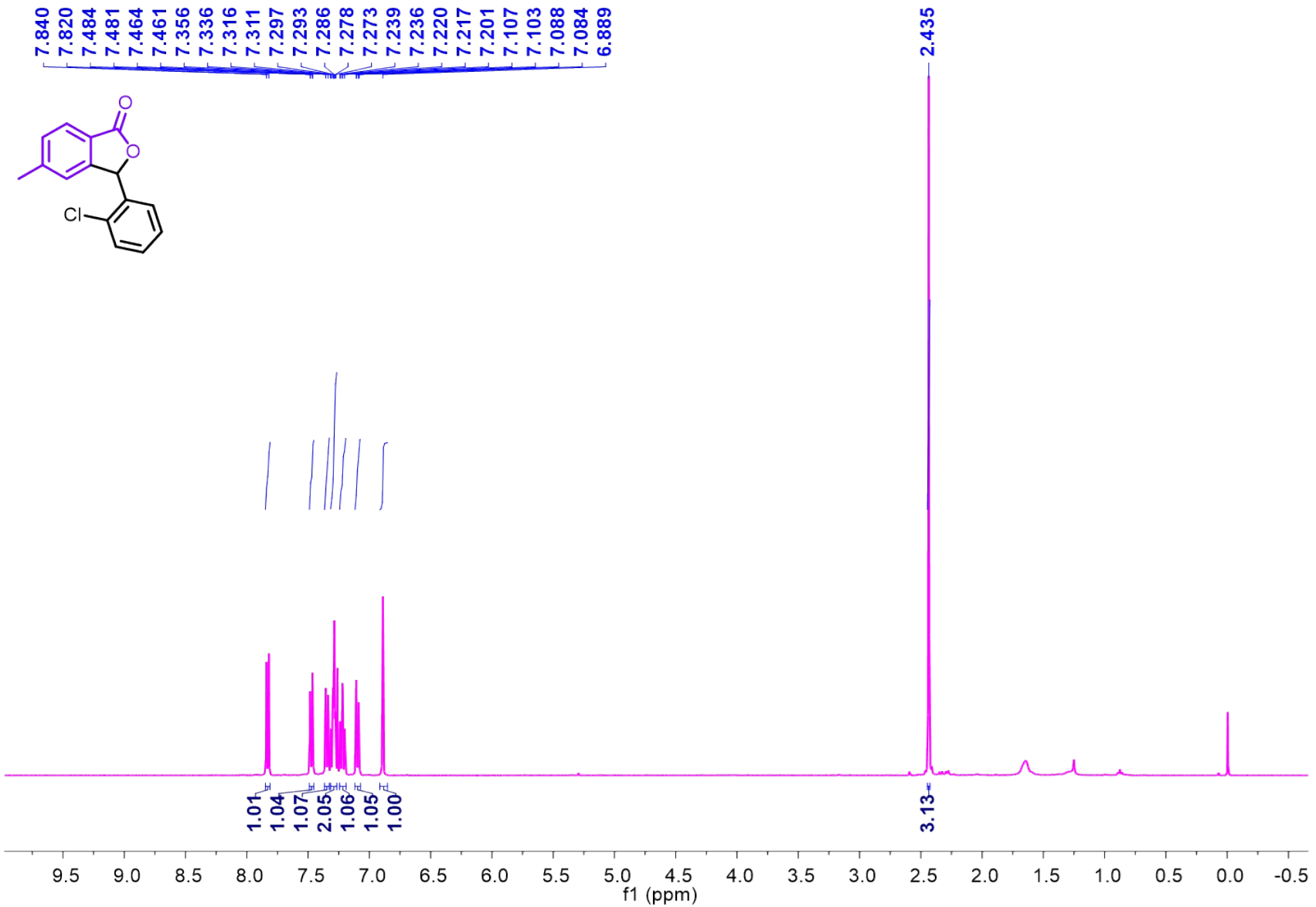


Figure S80. ^{1}H NMR spectra of 3-(2-chlorophenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3d**) in $CDCl_3$.

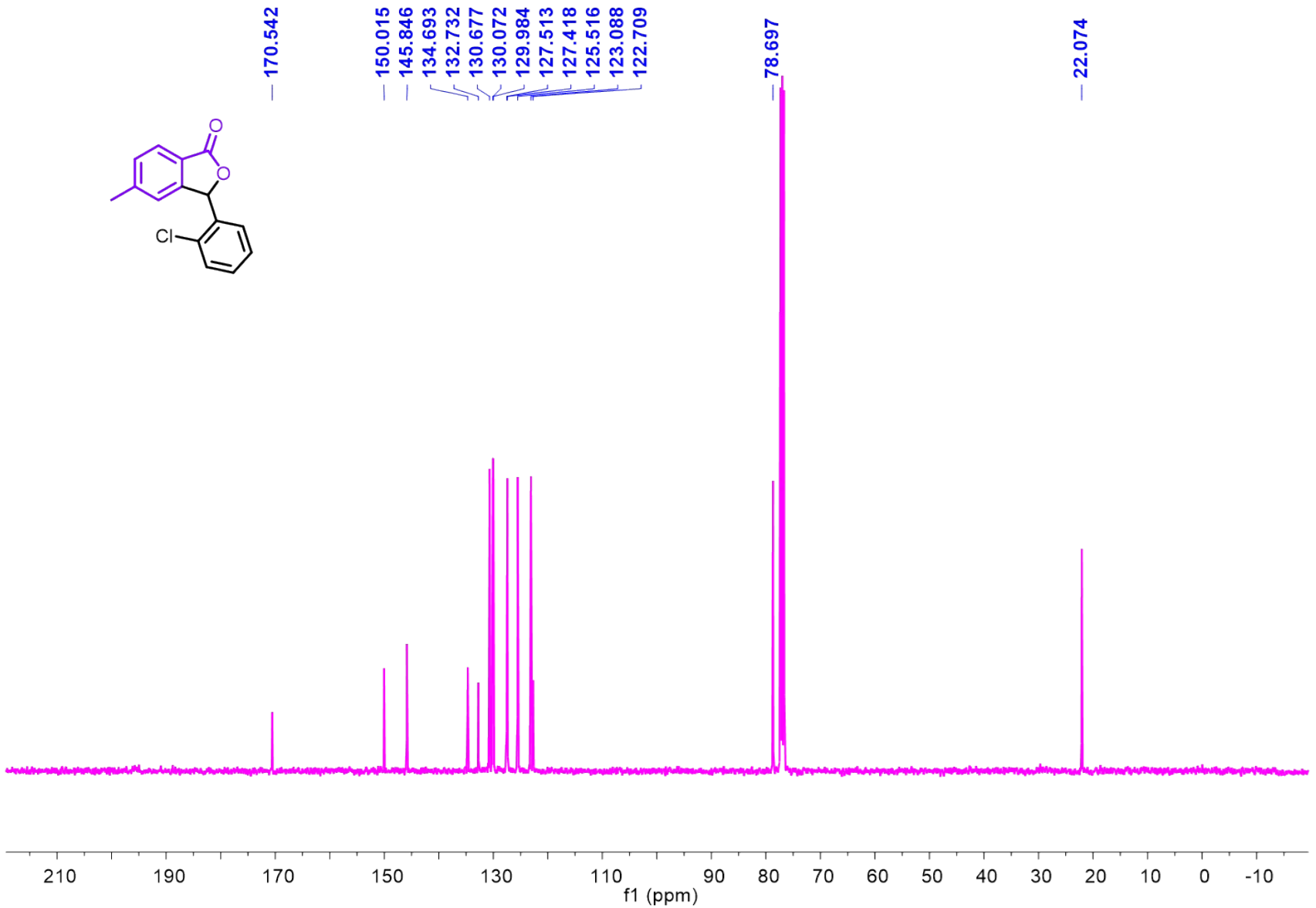


Figure S81. ^{13}C NMR spectra of 3-(2-chlorophenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3d**) in $CDCl_3$.

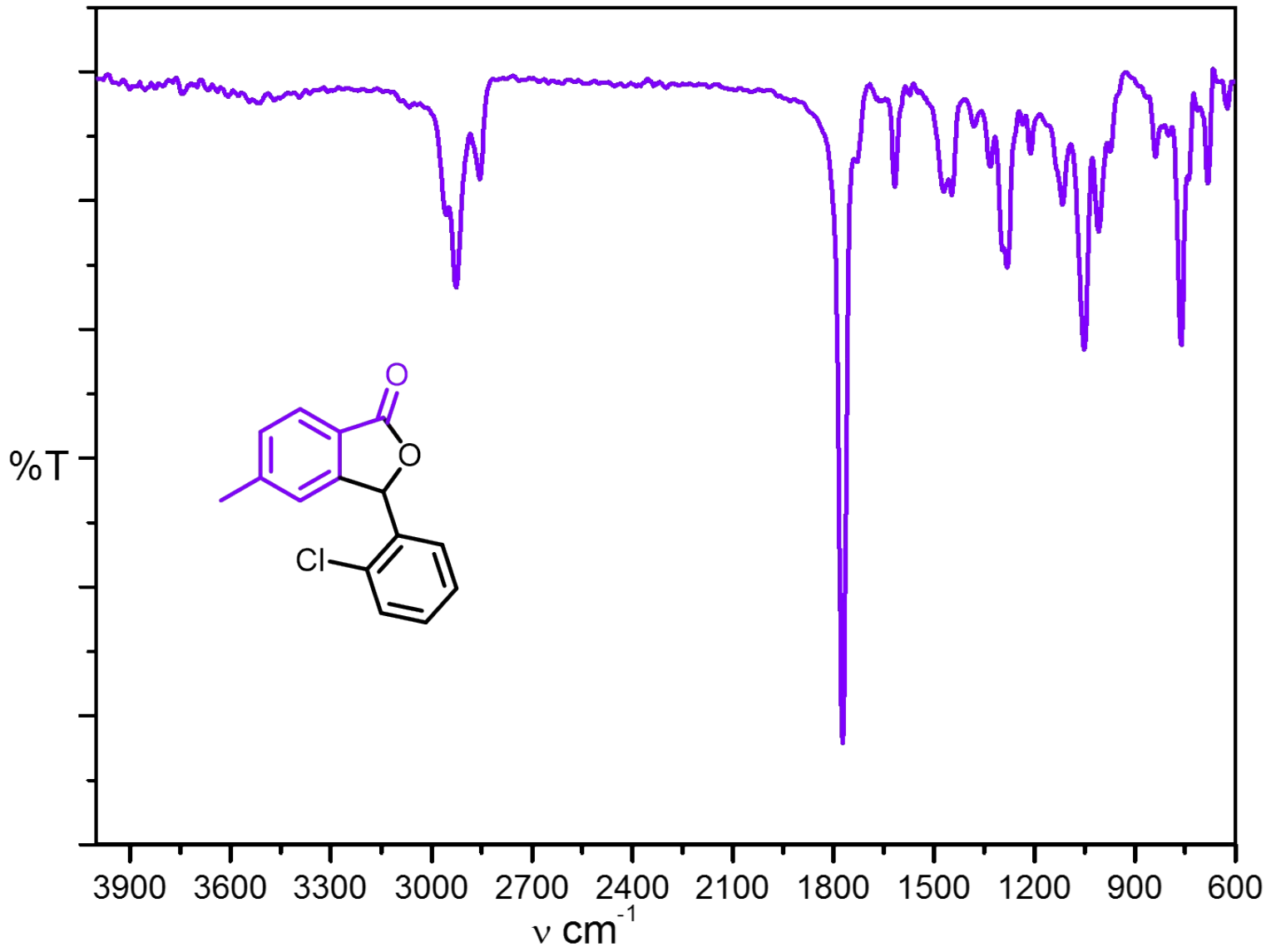


Figure S82. IR spectra of 3-(2-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3d**).

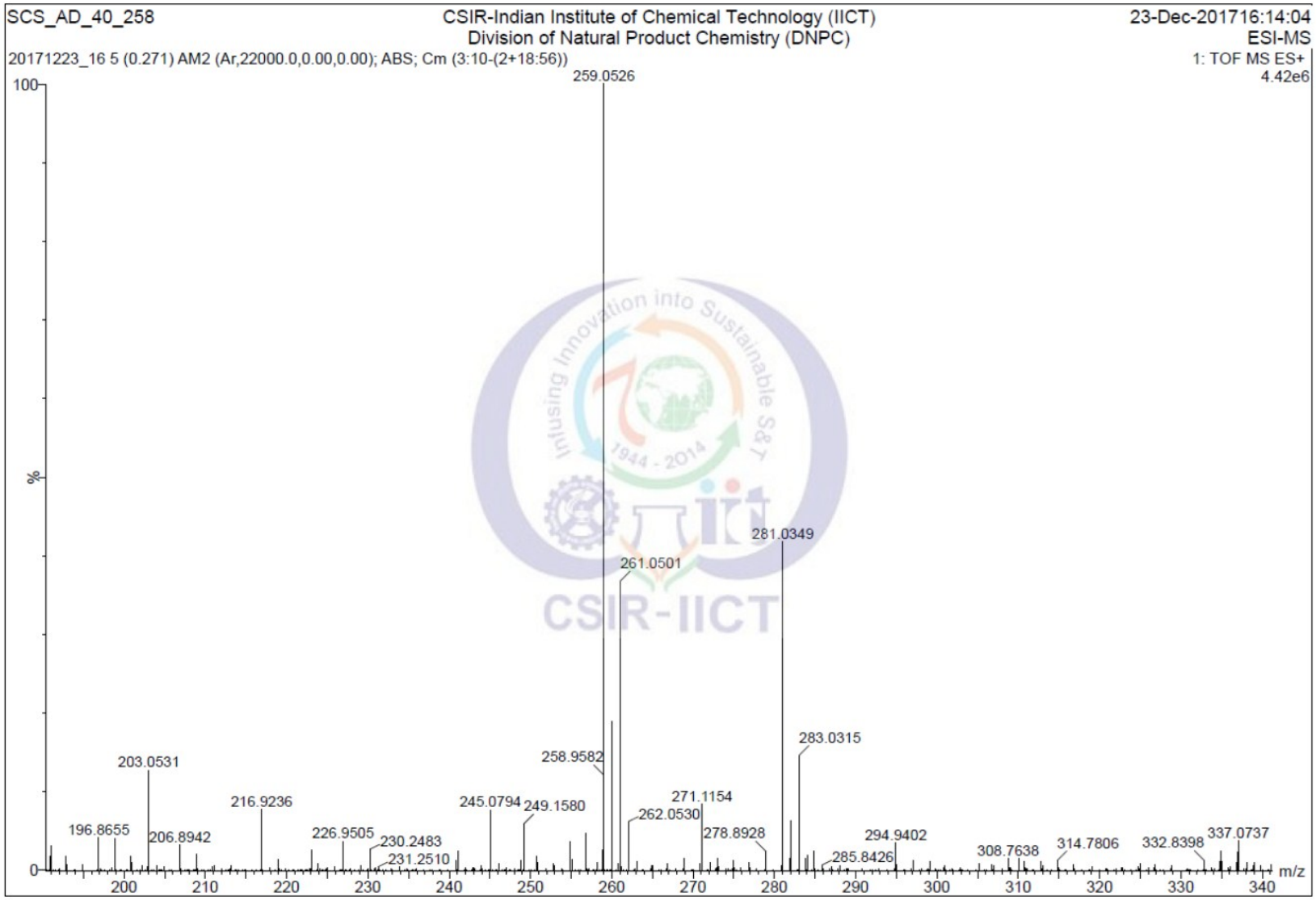


Figure S83. HRMS spctra of 3-(2-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3d**).

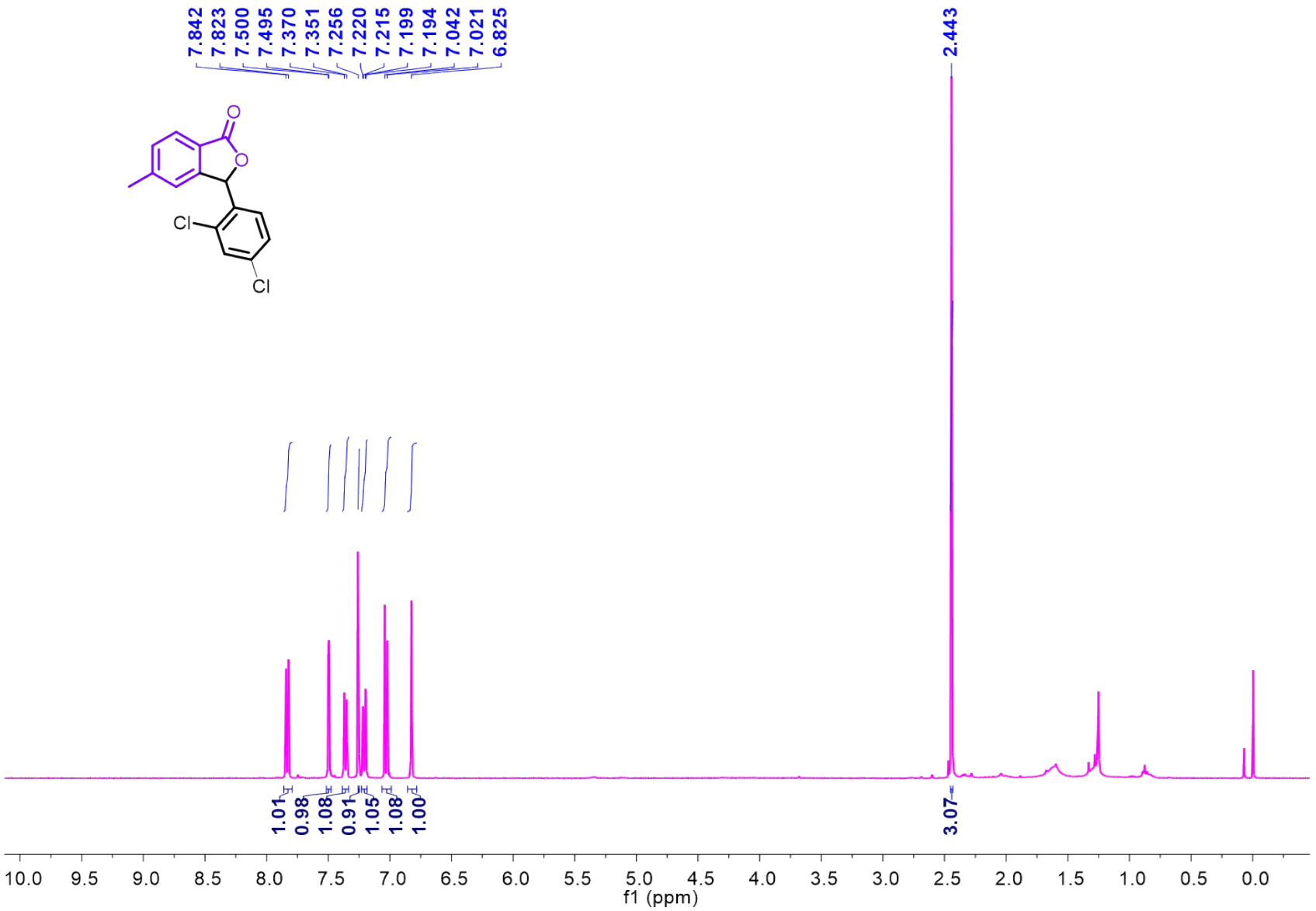


Figure S84. ^{1}H NMR spectra of 3-(2, 4-dichlorophenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3e**) in $CDCl_3$

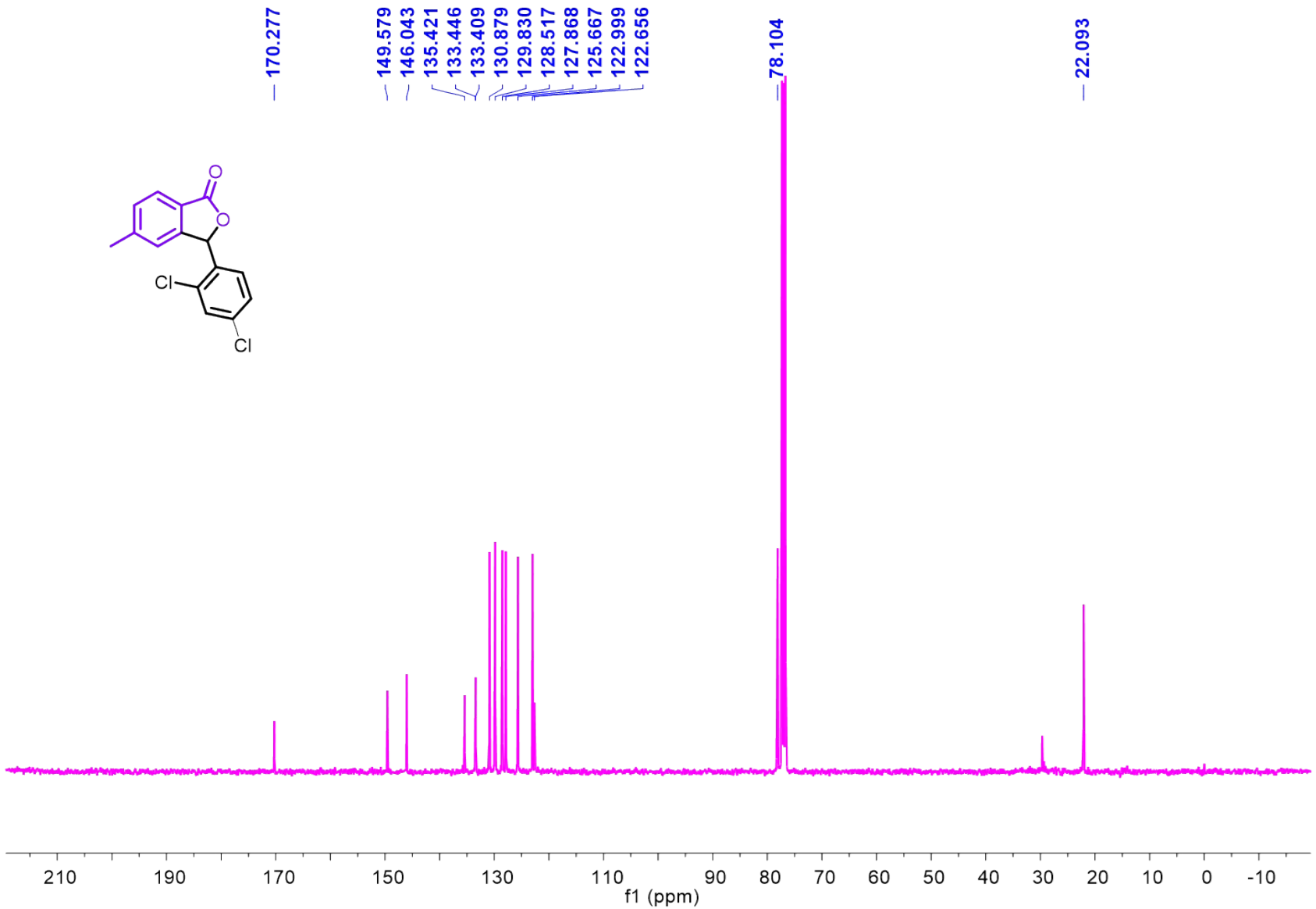


Figure S85. ^{13}C NMR spectra of 3-(2, 4-dichlorophenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3e**) in $CDCl_3$.

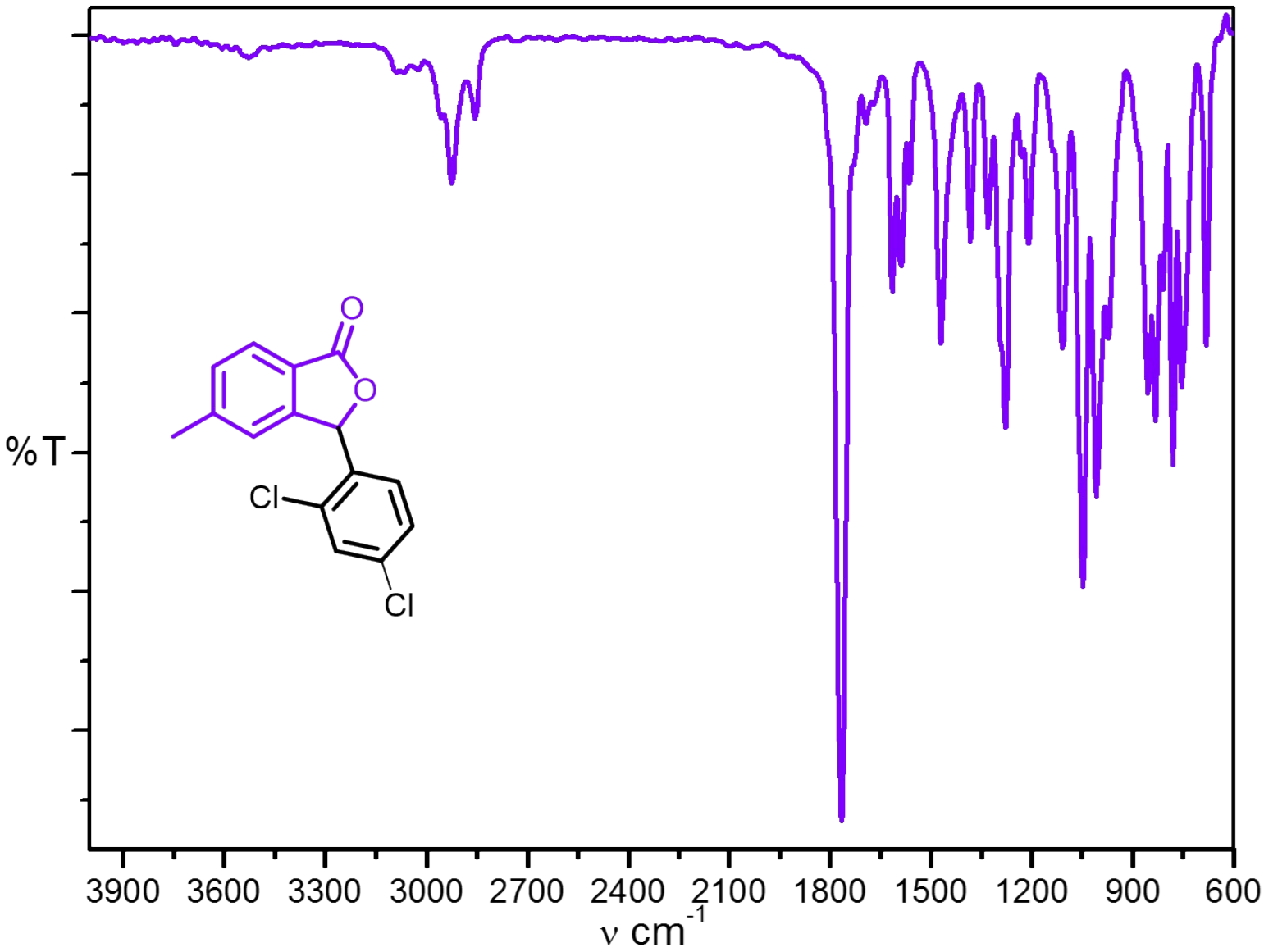


Figure S86. IR spectra of 3-(2, 4-dichlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3e**).

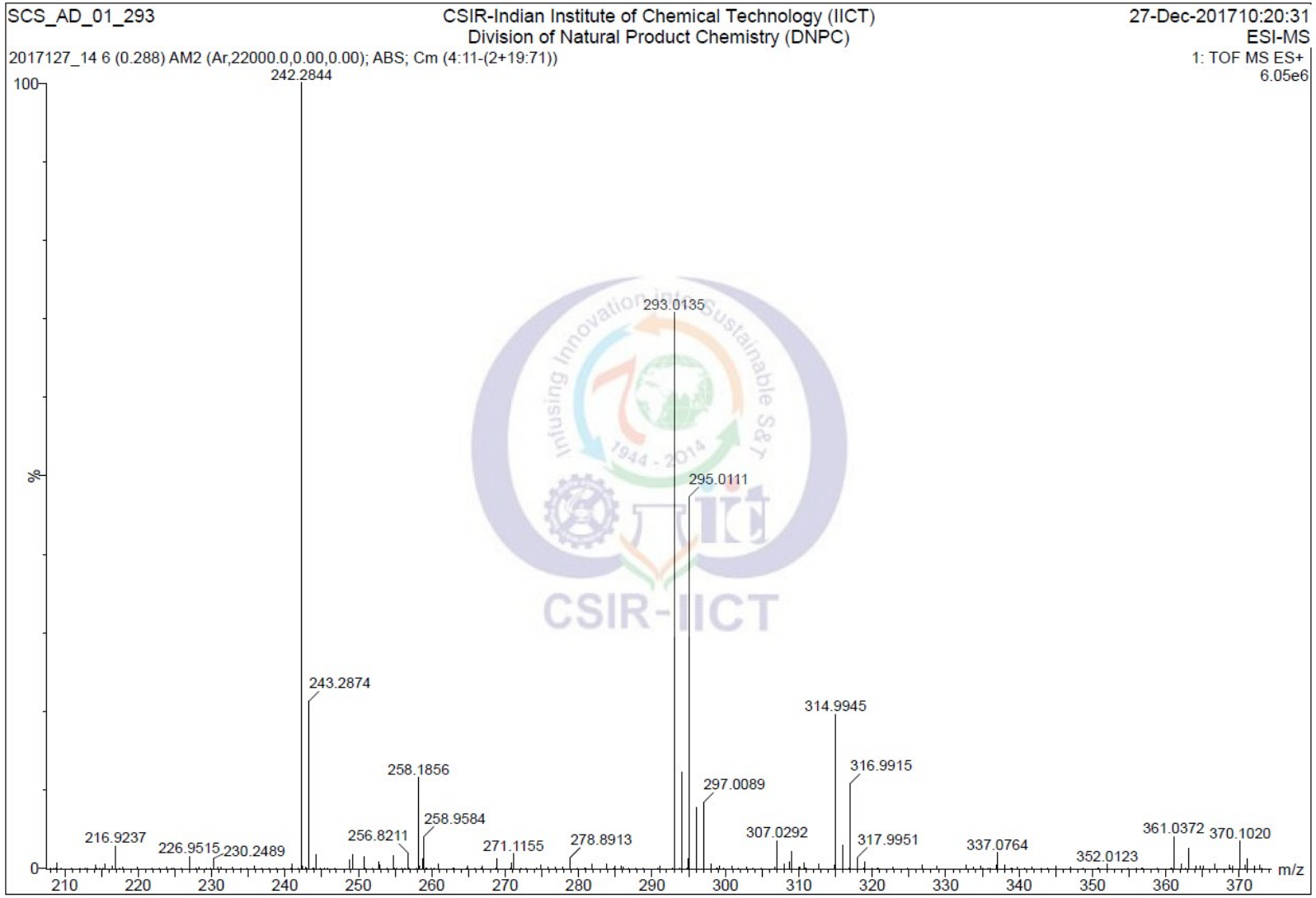


Figure S87. HRMS spctra of 3-(2, 4-dichlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3e**).

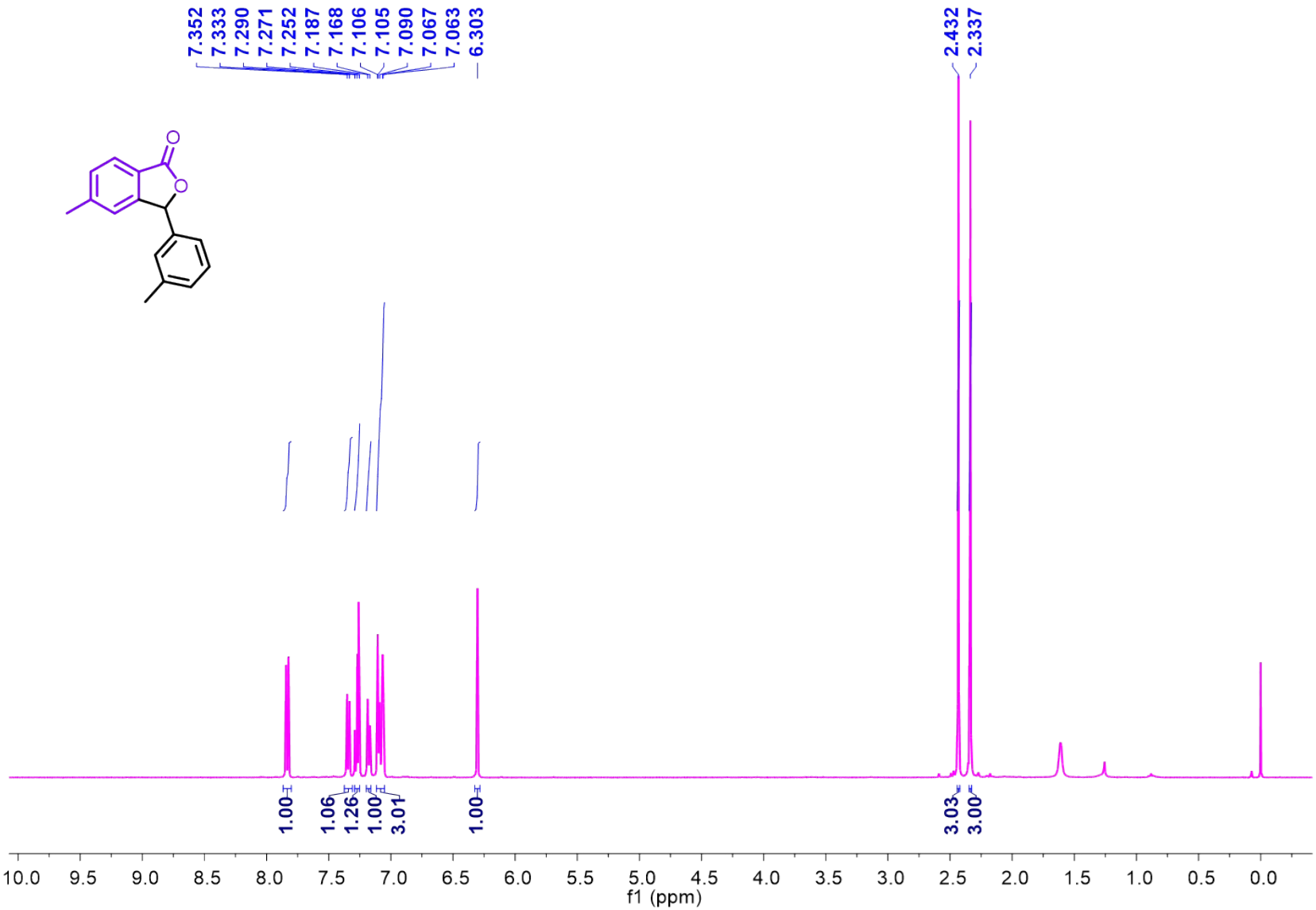


Figure S88. ^{1}H NMR spectra of 5-methyl-3-(m-tolyl) iso-benzofuran-1-(3*H*)-one (**3f**) in $CDCl_3$.

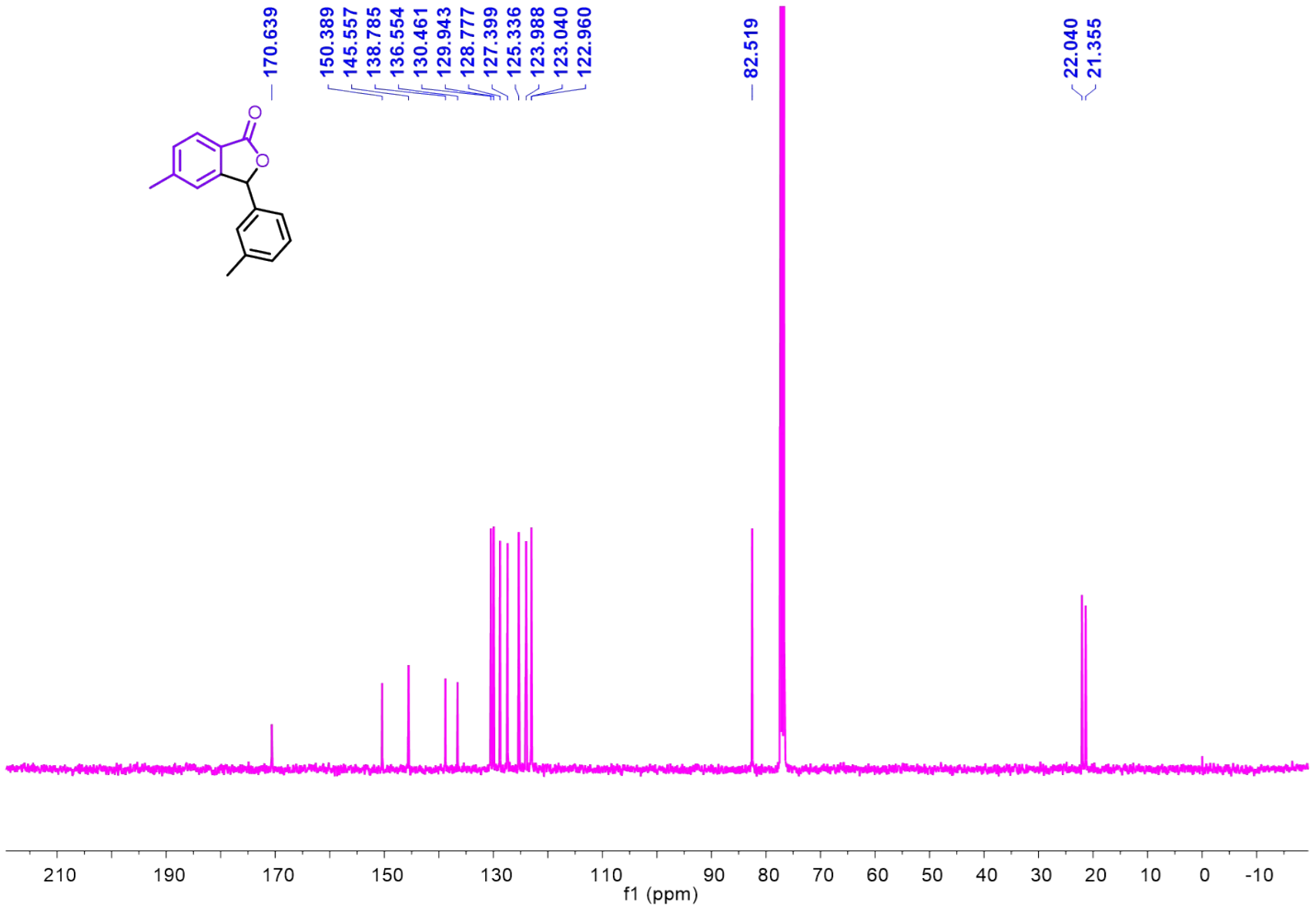


Figure S89. ^{13}C NMR spectra of 5-methyl-3-(m-tolyl) iso-benzofuran-1-(3*H*)-one (**3f**) in $CDCl_3$.

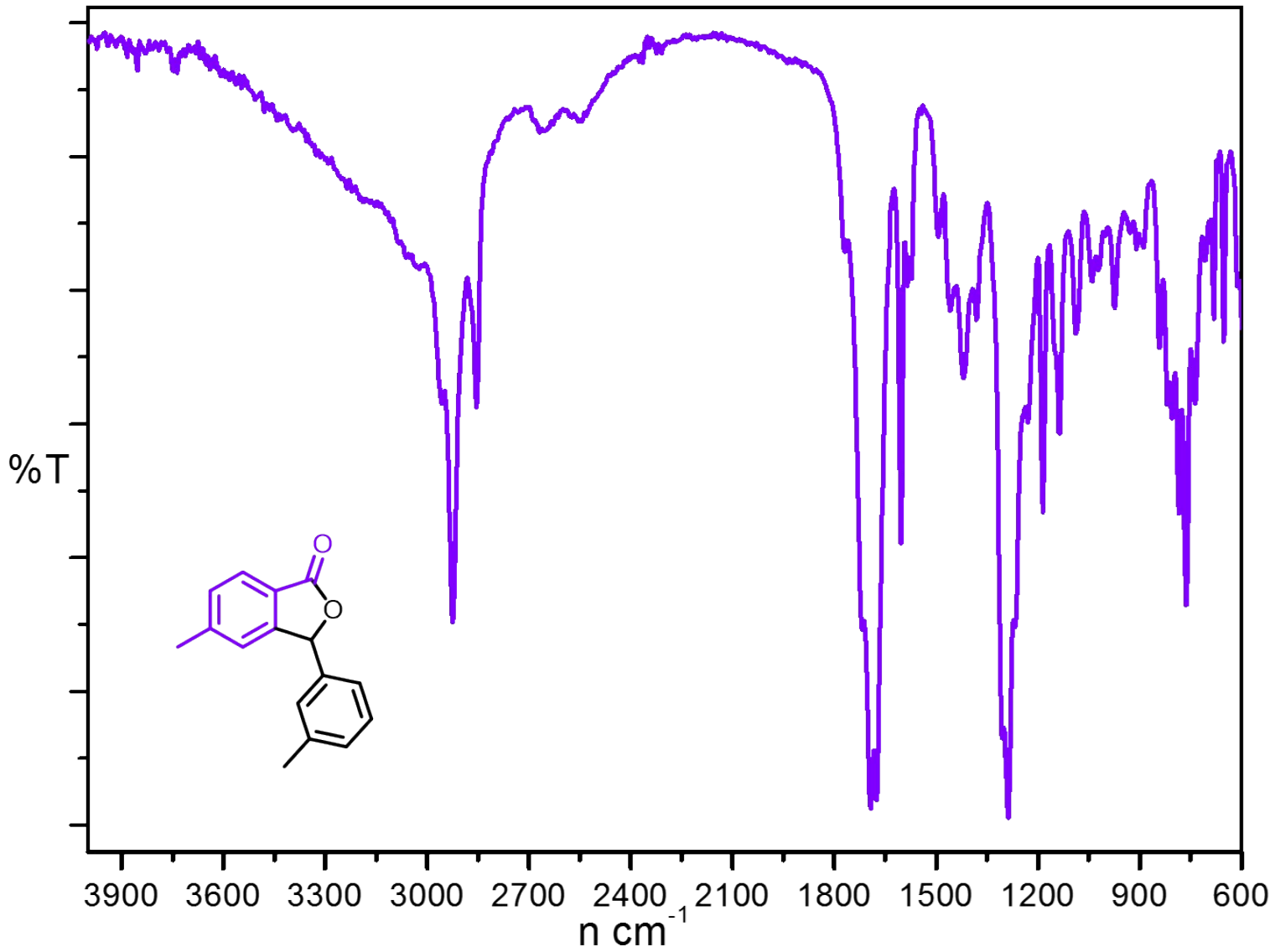


Figure S90. IR spectra of 5-methyl-3-(m-tolyl) isobenzofuran-1-(3*H*)-one (**3f**).

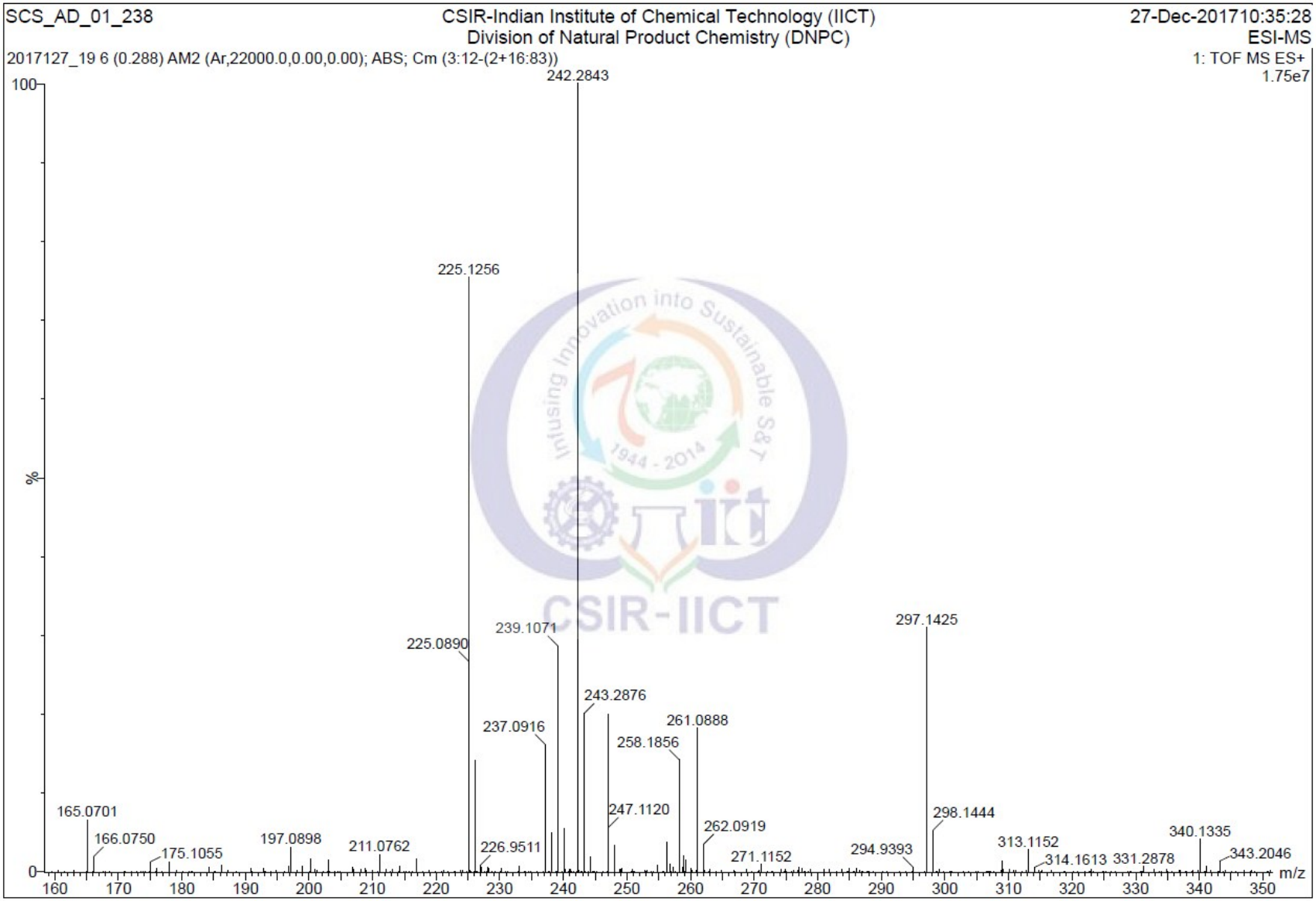


Figure S91. HRMS spctra of 5-methyl-3-(m-tolyl) isobenzofuran-1-(3*H*)-one (**3f**).

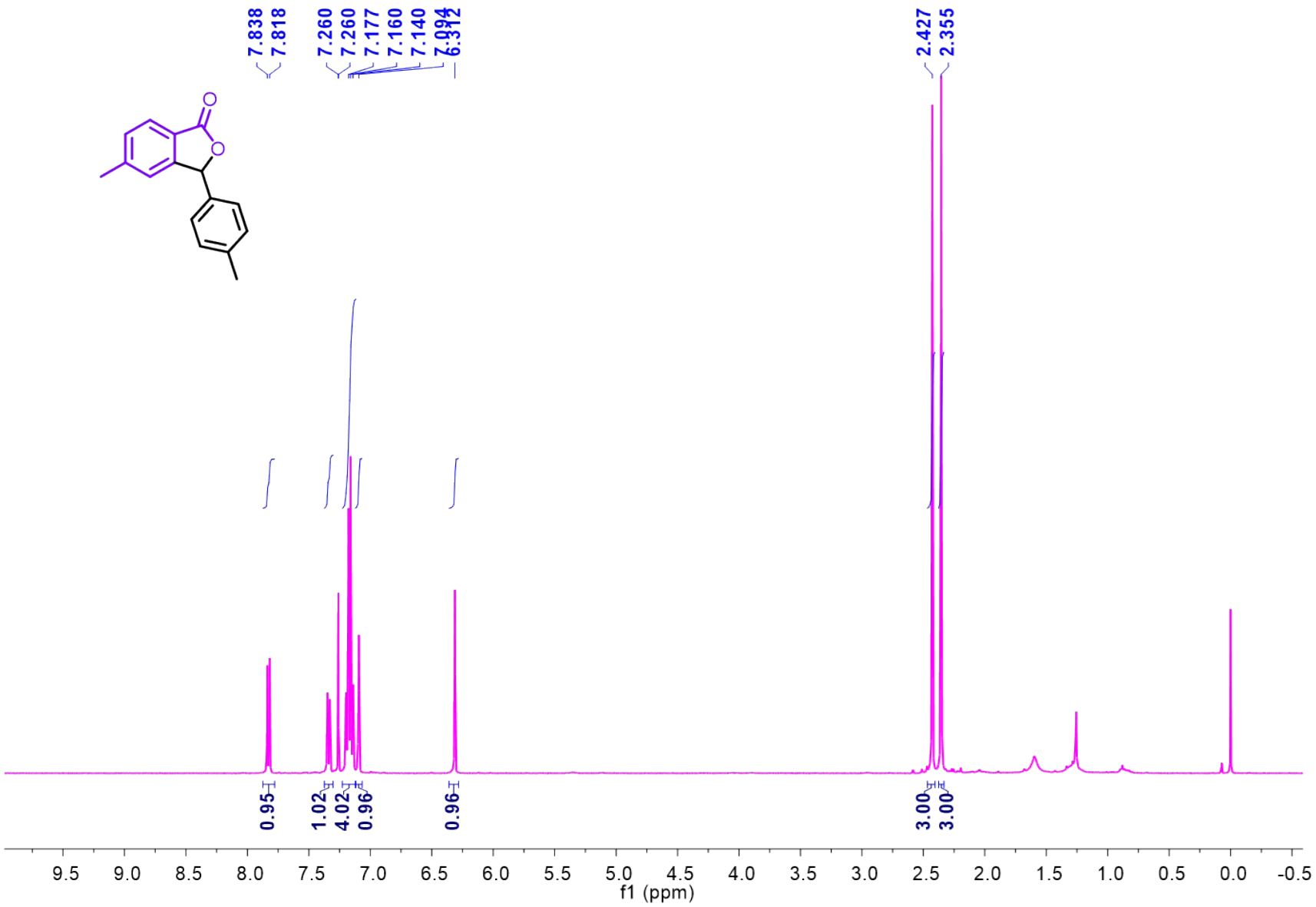


Figure S92. ^{1}H NMR spectra of 5-methyl-3-(p-tolyl) iso-benzofuran-1-(3*H*)-one (**3g**) in $CDCl_3$.

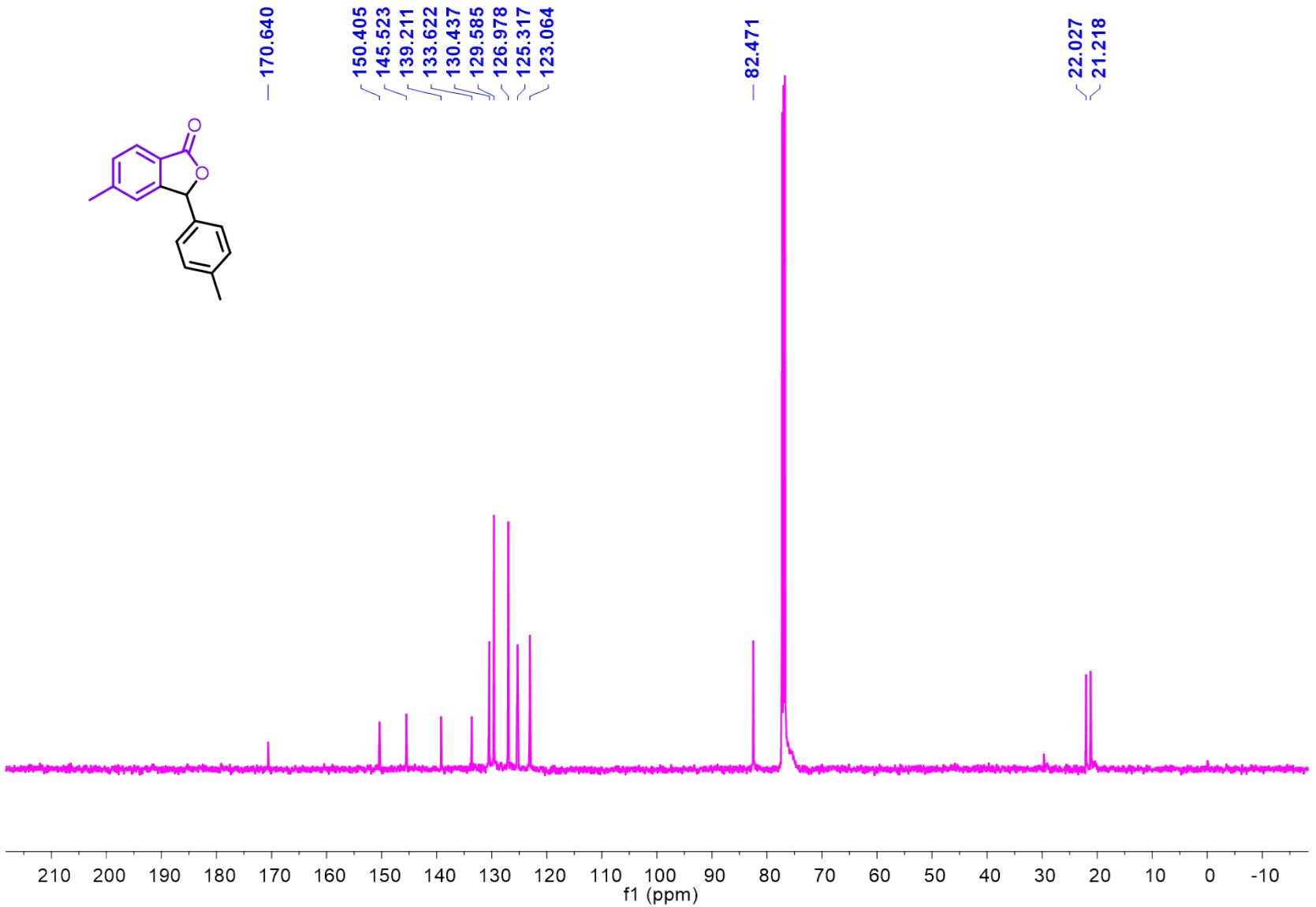


Figure S93. ^{13}C NMR spectra of 5-methyl-3-(p-tolyl) iso-benzofuran-1-(3*H*)-one (**3g**) in $CDCl_3$.

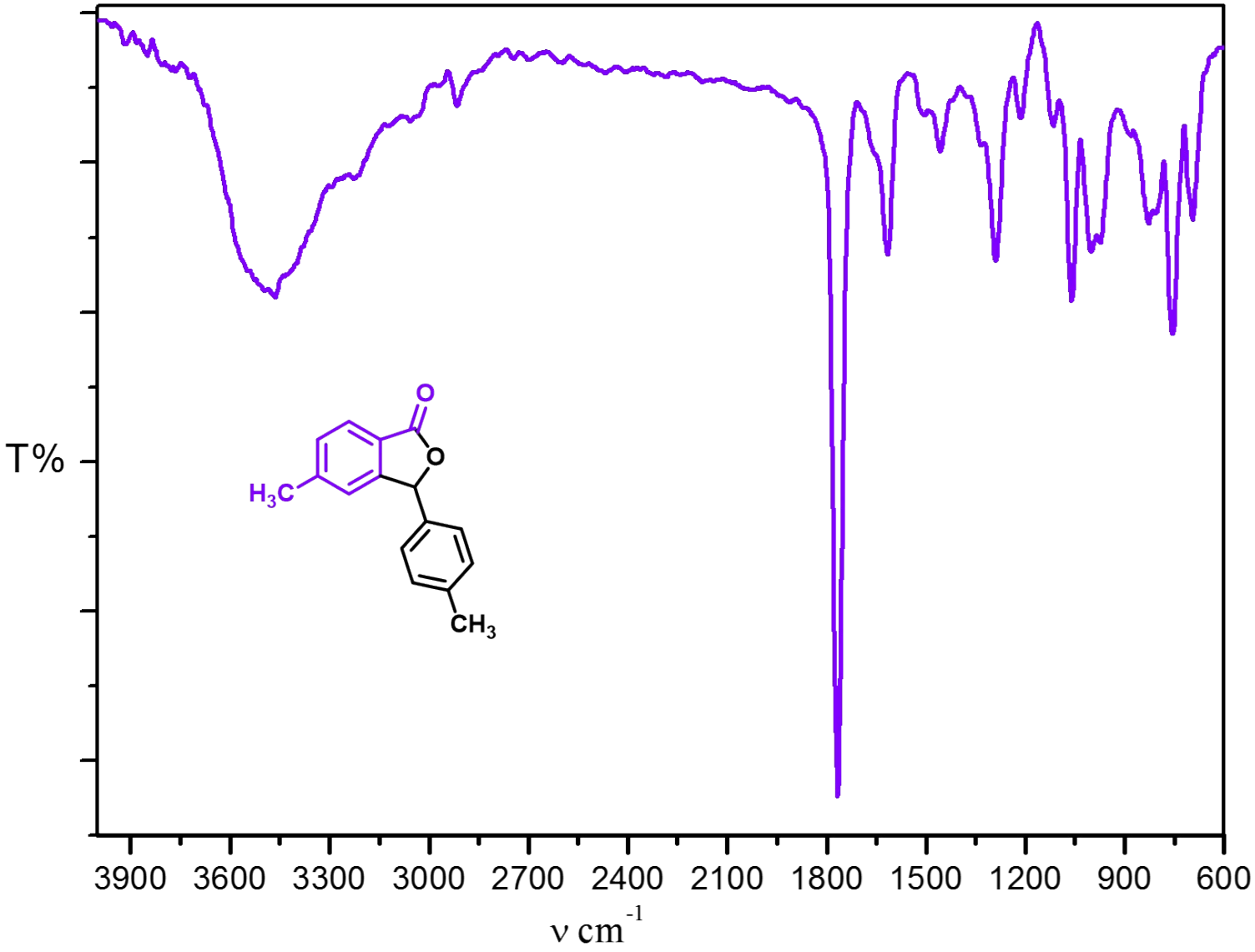


Figure S94. IR spectra of 5-methyl-3-(p-tolyl) isobenzofuran-1-(3*H*)-one (**3g**).

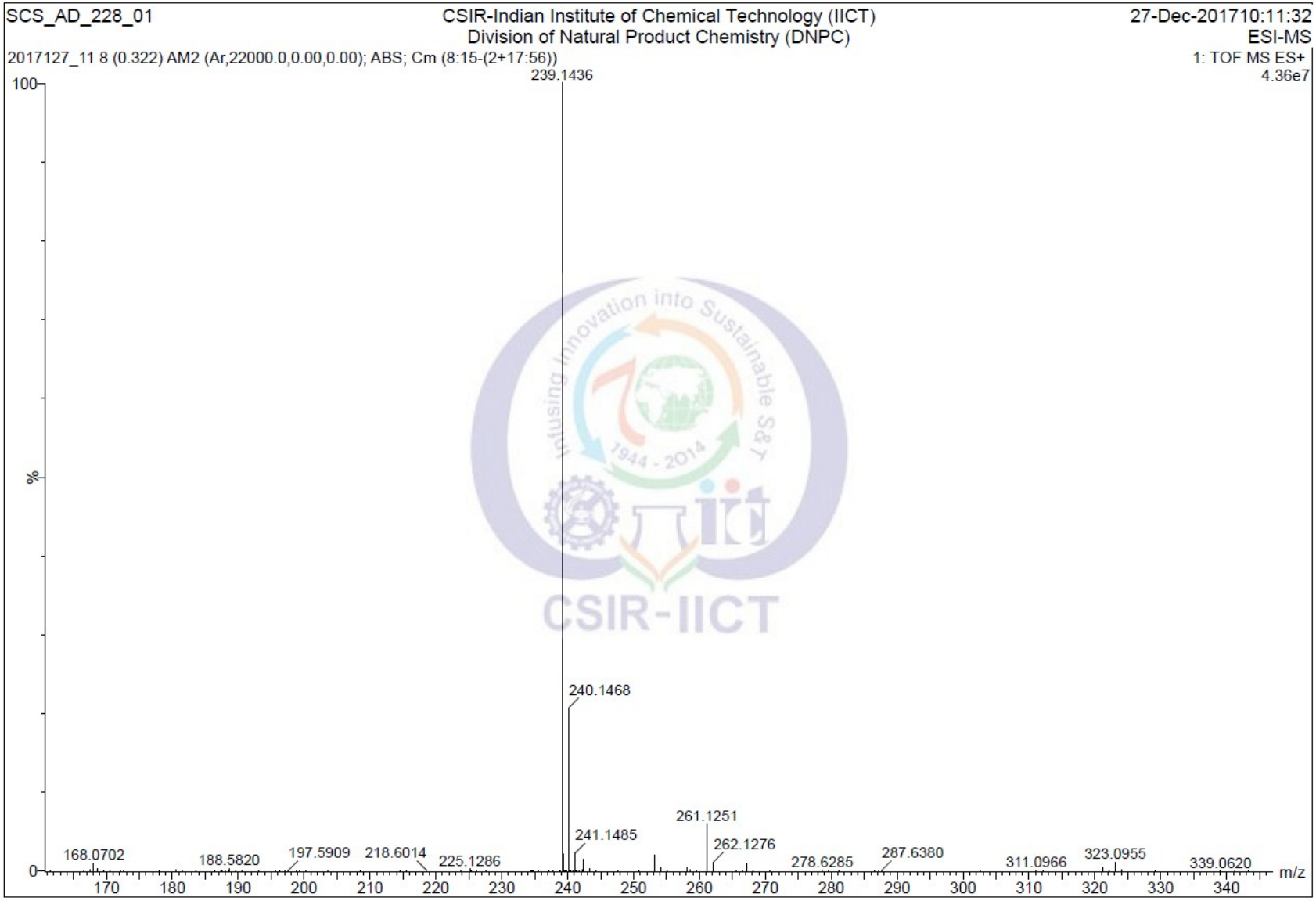


Figure S95. HRMS spctra of 5-methyl-3-(p-tolyl) isobenzofuran-1-(3*H*)-one (**3g**).

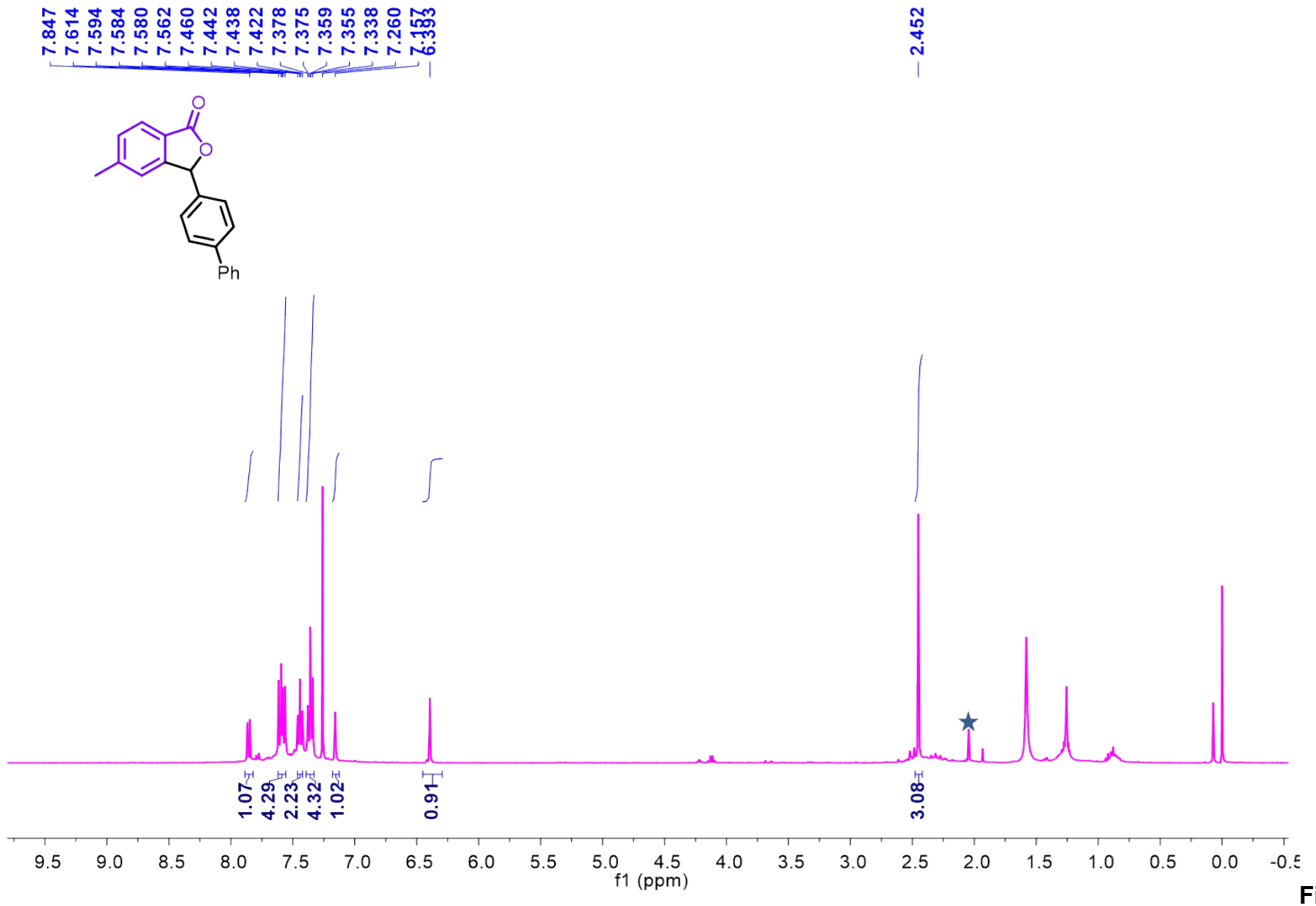


Figure S96. ^{1}H NMR spectra of 3-([1, 1'-biphenyl]-4-yl)-5-methyliso-benzofuran-1-(3*H*)-one (**3h**) in $CDCl_3$. (★ Solvent impurity)

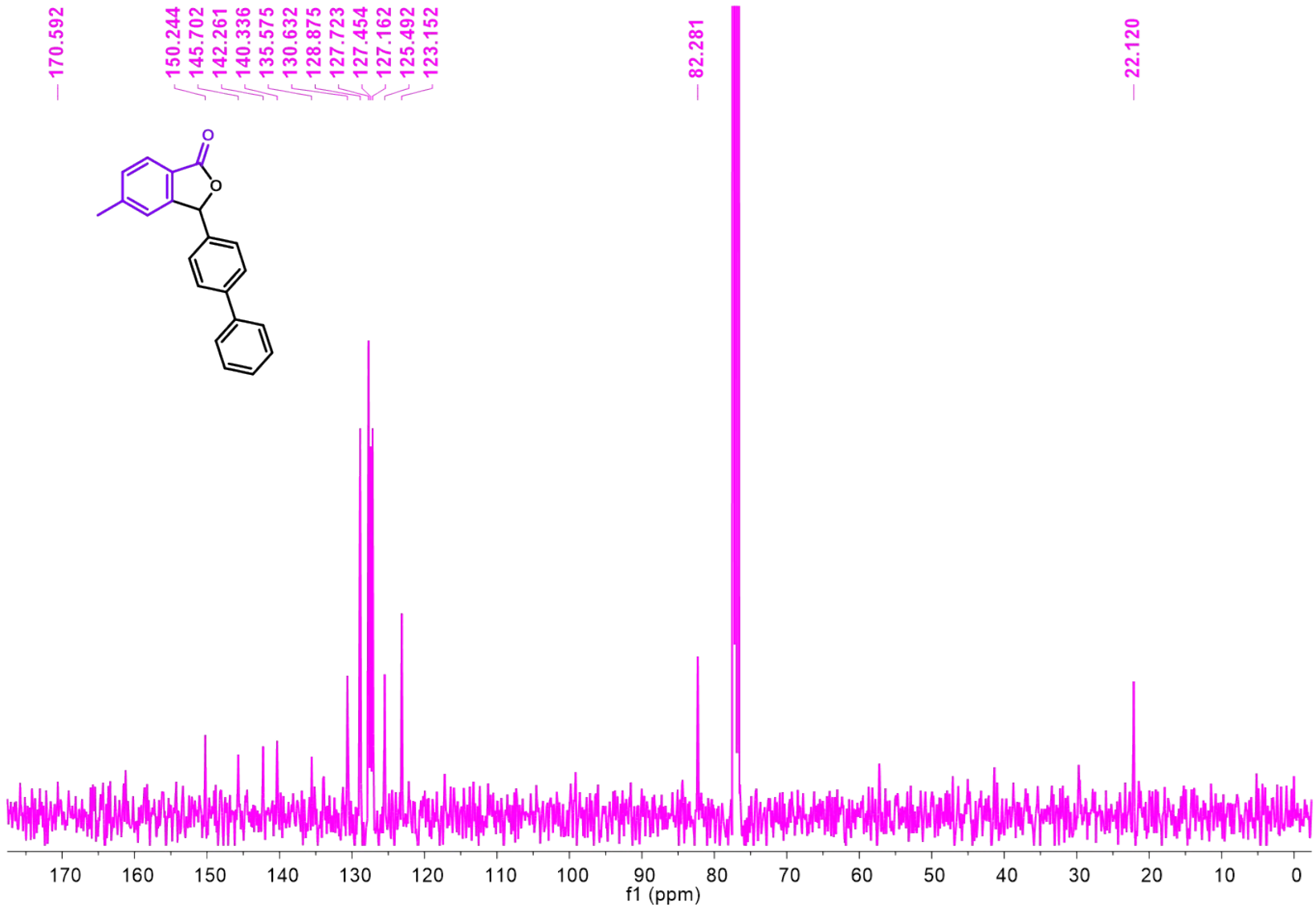


Figure S97. ^{13}C NMR spectra of 3-([1, 1'-biphenyl]-4-yl)-5-methyliso-benzofuran-1-(3*H*)-one (**3h**) in $CDCl_3$.

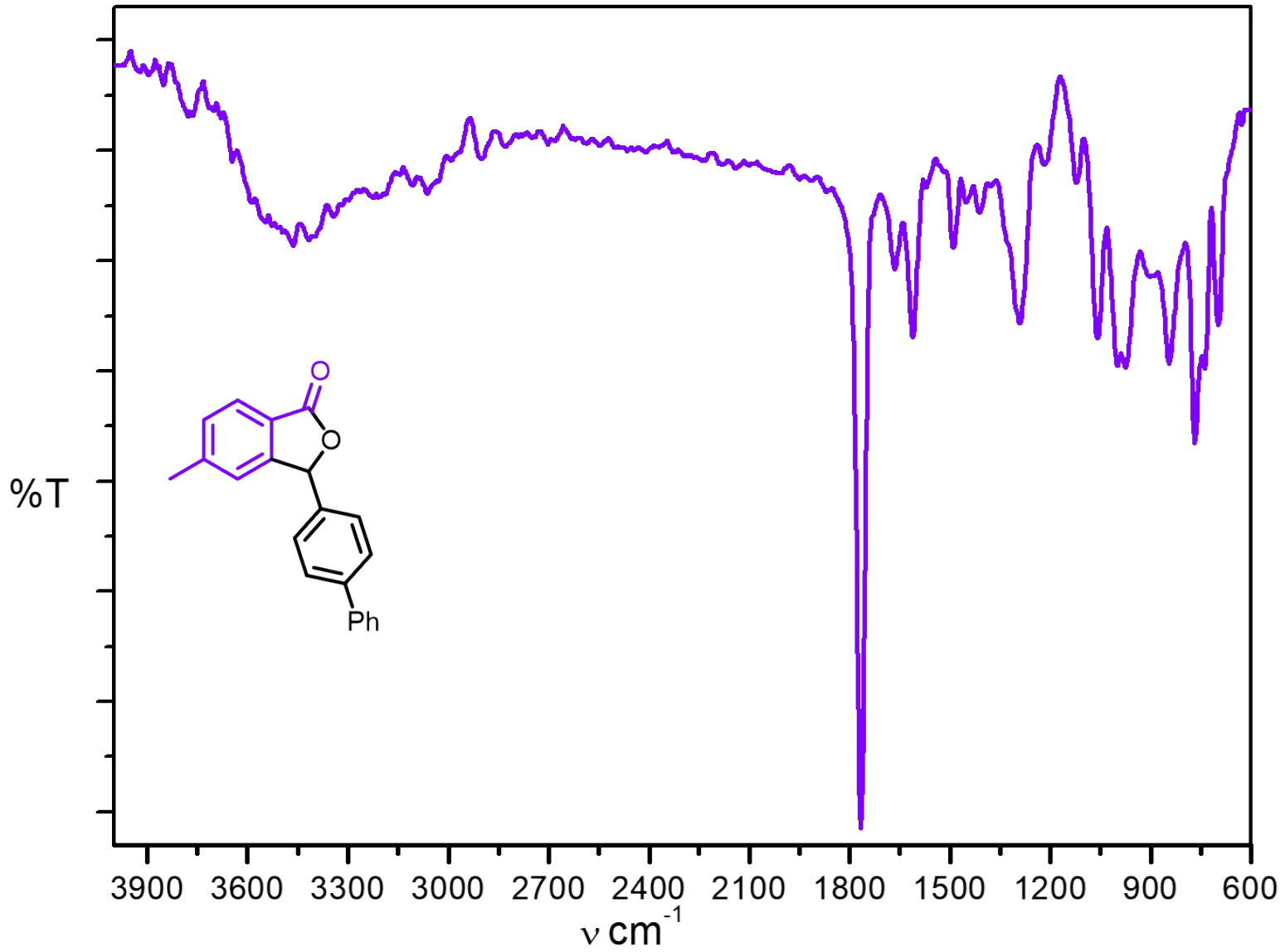


Figure S98. IR spectra of 3-([1, 1'-biphenyl]-4-yl)-5-methylisobenzofuran-1-(3*H*)-one (**3h**).

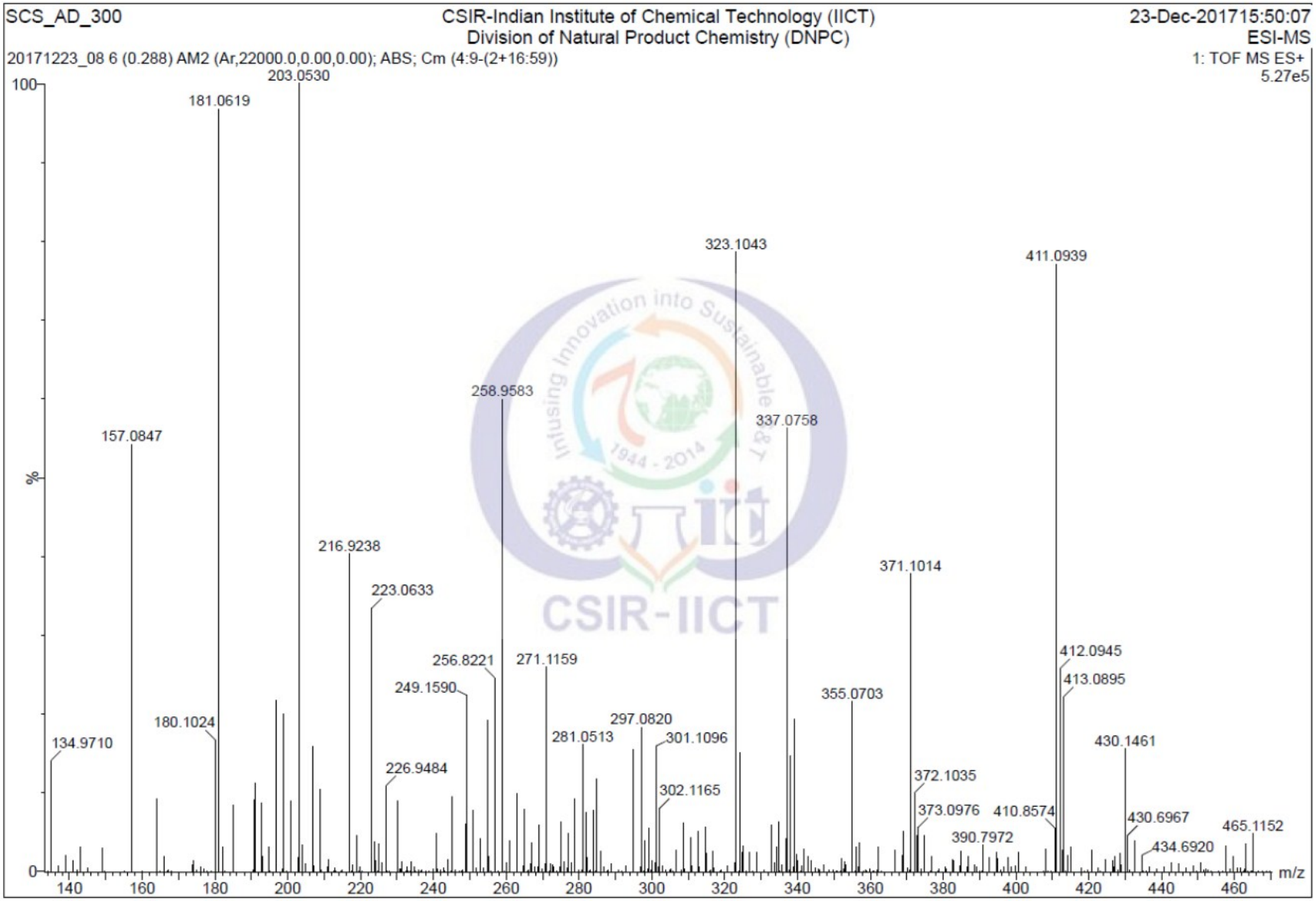


Figure S99. HRMS spctra of 3-([1, 1'-biphenyl]-4-yl)-5-methylisobenzofuran-1-(3*H*)-one (**3h**).

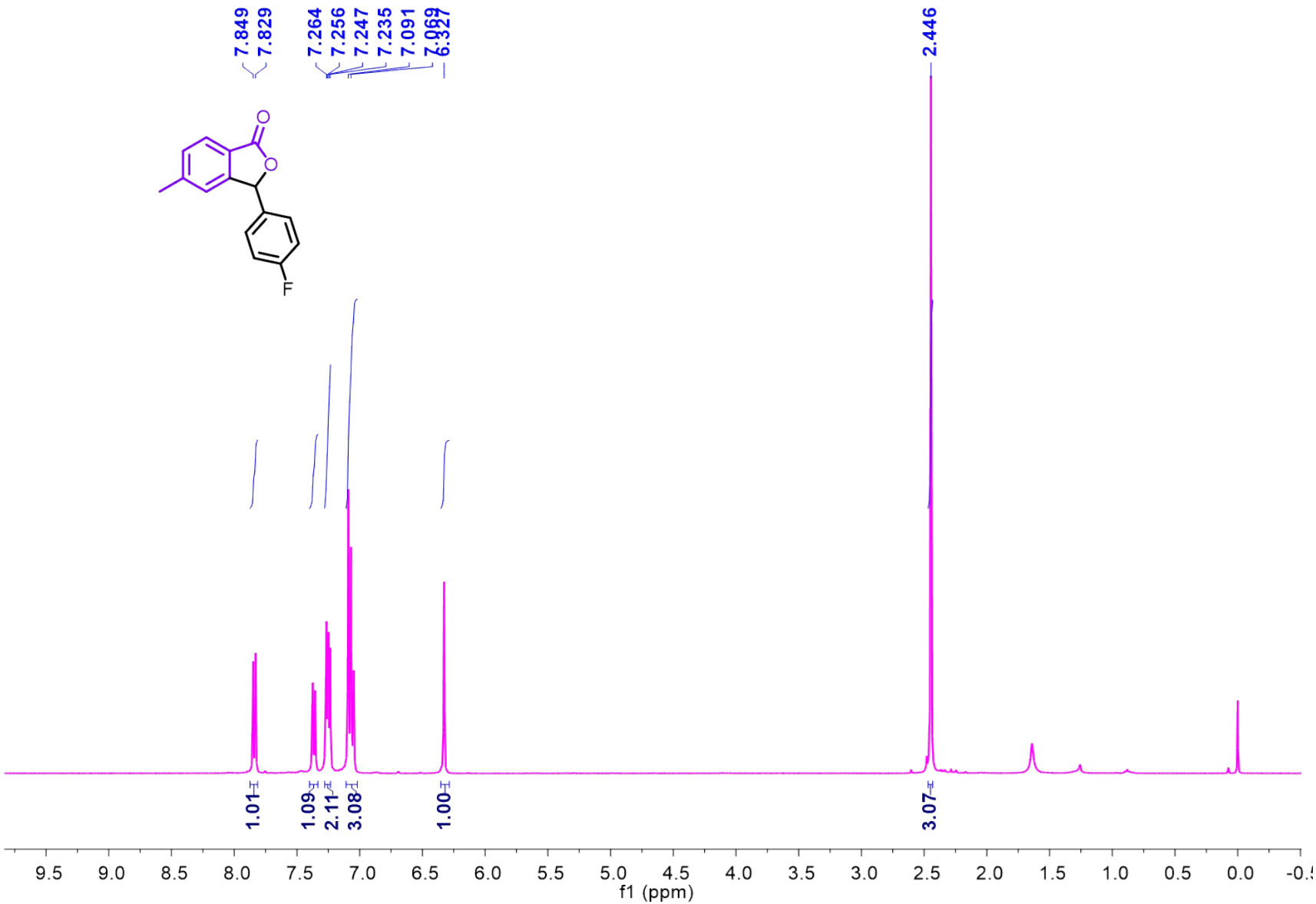


Figure S100. ^{1}H NMR spectra of 3-(4-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3i**) in $CDCl_3$.

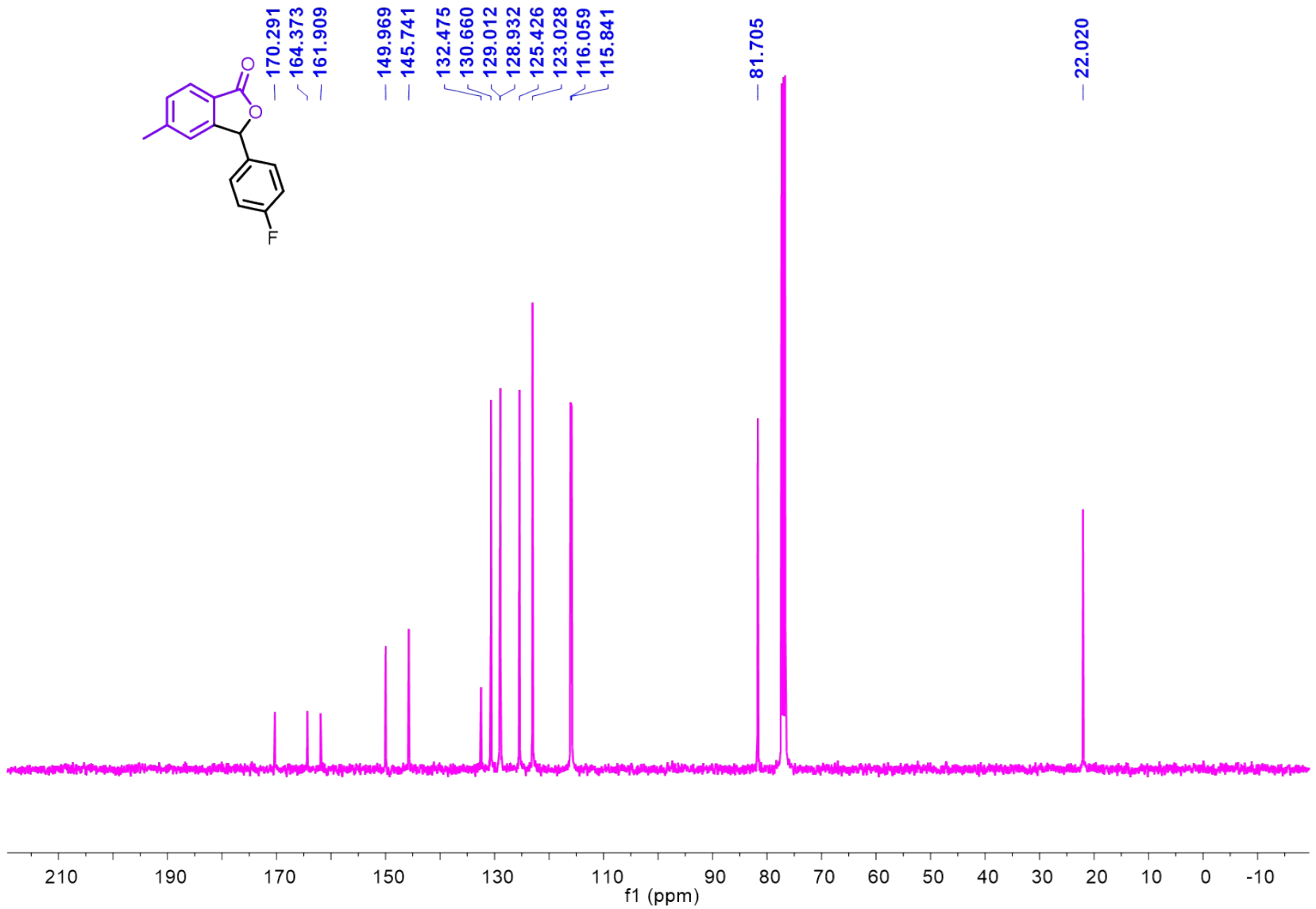


Figure S101. ^{13}C NMR spectra of 3-(4-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3i**) in $CDCl_3$.

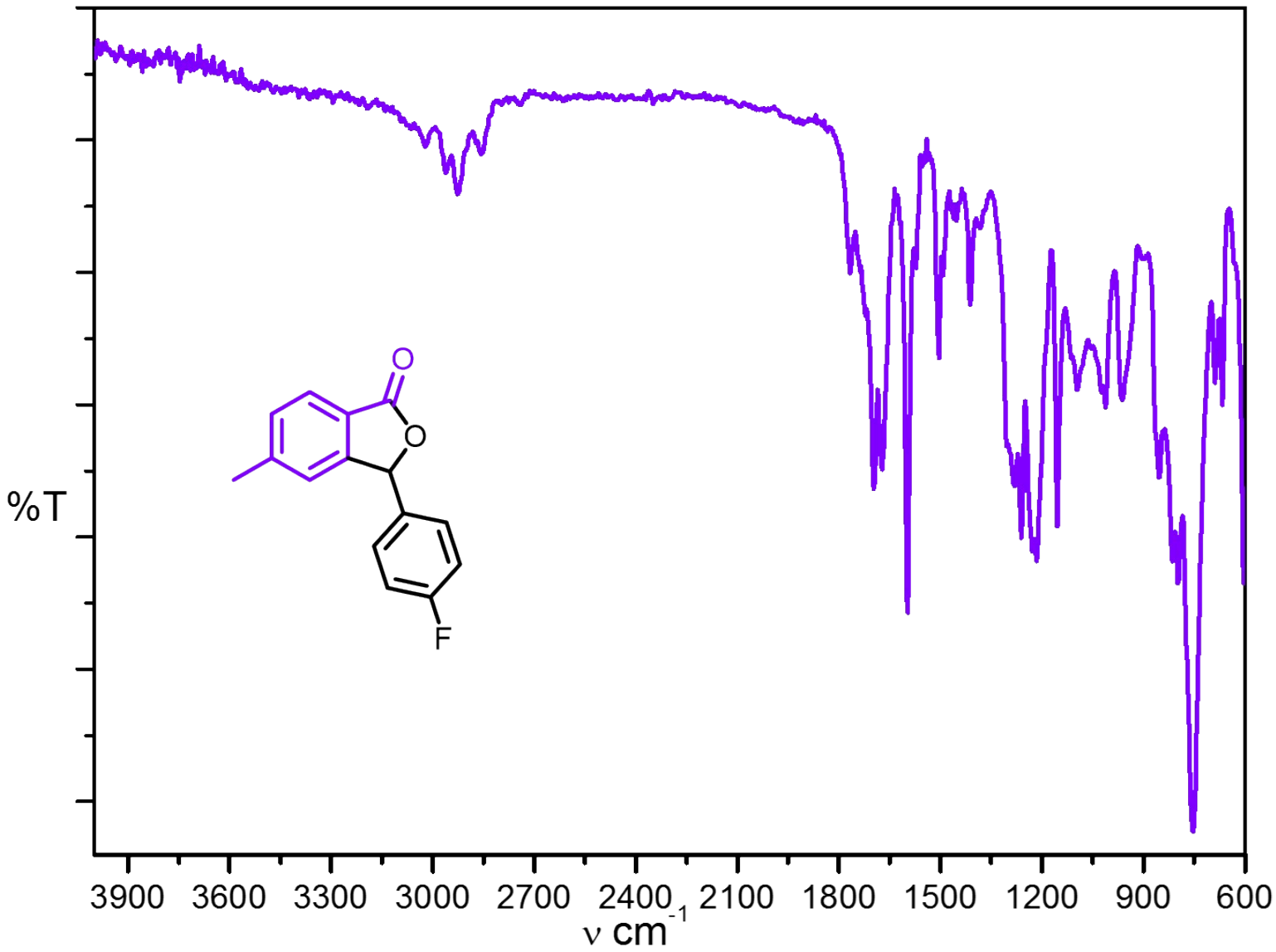


Figure S102. IR spectra of 3-(4-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3i**).

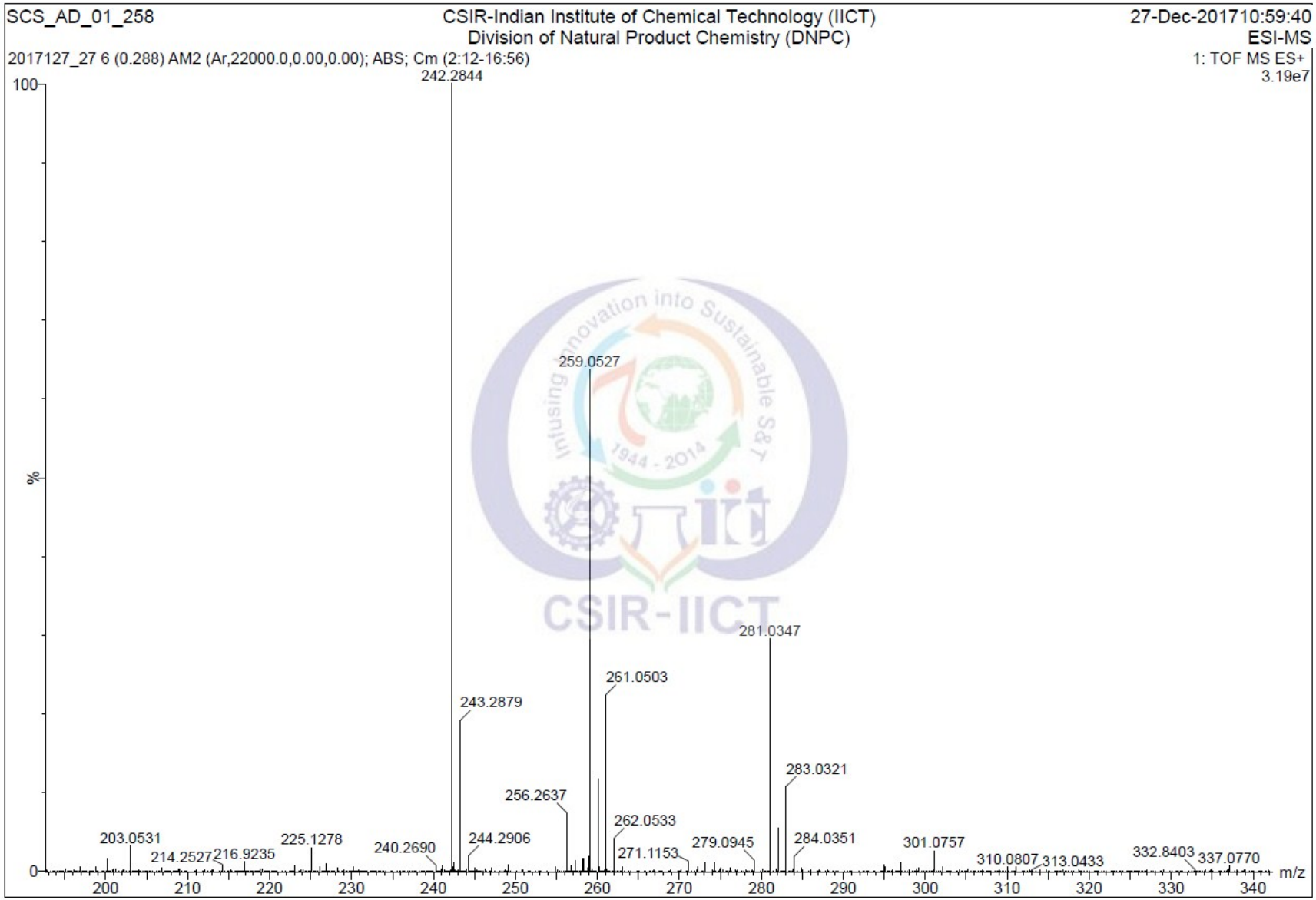


Figure S103. HRMS spctra of 3-(4-flurophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3i**).

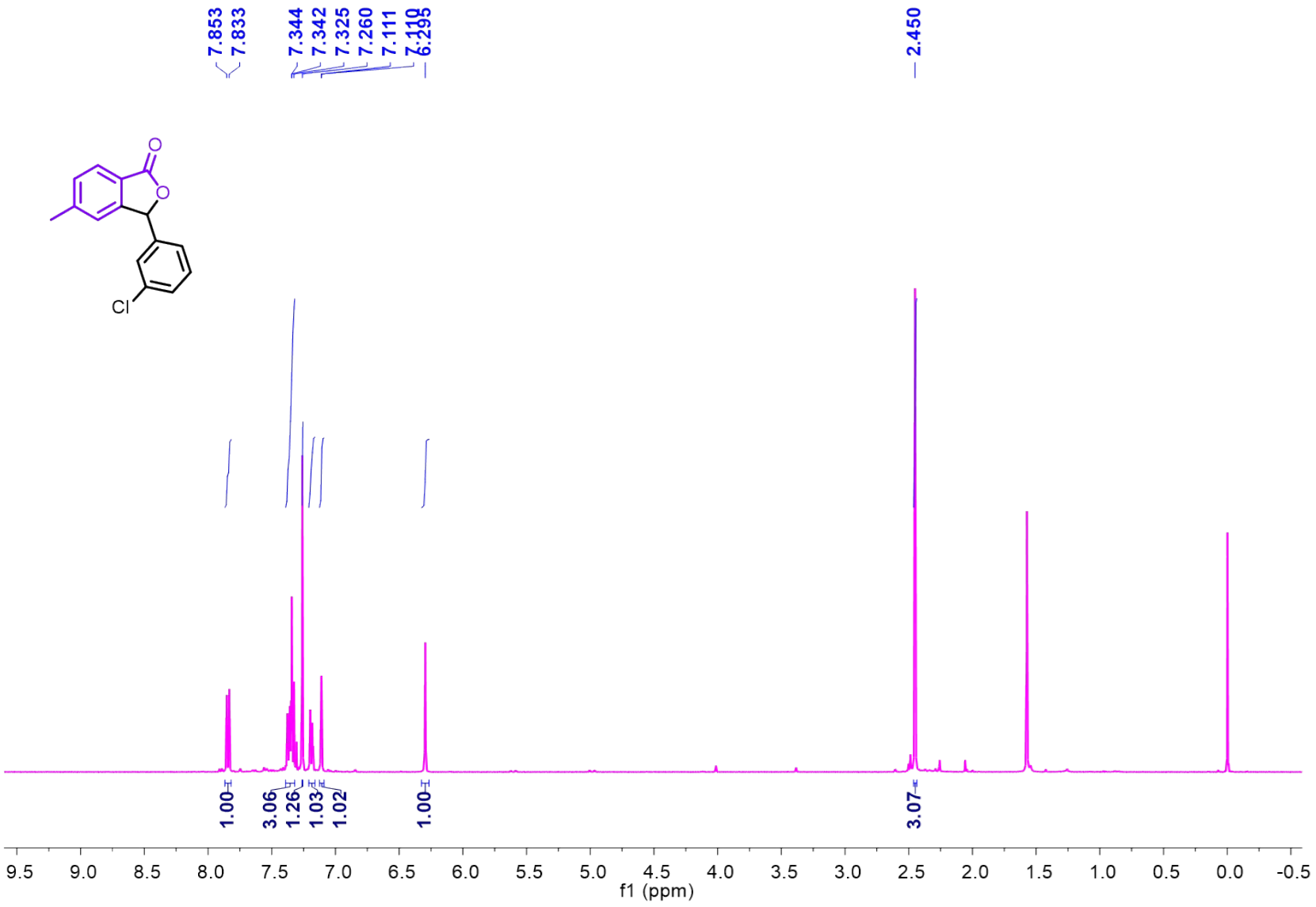


Figure S104. ^{1}H NMR spectra of 3-(3-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3j**) in $CDCl_3$.

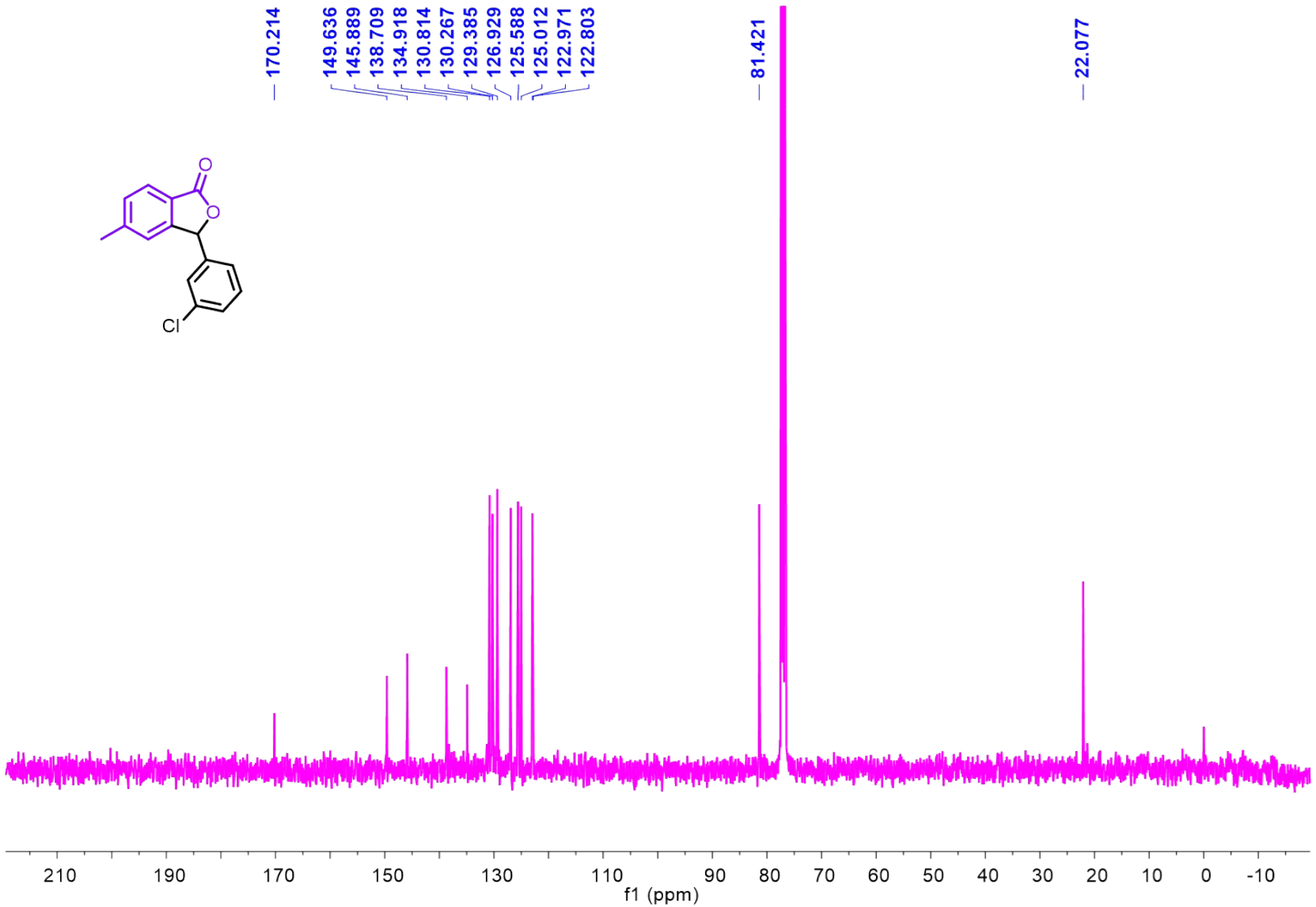


Figure S105. ^{13}C NMR spectra of 3-(3-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3j**) in $CDCl_3$.

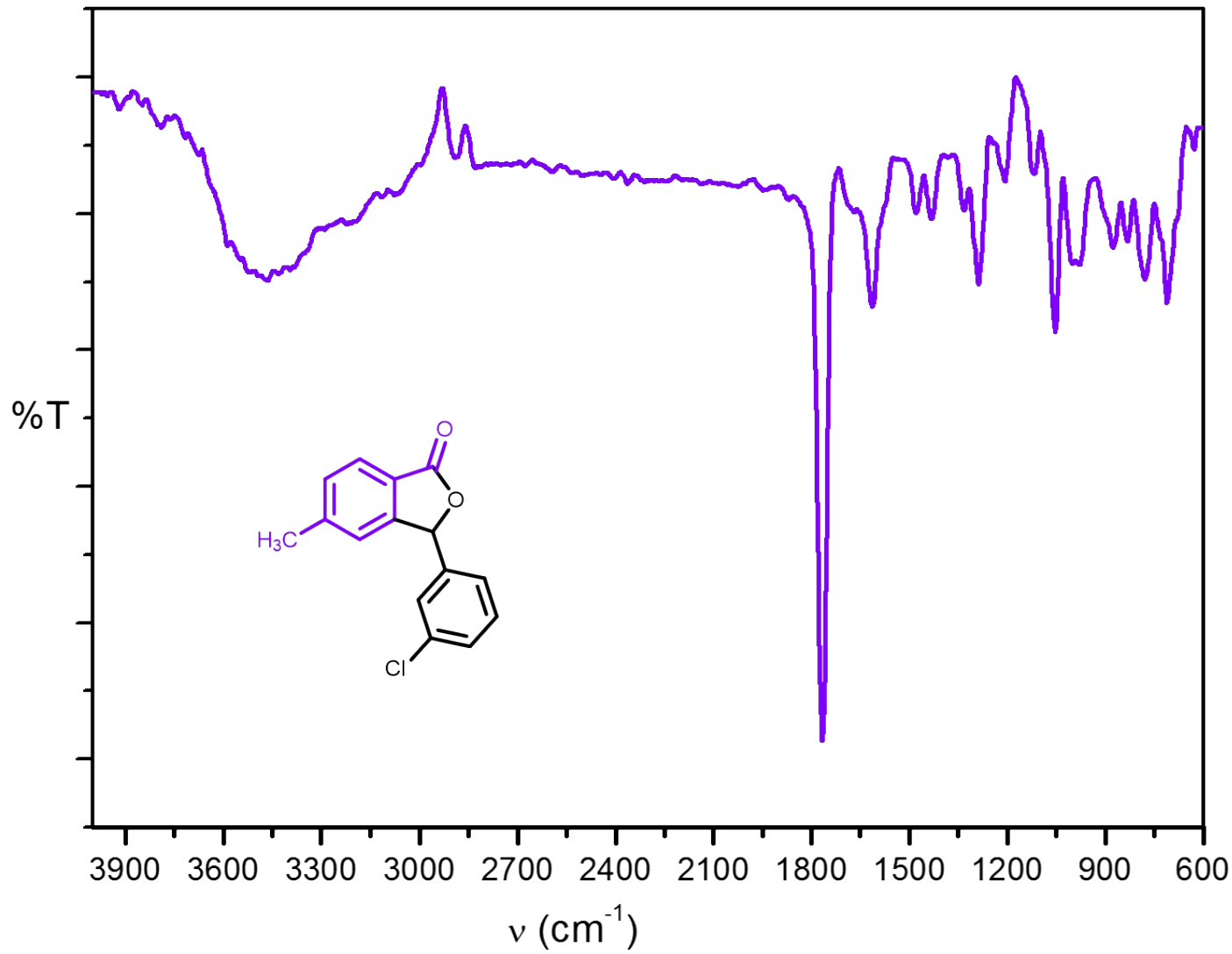


Figure S106. IR spectra of 3-(3-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3j**).

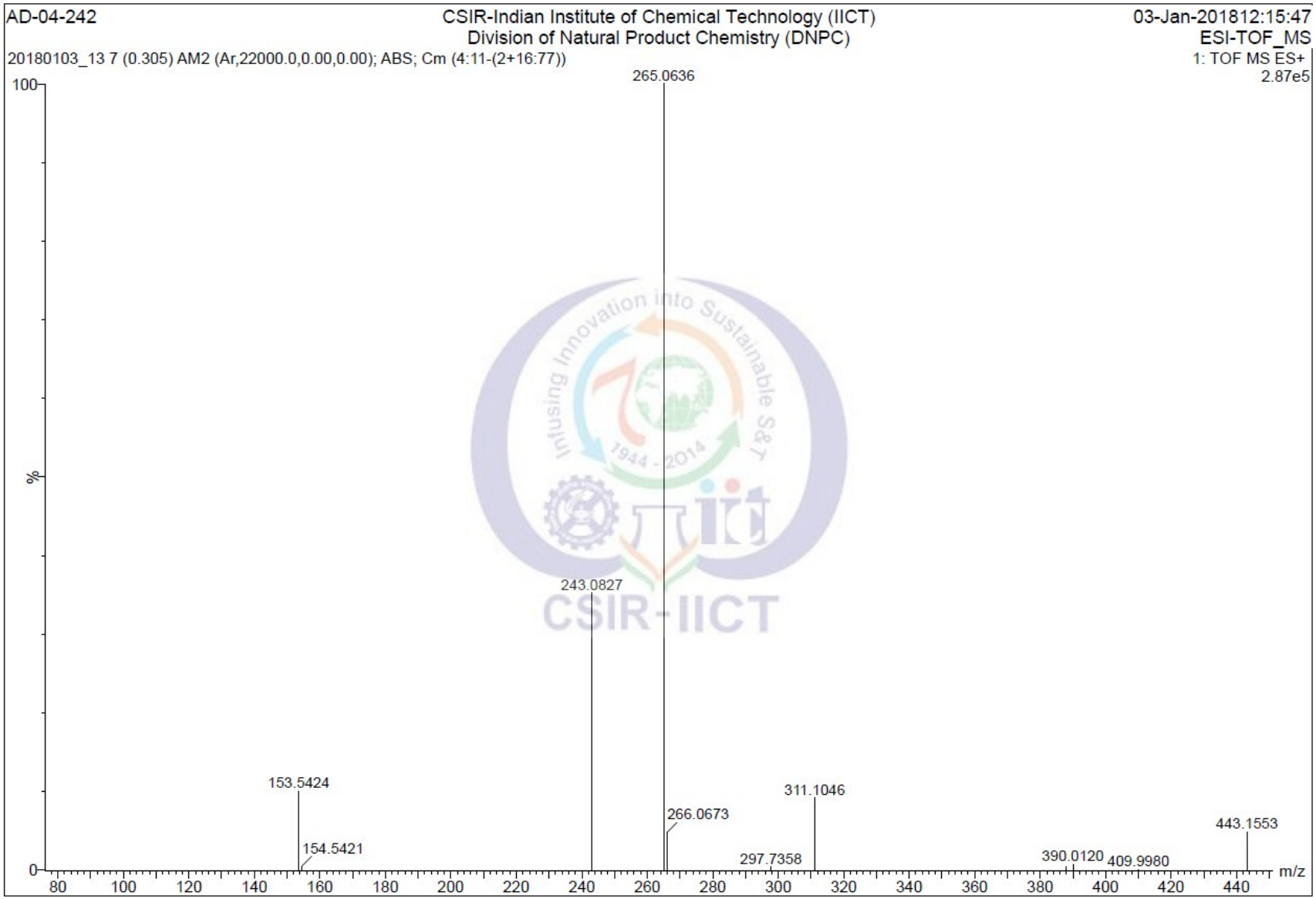


Figure S107. HRMS spctra of 3-(3-chlorophenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3j**).

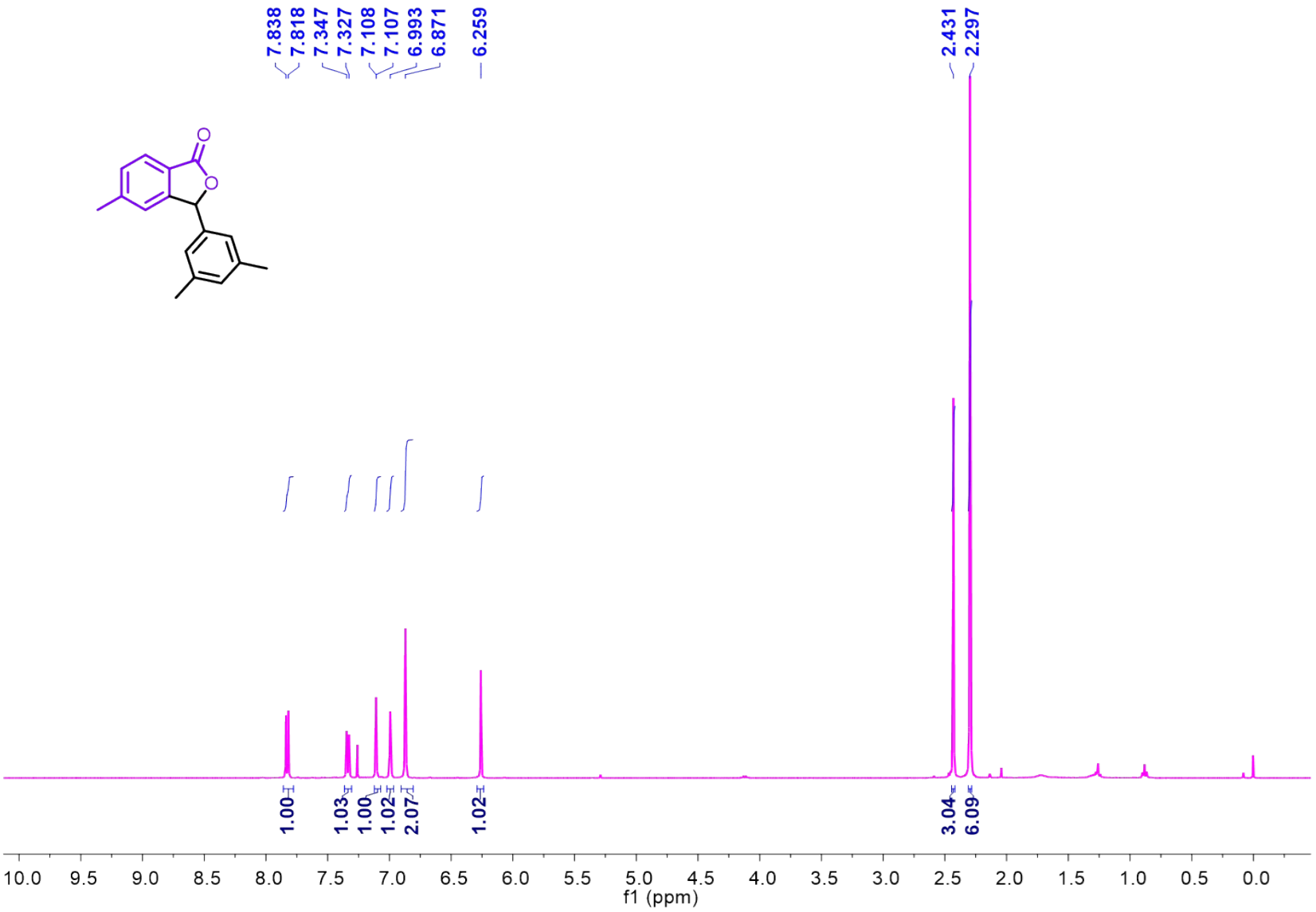


Figure S108.[1]H NMR spectra of 3-(3, 5-dimethylphenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3k**) in $CDCl_3$.

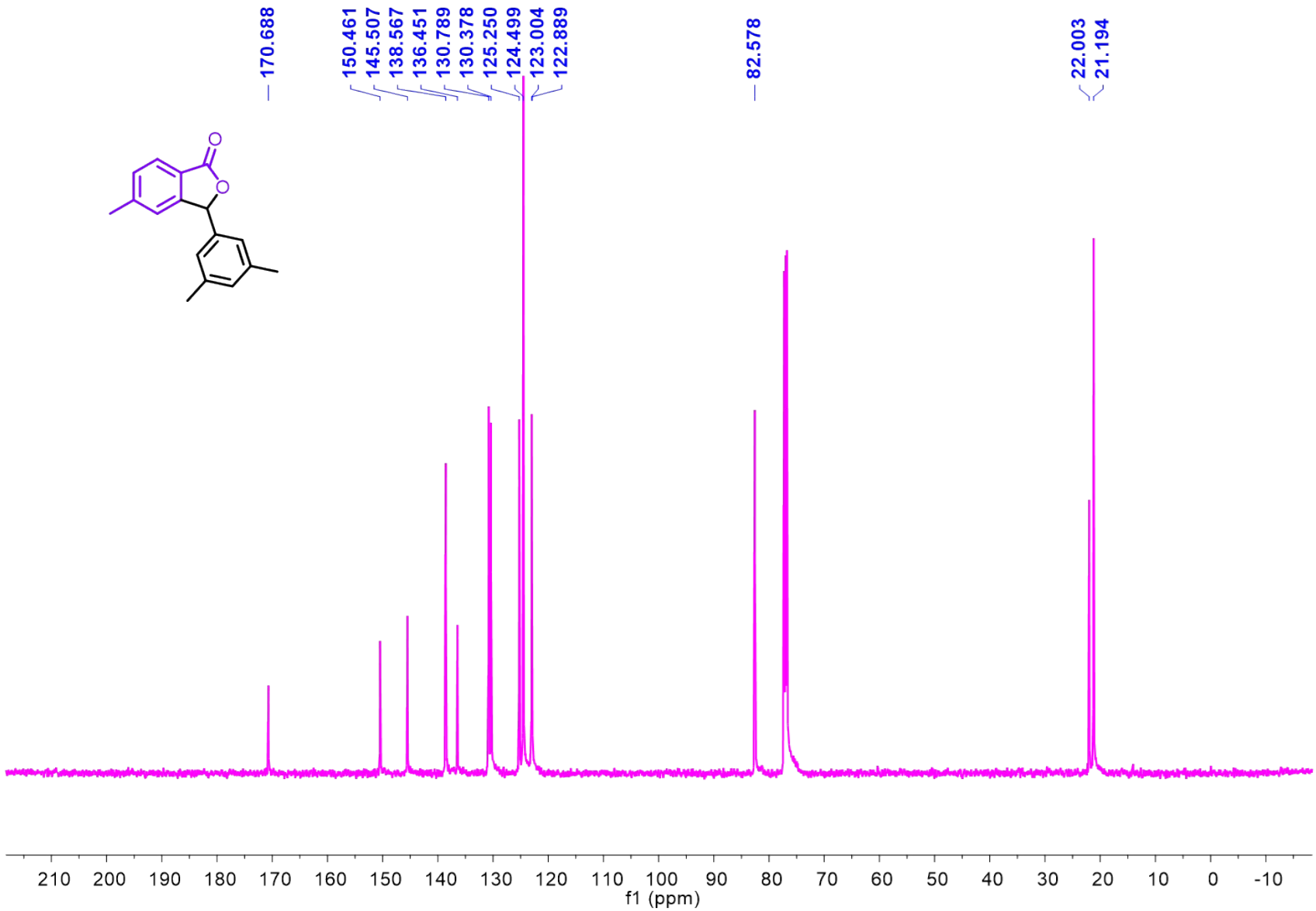


Figure S109. ^{13}C NMR spectra of 3-(3, 5-dimethylphenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3k**) in $CDCl_3$.

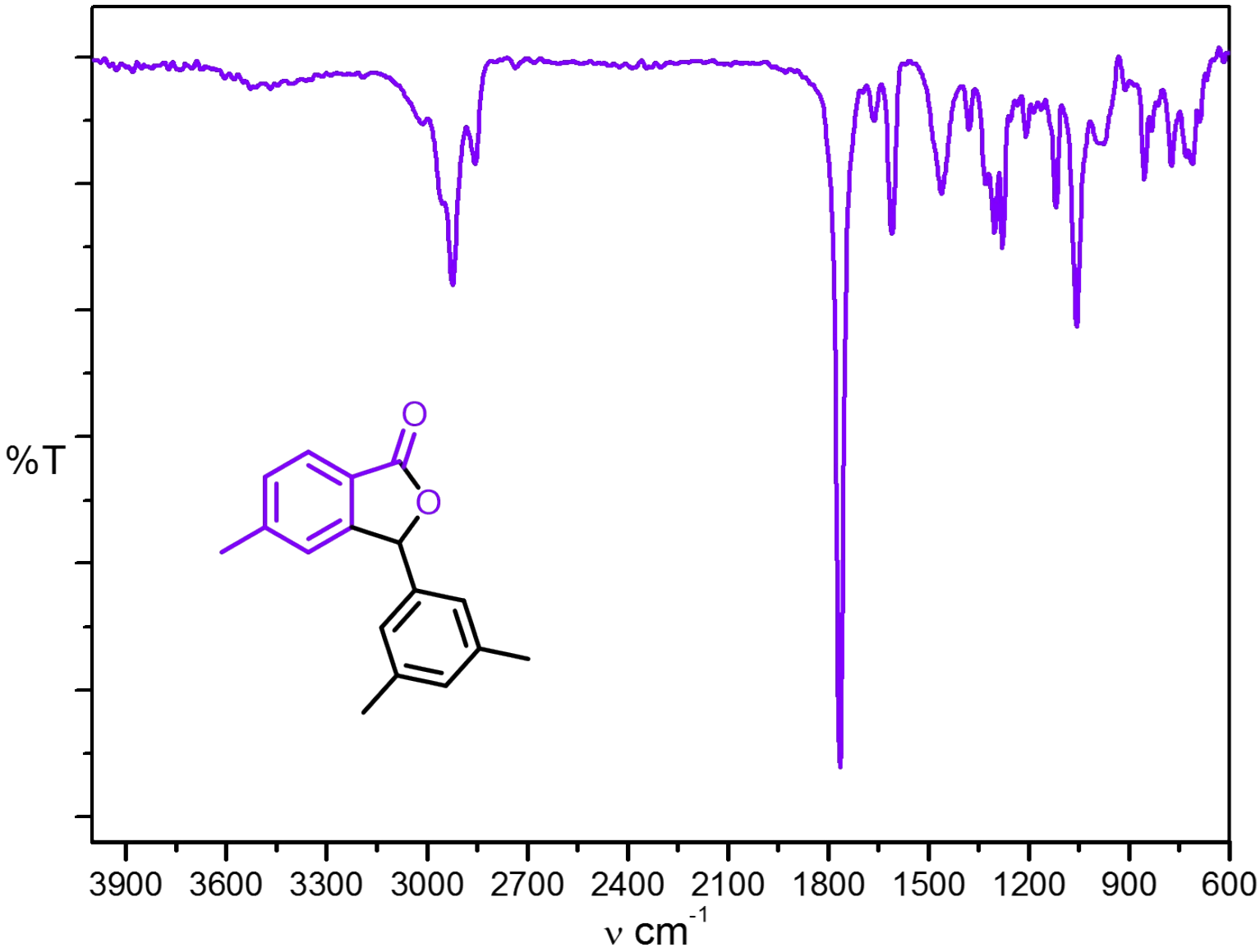


Figure S110. IR spectra of 3-(3, 5-dimethylphenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3k**).

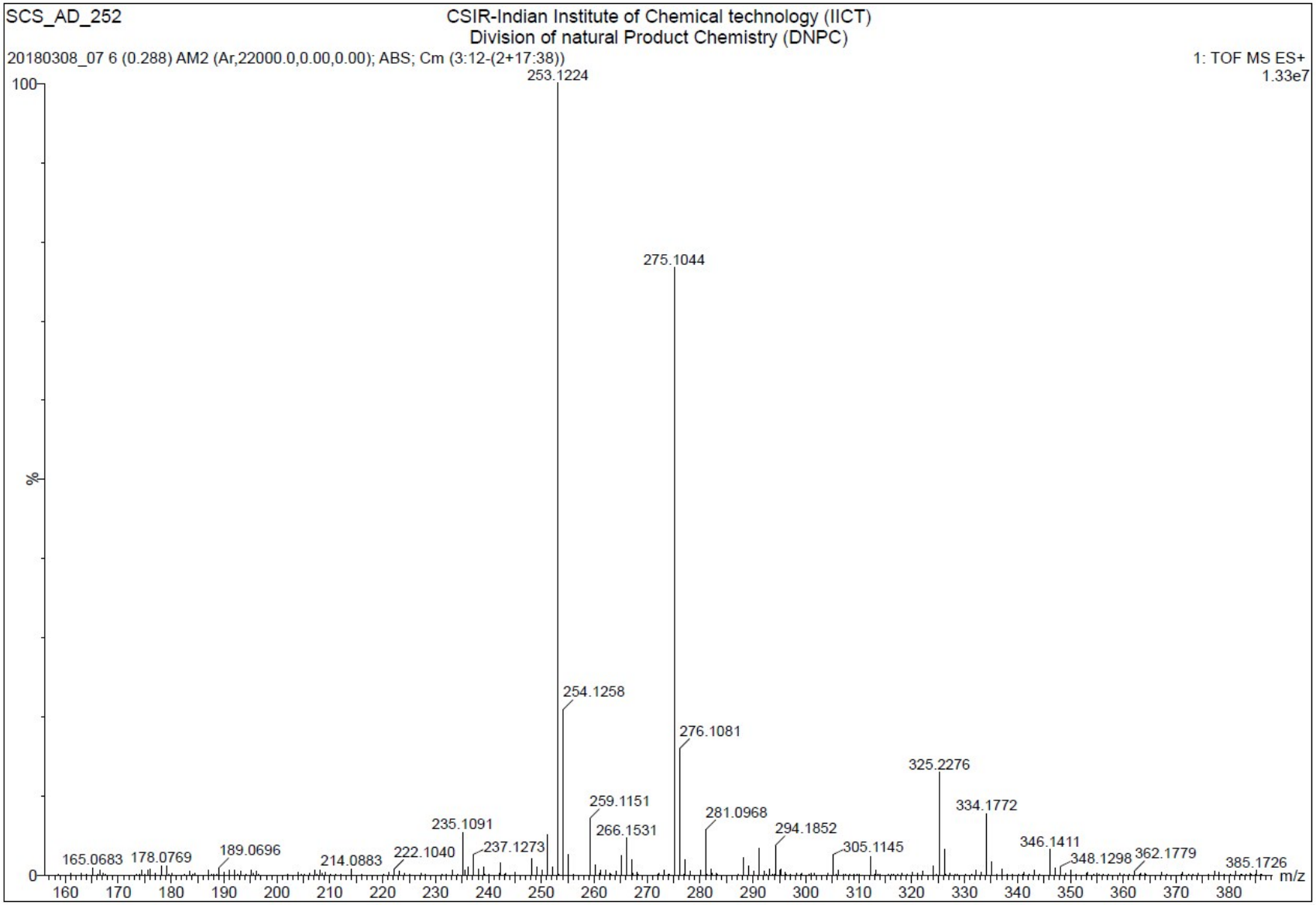
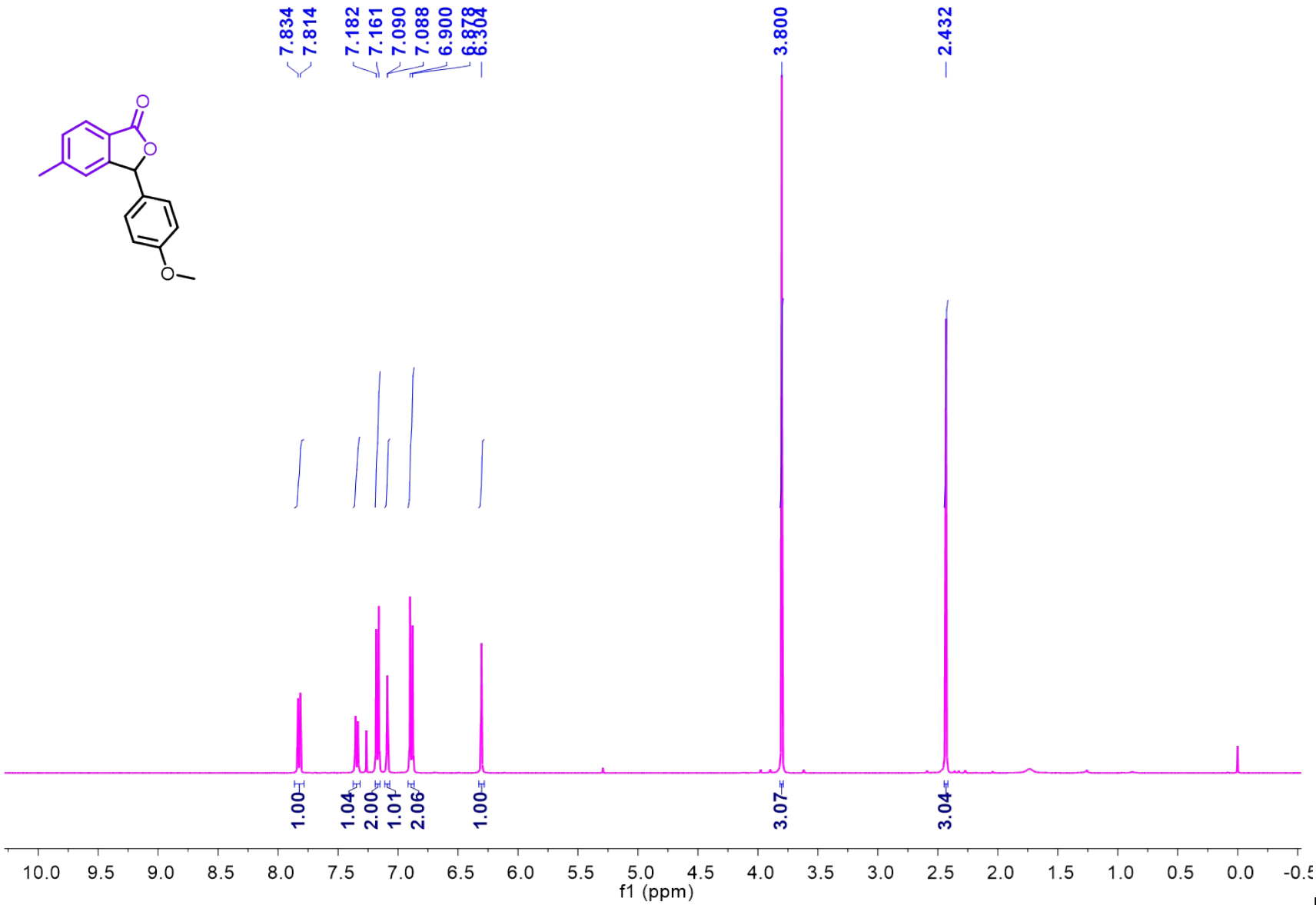


Figure S111. HRMS spctra of 3-(3, 5-dimethylphenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3k**).


7.834
7.814
7.182
7.161
7.090
7.088
6.900
6.878
6.304
3.800
2.432
1.00
1.04
2.00
1.01
2.06
1.00
3.07
3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

Figu

re S112. ^{1}H NMR spectra of 3-(4-methoxyphenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3l**) in $CDCl_3$.

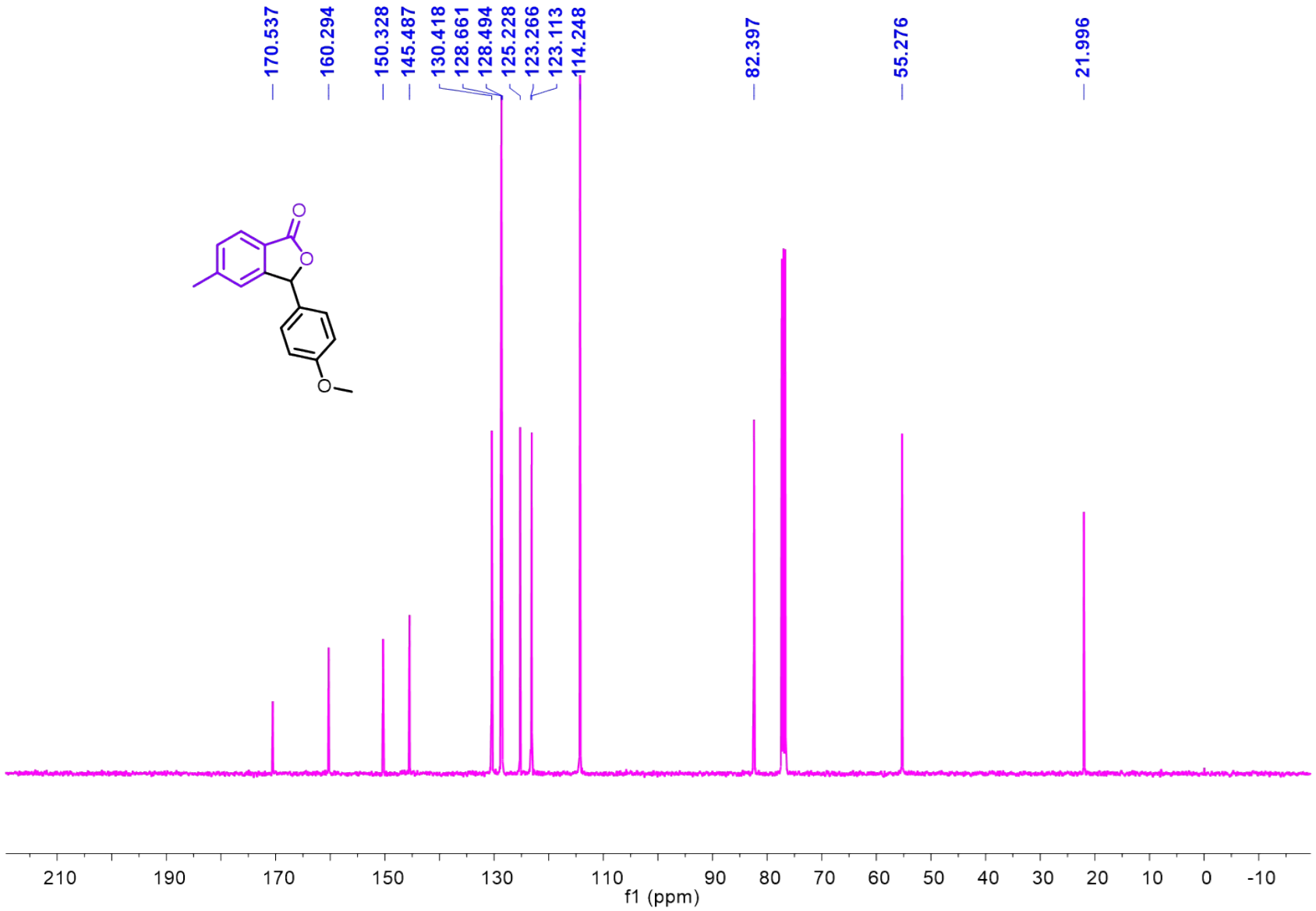


Figure S113. ^{13}C NMR spectra of 3-(4-methoxyphenyl)-5-methyliso-benzofuran-1-(3*H*)-one (**3l**) in $CDCl_3$.

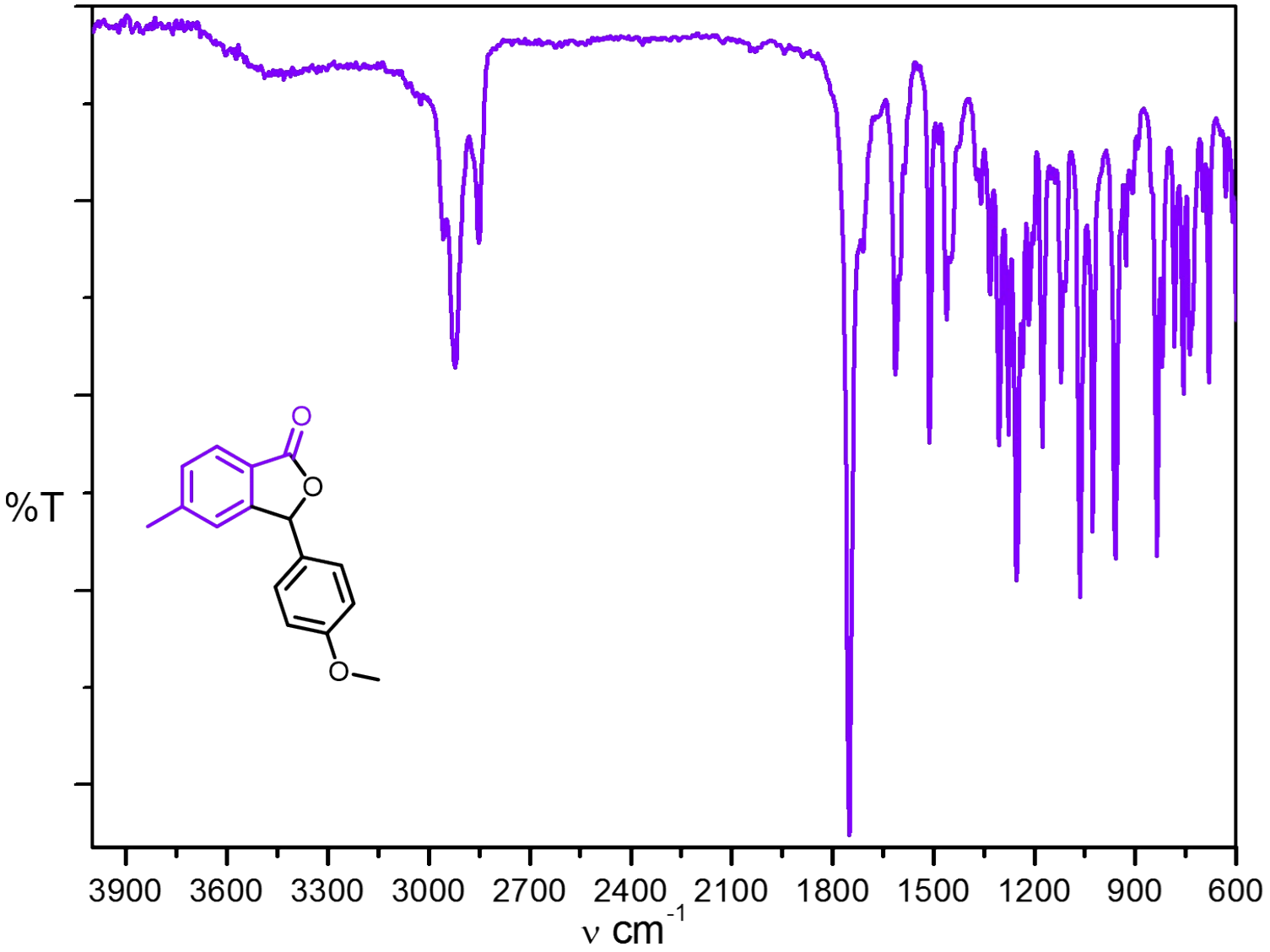


Figure S114. IR spectra of 3-(4-methoxyphenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3l**).

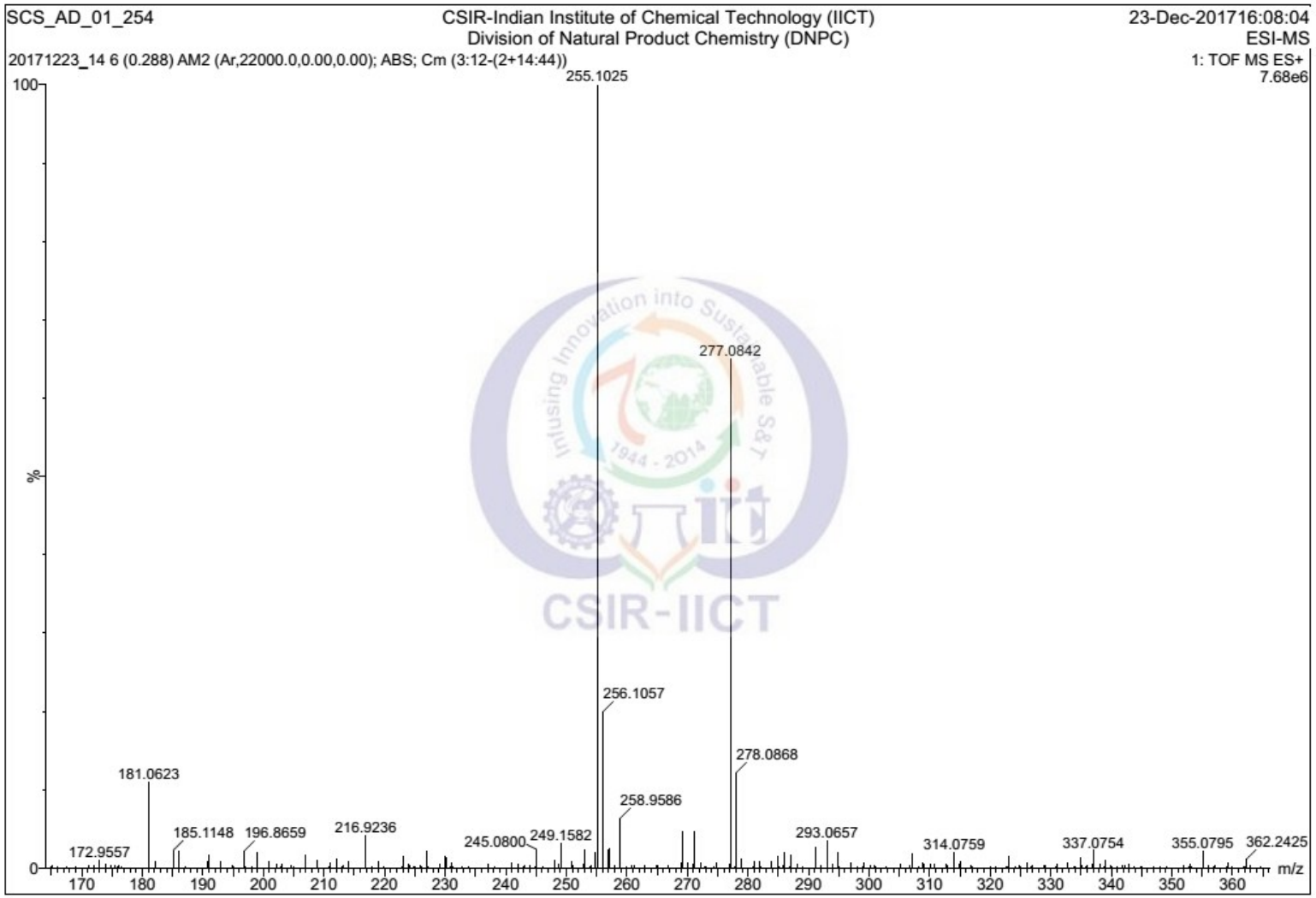


Figure 115. HRMS spctra of 3-(4-methoxyphenyl)-5-methylisobenzofuran-1-(3*H*)-one (**3l**).

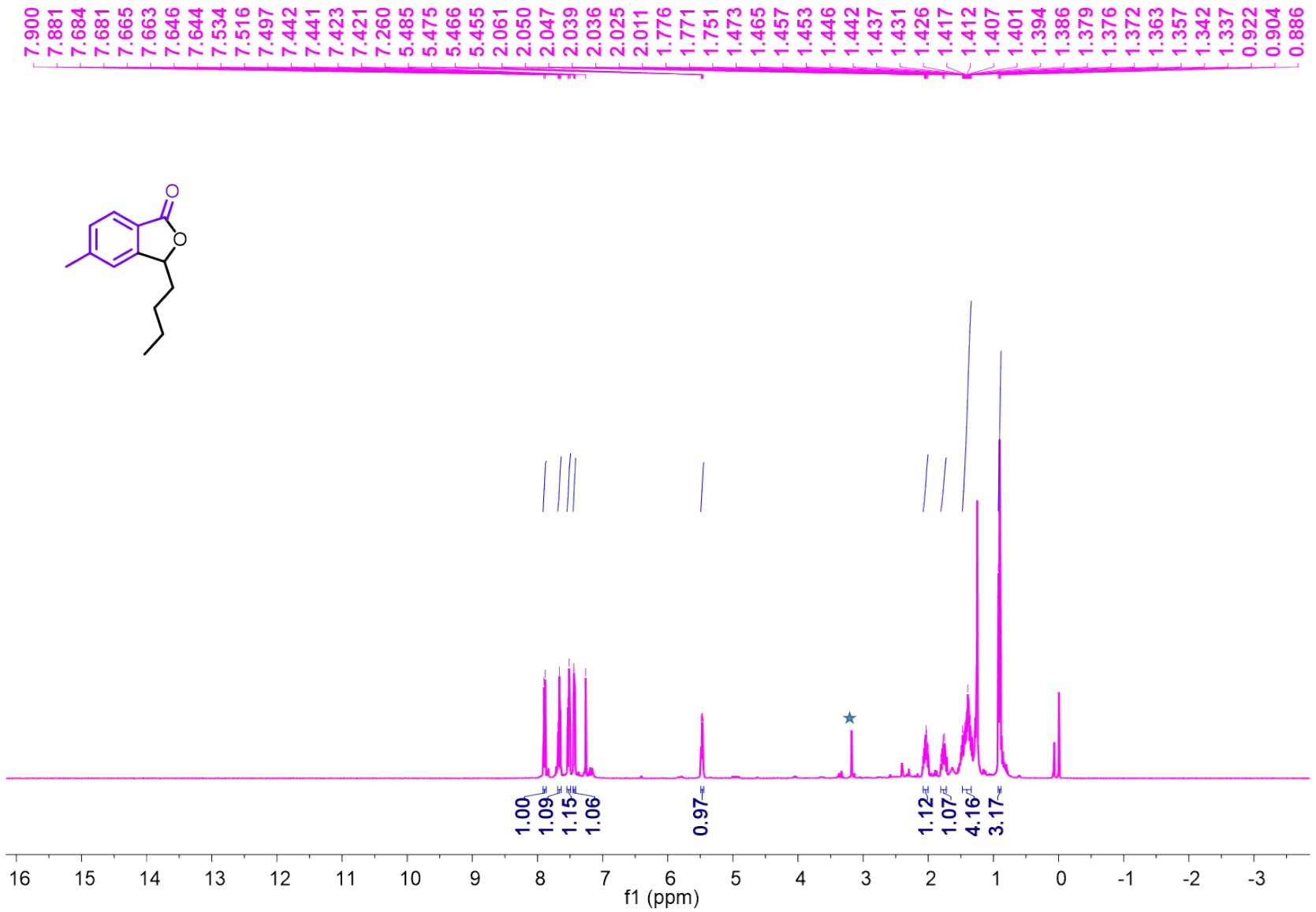


Figure S116. ^{1}H NMR spectra of 3-butylisobenzofuran-1(3H)-one (**3m**) in $CDCl_3$ (* Solvent impurity).

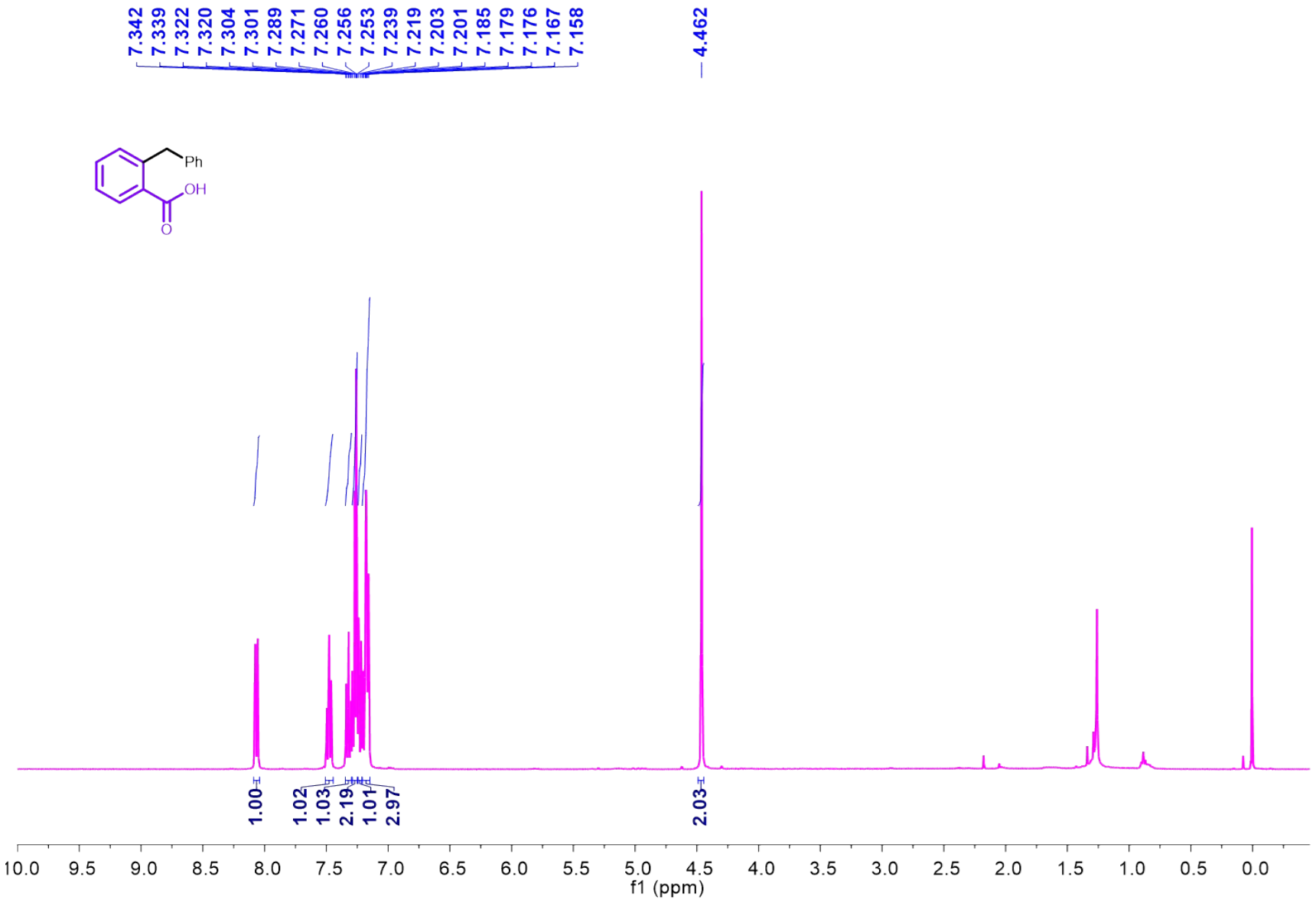


Figure S117. ^{1}H NMR spectra of 2-benzylbenzoic acid (**5a**) in $CDCl_3$.

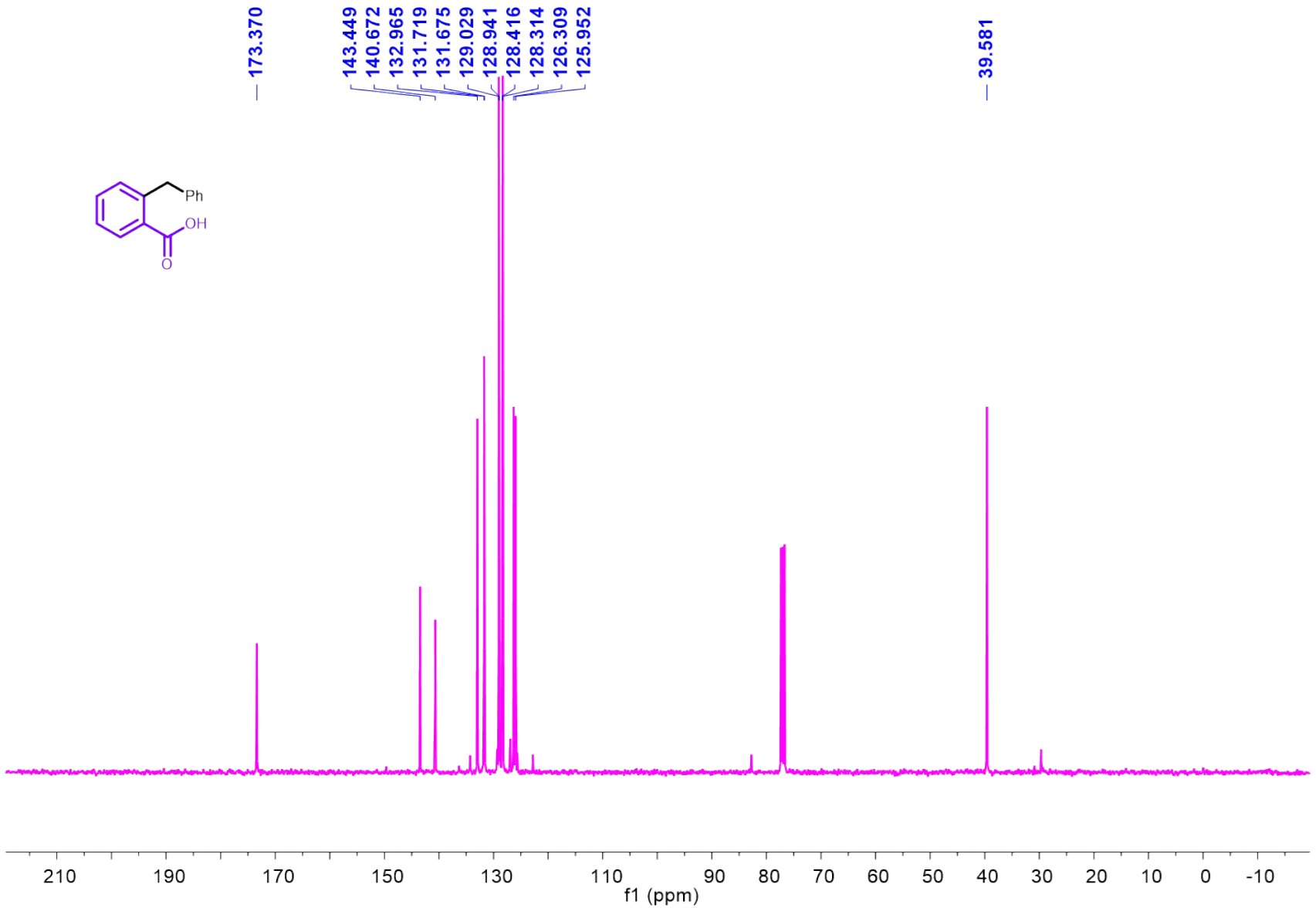


Figure S118.[13]C NMR spectra of 2-benzylbenzoic acid (**5a**) in $CDCl_3$.

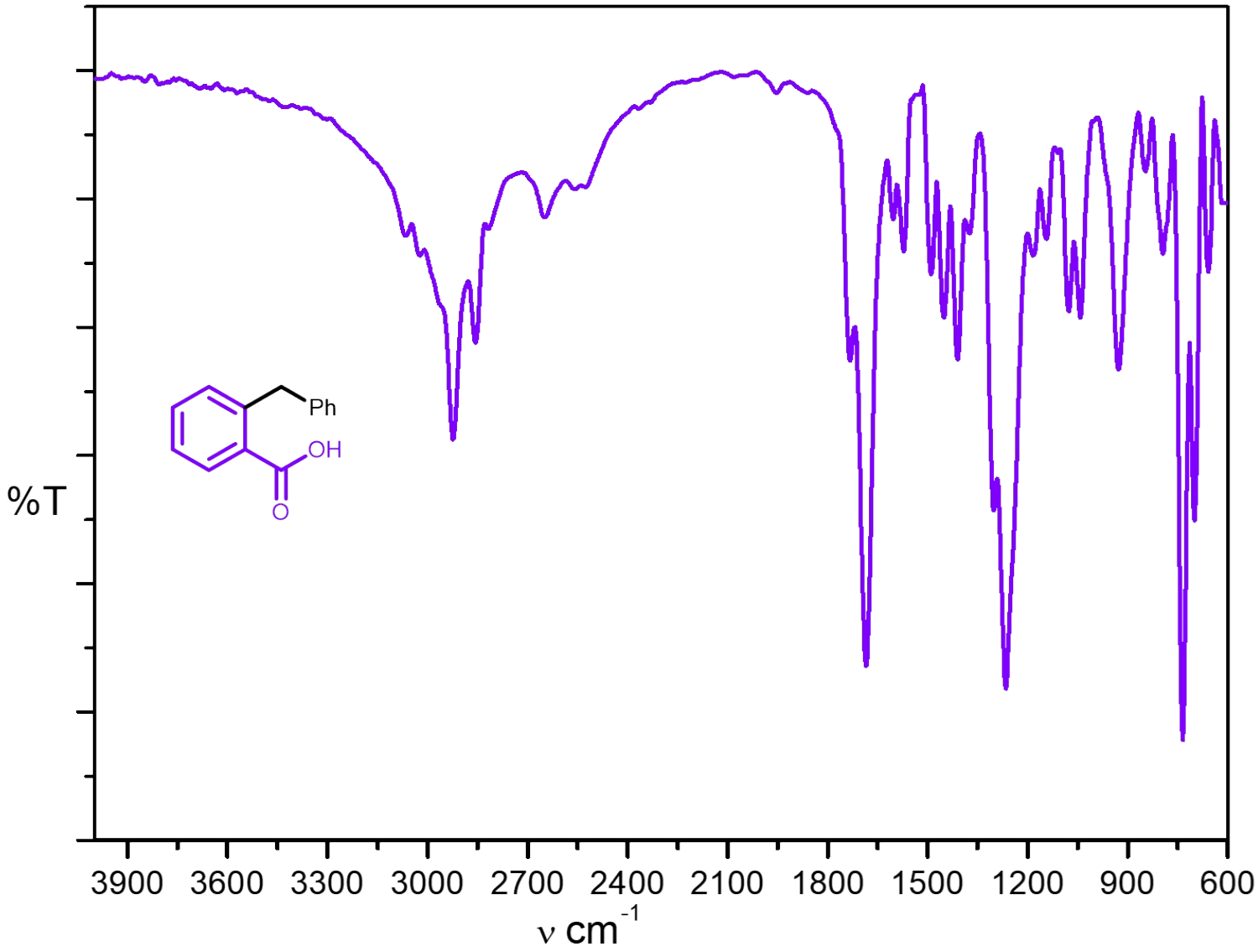


Figure S119. IR spctra of 2-benzylbenzoic acid (**5a**).

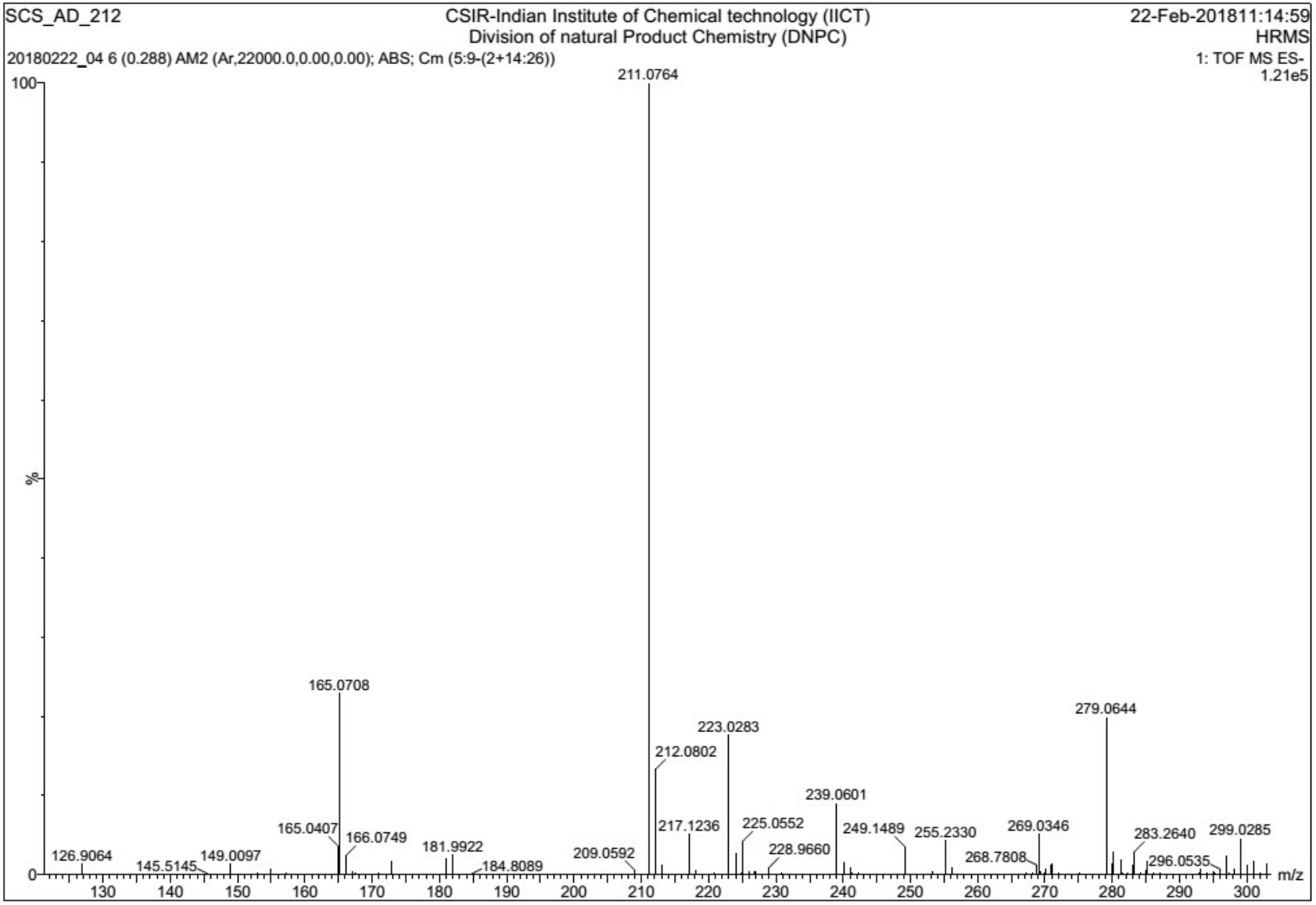


Figure S120. HRMS spctra of 2-benzylbenzoic acid (**5a**).

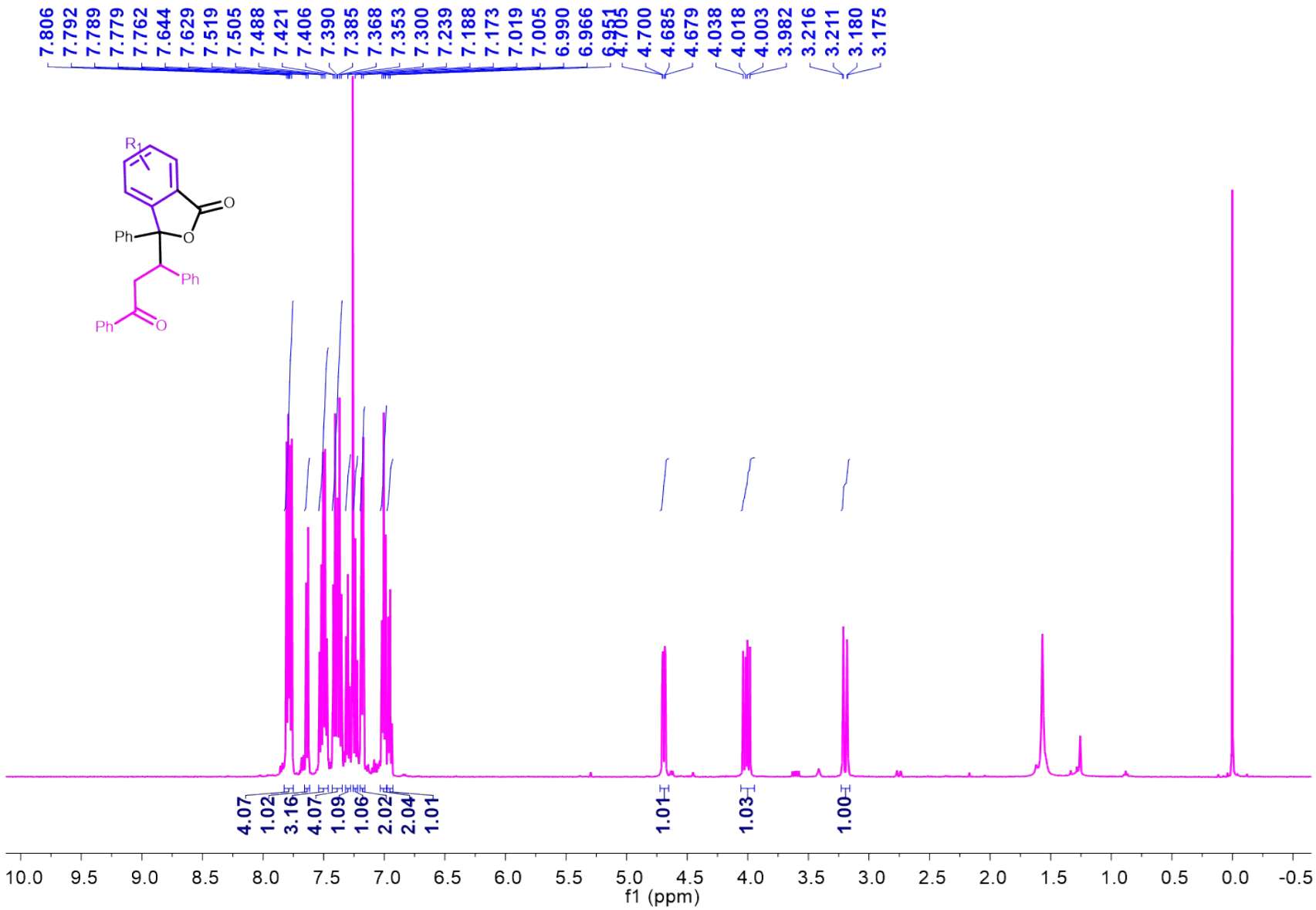


Figure S121. ^{1}H NMR spectra of 3-(3-oxo-1,3-diphenylpropyl)-3-phenylisobenzofuran-1(3H)-one (**6a**) in $CDCl_3$.

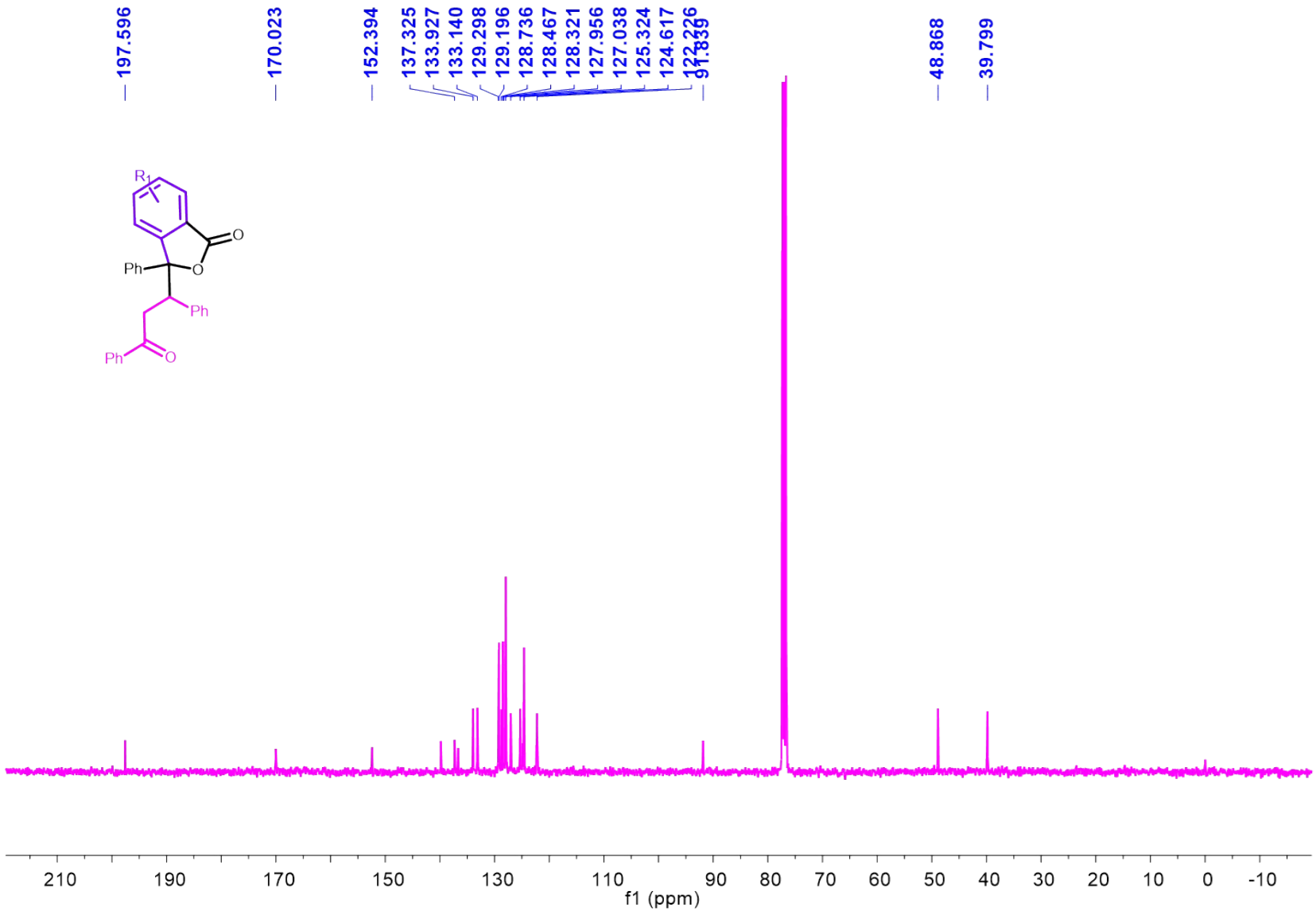


Figure S122.[13]C NMR spectra of 3-(3-oxo-1,3-diphenylpropyl)-3-phenylisobenzofuran-1(3H)-one (**6a**) in $CDCl_3$.

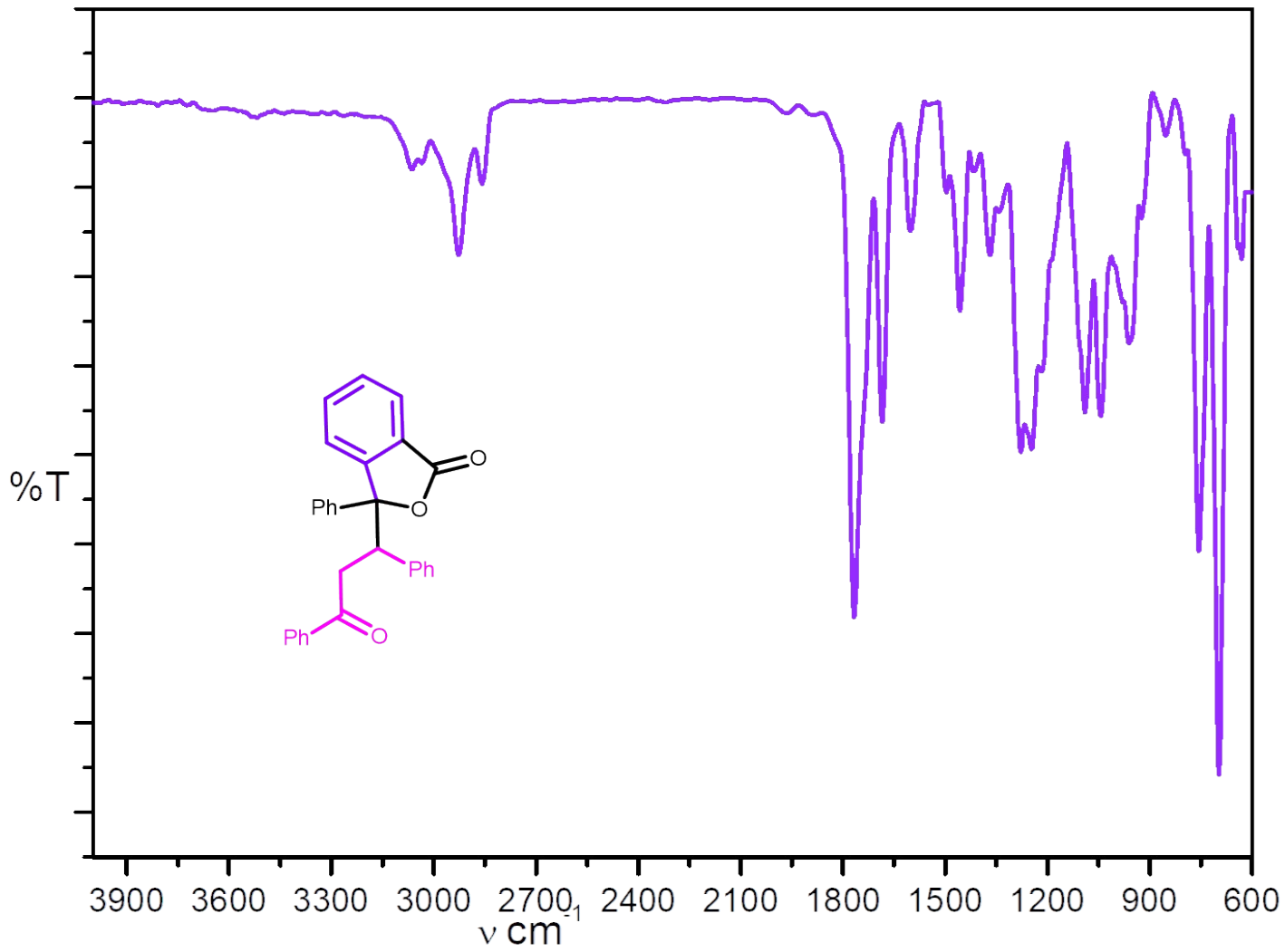


Figure S123. IR spctra of 3-(3-oxo-1,3-diphenylpropyl)-3-phenylisobenzofuran-1(3H)-one (**6a**).

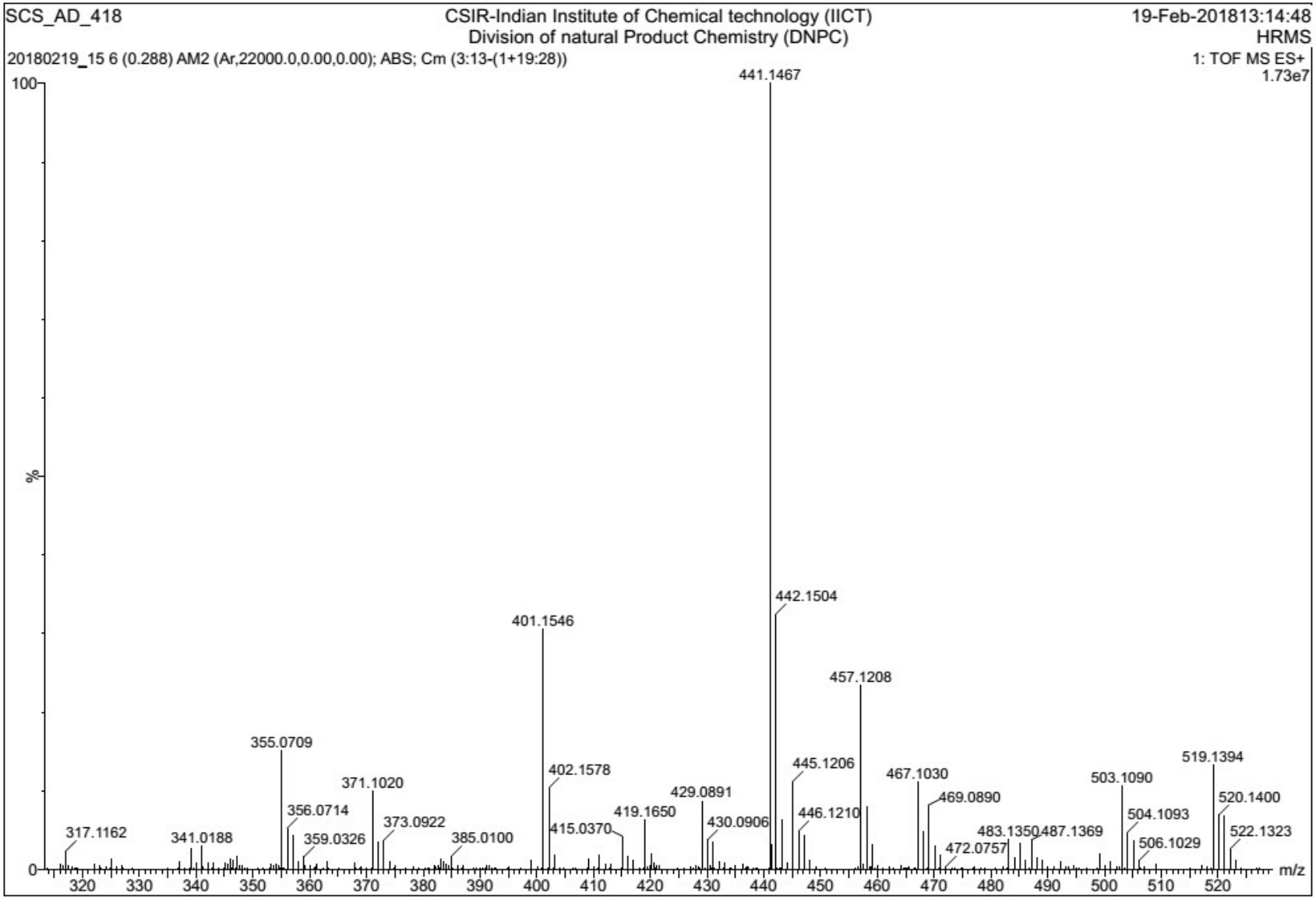
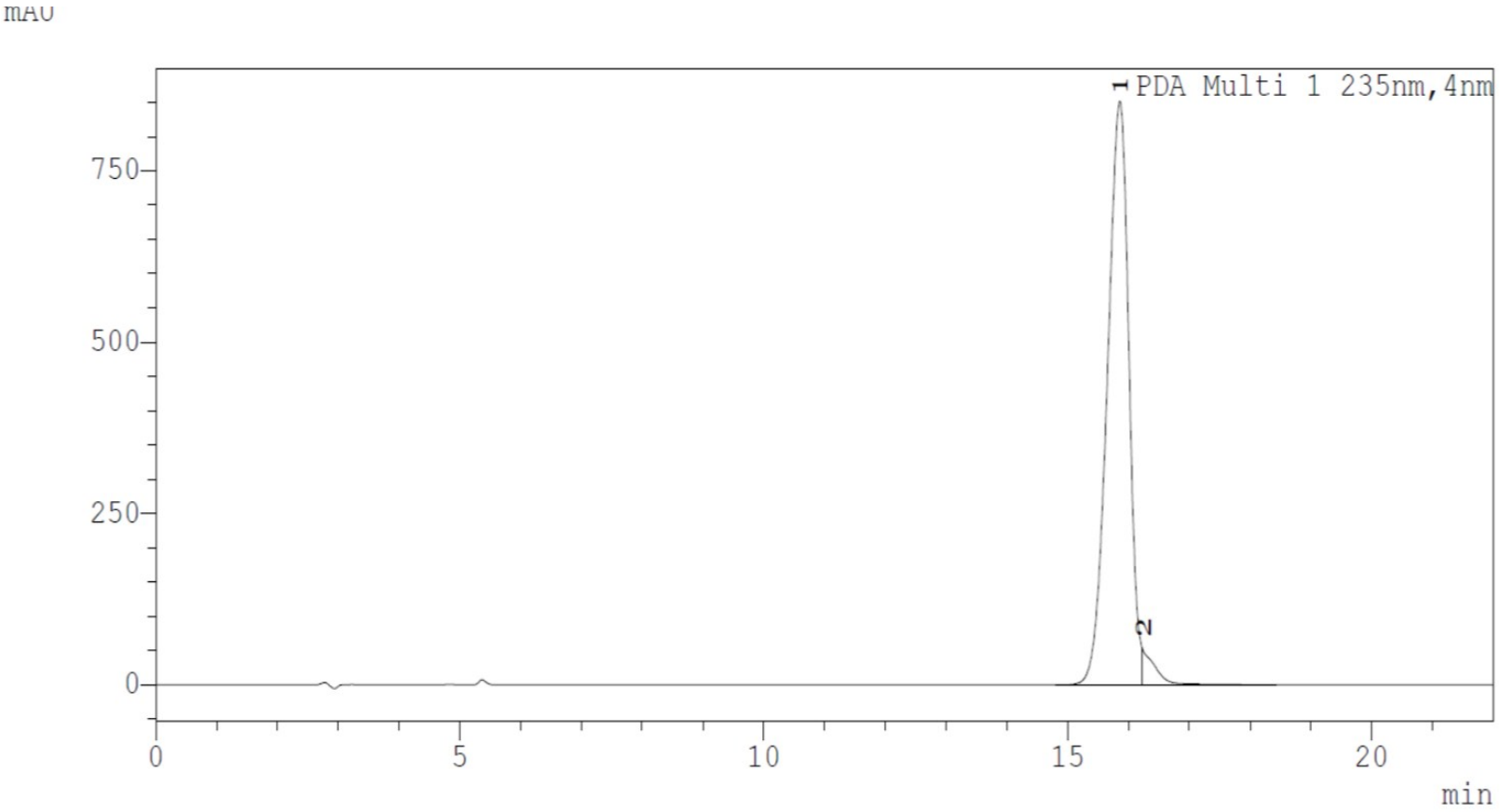


Figure S124. HRMS spctra of 3-(3-oxo-1,3-diphenylpropyl)-3-phenylisobenzofuran-1(3H)-one (**6a**).



Peak Table

PDA Ch1 235nm

Peak#	Ret. Time	Peak Start	Peak End	Area	Area%
1	15.858	14.805	16.224	#########	96.421
2	16.240	16.224	18.432	773380	3.579
Total				#########	100.000

Figure S125. HPLC of 3-(3-oxo-1,3-diphenylpropyl)-3-phenylisobenzofuran-1(3H)-one (**6a**) in $CDCl_3$.