Electronic Supplementary Information

Concise Synthesis of Tetrasubstituted Furan-Based Schiff Base Compounds *via* One-pot Method

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1. General Information

1.1. Conventional Reagents and Equipment

The determination of melting point (m.p.) was completed on the X-5 digital melting point instrument without correction. The flash column chromatography operation uses 200-300 mesh silica gel. The ^{1}H and ^{13}C NMR spectra were obtained by a 600 MHz Bruker spectrometer. High resolution mass spectrometry (HR-MS) was recorded on a Thermo Fisher Technologies (USA) MAT95XP high resolution mass spectrometer. The single crystal structure was determined by Agilent Gemini E-type X-ray single crystal diffractometer with Mo as the target. The BSC-1 model product produced by Suzhou Antai Air Technology Co., Ltd.is selected for the biological safety cabinet.

All reagents and solvents are commercially available and do not require further purification. α-hydroxy ketones are synthesized from various aldehydes according to the method reported in literature [1].

1.2. Activation of Strain and Preparation of Bacterial Suspension

According to the method of reference [2], *Escherichia coli* ATCC 43894 and *Staphylococcus aureus* ATCC 25923 frozen at -80 °C were inoculated on LB agar plate by streak plate method to disperse them. After that, these plates were placed in a biochemical incubator at 37 °C for 24 hours. A single colony was picked from agar plate with inoculation ring, inoculated into 2 mL liquid LB broth, and cultured for 12 hours. Then, 50 μL of bacterial suspension was diluted at a ratio of 1:100 for further expansion of culture until the strain reached the logarithmic growth phase.

1.3. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) Assays

According to the literature [3, 4], the bacterial suspension cultured to the logarithmic phase was diluted with LB broth to OD600 = 0.1 for the subsequent use. Then, 4 mg of the tested compound was dissolved to prepare a test stock solution with a concentration of 2 mg/mL. In 96-well plates, LB

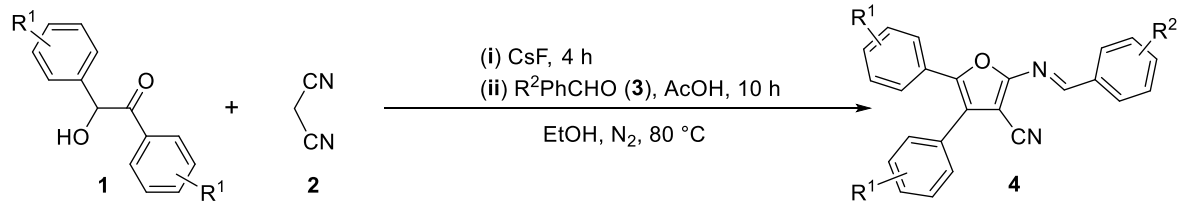
broth was used to serially dilute the sample stock solution to a total volume of 180 μL to obtain the desired concentration range. Subsequently, an equal volume (20 μL) of diluted bacterial suspension was added to each well, and the final concentrations of the compounds were 1000, 500, 250, 125, 62.5, 31.25 and 15.625 μg/mL, respectively.

Subsequently, the bacterial suspensions were incubated in a 37 °C thermostatic incubator (*Escherichia coli* for 18 hours, *Staphylococcus aureus* for 18-20 hours). A bacterial suspension without the compound served as the negative control, while LB broth without bacteria and compound served as the positive control. Each concentration was tested in triplicate, with three technical replicates, to accurately determine the MIC for each bacterial strain.

The minimum inhibitory concentration (MIC) refers to the minimum concentration at which the compound can inhibit bacterial growth without visible bacteria.

2. Experimental Part

2.1. Experimental Procedure for Compounds 4a - 4am



Scheme S1. The synthetic route for compounds **4**

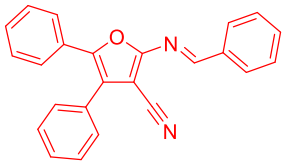
As **Scheme S1**, in a 50 mL round-bottom flask, *α*-hydroxy ketone **1**, malononitrile **2**, and cesium fluoride were sequentially added. Subsequently, 5 mL of ethanol was added as the solvent. Then, under the atmosphere of nitrogen, the mixture was refluxed at 80 ºC for 4 hours.

After the initial reaction reaches 4 hours, the reaction mixture is stirred, and the second-stage aldehyde precursor and acetic acid are promptly added. The system is degassed and purged with nitrogen gas, then maintained at 80 °C for an additional 10 hours to ensure complete conversion.

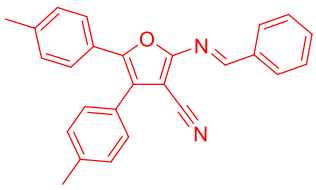
Upon completion, the solvent ethanol was removed *via* rotary evaporation, and the pH of the aqueous phase of the residual was adjusted to neutrality. The organic layer was subjected to three successive extractions with ethyl acetate (3×15 mL). Then, the combined organic extracts were dried over anhydrous sodium sulfate.

After filtration, the obtained organic layer was concentrated under the reduced pressure to afford the crude product. Finally, the further purification was subsequently performed by using column chromatography with an eluent system of petroleum ether/ethyl acetate (30:1 v/v), yielding the target compounds **4a** - **4am**.

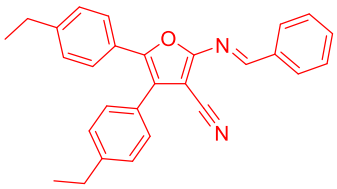
2.2. Characterization Data for All Products 4a - 4am



(*E*)-2-Benzylideneamino-4,5-diphenylfuran-3-carbonitrile (**4a**), yellow solid (60.6 mg, yield 87%), m.p. 158.7-160.3 ºC; ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm: 9.16 (*s*, 1H, -N=CH-), 8.11-8.03 (*m*, 2H, ArH), 7.65-7.52 (*m*, 8H, ArH), 7.50-7.38 (*m*, 5H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm: 162.6, 159.6, 145.9, 135.5, 133.8, 130.4, 130.2, 129.8, 129.7, 129.6, 129.5, 129.4, 128.9, 126.6, 124.0, 113.7, 94.2; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{17}N_2O$ $[M+H]^+$: 349.1335, Found: 349.1331.

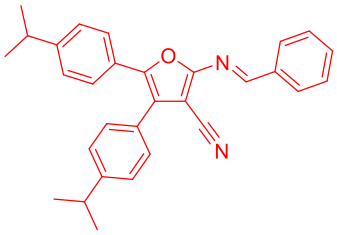


(*E*)-2-Benzylideneamino-4,5-di-*p*-tolylfuran-3-carbonitrile (**4b**), yellow solid (60.2 mg, yield 80%), m.p. 172.6-174.3 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 9.12 (*s*, 1H, -N=CH-), 8.06 (*d*, J = 8.4 Hz, 2H, ArH), 7.65-7.57 (*m*, 3H, ArH), 7.43 (*d*, J = 8.4 Hz, 2H, ArH), 7.36-7.31 (*m*, 4H, ArH), 7.20 (*d*, J = 8.4 Hz, 2H, ArH), 2.38 (*s*, 3H, CH_3), 2.30 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 161.9, 159.3, 146.0, 139.4, 138.9, 135.5, 133.6, 130.3, 130.1, 129.9, 129.7, 129.3, 127.4, 126.5, 126.2, 123.3, 113.7, 94.2, 21.4; ESI-HRMS, *m/z*: Calcd for $C_{26}H_{21}N_2O$ $[M+H]^+$: 377.1648, Found: 377.1642.

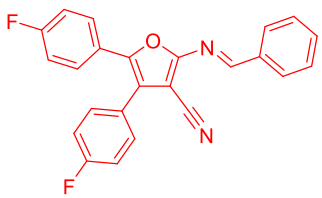


(*E*)-2-Benzylideneamino-4,5-bis(4-ethylphenyl)furan-3-carbonitrile (**4c**), yellow solid (56.6 mg, yield 70%), m.p. 180.4-182.3 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.90 (*s*, 1H, -N=CH-), 8.01 (*d*, J = 8.4 Hz, 2H, ArH), 7.52-7.48 (*m*, 2H, ArH), 7.45 (*d*, J = 8.4 Hz, 2H, ArH), 7.40 (*d*, J = 7.8 Hz,

2H, ArH), 7.30-7.25 (*m*, 3H, ArH), 7.15 (*d*, *J* = 7.8 Hz, 2H, ArH), 2.71 (*q*, *J* = 7.8 Hz, 2H, CH_2), 2.65 (*q*, *J* = 7.8 Hz, 2H, CH_2), 1.29 (*t*, *J* = 7.8 Hz, 3H, CH_3), 1.23 (*t*, *J* = 7.8 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 159.6 , 159.3, 146.3, 145.3, 144.8, 135.5, 132.9, 129.8, 129.1, 129.0, 128.7, 128.3, 127.7, 126.7, 126.6, 123.7, 113.8, 94.4, 28.8, 15.4, 15.3; ESI-HRMS, *m/z*: Calcd for $C_{28}H_{25}N_2O$ $[M+H]^+$: 405.1961, Found: 405.1967.

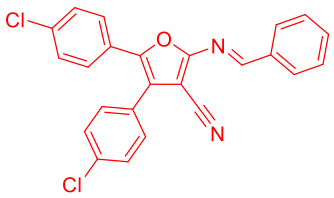


(*E*)-2-Benzylideneamino-4,5-bis(4-isopropylphenyl)furan-3-carbonitrile (**4d**), yellow solid (57.0 mg, yield 66%), m.p. 187.0-188.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), *δ*, ppm: 8.93 (*s*, 1H, -N=CH-), 8.05 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.58-7.55 (*m*, 1H, ArH), 7.54-7.50 (*m*, 4H, ArH), 7.45 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.33 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.22 (*d*, *J* = 8.4 Hz, 2H, ArH), 3.03-2.97 (*m*, 1H, CH), 2.96-2.91 (*m*, 1H, CH), 1.34 (*d*, *J* = 6.6 Hz, 6H, CH_3), 1.28 (*d*, *J* = 6.6 Hz, 6H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 159.6, 159.3, 149.9, 149.4, 146.3, 135.5, 132.9, 129.8, 129.1, 129.0, 127.7, 127.2, 126.8, 126.6, 123.7, 113.8, 94.5, 34.1, 34.0, 24.0, 23.9; ESI-HRMS, *m/z*: Calcd for $C_{30}H_{29}N_2O$ $[M+H]^+$: 433.2274, Found: 433.2280.

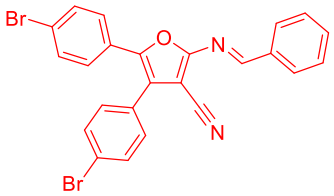


(*E*)-2-Benzylideneamino-4,5-bis(4-fluorophenyl)furan-3-carbonitrile (**4e**), yellow solid (69.1 mg, yield 90%), m.p. 153.4-154.9 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), *δ*, ppm: 8.90 (*s*, 1H, -N=CH-), 8.01 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.56 (*t*, *J* = 7.2 Hz, 1H, ArH), 7.50 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.49-7.46 (*m*, 2H, ArH), 7.45-7.42 (*m*, 2H, ArH), 7.17-7.13 (*m*, 2H, ArH), 7.05-7.01 (*m*, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 163.9 (*d*, *J* = 247.8 Hz), 163.0 (*d*, *J* = 249.3 Hz), 160.4, 159.5, 145.3, 135.2, 133.2, 131.1 (*d*, *J* = 7.8 Hz), 129.9, 129.1, 128.6 (*d*, *J* = 8.3 Hz), 126.1 (*d*, *J* = 3.3 Hz), 125.2 (*d*, *J* = 3.3 Hz), 122.9, 116.5 (*d*, *J* = 21.6 Hz), 116.1 (*d*, *J* = 21.8 Hz), 113.3, 94.0; ^{19}F NMR (564

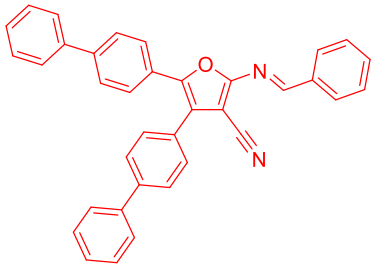
MHz, $CDCl_3$), δ, ppm: -110.663, -111.986; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{15}F_2N_2O$ $[M+H]^+$: 385.1147, Found: 385.1140.



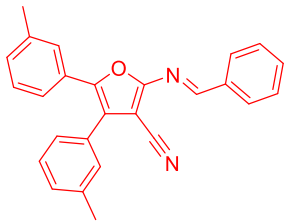
(*E*)-2-Benzylideneamino-4,5-bis(4-chlorophenyl)furan-3-carbonitrile (**4f**), yellow solid (69.1 mg, yield 83%), m.p. 151.3-153.3 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.94 (*s*, 1H, -N=CH-), 8.04 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.55 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.47 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.44 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.42-7.36 (*m*, 2H, ArH), 7.34 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.29-7.23 (*m*, 1H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.8, 159.9, 145.2, 135.2, 133.4, 130.5, 130.1, 129.7, 129.3, 129.2, 128.5, 127.8, 127.3, 126.7, 123.4, 113.2, 93.9; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{15}Cl_2N_2O$ $[M+H]^+$: 417.0561, Found: 417.0551.



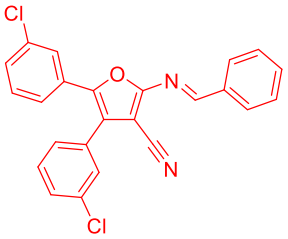
(*E*)-2-Benzylideneamino)-4,5-bis(4-bromophenyl)furan-3-carbonitrile (**4g**), yellow solid (68.2 mg, yield 82%), m.p. 165.3-167.1 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.88 (*s*, 1H, -N=CH-), 8.00 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.58 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.56-7.51 (*m*, 2H, ArH), 7.50 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.45 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.36- 7.31 (*m*, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.9, 159.9, 146.9, 132.7, 132.4, 132.2, 130.8, 130.4, 130.1, 129.7, 129.4, 129.2, 128.3, 128.0, 126.9, 113.1, 93.8; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{15}Br_2N_2O$ $[M+H]^+$: 504.9546, Found: 504.9536.



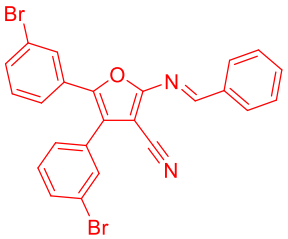
(*E*)-4,5-Di([1,1'-biphenyl]-4-yl)-2-benzylideneaminofuran-3-carbonitrile (**4h**), yellow solid (86.0 mg, yield 86%), m.p. 160.4-162.3 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.97 (*s*, 1H, -N=CH-), 8.05 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.71 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.68-7.64 (*m*, 5H, ArH), 7.62-7.60 (*m*, 3H, ArH), 7.59 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.57-7.51 (*m*, 5H, ArH), 7.49-7.46 (*m*, 2H, ArH), 7.45 (*d*, *J* = 8.4 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.2, 159.7, 146.1, 141.7, 140.2, 135.4, 134.6, 133.1, 130.0, 129.9, 129.7, 129.5, 129.2, 129.1, 129.0, 129.0, 127.9, 127.4, 127.3, 127.2, 127.1, 127.0, 126.9, 125.8, 113.5, 94.3; ESI-HRMS, *m/z*: Calcd for $C_{36}H_{25}N_2O$ $[M+H]^+$: 501.1961, Found: 501.1967.



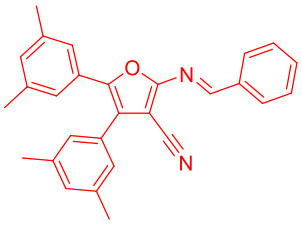
(*E*)-2-Benzylideneamino-4,5-di-*m*-tolylfuran-3-carbonitrile (**4i**), yellow solid (55.6 mg, yield 74%), m.p. 124.2-125.6 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.94 (*s*, 1H, -N=CH-), 8.04 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.56 (*t*, *J* = 7.2 Hz, 1H, ArH), 7.53-7.50 (*m*, 2H, ArH), 7.39 (*s*, 1H, ArH), 7.33 (*t*, *J* = 7.2 Hz, 1H, ArH), 7.30 (*s*, 1H, ArH), 7.29-7.25 (*m*, 2H, ArH), 7.23 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.18 (*t*, *J* = 7.2 Hz, 2H, ArH), 7.13 (*d*, *J* = 7.2 Hz, 2H, ArH), 2.39 (*s*, 3H, CH_3), 2.32 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.0, 159.5, 138.9, 138.5, 135.5, 134.6, 133.0, 130.3, 129.9, 129.8, 129.7, 129.6, 129.1, 129.0, 128.6, 127.1, 126.4, 123.9, 122.6, 113.6, 94.3, 21.6, 21.5; ESI-HRMS, *m/z*: Calcd for $C_{26}H_{21}N_2O$ $[M+H]^+$: 377.1648, Found: 377.1640.



(*E*)-2-Benzylideneamino-4,5-bis(3-chlorophenyl)furan-3-carbonitrile (**4j**), yellow solid (64.9 mg, yield 78%), m.p. 152.4-154.4 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.97 (*s*, 1H, -N=CH-), 8.07 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.61 (*t*, *J* = 7.2 Hz, 1H, ArH), 7.58 (*s*, 1H, ArH), 7.57-7.53 (*m*, 2H, ArH), 7.48 (*s*, 1H, ArH), 7.46-7.42 (*m*, 2H, ArH), 7.40-7.37 (*m*, 1H, ArH), 7.34-7.30 (*m*, 2H, ArH), 7.29-7.24 (*m*, 1H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 161.2, 160.0, 144.8, 135.3, 135.2, 135.0, 133.5, 131.7, 130.7, 130.4, 130.2, 130.1, 129.4, 129.3, 129.2, 127.5, 126.4, 124.6, 123.8, 123.3, 113.0, 93.9; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{15}Cl_2N_2O$ $[M+H]^+$: 417.0556, Found: 417.0552.

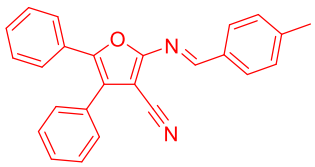


(*E*)-2-Benzylideneamino-4,5-bis(3-bromophenyl)furan-3-carbonitrile (**4k**), yellow solid (74.6 mg, yield 74%), m.p. 154.2-155.8 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.95 (*s*, 1H, -N=CH-), 8.05 (*d*, *J* = 7.2 Hz, 2H, ArH), 7.73 (*s*, 1H, ArH), 7.61 (*s*, 1H, ArH), 7.58 (*t*, *J* = 7.8 Hz, 2H, ArH), 7.53 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.52 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.46 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.41 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.37-7.31 (*m*, 2H, ArH), 7.17 (*t*, *J* = 7.8 Hz, 1H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 161.3, 160.0, 144.7, 135.2, 134.6, 133.5, 132.4, 132.2, 132.0, 131.0, 130.4, 130.2, 129.9, 129.3, 129.2, 128.0, 125.1, 123.7, 123.3, 123.1, 112.9, 93.9; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{15}Br_2N_2O$ $[M+H]^+$: 506.9526, Found: 506.9522.

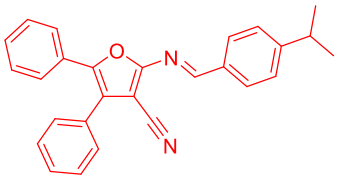


(*E*)-2-Benzylideneamino-4,5-bis(3,5-dimethylphenyl)furan-3-carbonitrile (**4l**), yellow solid

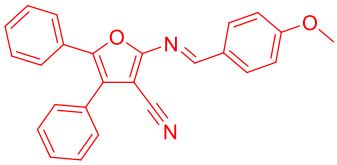
(50.9 mg, yield 63%), m.p. 192.7-194.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.93 (*s*, 1H, -N=CH-), 8.04 (*d*, *J* = 6.6 Hz, 2H, ArH), 7.57-7.54 (*m*, 1H, ArH), 7.52-7.50 (*m*, 2H, ArH), 7.17 (*s*, 2H, ArH), 7.10 (*s*, 2H, ArH), 7.05 (*s*, 1H, ArH), 6.95 (*s*, 1H, ArH), 2.34 (*s*, 6H, $2CH_3$), 2.26 (*s*, 6H, $2CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.7, 159.3, 146.3, 138.6, 138.2, 135.5, 132.9, 130.6, 130.4, 130.2, 129.9, 129.1, 129.0, 126.9, 124.3, 123.1, 113.7, 94.3, 21.4, 21.3; ESI-HRMS, *m/z*: Calcd for $C_{28}H_{25}N_2O$ $[M+H]^+$: 405.1961, Found: 405.1953.



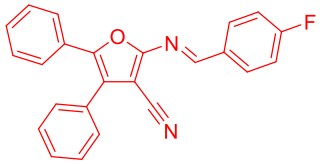
(*E*)-2-(4-Methylbenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4m**), yellow solid (52.1 mg, yield 72%), m.p. 163.7-165.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.89 (*s*, 1H, -N=CH-), 7.92 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.52 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.50-7.48 (*m*, 2H, ArH), 7.47-7.44 (*m*, 2H, ArH), 7.43-7.40 (*m*, 1H, ArH), 7.33-7.30 (*m*, 5H, ArH), 2.45 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.2, 159.9, 145.8, 144.1, 132.9, 130.4, 130.0, 129.9, 129.3, 129.2, 128.9, 128.8, 128.7, 126.6, 124.1, 113.7, 93.6, 22.0; ESI-HRMS, *m/z*: Calcd for $C_{25}H_{19}N_2O$ $[M+H]^+$: 363.1492, Found: 363.1494.



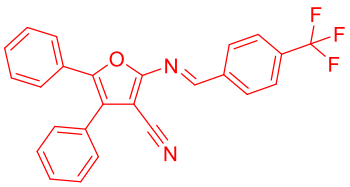
(*E*)-2-(4-Isopropylbenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4n**), yellow solid (50.7 mg, yield 65%), m.p. 171.6-173.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.91 (*s*, 1H, -N=CH-), 7.96 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.54-7.45 (*m*, 5H, ArH), 7.44-7.41 (*m*, 2H, ArH), 7.38 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.33-7.30 (*m*, 3H, ArH), 3.03-2.98 (*m*, 1H, CH), 1.31 (*d*, *J* = 6.6 Hz, 6H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.2, 159.9, 154.9, 145.8, 133.2, 130.4, 130.1, 129.2, 129.1, 128.9, 128.8, 128.7, 127.3, 126.5, 124.1, 113.7, 93.6, 34.5, 23.8; ESI-HRMS, *m/z*: Calcd for $C_{27}H_{23}N_2O$ $[M+H]^+$: 391.1805, Found: 391.1800.



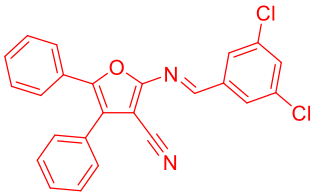
(*E*)-2-(4-Methoxybenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4o**), yellow solid (47.6 mg, yield 63%), m.p. 168.7-170.5 ºC; ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm: 9.09 (*s*, 1H, -N=CH-), 8.04 (*d*, *J* = 9.0 Hz, 2H, ArH), 7.55-7.50 (*m*, 5H, ArH), 7.48 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.41-7.34 (*m*, 3H, ArH), 7.15 (*d*, *J* = 9.0 Hz, 2H, ArH), 3.88 (*s*, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 150 MHz), δ, ppm: 164.1, 161.8, 160.2, 145.2, 132.4, 132.3, 130.5, 129.7, 129.5, 129.3, 129.0, 128.3, 126.4, 115.4, 113.9, 92.7, 56.2; ESI-HRMS, *m/z*: Calcd for $C_{25}H_{19}N_2O_2$ $[M+H]^+$: 379.1441, Found: 379.1442.



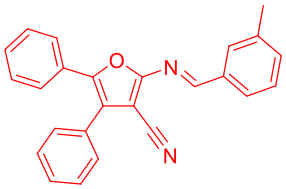
(*E*)-2-(4-Fluorobenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4p**), yellow solid (53.4 mg, yield 73%), m.p. 173.4-175.3 ºC; ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm: 9.13 (*s*, 1H, -N=CH-), 8.19-8.09 (*m*, 2H, ArH), 7.53-7.47 (*m*, 7H, ArH), 7.44-7.33 (*m*, 5H, ArH); ^{13}C NMR (DMSO-d_6, 150 MHz), δ, ppm: 165.5 (*d*, *J* = 251.4 Hz), 161.1, 159.4, 145.8, 132.7 (*d*, *J* = 9.5 Hz), 132.2, 130.3, 129.7, 129.5, 129.3, 128.8, 126.5, 123.9 (*d*, *J* = 3.2 Hz), 117.0 (*d*, *J* = 22.1 Hz), 113.5, 93.8; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{16}FN_2O$ $[M+H]^+$: 367.1241, Found: 367.1242.



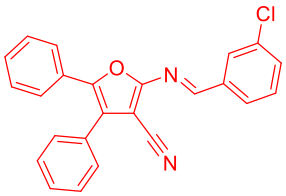
(*E*)-4,5-Diphenyl-2-(4-trifluoromethylbenzylideneamino)furan-3-carbonitrile (**4q**), yellow solid (62.4 mg, yield 75%), m.p. 176.7-178.4 ºC; ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm: 9.22 (*s*, 1H, -N=CH-), 8.25 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.93 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.55-7.51 (*m*, 5H, ArH), 7.48 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.41-7.37 (*m*, 3H, ArH); ^{13}C NMR (DMSO-d_6, 150 MHz), δ, ppm: 160.7, 158.8, 146.4, 139.0, 132.5 (*q*, *J* = 32.0 Hz), 130.6, 130.2, 129.7, 129.5, 129.3, 128.7, 126.6, 126.5 (*q*, *J* = 3.9 Hz), 125.3 (*q*, *J* = 271.2 Hz), 113.3, 95.8; ESI-HRMS, *m/z*: Calcd for $C_{25}H_{16}F_3N_2O$ $[M+H]^+$: 417.1209, Found: 417.1205.



(*E*)-2-(3,5-Dichlorobenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4r**), yellow solid (63.2 mg, yield 76%), m.p. 155.3-156.7 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.78 (*s*, 1H, -N=CH-), 7.89 (*s*, 1H, ArH), 7.88 (*s*, 1H, ArH), 7.52-7.49 (*m*, 3H, ArH), 7.49-7.43 (*m*, 5H, ArH), 7.34 (*s*, 1H, ArH), 7.33-7.31 (*m*, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 158.2, 156.4, 147.1, 138.2, 136.0, 134.3, 132.3, 129.3, 129.2, 129.1, 129.0, 128.9, 128.0, 127.7, 126.7, 125.4, 124.7, 113.1, 96.3; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{15}Cl_2N_2O$ $[M+H]^+$: 417.0556, Found: 417.0556.

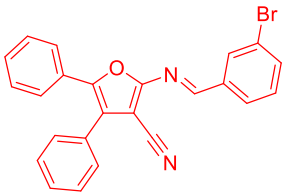


(*E*)-2-(3-Methylbenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4s**), yellow solid (48.5 mg, yield 67%), m.p. 154.4-156.3 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.90 (*s*, 1H, -N=CH-), 7.88 (*s*, 1H, ArH), 7.79 (*d*, J = 7.2 Hz, 1H, ArH), 7.52 (*d*, J = 7.8 Hz, 2H, ArH), 7.50-7.48 (*m*, 2H, ArH), 7.46 (*d*, J = 8.4 Hz, 2H, ArH), 7.44-7.41 (*m*, 2H, ArH), 7.40 (*d*, J = 7.2 Hz, 1H, ArH), 7.33-7.31 (*m*, 3H, ArH), 2.45 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.4, 159.7, 146.0, 139.0, 135.3, 134.0, 130.4, 130.0, 129.3, 129.2, 129.0, 128.9, 128.8, 128.7, 127.6, 126.6, 124.2, 113.6, 94.0, 21.4; ESI-HRMS, *m/z*: Calcd for $C_{25}H_{19}N_2O$ $[M+H]^+$: 363.1492, Found: 363.1486.

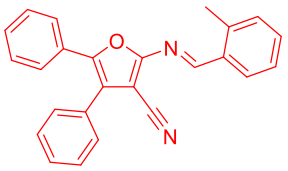


(*E*)-2-(3-Chlorobenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4t**), yellow solid (54.2 mg, yield 71%), m.p. 139.7-141.6 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.86 (*s*, 1H, -N=CH-), 8.03 (*s*, 1H, ArH), 7.89-7.86 (*m*, 1H, ArH), 7.53-7.49 (*m*, 3H, ArH), 7.48-7.45 (*m*, 4H, ArH), 7.44-7.41 (*m*, 2H, ArH), 7.34-7.31 (*m*, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 158.8, 158.0, 146.5, 137.0,

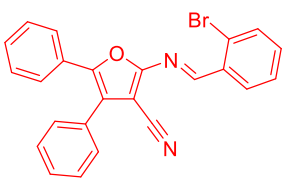
133.3, 134.4, 132.7, 130.4, 130.3, 130.1, 129.3, 129.2, 129.1, 128.7, 128.0, 126.6, 125.3, 113.2, 95.2; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{16}ClN_2O$ $[M+H]^+$: 383.0946, Found: 383.0938.



(*E*)-2-(3-Bromobenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4u**), yellow solid (58.8 mg, yield 69%), m.p. 146.3-147.7 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.84 (*s*, 1H, -N=CH-), 8.18 (*s*, 1H, ArH), 7.92 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.66 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.53-7.50 (*m*, 2H, ArH), 7.49-7.42 (*m*, 5H, ArH), 7.38 (*t*, *J* = 7.8 Hz, 1H, ArH), 7.34-7.31 (*m*, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 158.9, 158.1, 146.6, 137.4, 135.7, 132.2, 130.6, 130.2, 129.3, 129.2, 129.1, 129.0, 128.8, 128.5, 127.6, 126.7, 124.5, 123.4, 113.3, 95.4; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{16}BrN_2O$ $[M+H]^+$: 427.0441, Found: 427.0437.

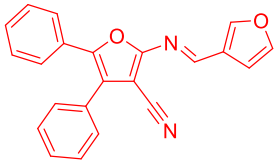


(*E*)-2-(2-Methylbenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4v**), yellow solid (36.9 mg, yield 51%), m.p. 155.7-157.6 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 9.23 (*s*, 1H, -N=CH-), 8.22 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.52 (*d*, *J* = 6.6 Hz, 2H, ArH), 7.50 (*d*, *J* = 6.6 Hz, 2H, ArH), 7.48-7.45 (*m,* 2H, ArH), 7.44-7.41 (*m*, 2H, ArH), 7.35-7.31 (*m*, 4H, ArH), 7.28 (*d*, *J* = 7.8 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.1, 158.8, 146.0, 140.5, 133.3, 132.7, 131.5, 130.4, 129.3, 129.2, 129.1, 128.9, 128.8, 128.7, 126.7, 126.6, 124.2, 113.7, 93.8, 19.9; ESI-HRMS, *m/z*: Calcd for $C_{25}H_{19}N_2O$ $[M+H]^+$: 363.1492, Found: 363.1483.

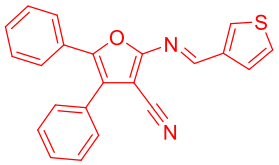


(*E*)-2-(2-Bromobenzylideneamino)-4,5-diphenylfuran-3-carbonitrile (**4w**), yellow solid (48.6

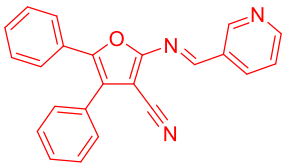
mg, yield 57%), m.p. 148.6-150.4 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 9.29 (*s*, 1H, -N=CH-), 8.40 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.66 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.54-7.52 (*m*, 2H, ArH), 7.50-7.43 (*m*, 6H, ArH), 7.40-7.36 (*m*, 1H, ArH), 7.34-7.31 (*m*, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.0, 158.5, 146.6, 135.4, 133.8, 133.5, 130.1, 129.6, 129.2, 129.1, 128.8, 128.7, 128.5, 128.0, 127.3, 126.6, 125.3, 124.4, 113.2, 95.6; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{16}BrN_2O$ $[M+H]^+$: 427.0441, Found: 427.0432.



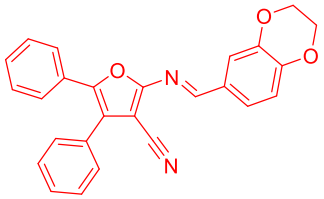
(*E*)-2-(Furan-3-ylmethyleneamino)-4,5-diphenylfuran-3-carbonitrile (**4x**), yellow solid (54.1 mg, yield 80%), m.p. 171.7-173.7 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.90 (*s*, 1H, -N=CH-), 8.03 (*s*, 1H, ArH), 7.53 (*d*, *J* = 2.4 Hz, 1H, ArH), 7.50-7.45 (*m*, 5H, ArH), 7.44-7.40 (*m*, 2H, ArH), 7.32-7.29 (*m*, 3H, ArH), 7.04 (*d*, *J* = 2.4 Hz, 1H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.8, 152.0, 151.4, 149.0, 145.7, 145.0, 130.3, 129.2, 129.1, 128.8, 128.6, 126.4, 125.3, 124.0, 113.5, 107.9, 107.1, 93.0; ESI-HRMS, *m/z*: Calcd for $C_{22}H_{15}N_2O_2$ $[M+H]^+$: 339.1128, Found: 339.1121.



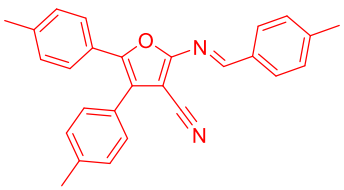
(*E*)-4,5-Diphenyl-2-(thiophen-3-ylmethyleneamino)furan-3-carbonitrile (**4y**), yellow solid (55.2 mg, yield 78%), m.p. 164.6-166.4 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.93 (*s*, 1H, -N=CH-), 8.00 (*d*, *J* = 3.0 Hz, 1H, ArH), 7.78 (*d*, *J* = 3.0 Hz, 1H, ArH), 7.51-7.49 (*m*, 2H, ArH), 7.48-7.46 (*m*, 2H, ArH), 7.45 (*s*, 1H, ArH), 7.44-7.40 (*m*, 4H, ArH), 7.32-7.30 (*m*, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.8, 153.9, 145.9, 140.3, 133.6, 130.4, 129.3, 129.2, 128.9, 128.8, 128.7, 127.4, 126.6, 126.3, 125.4, 124.2, 113.6, 93.6; ESI-HRMS, *m/z*: Calcd for $C_{22}H_{15}N_2OS$ $[M+H]^+$: 355.0900, Found: 355.0892.



(*E*)-4,5-Diphenyl-2-(pyridin-3-ylmethyleneamino)furan-3-carbonitrile (**4z**), yellow solid (56.5 mg, yield 81%), m.p. 189.7-191.6 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 9.06 (*s*, 1H, -N=CH-), 8.93 (*s*, 1H, ArH), 8.74 (*d*, *J* = 6.6 Hz, 1H, ArH), 8.47 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.53-7.51 (*m*, 2H, ArH), 7.49-7.46 (*m*, 3H, ArH), 7.45-7.43 (*m*, 3H, ArH), 7.34-7.31 (*m*, 3H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 158.6, 156.4, 152.9, 151.7, 146.9, 135.6, 131.4, 130.1, 129.3, 129.2, 129.0, 128.8, 126.7, 124.5, 124.4, 113.1, 96.0; ESI-HRMS, *m/z*: Calcd for $C_{23}H_{16}N_3O$ $[M+H]^+$: 350.1288, Found: 350.1280.

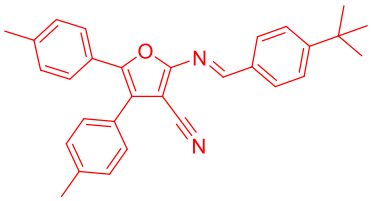


(*E*)-2-(((2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)methylene)amino)-4,5-diphenylfuran-3-carbonitrile (**4aa**), yellow solid (58.5 mg, yield 72%), m.p. 148.7-150.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.81 (*s*, 1H, -N=CH-), 7.60 (*s*, 1H, ArH), 7.55-7.49 (*m*, 5H, ArH), 7.48 (*d*, *J* = 8.4 Hz, 1H, ArH), 7.46-7.42 (*m*, 2H, ArH), 7.34-7.31 (*m*, 3H, ArH), 7.00 (*d*, *J* = 8.4 Hz, 1H, ArH), 4.38-4.35 (*m*, 2H, OCH_2), 4.34-4.32 (*m*, 2H, OCH_2); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.0, 159.5, 148.4, 145.6, 144.2, 130.5, 129.3, 129.2, 128.9, 128.8, 128.7, 126.6, 124.4, 124.1, 118.4, 118.0, 113.8, 93.1, 64.9, 64.2; ESI-HRMS, *m/z*: Calcd for $C_{26}H_{19}N_2O_3$ $[M+H]^+$: 407.1390, Found: 407.1393.

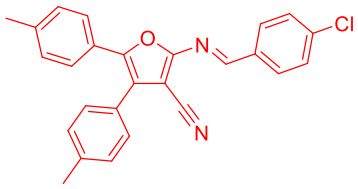


(*E*)-2-(4-Methylbenzylideneamino)-4,5-di-*p*-tolylfuran-3-carbonitrile (**4ab**), yellow solid (54.6 mg, yield 70%), m.p. 197.9-198.1 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.86 (*s*, 1H, -N=CH-), 7.91 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.42 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.37 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.31 (*d*,

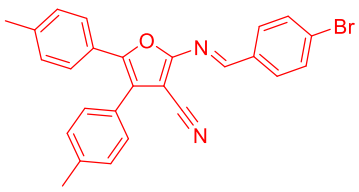
J = 7.8 Hz, 2H, ArH), 7.25 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.12 (*d*, *J* = 7.8 Hz, 2H, ArH), 2.45 (*s*, 3H, CH_3), 2.42 (*s*, 3H, CH_3), 2.35 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 160.0, 159.6, 146.0, 143.9, 138.9, 138.5, 132.9, 129.9, 129.8, 129.4, 129.0, 127.5, 126.5, 126.4, 123.5, 113.9, 93.7, 22.0, 21.5; ESI-HRMS, *m/z*: Calcd for $C_{27}H_{23}N_2O$ $[M+H]^+$: 391.1805, Found: 391.1797.



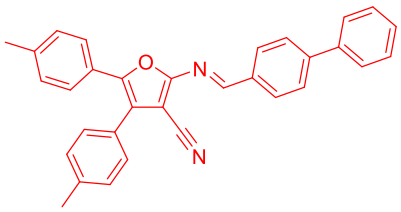
(*E*)-2-(4-(*tert*-Butyl)benzylideneamino)-4,5-di-*p*-tolylfuran-3-carbonitrile (**4ac**), yellow solid (51.8 mg, yield 60%), m.p. 188.2-189.8 ºC; ^1H NMR (600 MHz, $CDCl_3$), *δ*, ppm: 8.89 (*s*, 1H, -N=CH-), 7.96 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.54 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.43 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.38 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.25 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.13 (*d*, *J* = 7.8 Hz, 2H, ArH), 2.42 (*s*, 3H, CH_3), 2.36 (*s*, 3H, CH_3), 1.39 (*s*, 9H, $3CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 159.6, 156.9, 146.0, 138.9, 138.5, 132.9, 129.9, 129.8, 129.4, 129.1, 127.6, 126.6, 126.5, 126.1, 123.5, 113.9, 93.7, 35.4, 31.2, 21.5; ESI-HRMS, *m/z*: Calcd for $C_{30}H_{29}N_2O$ $[M+H]^+$: 433.2274, Found: 433.2270.



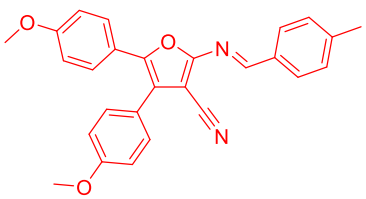
(*E*)-2-(4-Chlorobenzylideneamino)-4,5-di-*p*-tolylfuran-3-carbonitrile (**4ad**), yellow solid (62.3 mg, yield 76%), m.p. 150.7-152.5 ºC; ^1H NMR (600 MHz, $CDCl_3$), *δ*, ppm: 8.82 (*s*, 1H, -N=CH-), 7.94 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.47 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.41 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.36 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.24 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.24 (*d*, *J* = 7.8 Hz, 2H, ArH), 2.41 (*s*, 3H, CH_3), 2.35 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 158.8, 157.8, 146.5, 139.2, 139.0, 138.7, 134.0, 130.8, 130.0, 129.5, 129.0, 127.3, 126.5, 126.4, 123.7, 113.6, 94.9, 21.5; ESI-HRMS, *m/z*: Calcd for $C_{26}H_{20}ClN_2O$ $[M+H]^+$: 411.1259, Found: 411.1250.



(*E*)-2-(4-Bromobenzylideneamino)-4,5-di-*p*-tolylfuran-3-carbonitrile (**4ae**), yellow solid (65.4 mg, yield 72%), m.p. 145.7-147.4 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.80 (*s*, 1H, -N=CH-), 7.86 (*d*, *J* = 6.6 Hz, 2H, ArH), 7.63 (*d*, *J* = 6.6 Hz, 2H, ArH), 7.41 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.36 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.24 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.12 (*d*, *J* = 7.8 Hz, 2H, ArH), 2.41 (*s*, 3H, CH_3), 2.35 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 158.8, 157.9, 146.5, 139.2, 138.7, 134.3, 132.4, 131.0, 129.9, 129.5, 127.7, 127.3, 126.5, 126.3, 123.8, 113.6, 95.0, 21.5; ESI-HRMS, *m/z*: Calcd for $C_{26}H_{20}BrN_2O$ $[M+H]^+$: 455.0754, Found: 455.0745.

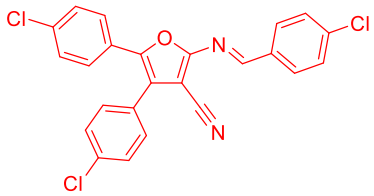


(*E*)-2-([1,1'-Biphenyl]-4-ylmethyleneamino)-4,5-di-*p*-tolylfuran-3-carbonitrile (**4af**), yellow solid (76.8 mg, yield 85%), m.p. 215.1-216.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.93 (*s*, 1H, -N=CH-), 8.08 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.74 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.67 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.51-7.47 (*m*, 2H, ArH-), 7.43-7.41 (*m*, 3H, ArH), 7.38 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.25 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.14 (*d*, *J* = 7.8 Hz, 2H, ArH), 2.42 (*s*, 3H, CH_3), 2.36 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.4, 159.0, 146.3, 145.6, 140.1, 139.1, 138.6, 134.4, 130.4, 129.9, 129.5, 129.2, 129.1, 128.4, 127.7, 127.5, 127.4, 126.5, 123.7, 113.8, 94.3, 21.6, 21.5; ESI-HRMS, *m/z*: Calcd for $C_{32}H_{25}N_2O$ $[M+H]^+$: 453.1961, Found: 453.1951.

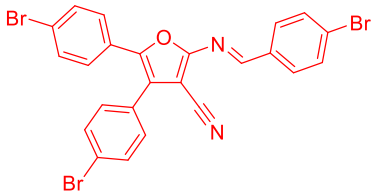


(*E*)-4,5-Bis(4-methoxyphenyl)-2-(4-methylbenzylideneamino)furan-3-carbonitrile (**4ag**), yellow solid (57.4 mg, yield 68%), m.p. 187.7-189.5 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.85 (*s*, 1H,

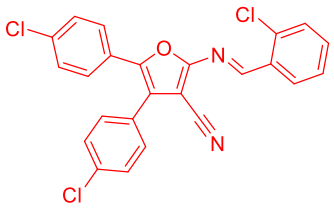
-N=CH-), 7.90 (*d*, *J* = 7.8 Hz, 2H, ArH), 7.45 (*d*, *J* = 9.0 Hz, ArH), 7.39 (*d*, *J* = 9.0 Hz, 2H, ArH), 7.30 (*d*, *J* = 7.8 Hz, 2H, ArH), 6.97 (*d*, *J* = 9.0 Hz, 2H, ArH), 6.84 (*d*, *J* = 9.0 Hz, 2H, ArH), 3.86 (*s*, 3H, OCH_3), 3.81 (*s*, 3H, OCH_3), 2.44 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 160.0, 159.8, 159.4, 145.8, 143.9, 133.0, 132.5, 130.5, 130.0, 129.9, 129.8, 128.0, 122.8, 122.4, 114.6, 114.2, 114.0, 93.7, 55.4, 22.0; ESI-HRMS, *m/z*: Calcd for $C_{27}H_{23}N_2O_3$ $[M+H]^+$: 423.1703, Found: 423.1695.



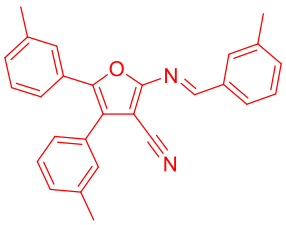
(*E*)-2-(4-Chlorobenzylideneamino)-4,5-bis(4-chlorophenyl)furan-3-carbonitrile (**4ah**), yellow solid (82.8 mg, yield 92%), m.p. 209.8-210.2 ºC; ^1H NMR (600 MHz, $CDCl_3$), *δ*, ppm: 8.82 (*s*, 1H, -N=CH-), 7.93 (*d*, *J* = 6.6 Hz, 2H, ArH), 7.47 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.43 (*d*, *J* = 9.0 Hz, 2H, ArH), 7.41 (*d*, *J* = 9.0 Hz, 2H, ArH), 7.38 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.30 (*d*, *J* = 6.6 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 159.3, 159.0, 145.5, 139.5, 135.3, 135.2, 133.6, 131.0, 130.4, 129.7, 129.5, 129.2, 128.3, 127.8, 127.1, 126.6, 123.4, 113.0, 94.4; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{14}Cl_3N_2O$ $[M+H]^+$: 451.0166, Found: 451.0156.



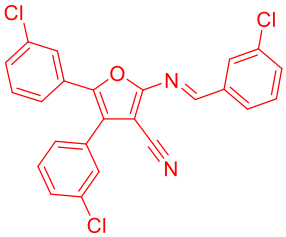
(*E*)-2-(4-Bromobenzylideneamino)-4,5-bis(4-bromophenyl)furan-3-carbonitrile (**4ai**), yellow solid (97.6 mg, yield 84%), m.p. 191.5-193.4 ºC; ^1H NMR (600 MHz, $CDCl_3$), *δ*, ppm: 8.84 (*s*, 1H, -N=CH-), 7.87 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.65 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.59 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.47 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.35 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.32 (*d*, *J* = 8.4 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), *δ*, ppm: 159.4, 159.2, 145.5, 134.1, 132,7, 132.6, 132.2, 131.9, 131.2, 130.7, 130.6, 128.8, 128.0, 127.6, 126.9, 123.5, 113.0, 94.4; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{14}Br_3N_2O$ $[M+H]^+$: 582.8651, Found: 582.8641.



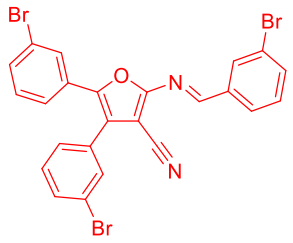
(*E*)-2-(2-Chlorobenzylideneamino)-4,5-bis(4-chlorophenyl)furan-3-carbonitrile (**4aj**), yellow solid (69.5 mg, yield 77%), m.p. 200.3-202.1 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 9.33 (*s*, 1H, -N=CH-), 8.39 (*d*, *J* = 9.0 Hz, 1H, ArH), 7.48-7.46 (*m*, 2H, ArH), 7.45 (*d*, *J* = 8.4 Hz, 2H, ArH), 7.43 (*d*, *J* = 9.0 Hz, 2H, ArH), 7.41 (*d*, *J* = 8.4 Hz, 3H, ArH), 7.32 (*d*, *J* = 9.0 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.4, 156.7, 145.6, 137.3, 135.3, 135.2, 133.9, 132.3, 130.4, 130.3, 129.7, 129.2, 129.1, 127.8, 127.4, 127.0, 126.5, 123.5, 112.8, 95.2; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{14}Cl_3N_2O$ $[M+H]^+$: 451.0166, Found: 451.0164.



(*E*)-2-(3-Methylbenzylideneamino)-4,5-di-*m*-tolylfuran-3-carbonitrile (**4ak**), yellow solid (40.6 mg, yield 52%), m.p. 171.3-173.2 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.91 (*s*, 1H, -N=CH-), 7.89 (*s*, 1H, ArH), 7.80 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.40 (*t*, *J* = 7.8 Hz, 1H, ArH), 7.37 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.33 (*t*, *J* = 7.8 Hz, 1H, ArH), 7.31 (*s*, 1H, ArH), 7.30- 7.26 (*m*, 3H, ArH), 7.23 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.18 (*t*, *J* = 7.8 Hz, 1H, ArH), 7.13 (*d*, *J* = 7.8 Hz, 1H, ArH), 2.45 (*s*, 3H, CH_3), 2.39 (*s*, 3H, CH_3), 2.32 (*s*, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 160.3, 159.6, 146.1, 139.0, 138.8, 138.5, 135.4, 134.0, 130.0, 129.8, 129.7, 129.6, 129.1, 129.0, 128.9, 128.6, 127.6, 127.4, 127.0, 126.4, 124.3, 123.8, 113.7, 94.0, 21.6, 21.5, 21.4; ESI-HRMS, *m/z*: Calcd for $C_{27}H_{23}N_2O$ $[M+H]^+$: 391.1805, Found: 391.1814.

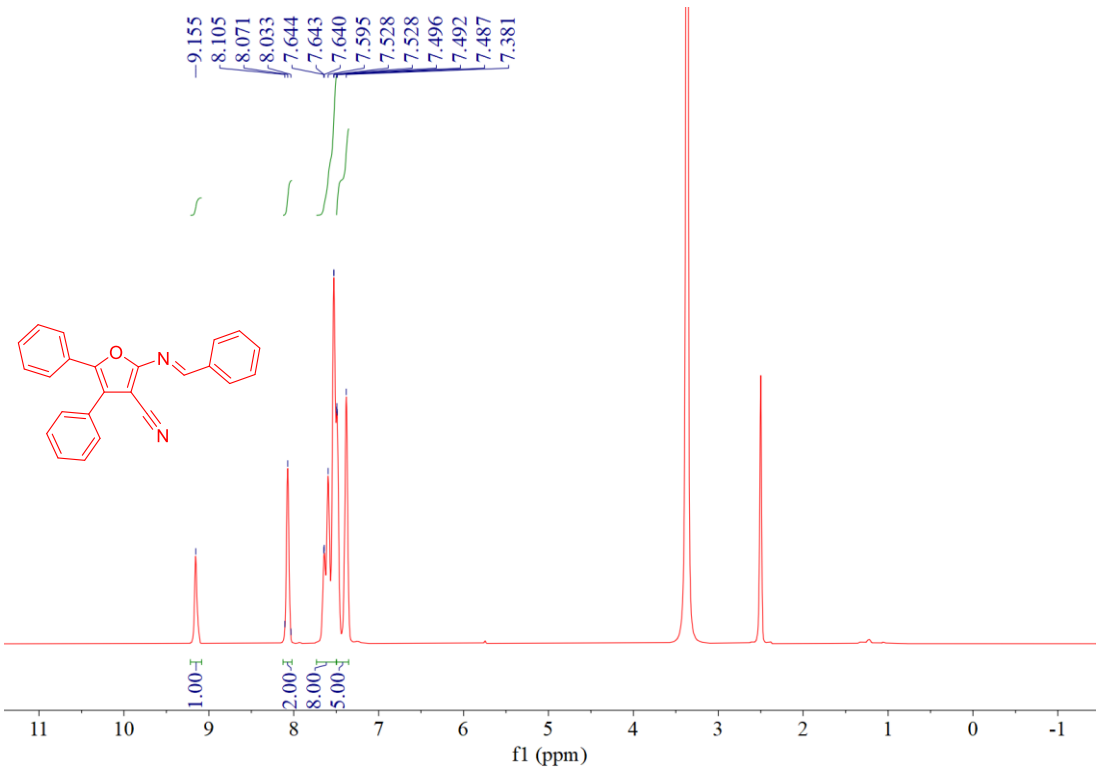


(*E*)-2-(3-Chlorobenzylideneamino)-4,5-bis(3-chlorophenyl)furan-3-carbonitrile (**4al**), yellow solid (65.8 mg, yield 73%), m.p. 175.3-177.1 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.88 (*s*, 1H, -N=CH-), 8.05 (*s*, 1H, ArH), 7.89 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.55 (*s*, 1H, ArH), 7.54 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.46-7.43 (*m*, 3H, ArH), 7.42 (*s*, 1H, ArH), 7.36 (*d*, *J* = 8.4 Hz, 1H, ArH), 7.32 (*d*, *J* = 8.4 Hz, 1H, ArH), 7.28 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.25 (*d*, *J* = 7.8 Hz, 1H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.2, 159.1, 145.2, 136.8, 135.4, 135.2, 135.0, 133.1, 131.4, 130.7, 130.3, 130.1, 130.0, 129.4, 129.3, 129.2, 129.1, 128.2, 127.4, 126.4, 124.6, 123.8, 112.6, 94.9; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{14}Cl_3N_2O$ $[M+H]^+$: 451.0166, Found: 451.0165.

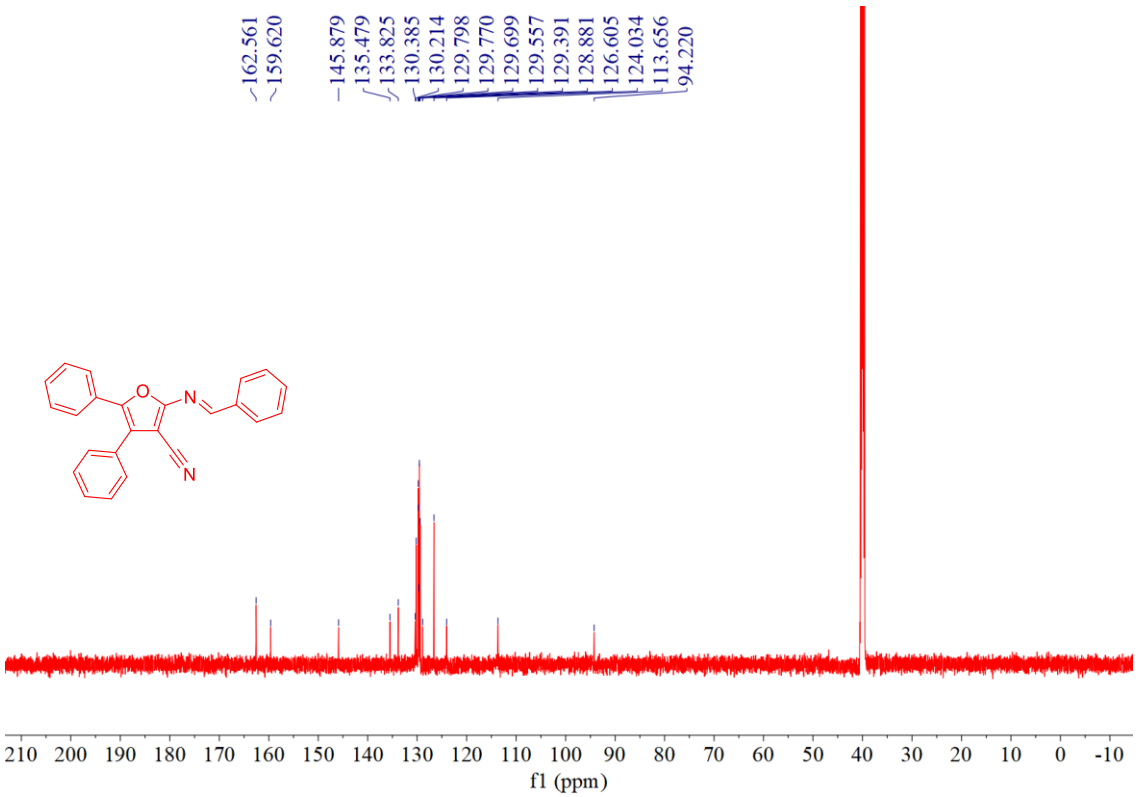


(*E*)-2-(3-Bromobenzylideneamino)-4,5-bis(3-bromophenyl)furan-3-carbonitrile (**4am**), yellow solid (74.5 mg, yield 64%), m.p. 156.0-157.8 ºC; ^{1}H NMR (600 MHz, $CDCl_3$), δ, ppm: 8.85 (*s*, 1H, -N=CH-), 8.19 (*s*, 1H, ArH), 7.93 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.71 (*s*, 1H, ArH), 7.68 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.60 (*s*, 1H, ArH), 7.59 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.46 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.42-7.37 (*m*, 2H, ArH), 7.36 (*t*, *J* = 7.8 Hz, 1H, ArH), 7.32 (*d*, *J* = 7.8 Hz, 1H, ArH), 7.17 (*t*, *J* = 7.8 Hz, 1H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$), δ, ppm: 159.2, 159.1, 145.1, 137.1, 136.1, 132.4, 132.3, 132.0, 131.7, 131.0, 130.7, 130.4, 129.3, 128.7, 127.9, 125.1, 123.8, 123.5, 123.3, 123.1, 112.7, 94.9; ESI-HRMS, *m/z*: Calcd for $C_{24}H_{14}Br_3N_2O$ $[M+H]^+$: 584.8636, Found: 584.8613.

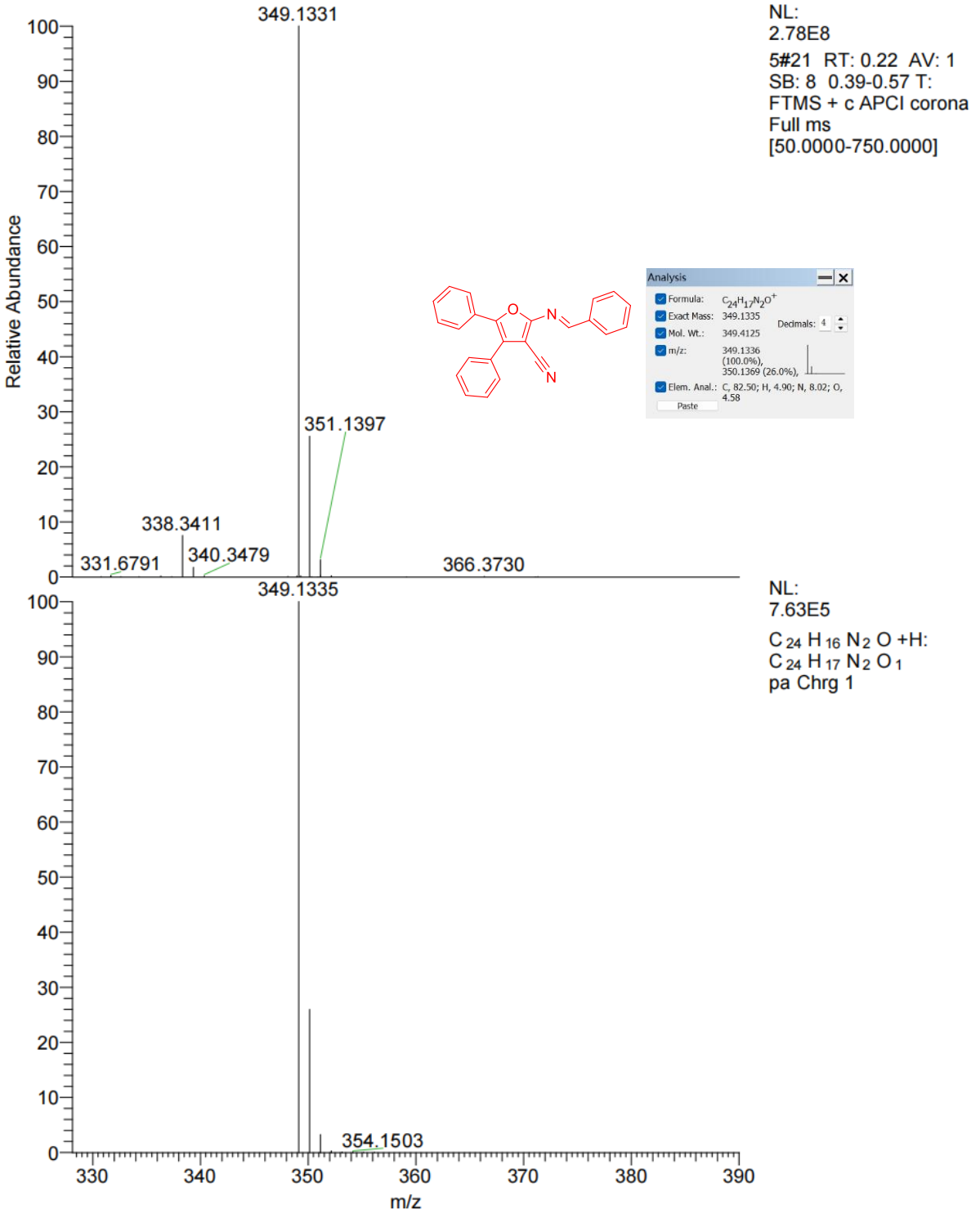
2.3. NMR Spectra for All Products 4a - 4am



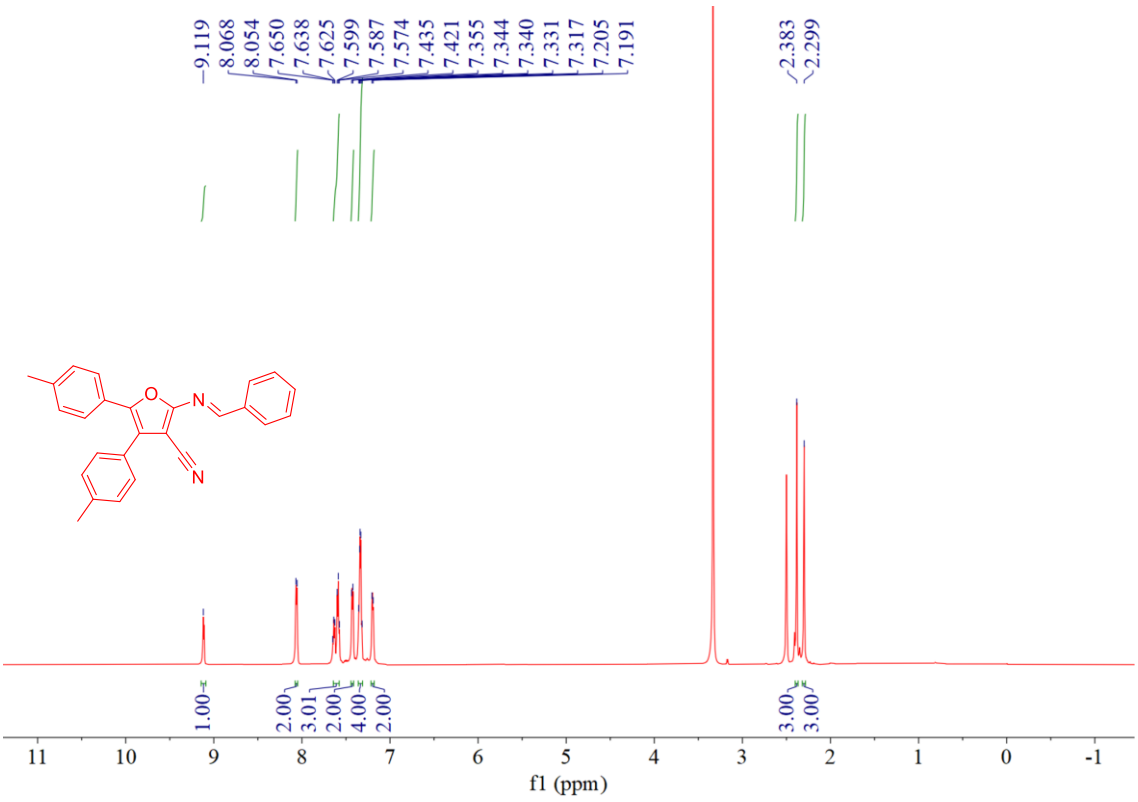
^{1}H NMR spectrum of compound **4a**



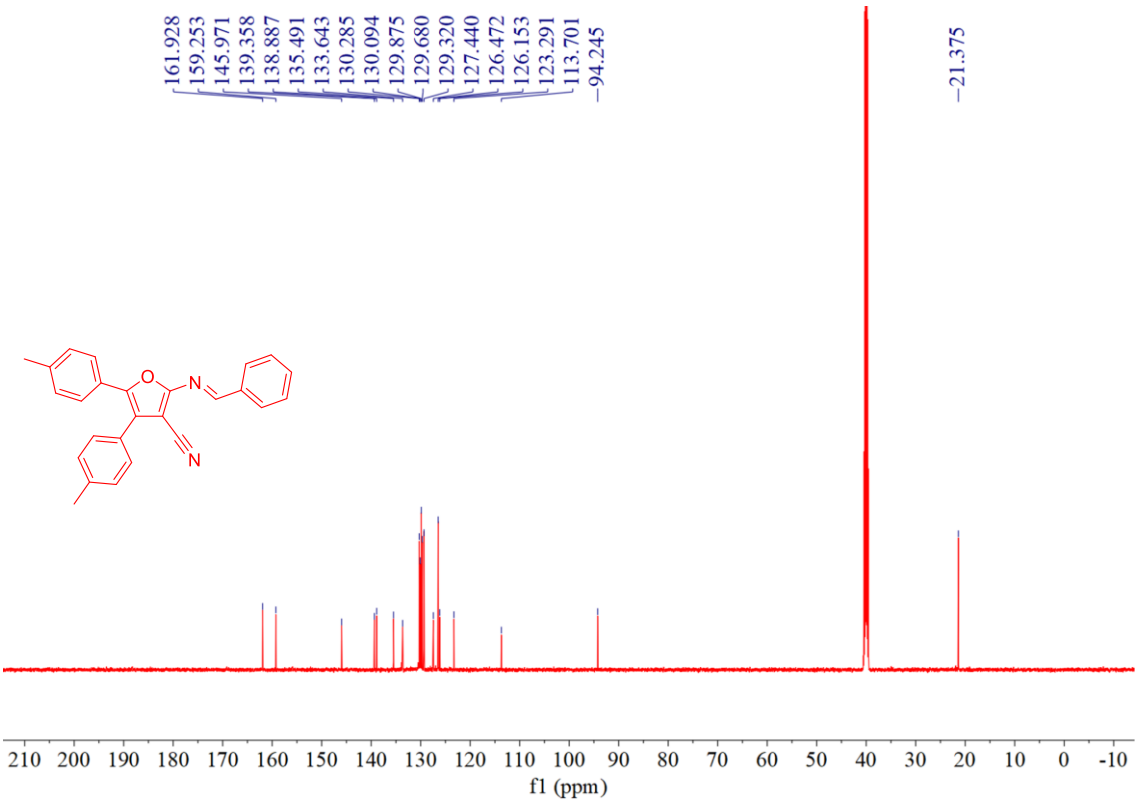
^{13}C NMR spectrum of compound **4a**



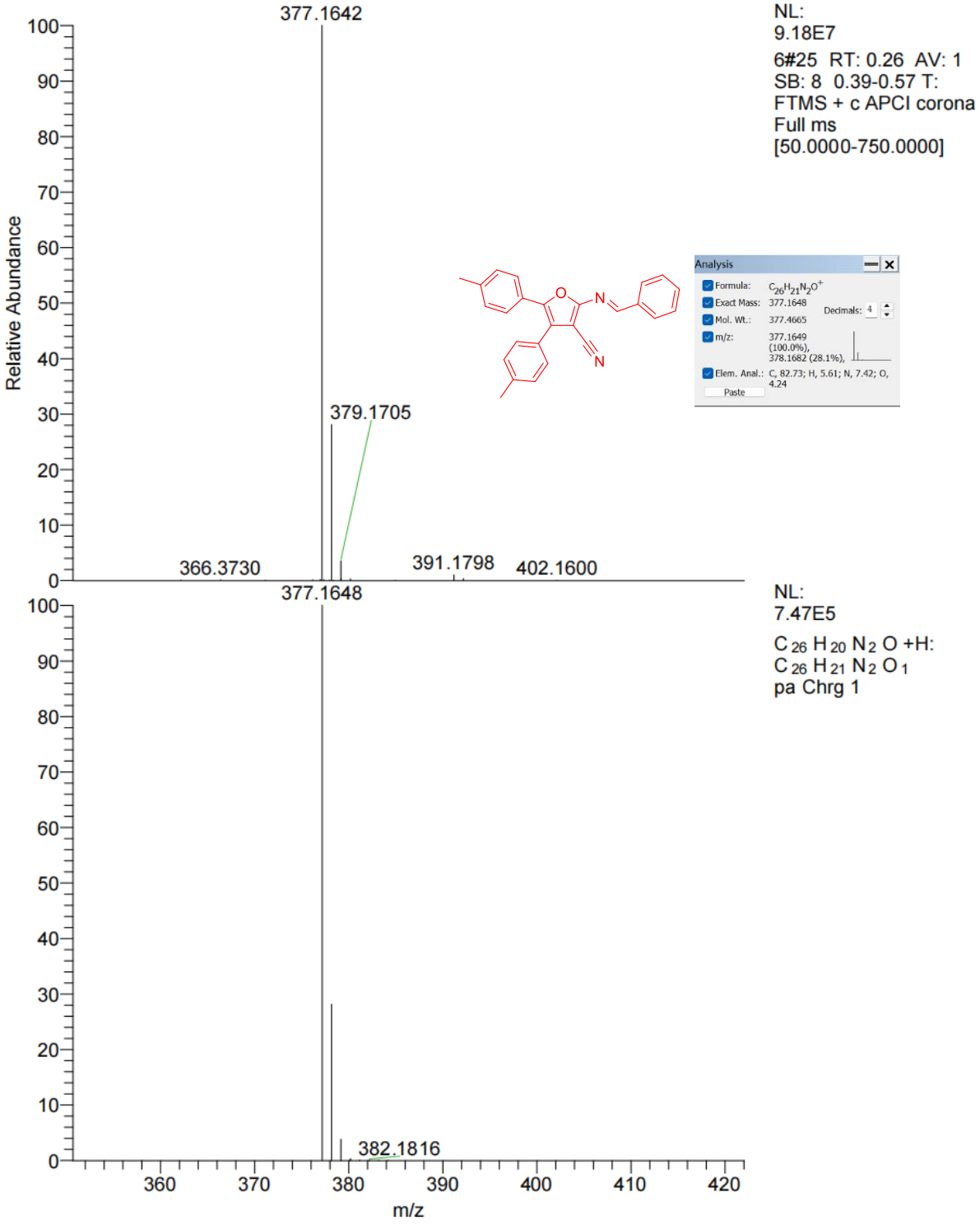
HR-MS spectrum of compound **4a**



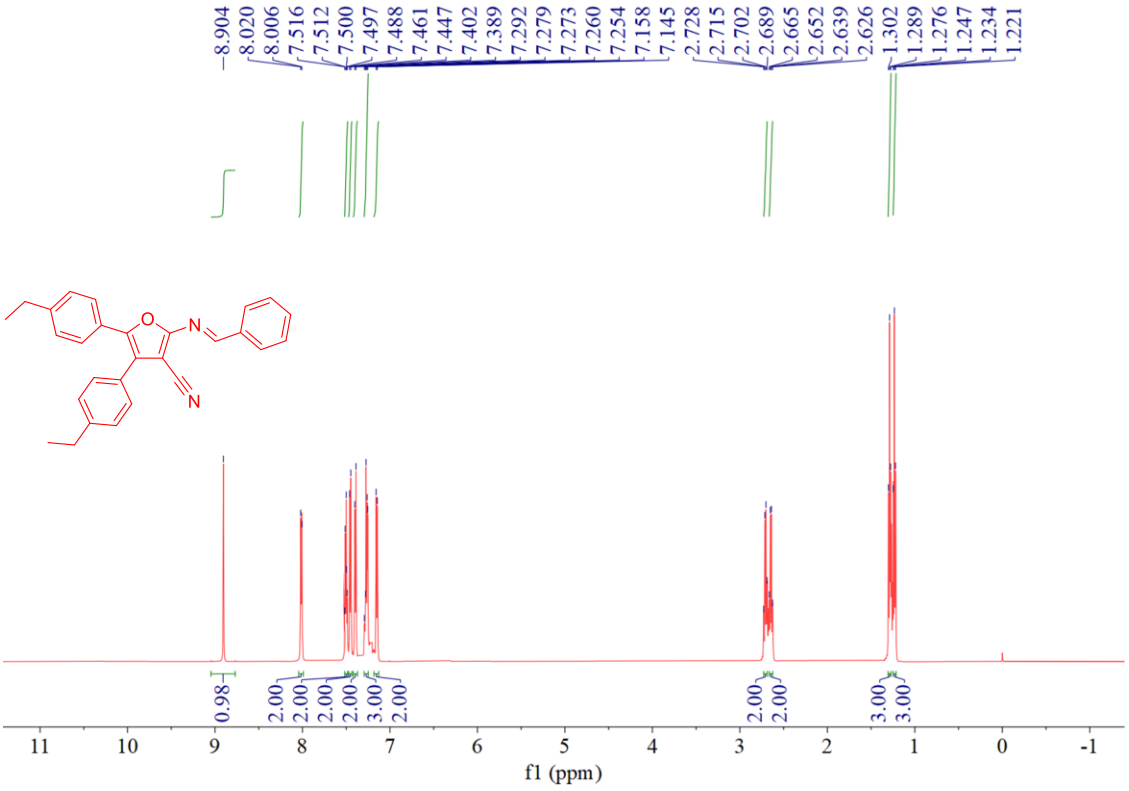
^{1}H NMR spectrum of compound **4b**



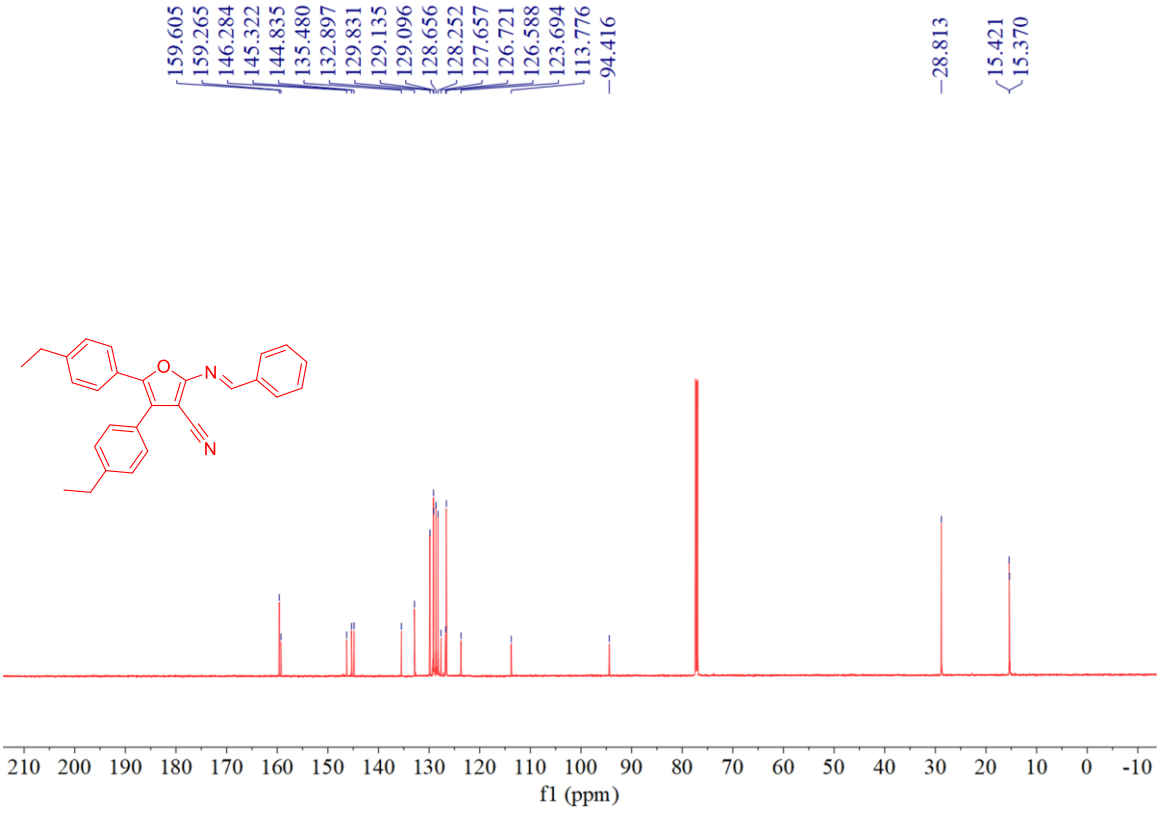
^{13}C NMR spectrum of compound **4b**



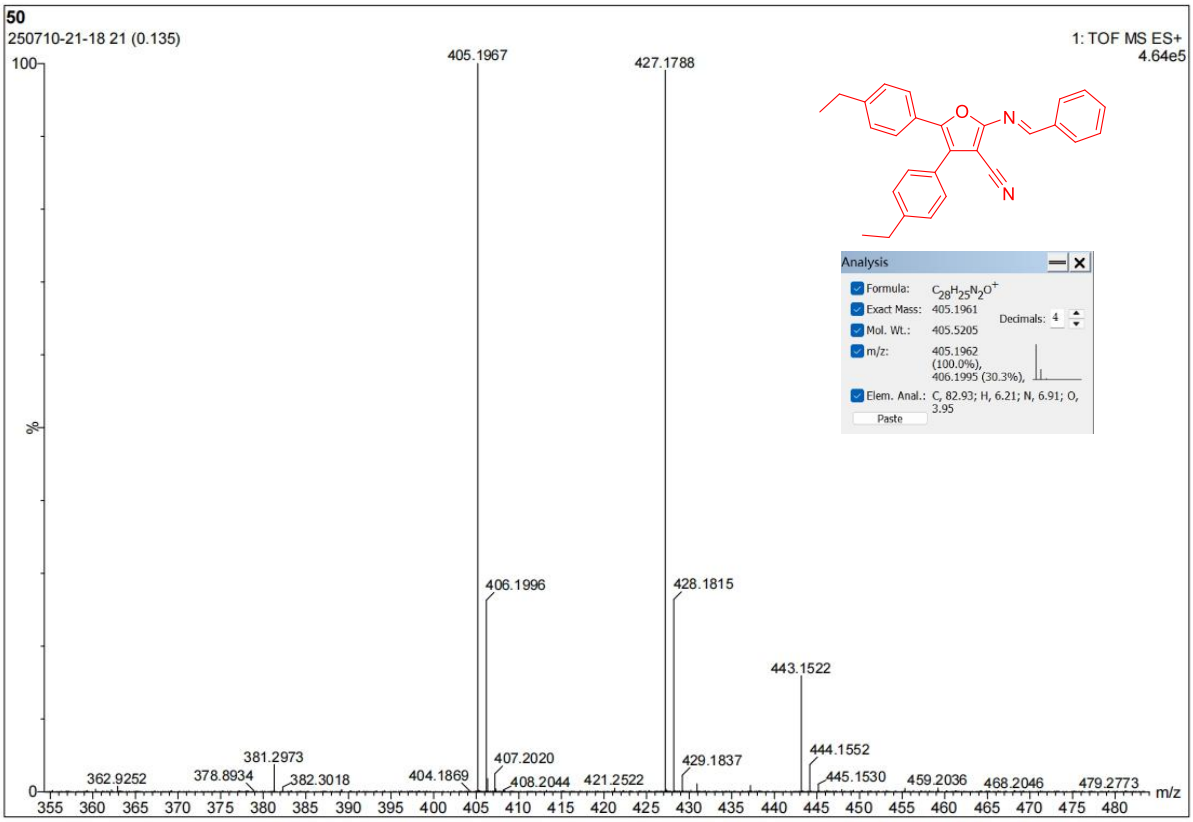
HR-MS spectrum of compound **4b**



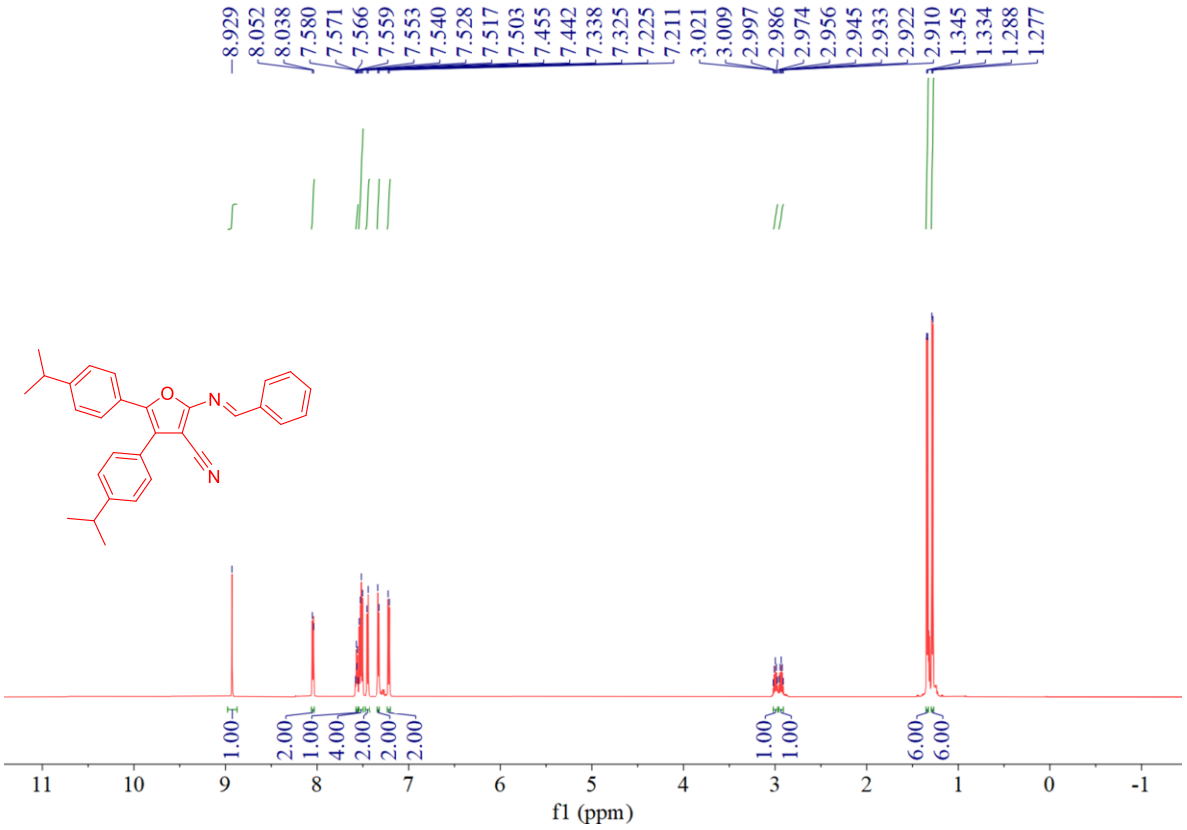
^{1}H NMR spectrum of compound **4c**



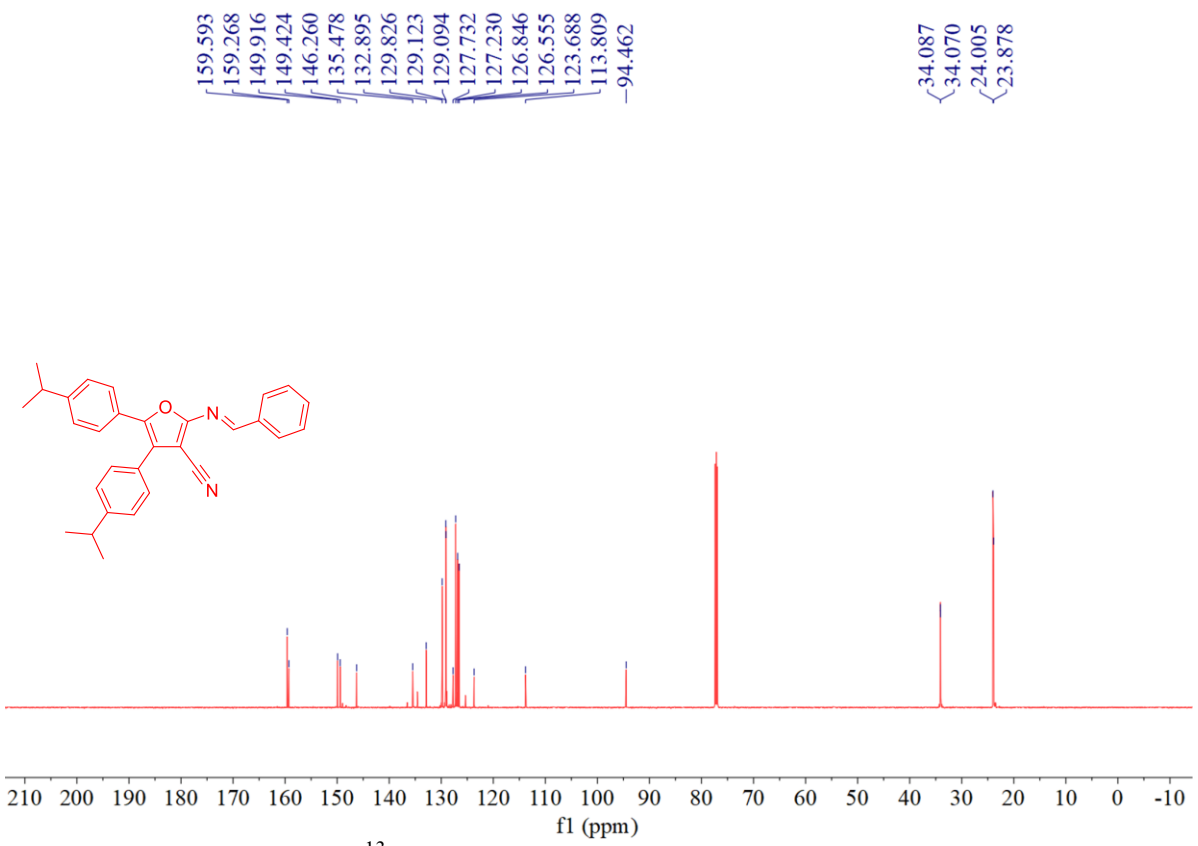
^{13}C NMR spectrum of compound **4c**



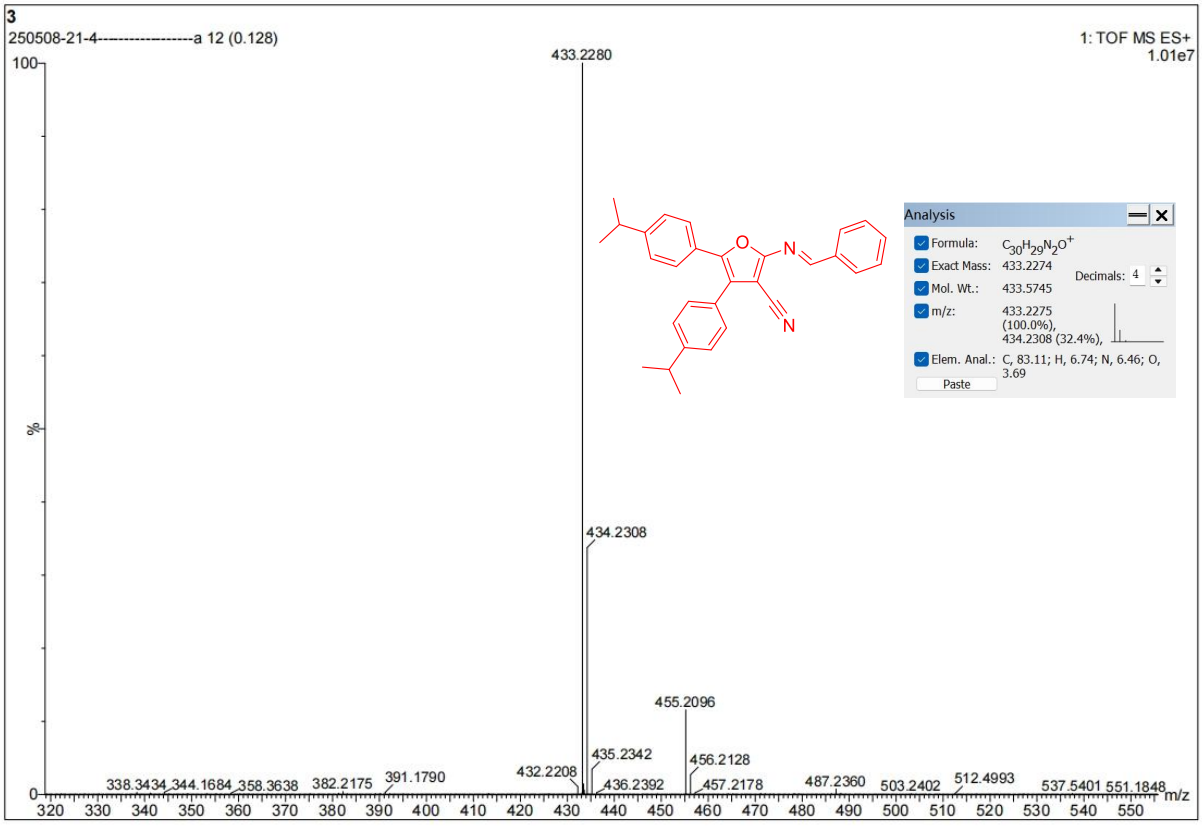
HR-MS spectrum of compound **4c**



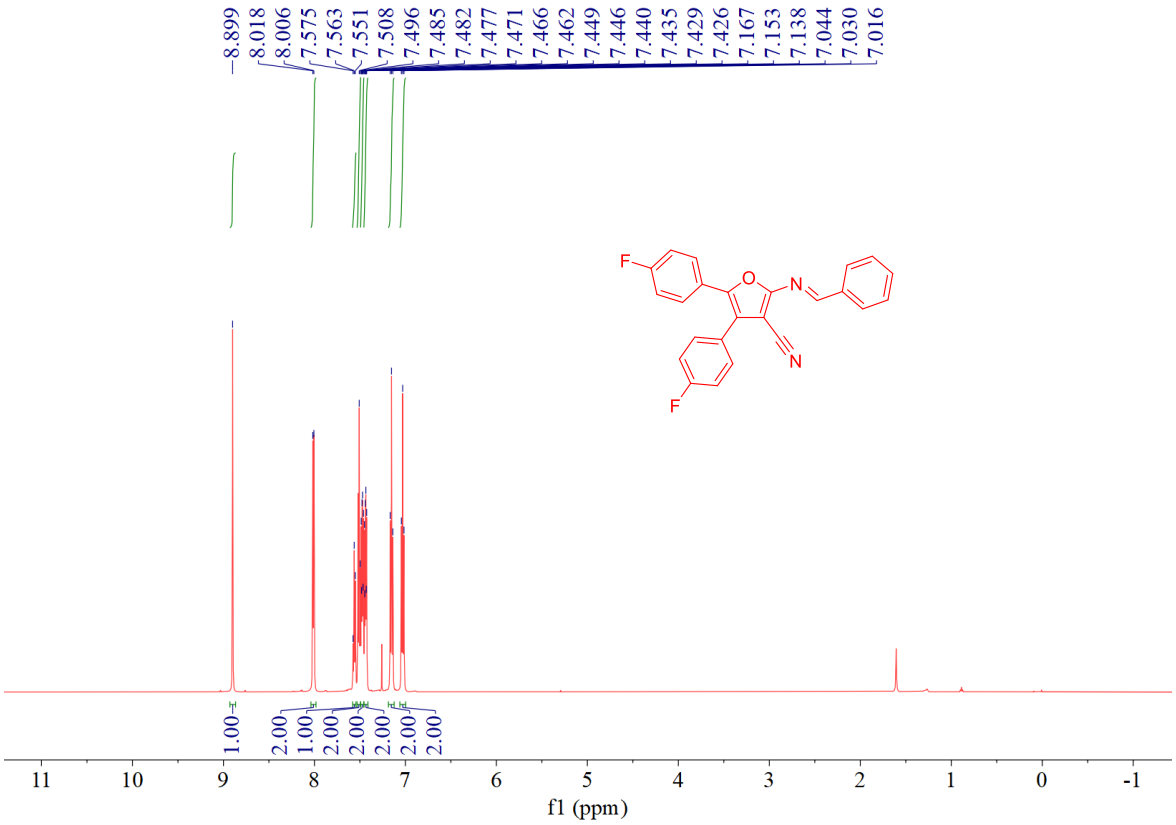
^{1}H NMR spectrum of compound **4d**



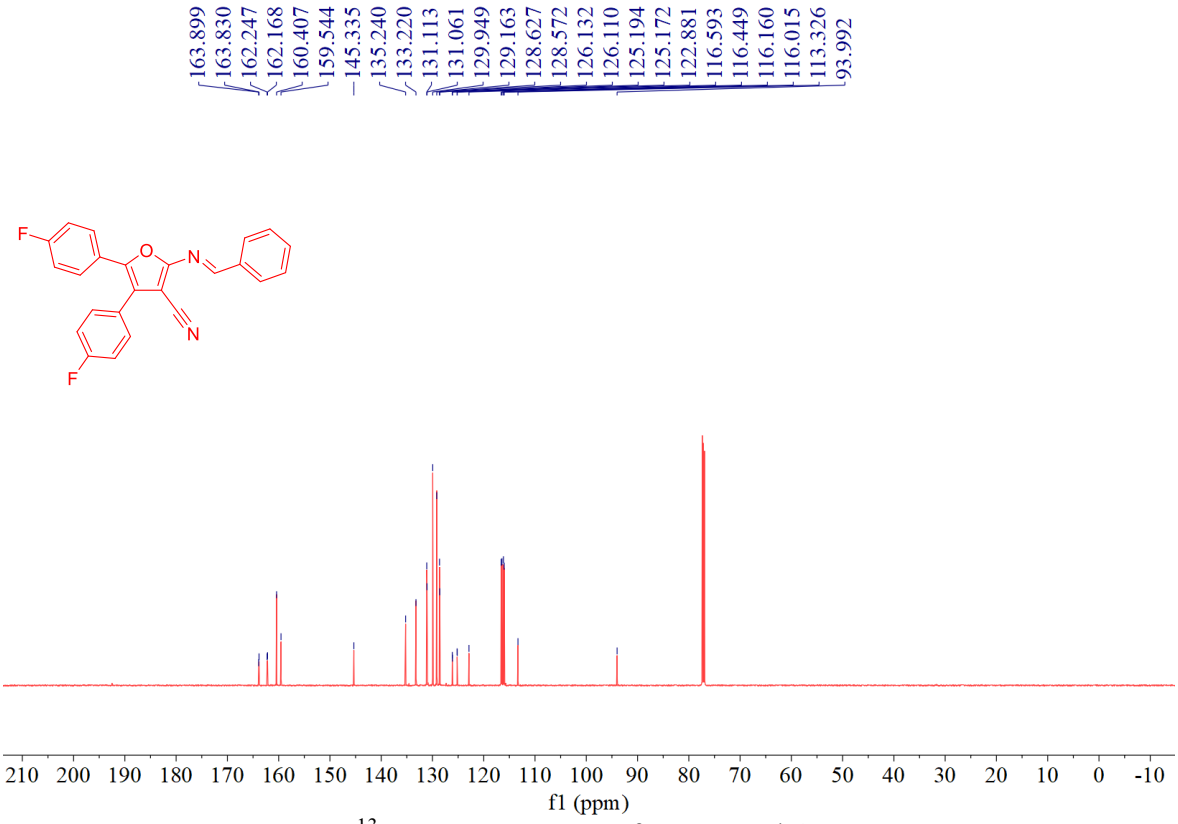
^{13}C NMR spectrum of compound **4d**



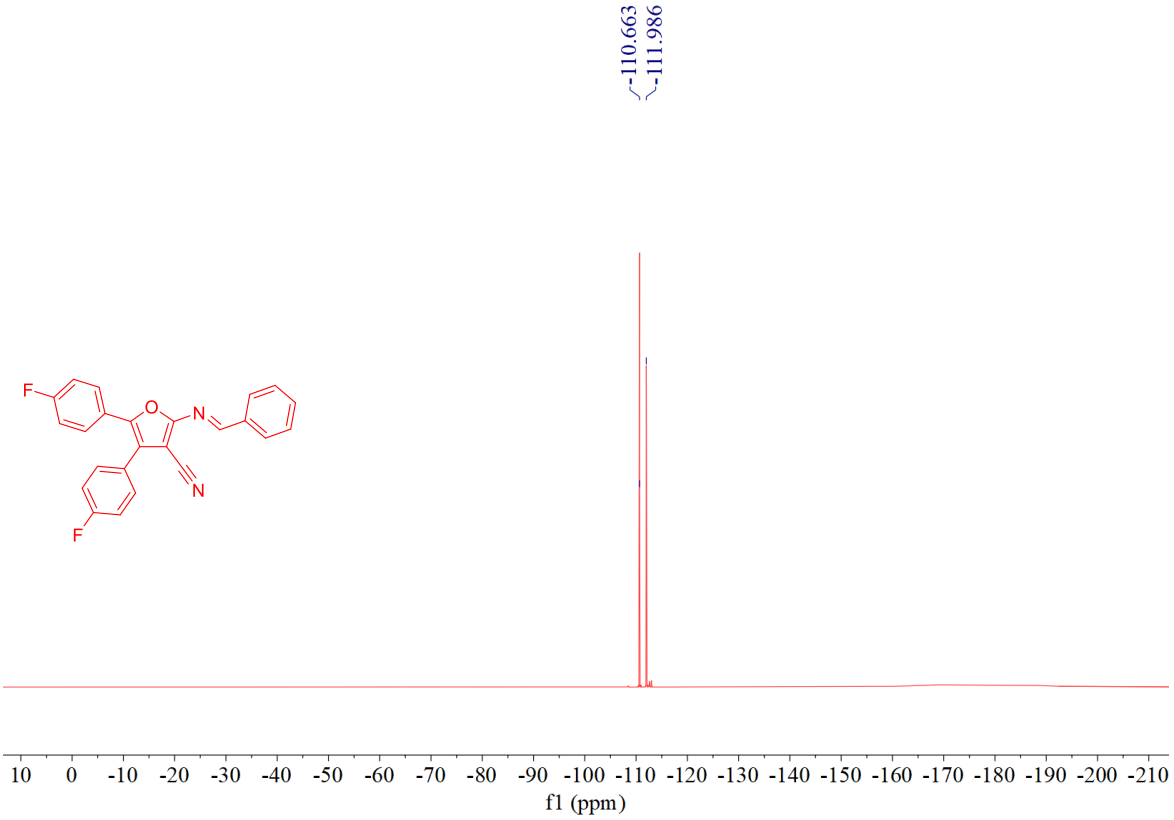
HR-MS spectrum of compound **4d**



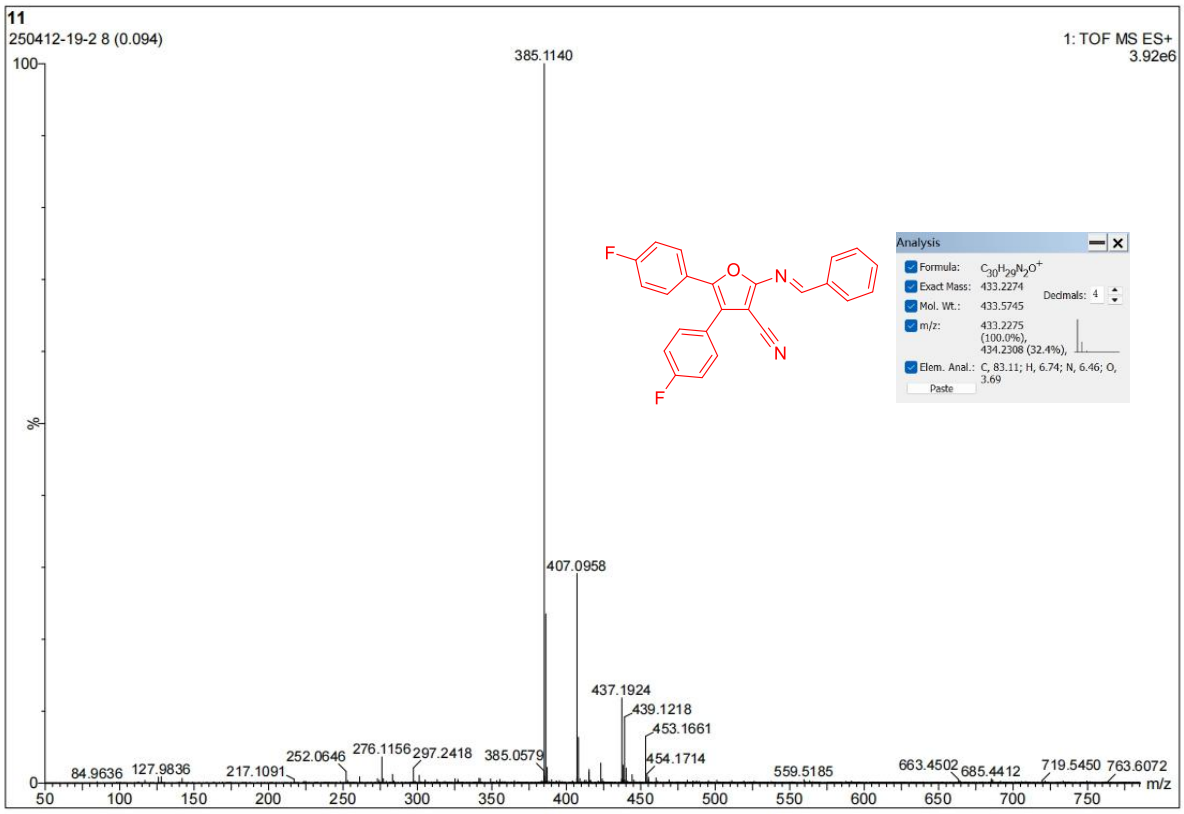
^{1}H NMR spectrum of compound **4e**



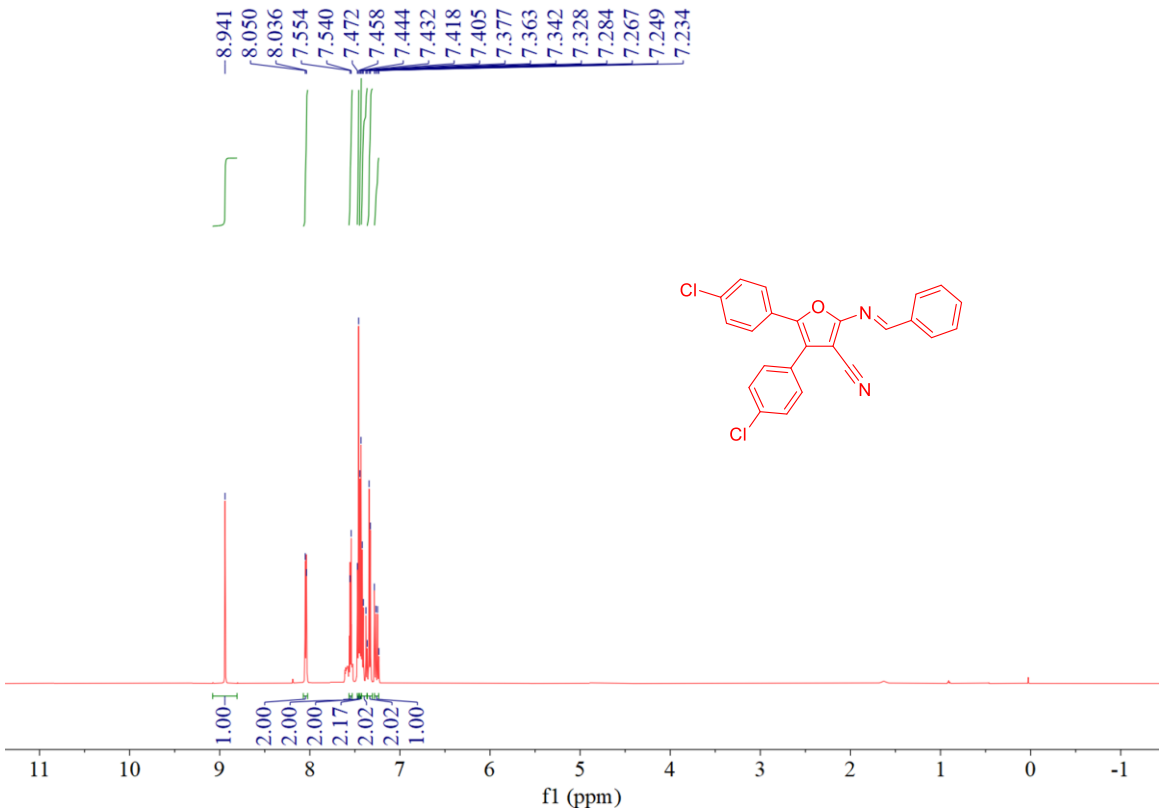
^{13}C NMR spectrum of compound **4e**



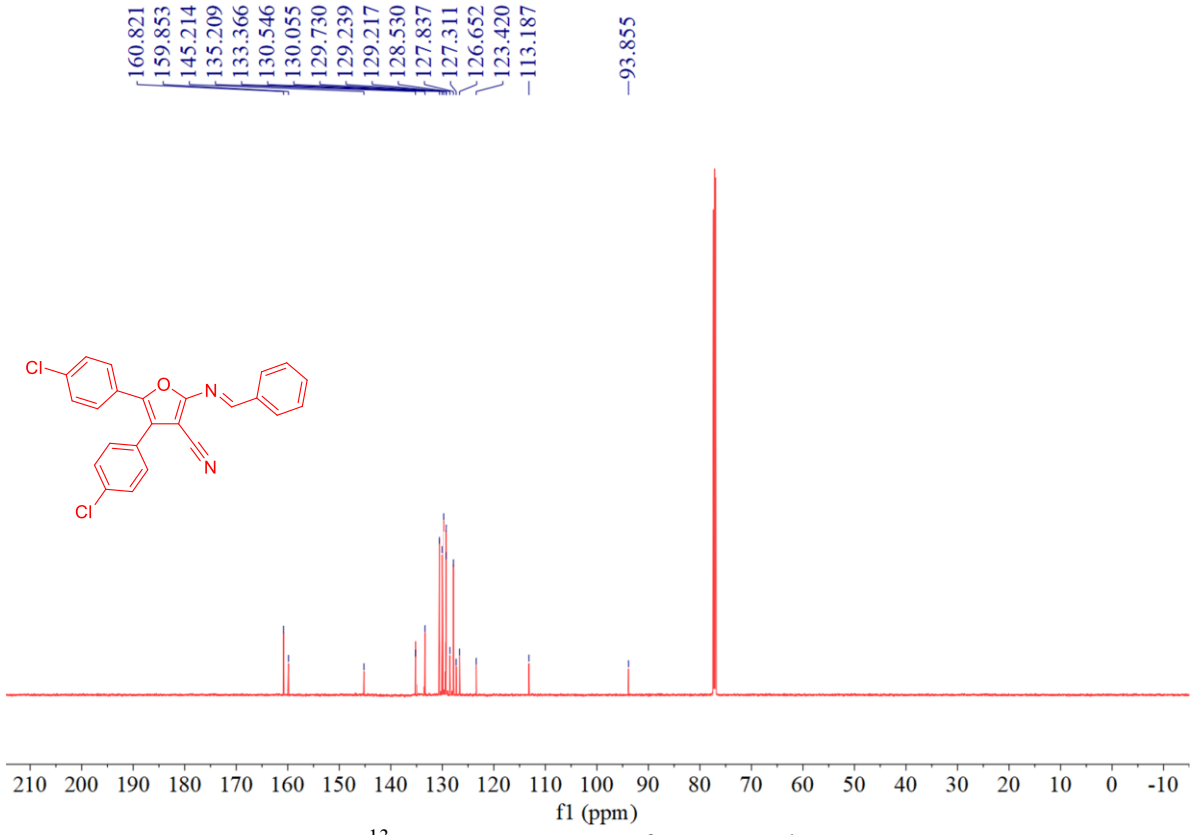
^{19}F NMR spectrum of compound **4e**



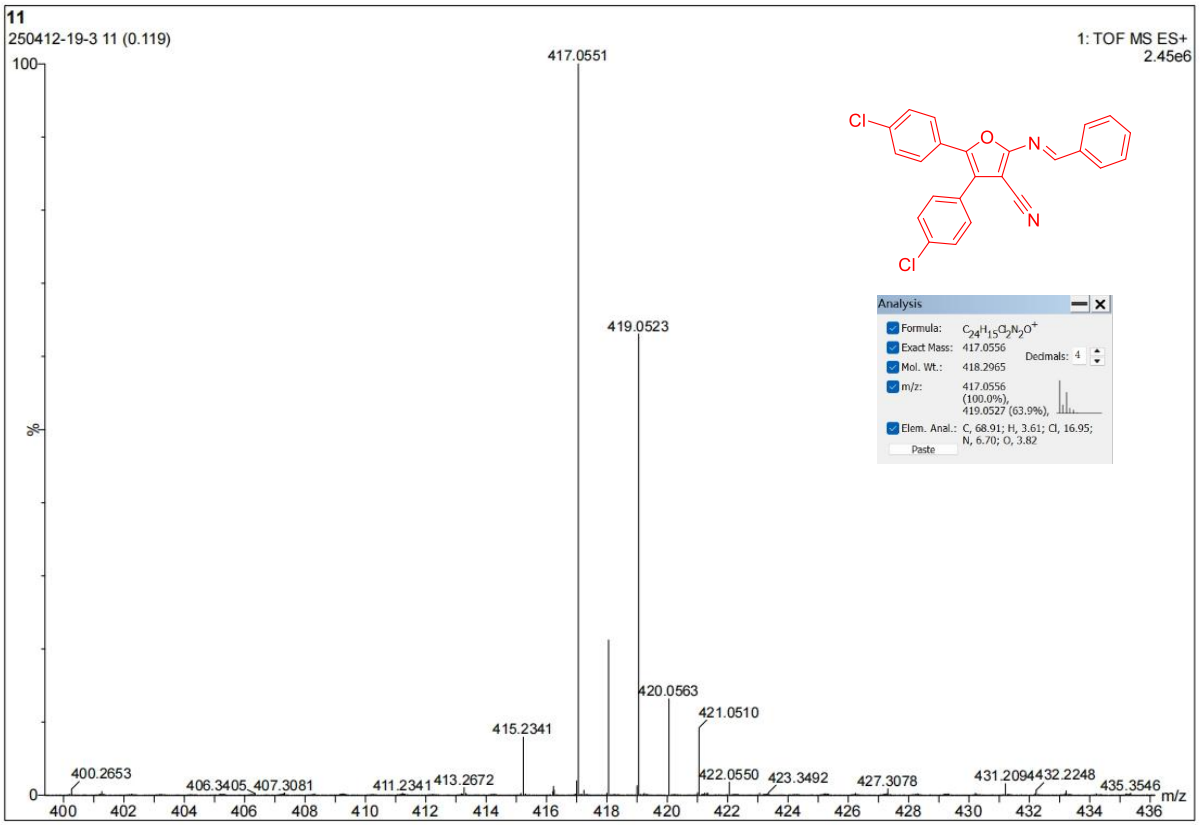
HR-MS spectrum of compound **4e**



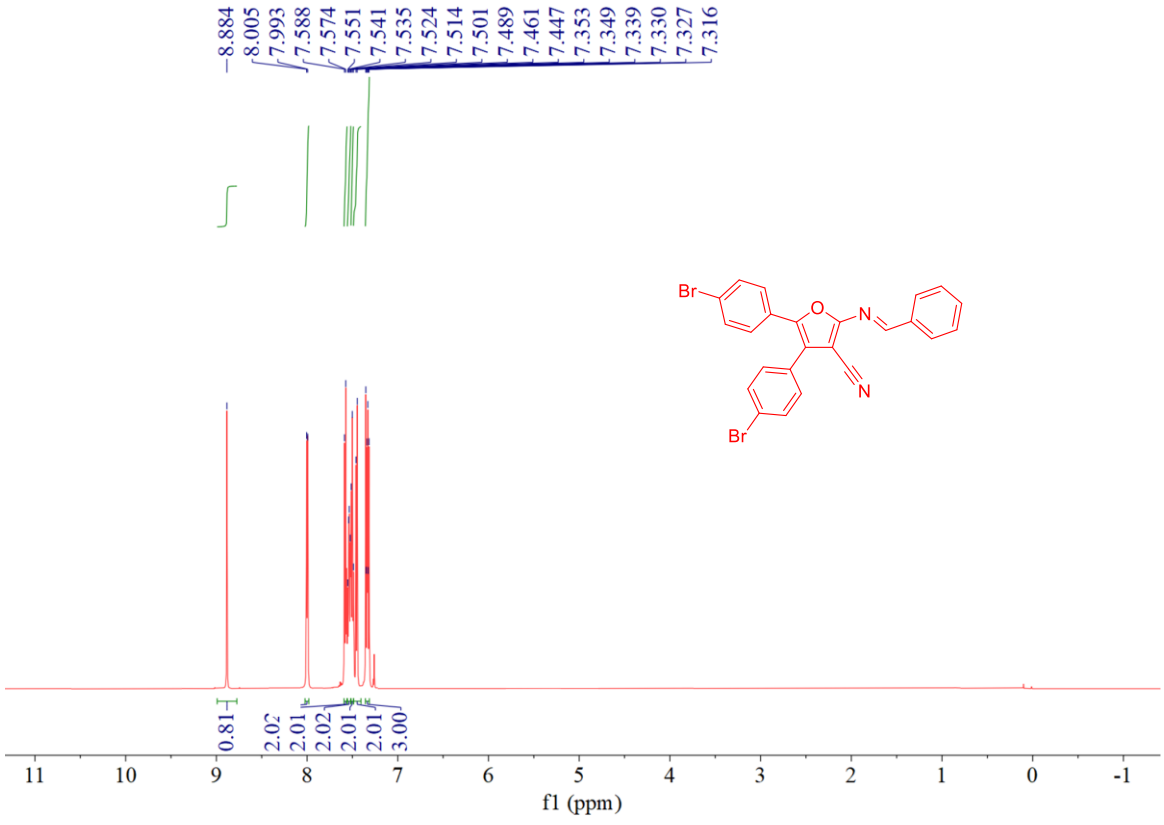
^{1}H NMR spectrum of compound **4f**



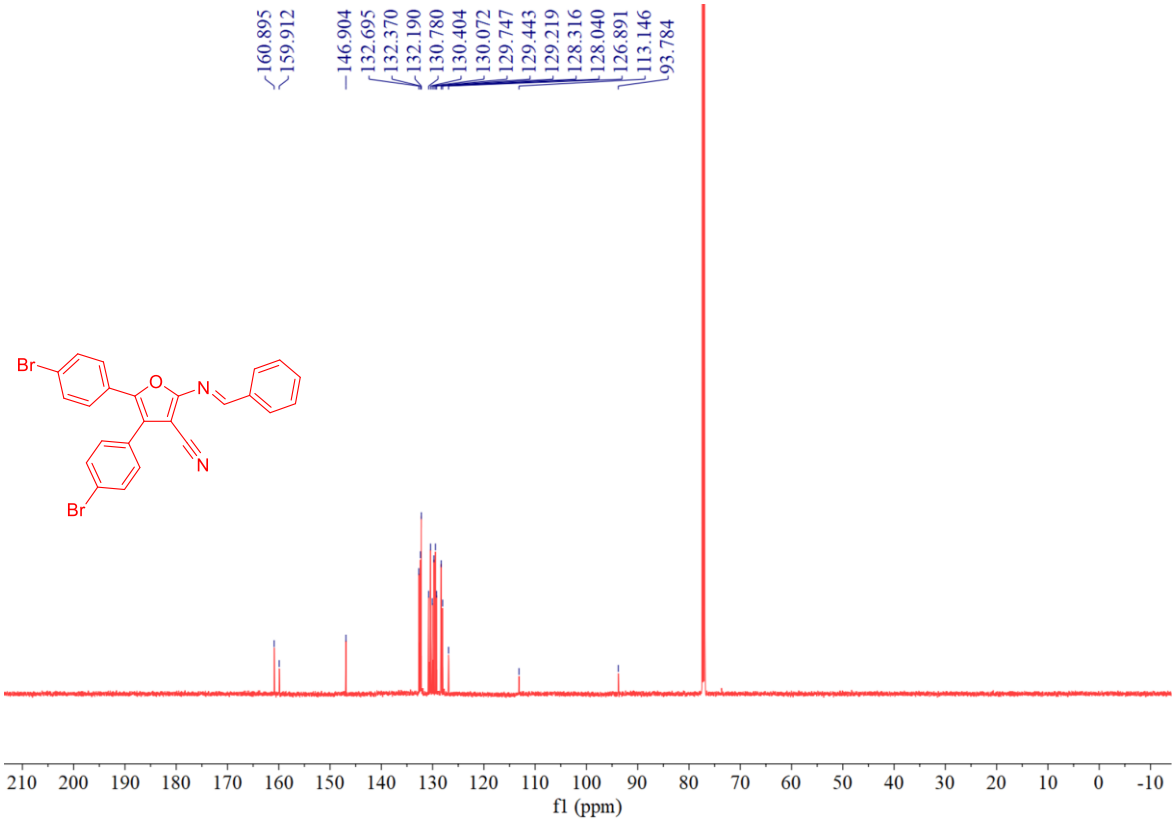
^{13}C NMR spectrum of compound **4f**



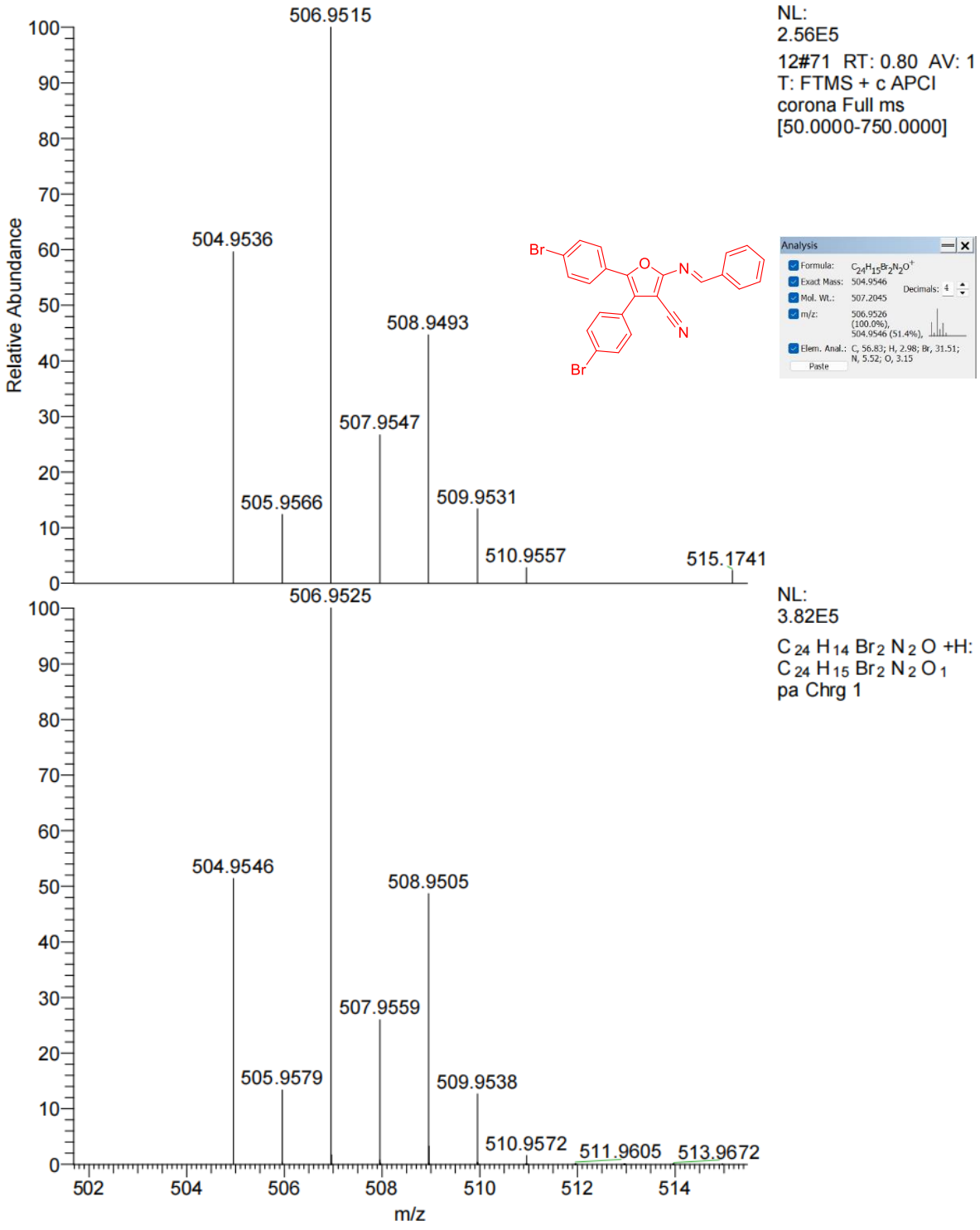
HR-MS spectrum of compound **4f**



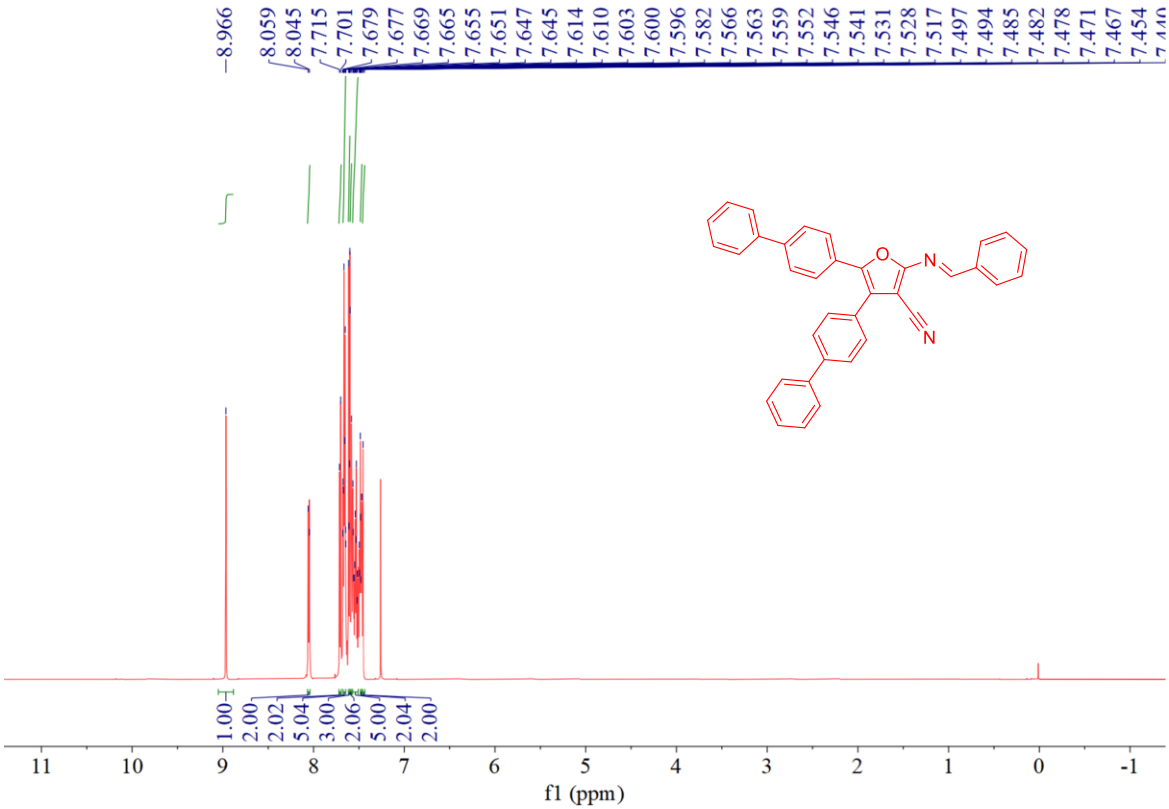
^{1}H NMR spectrum of compound **4g**



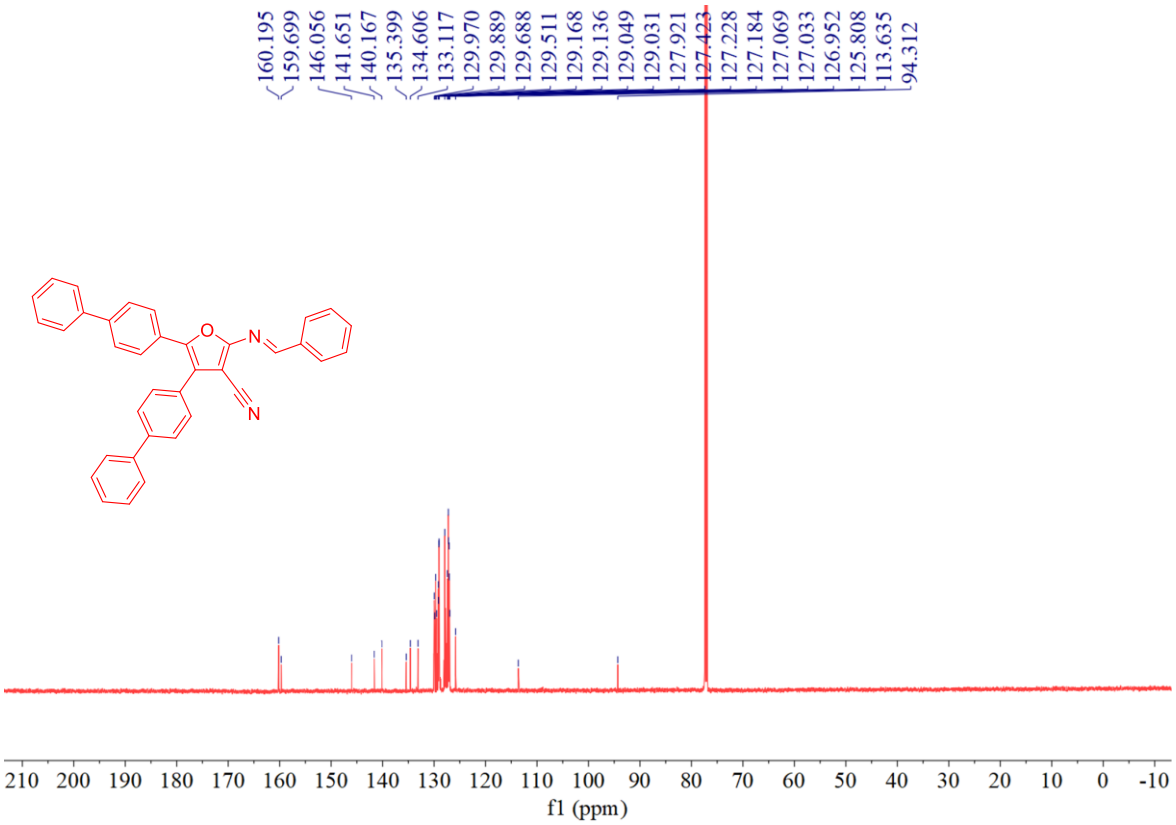
^{13}C NMR spectrum of compound **4g**



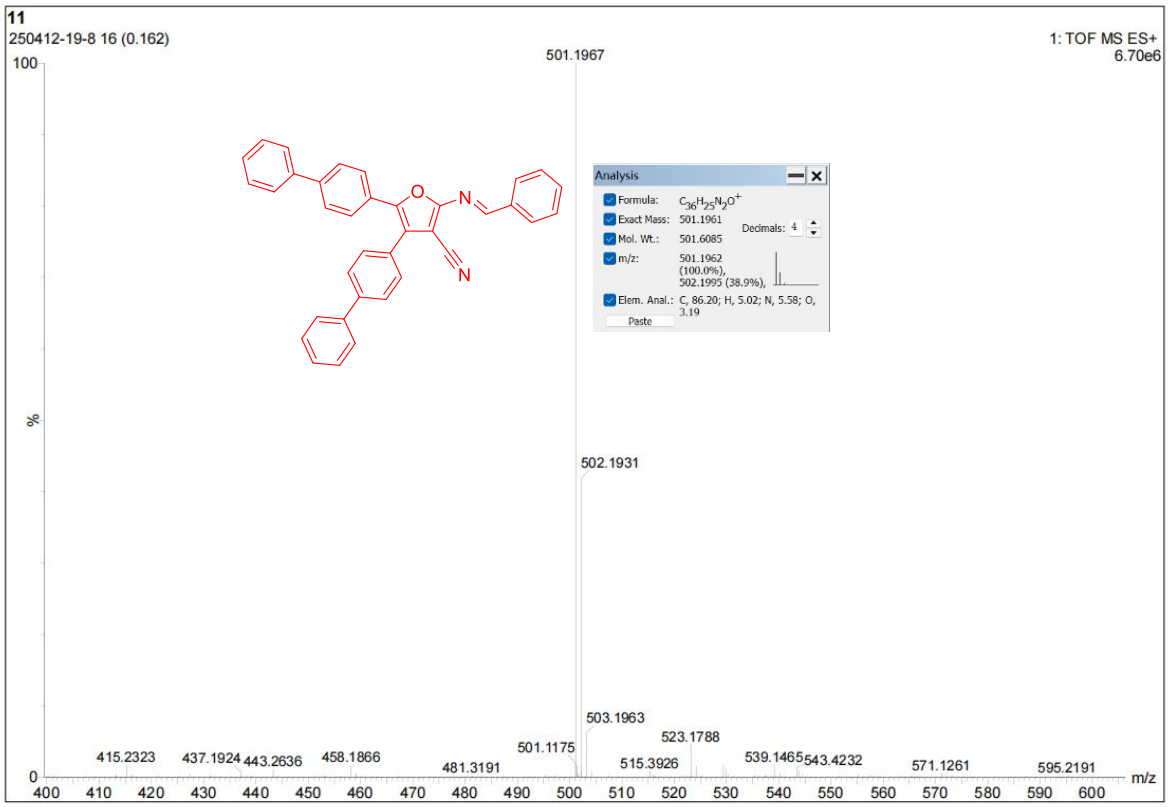
HR-MS spectrum of compound **4g**



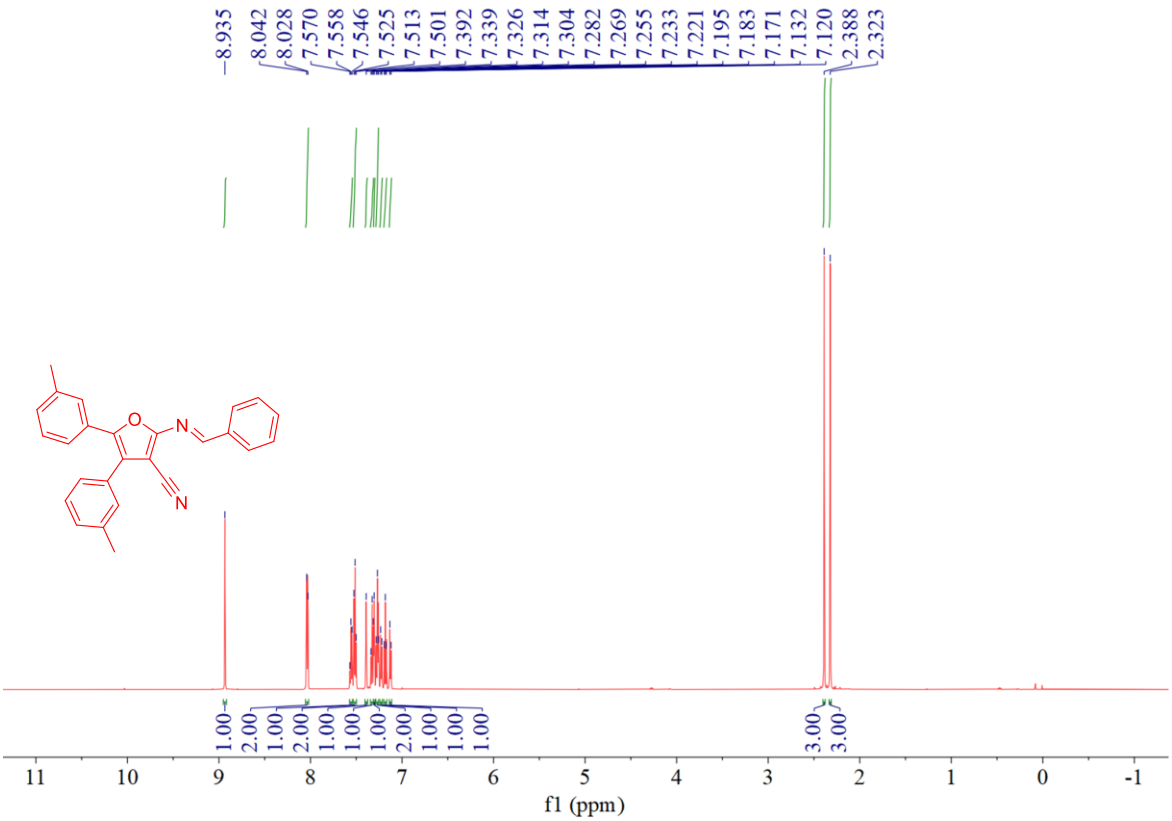
^{1}H NMR spectrum of compound **4h**



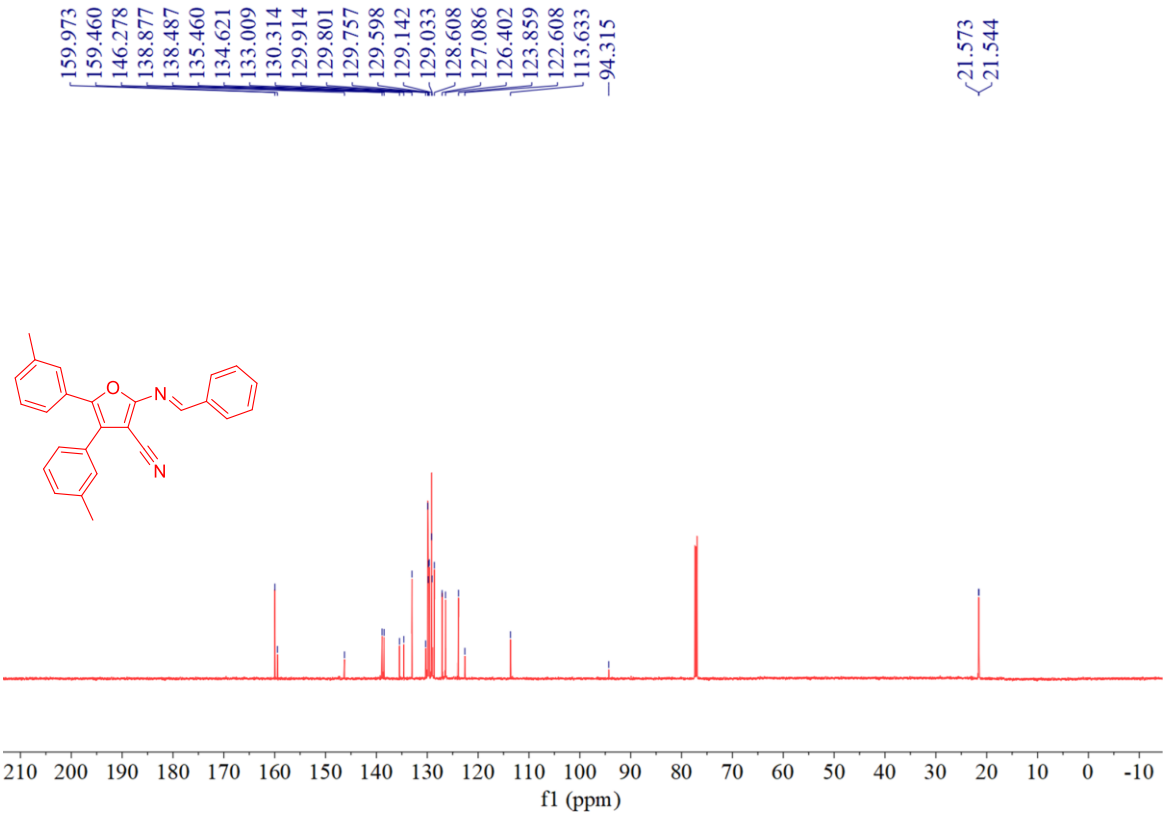
^{13}C NMR spectrum of compound **4h**



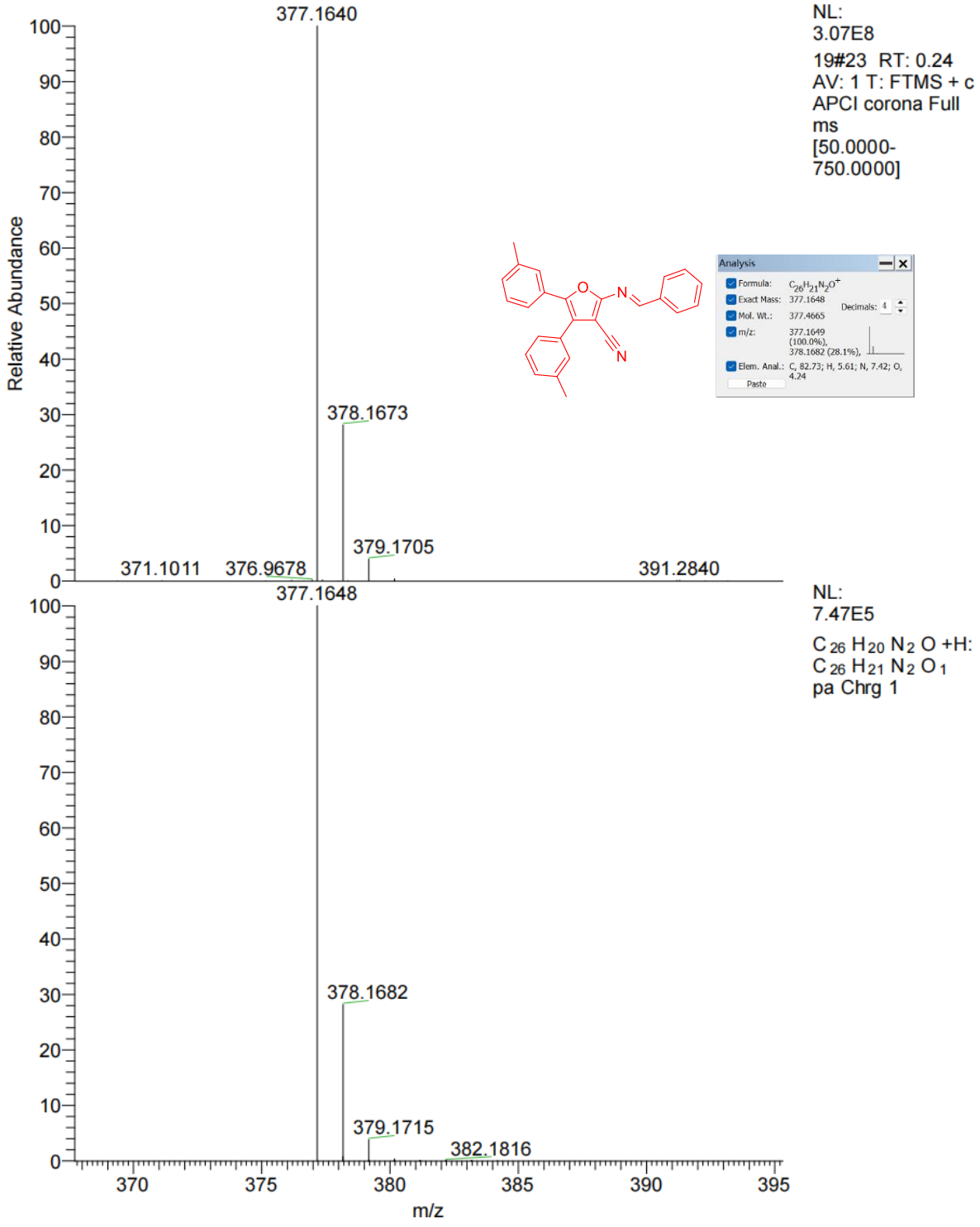
HR-MS spectrum of compound **4h**



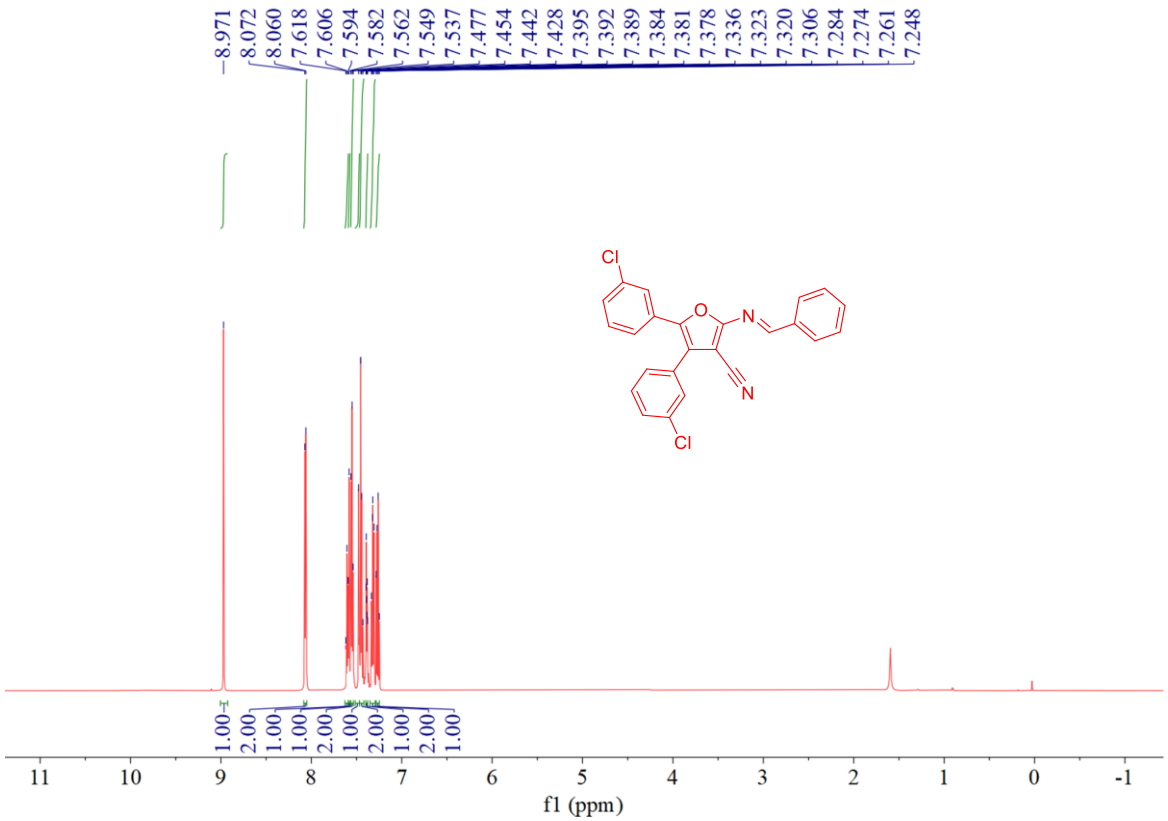
^{1}H NMR spectrum of compound **4i**



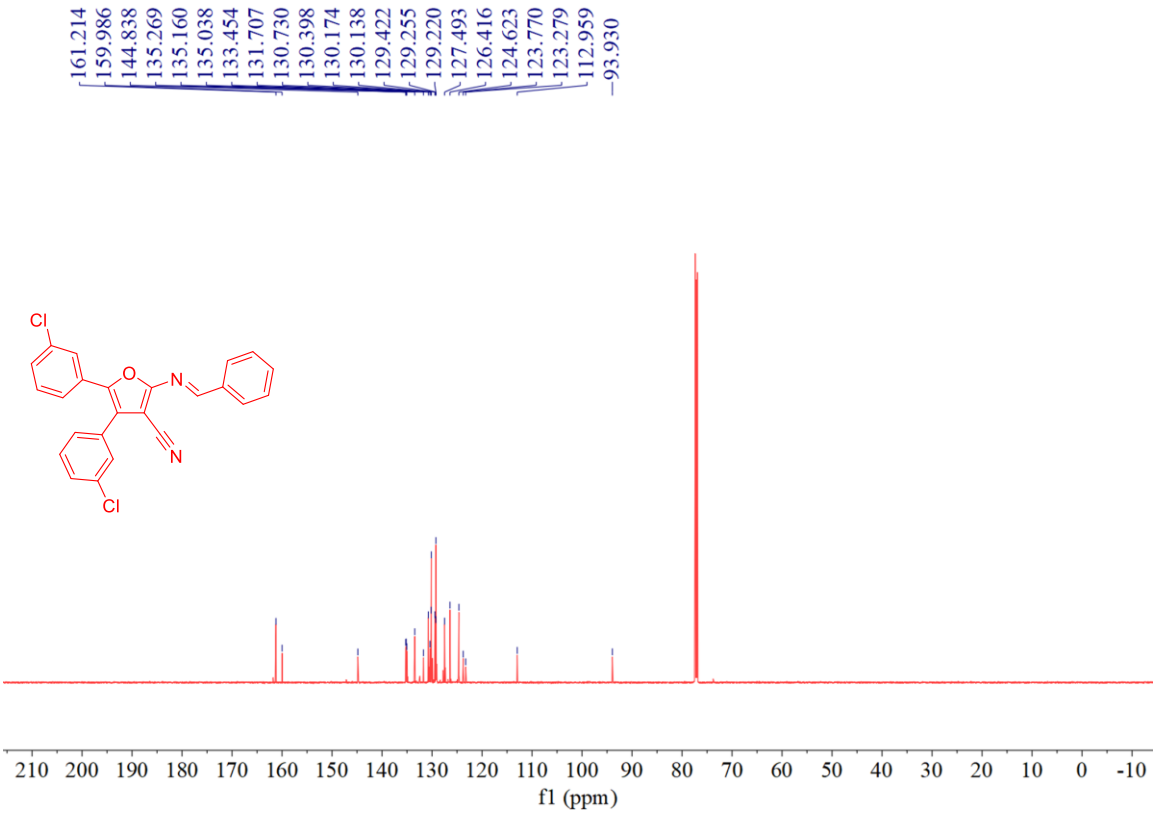
^{13}C NMR spectrum of compound **4i**



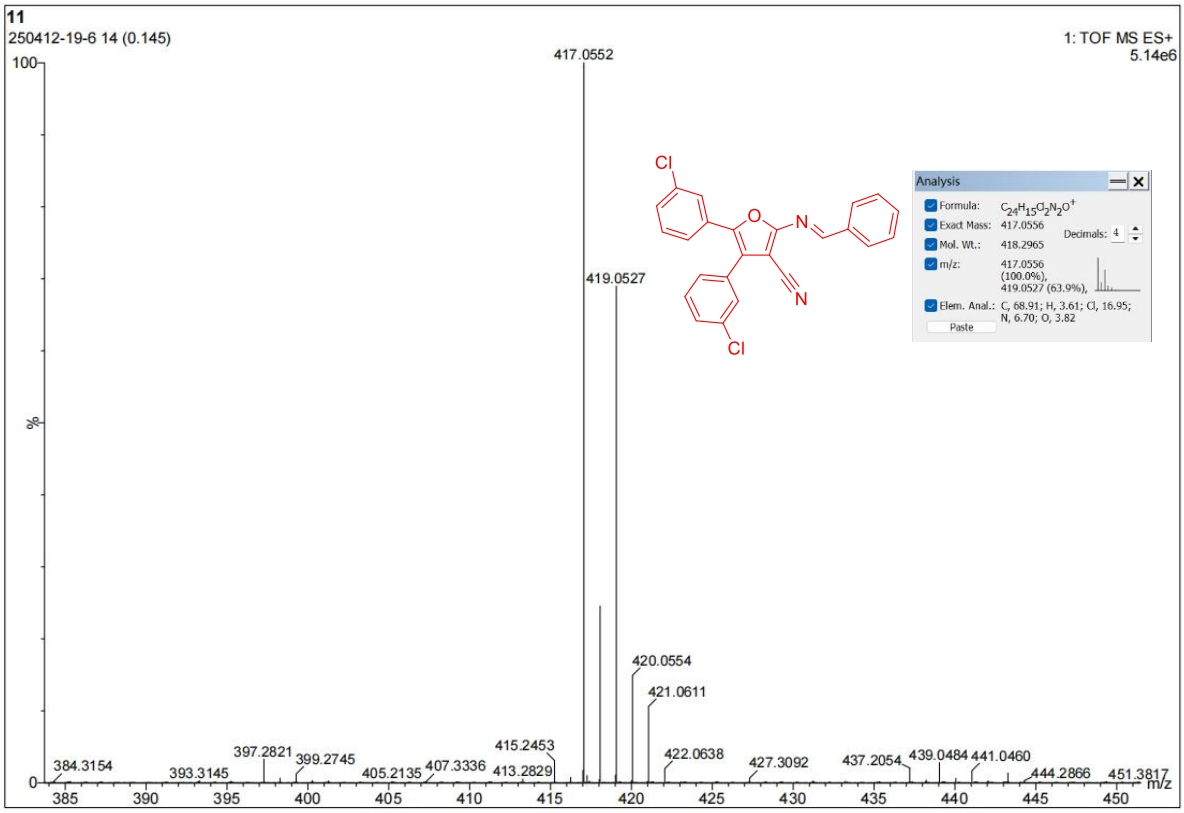
HR-MS spectrum of compound **4i**



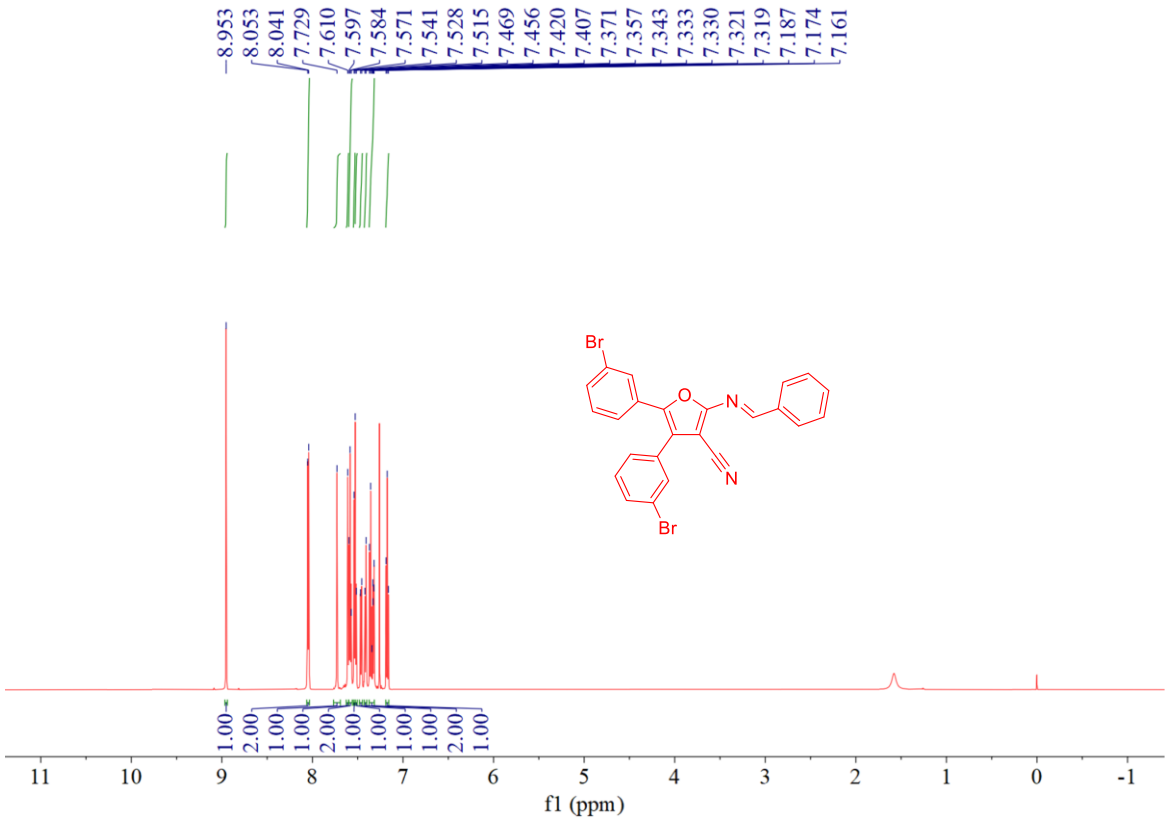
^{1}H NMR spectrum of compound **4j**



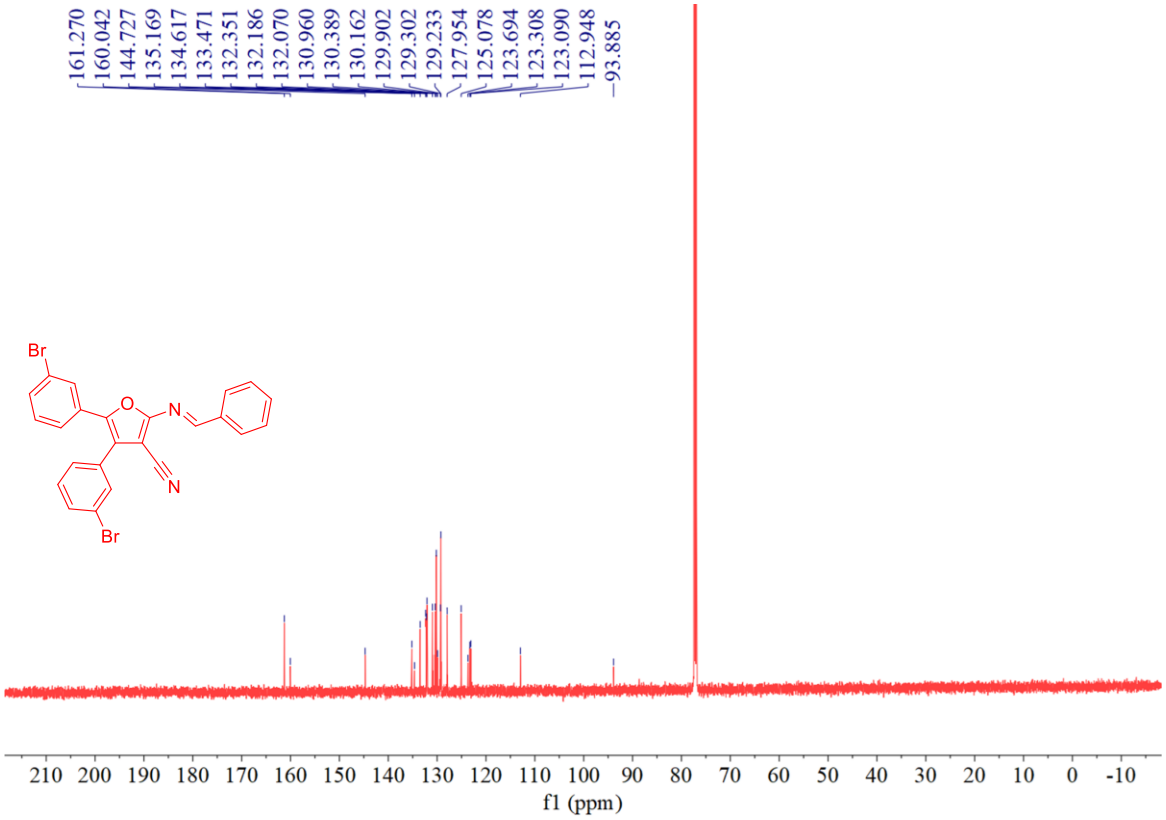
^{13}C NMR spectrum of compound **4j**



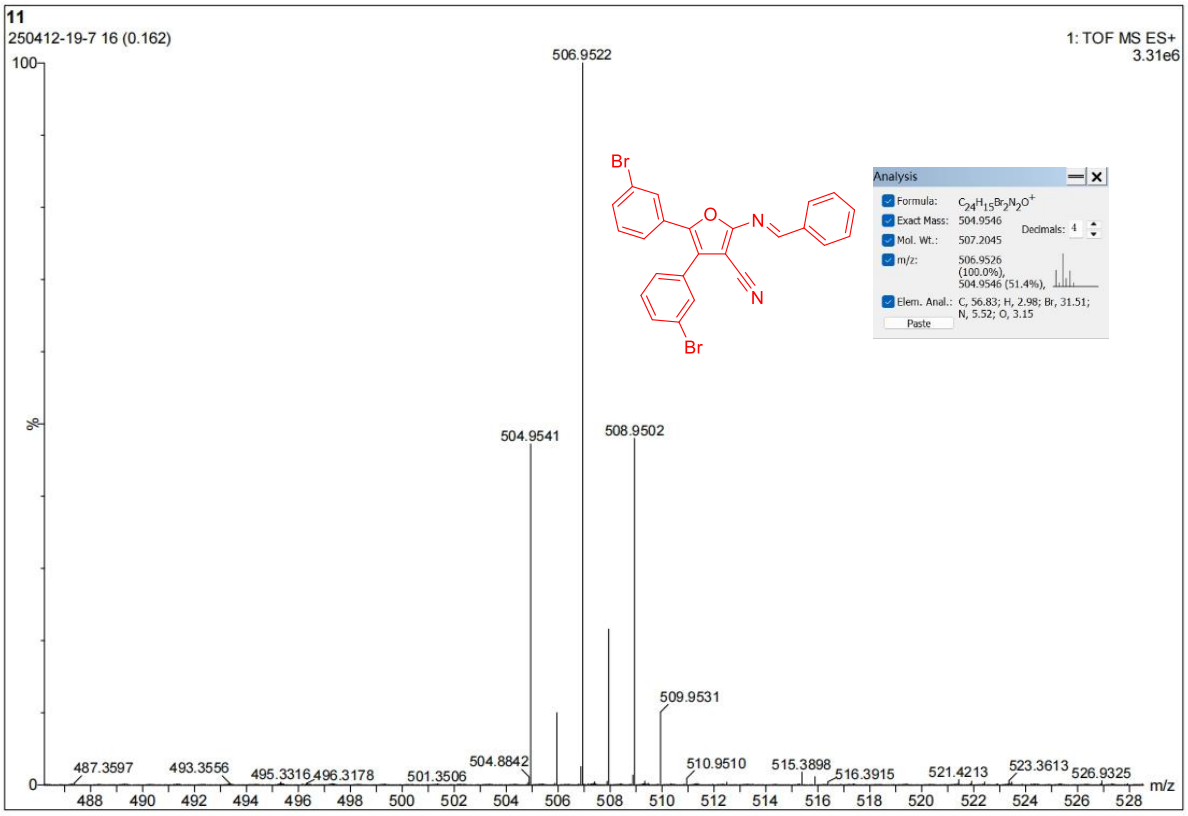
HR-MS spectrum of compound **4j**



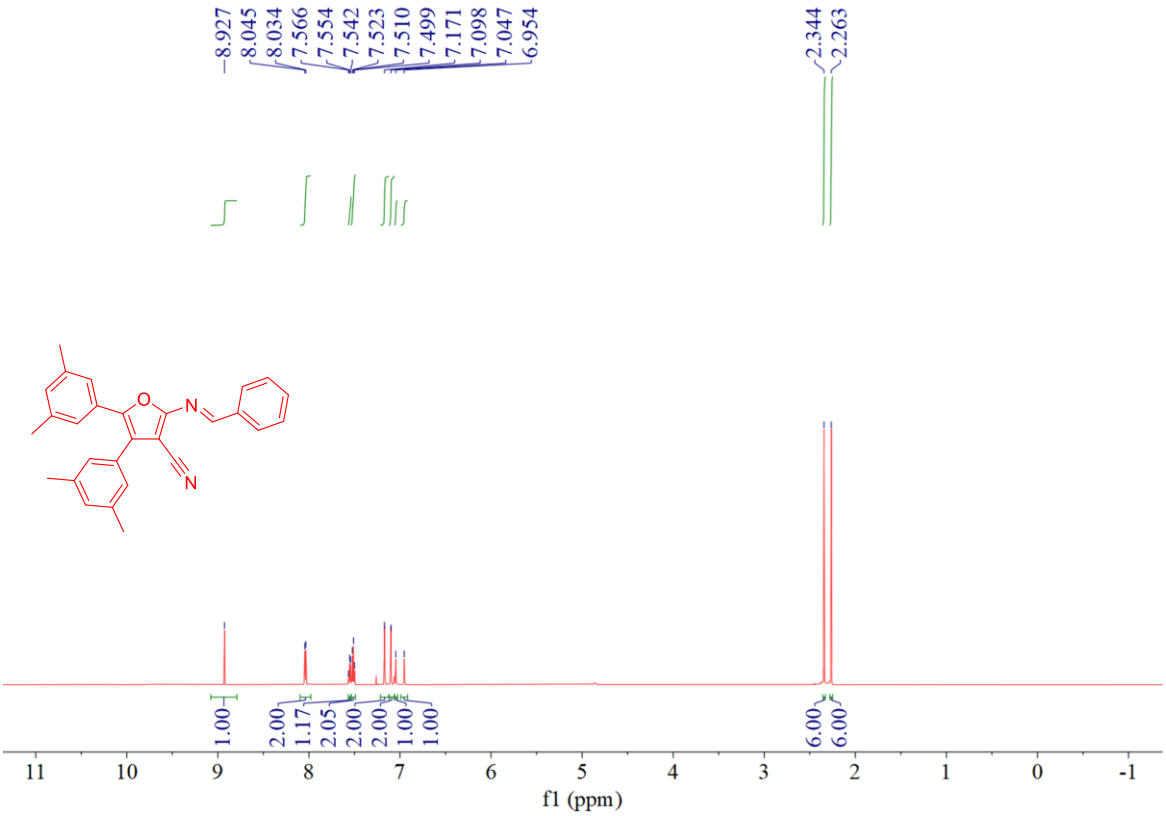
^{1}H NMR spectrum of compound **4k**



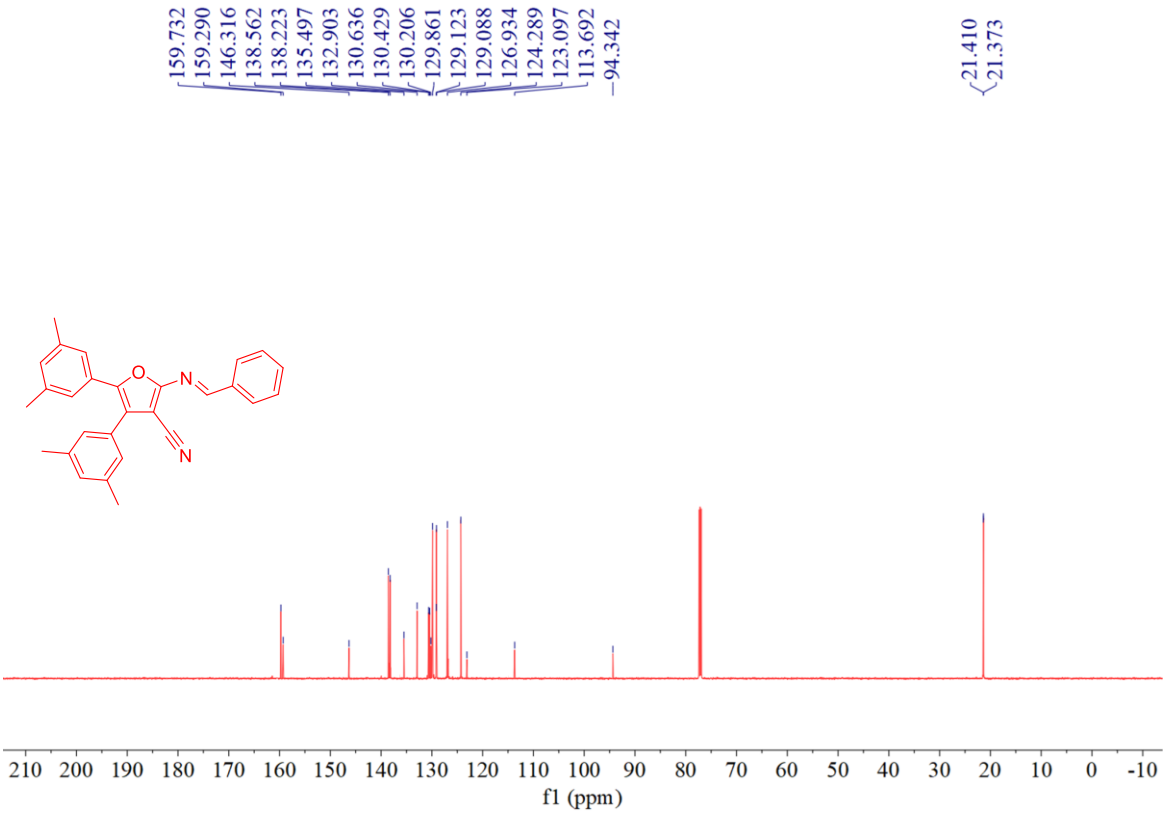
^{13}C NMR spectrum of compound **4k**



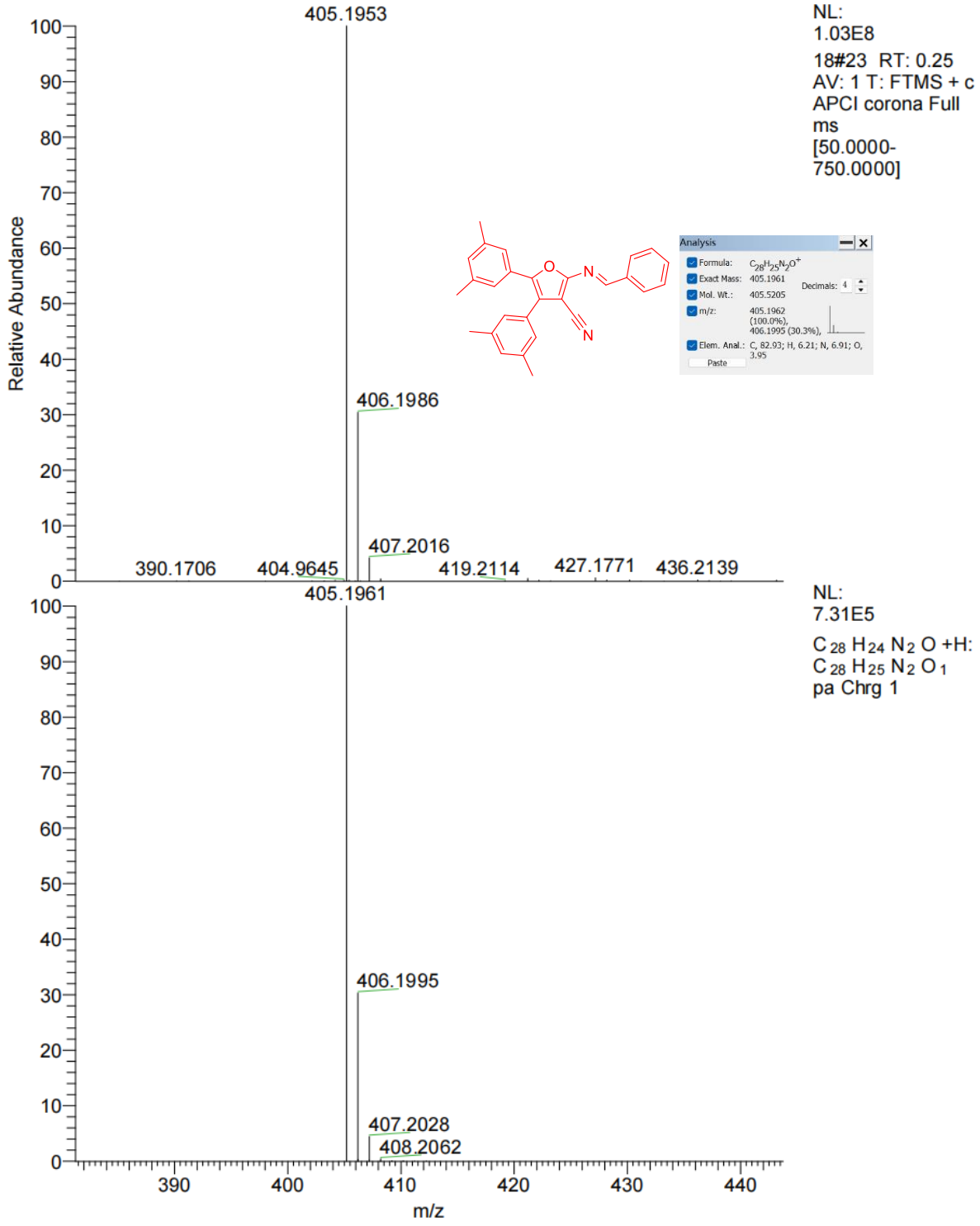
HR-MS spectrum of compound **4k**



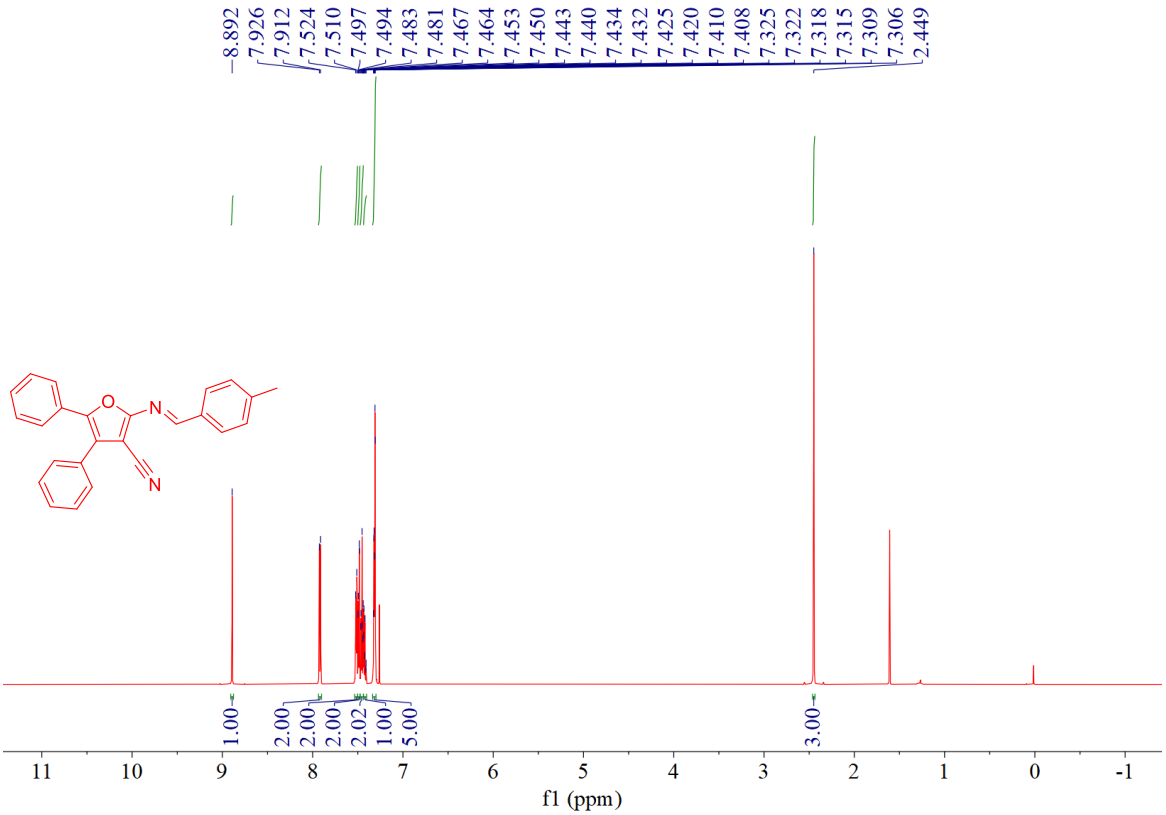
^{1}H NMR spectrum of compound **4l**



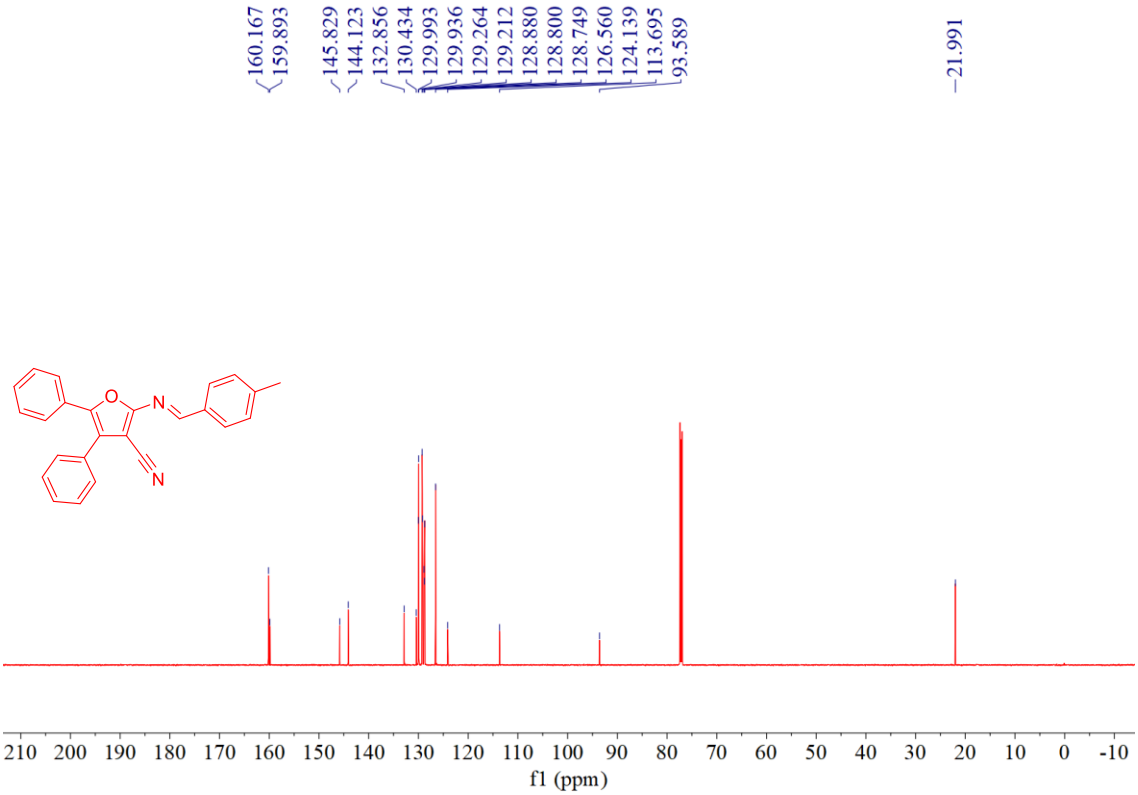
^{13}C NMR spectrum of compound **4l**



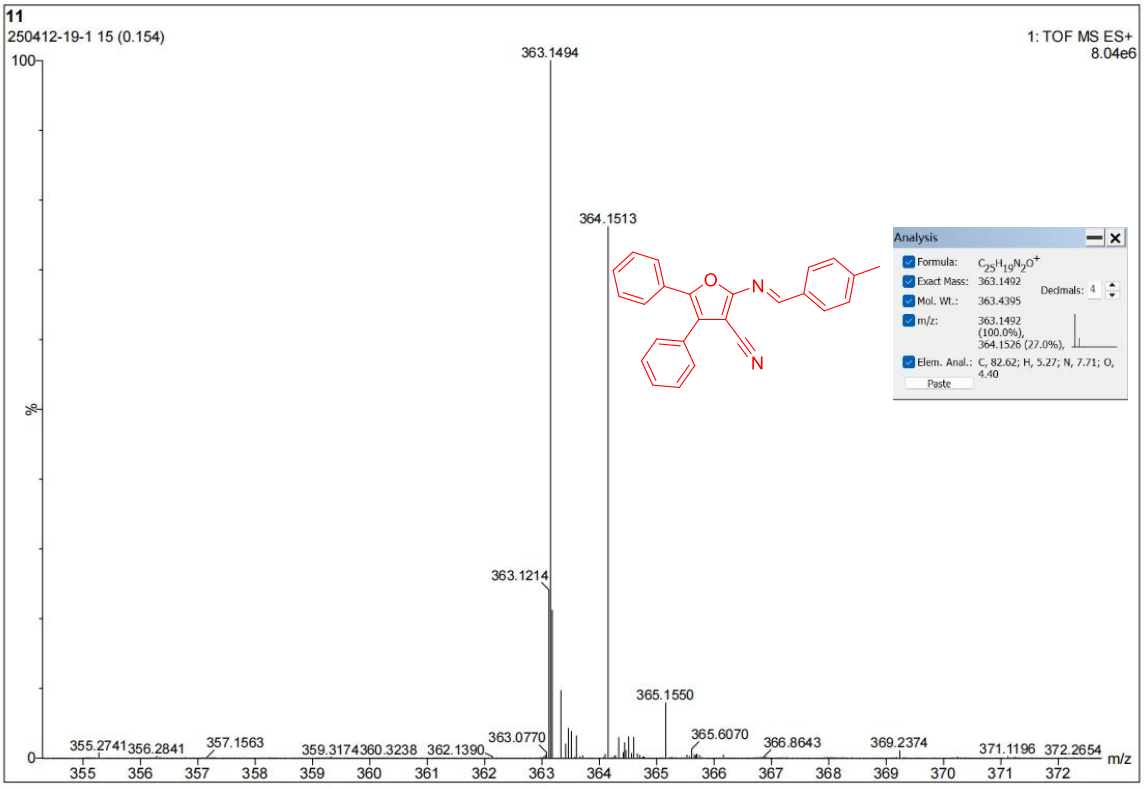
HR-MS spectrum of compound **4l**



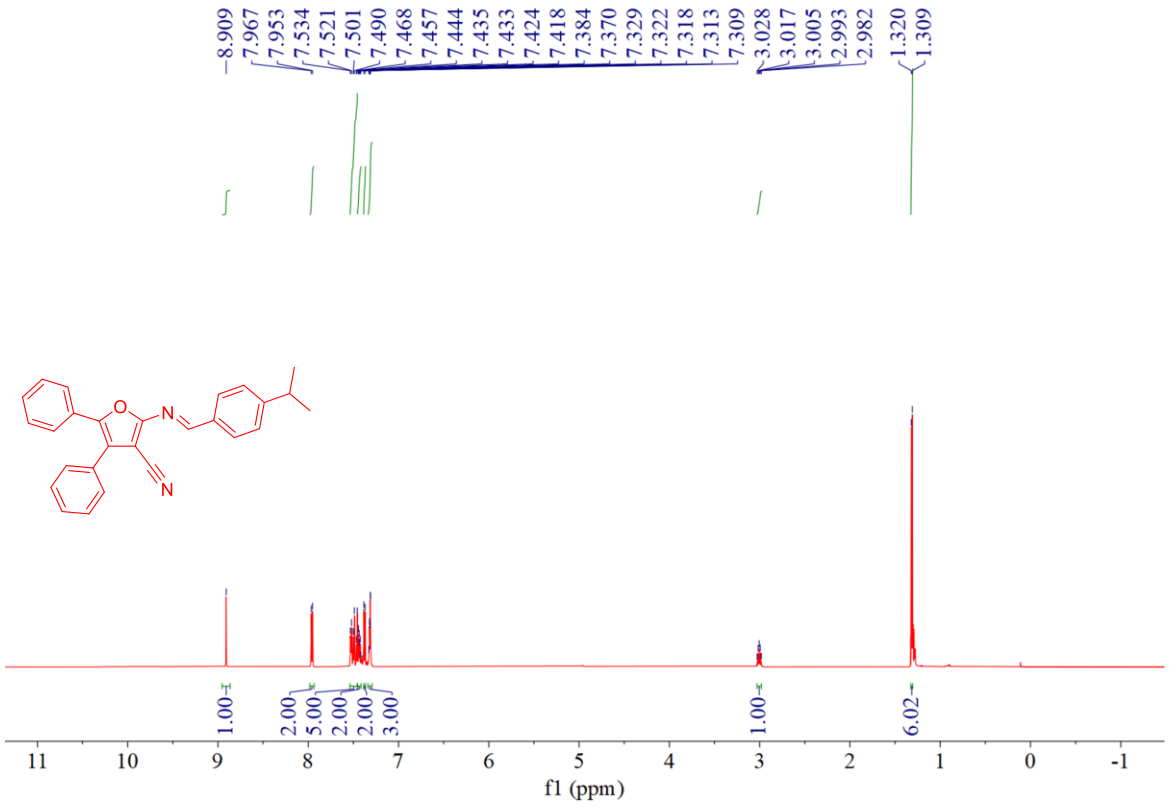
^{1}H NMR spectrum of compound **4m**



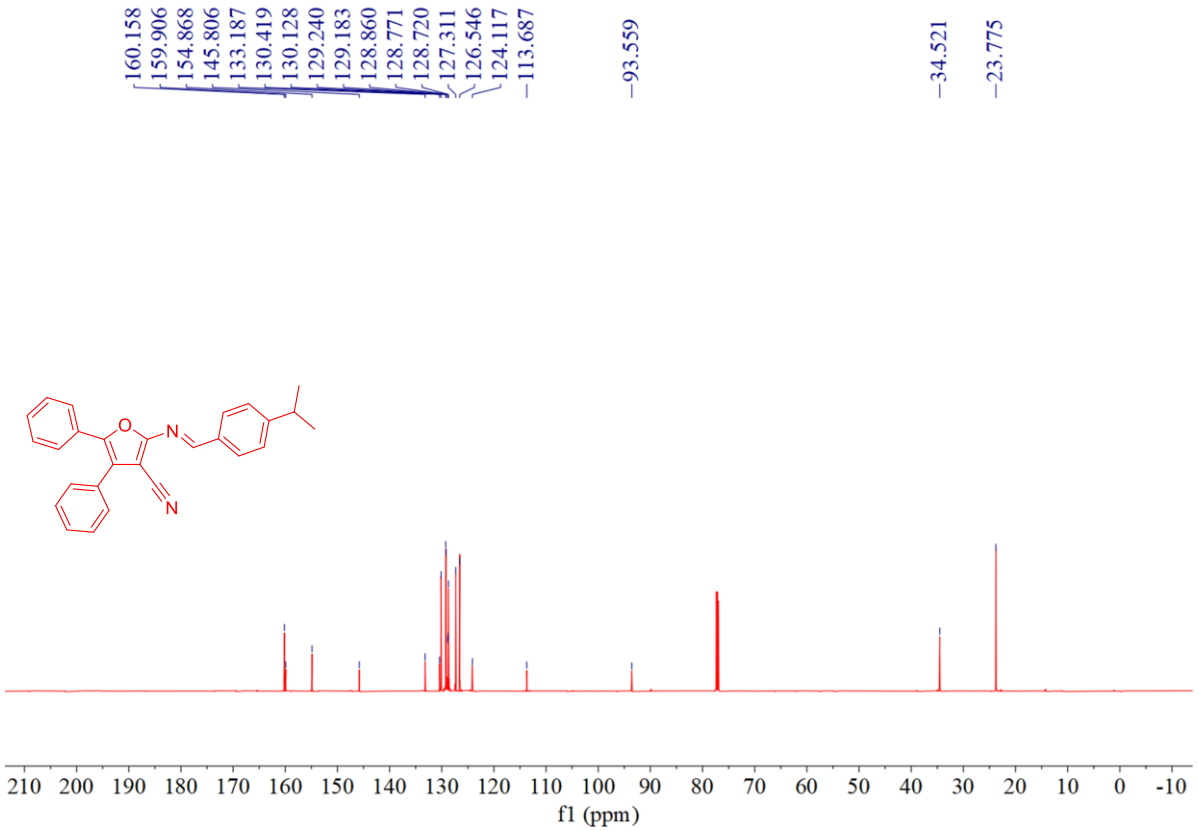
^{13}C NMR spectrum of compound **4m**



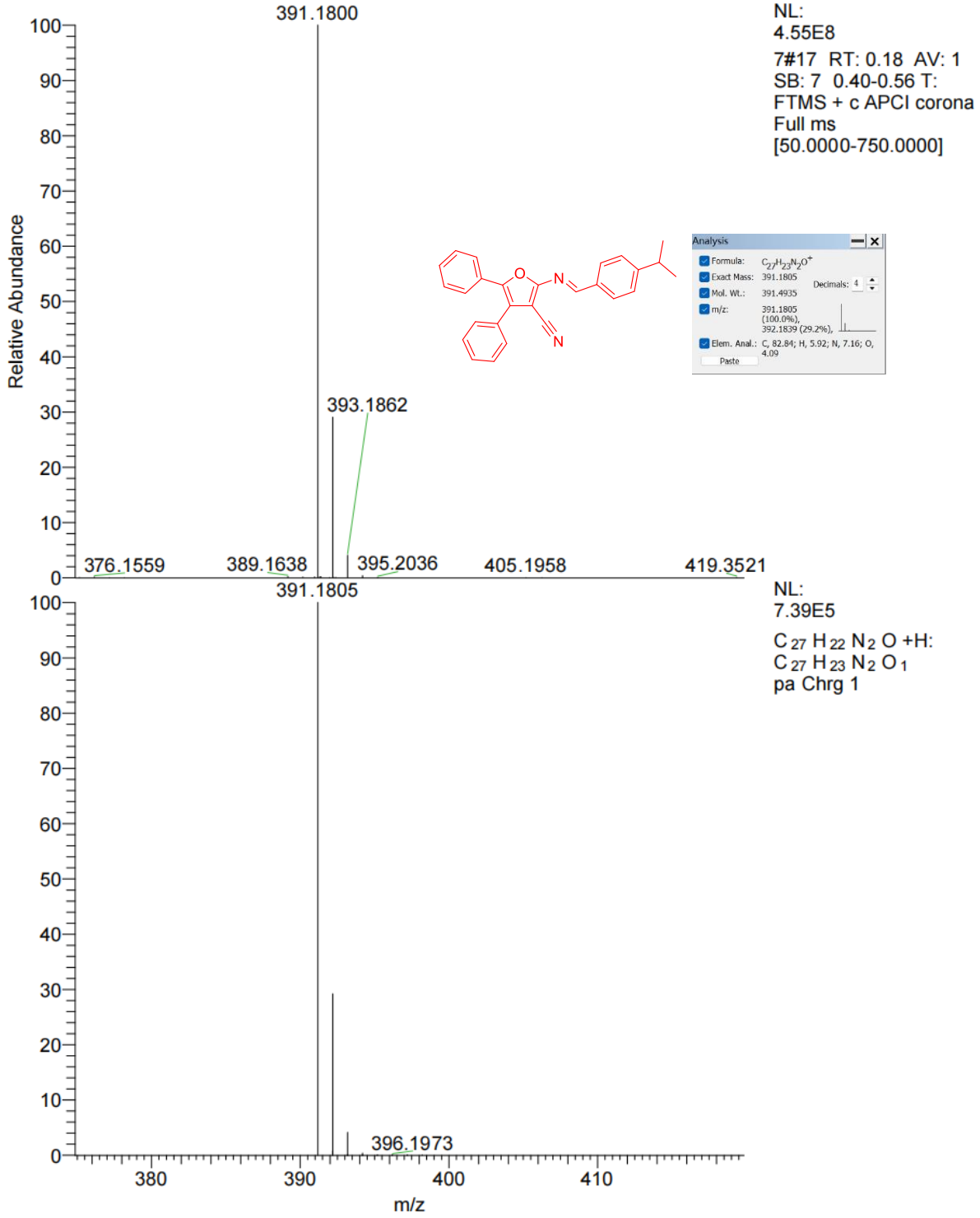
HR-MS spectrum of compound **4m**



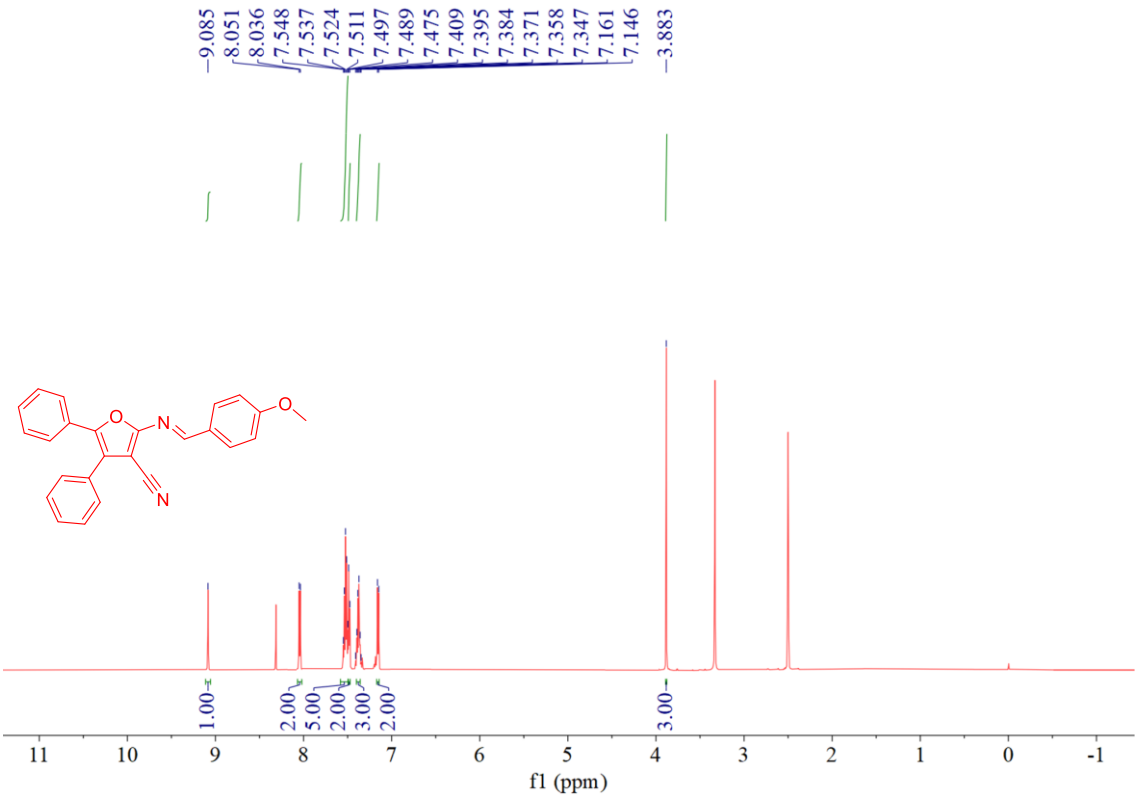
^{1}H NMR spectrum of compound **4n**



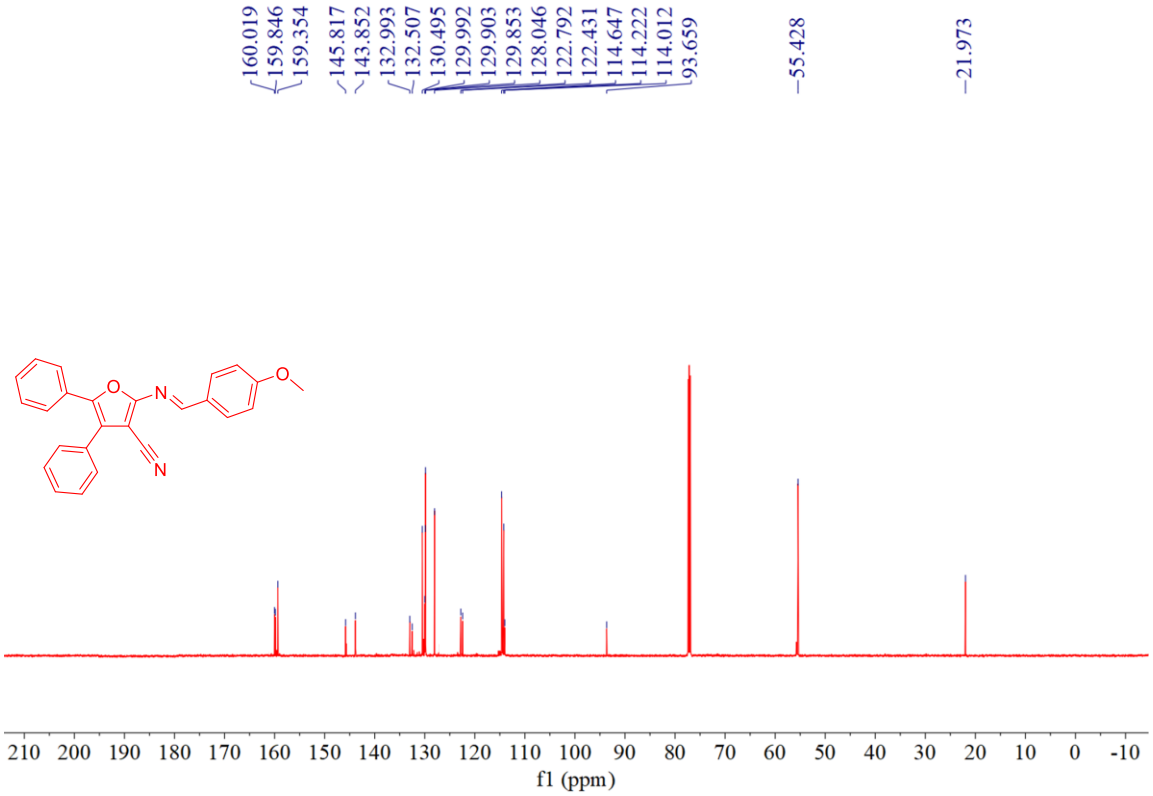
^{13}C NMR spectrum of compound **4n**



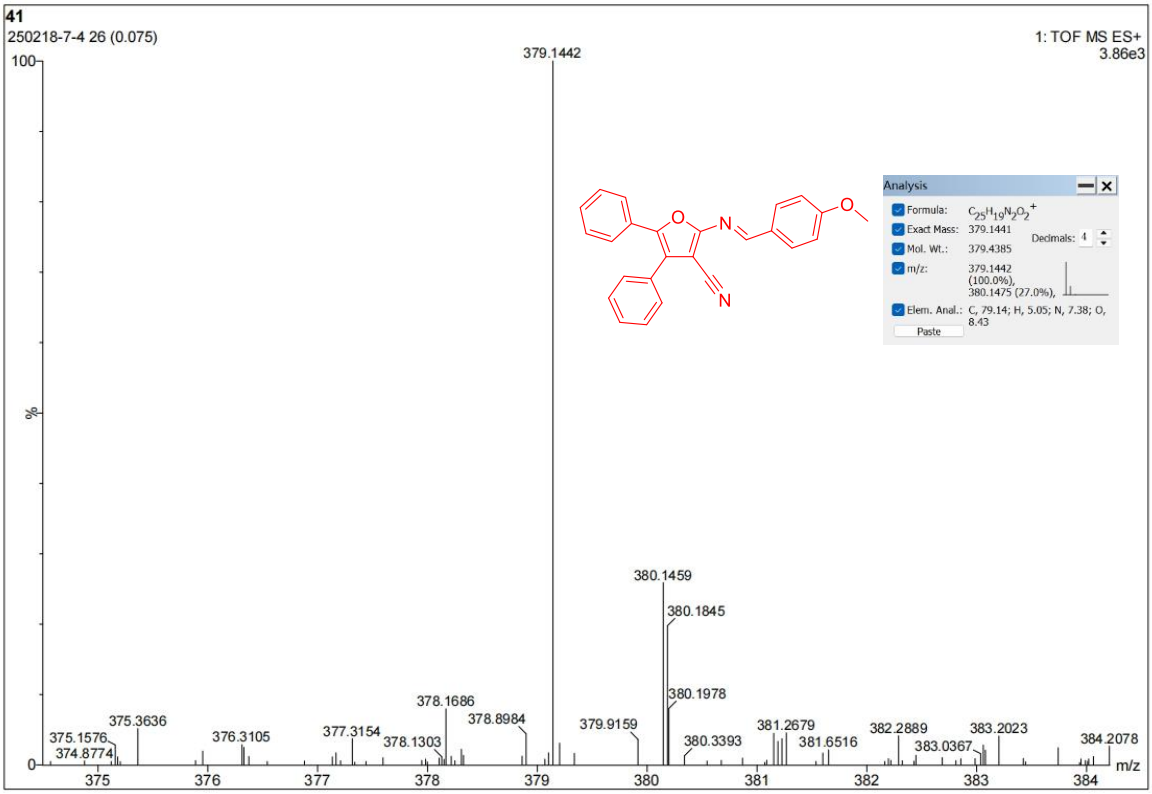
HR-MS spectrum of compound **4n**



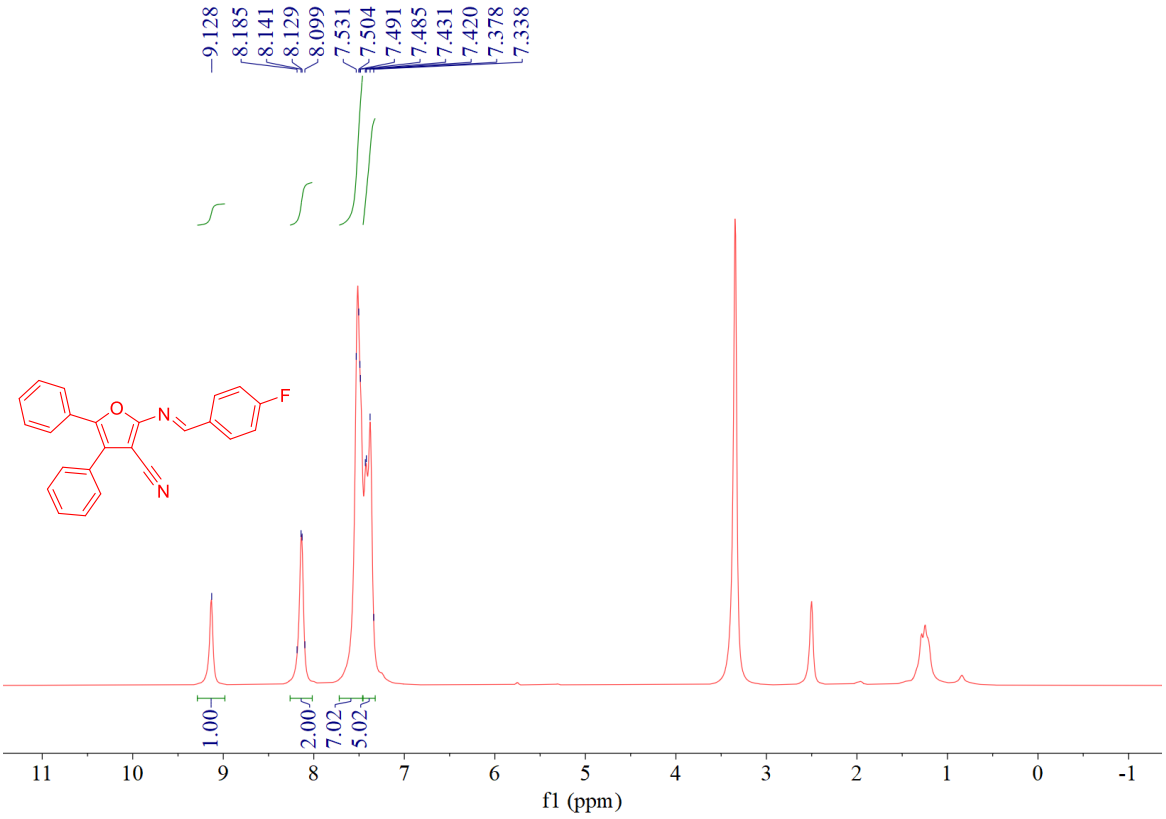
^{1}H NMR spectrum of compound **4o**



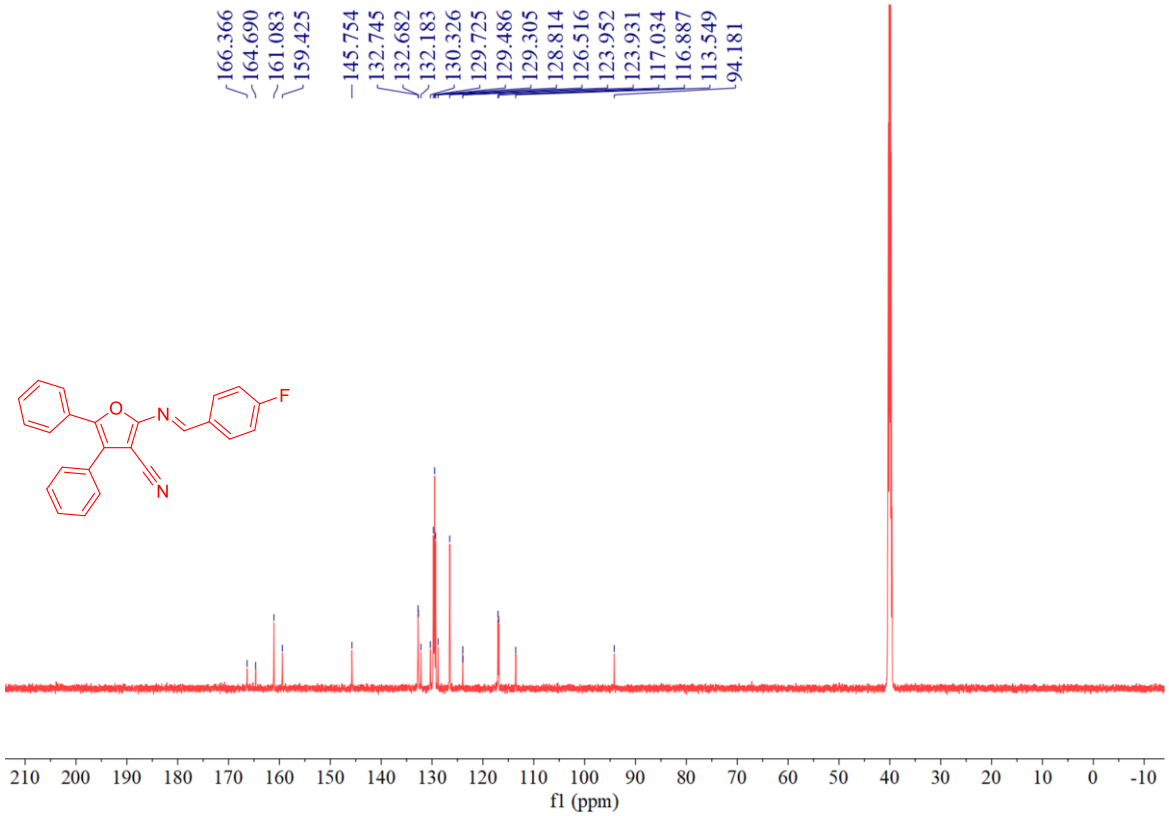
^{13}C NMR spectrum of compound **4o**



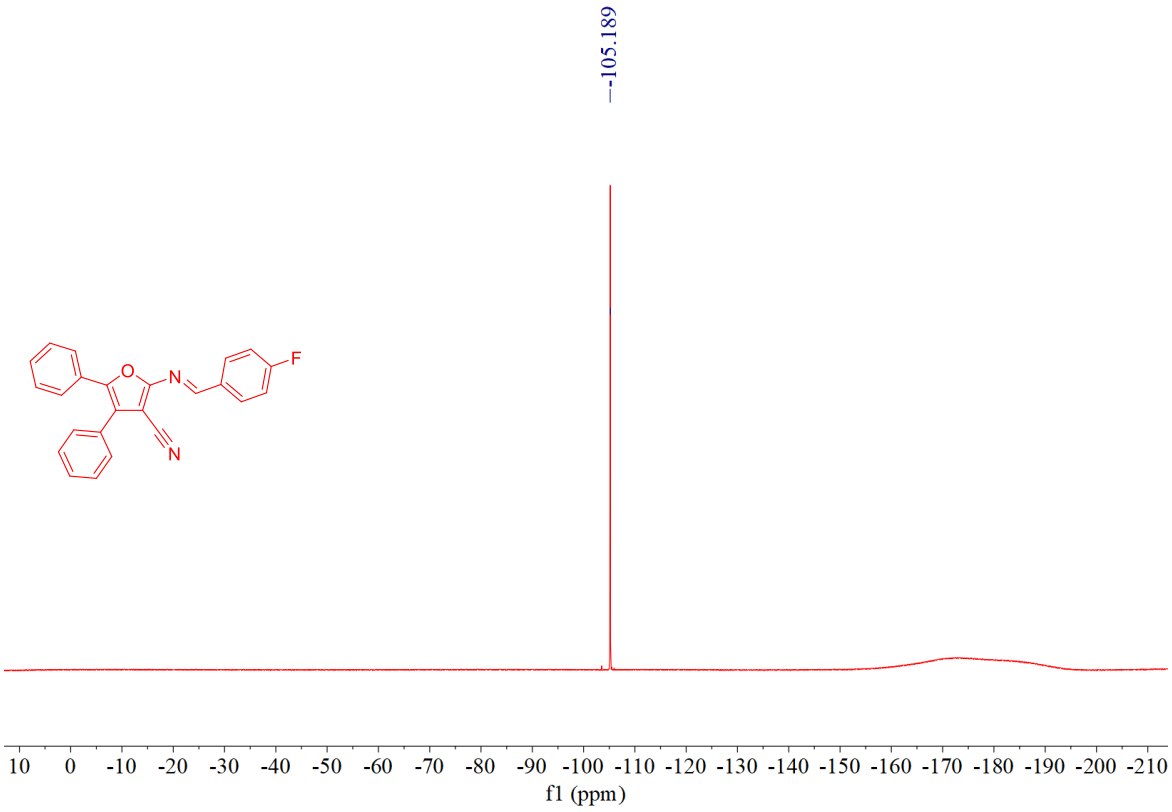
HR-MS spectrum of compound **4o**



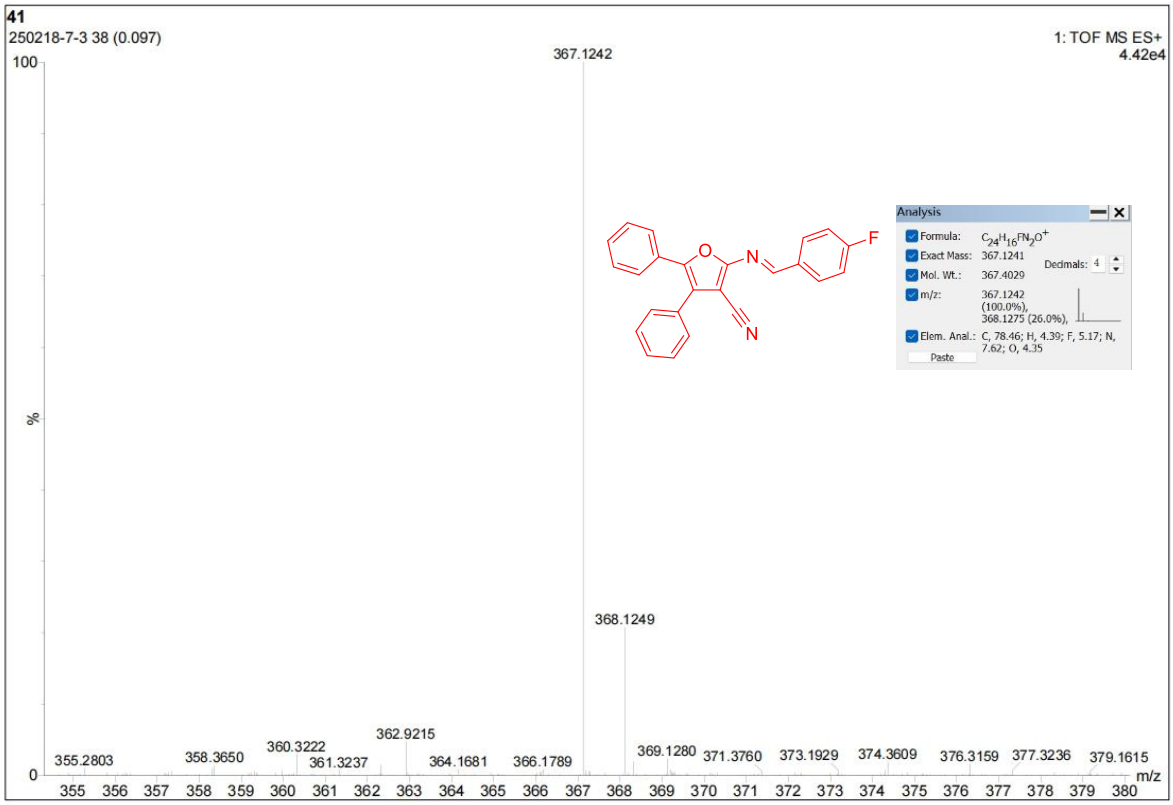
^{1}H NMR spectrum of compound **4p**



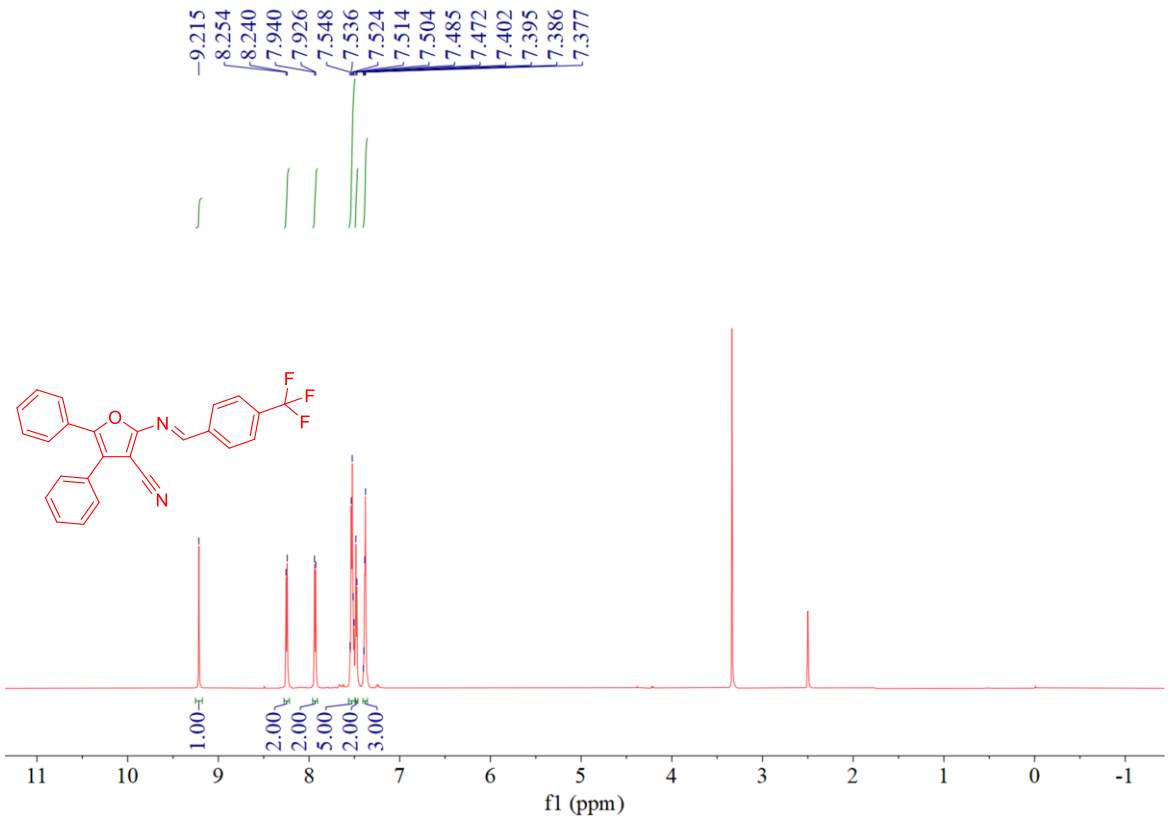
^{13}C NMR spectrum of compound **4p**



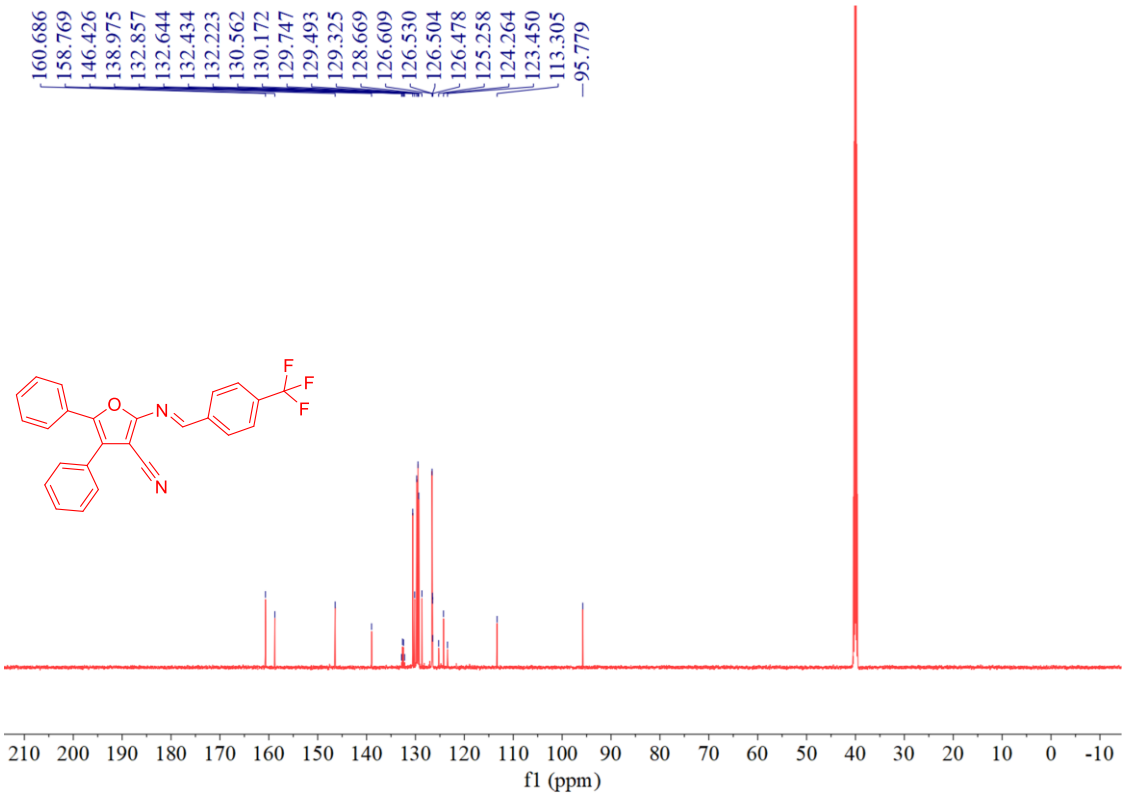
^{19}F NMR spectrum of compound **4p**



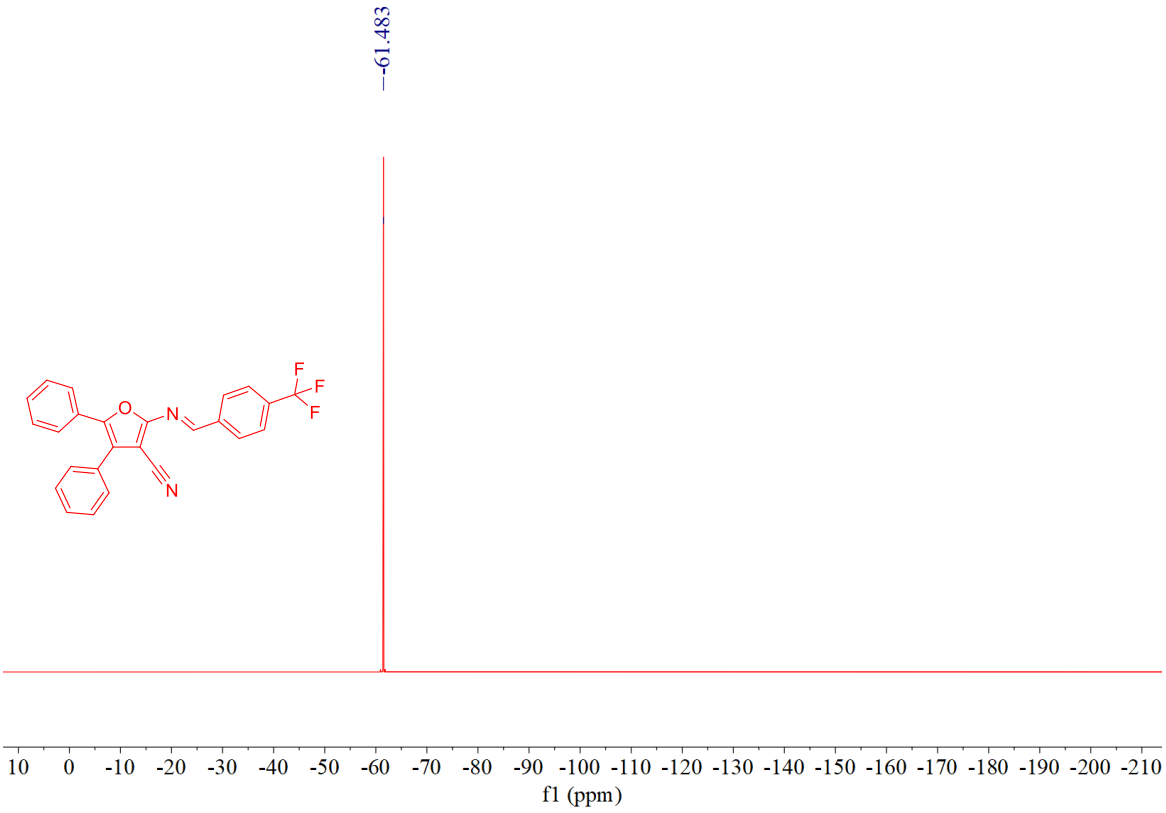
HR-MS spectrum of compound **4p**



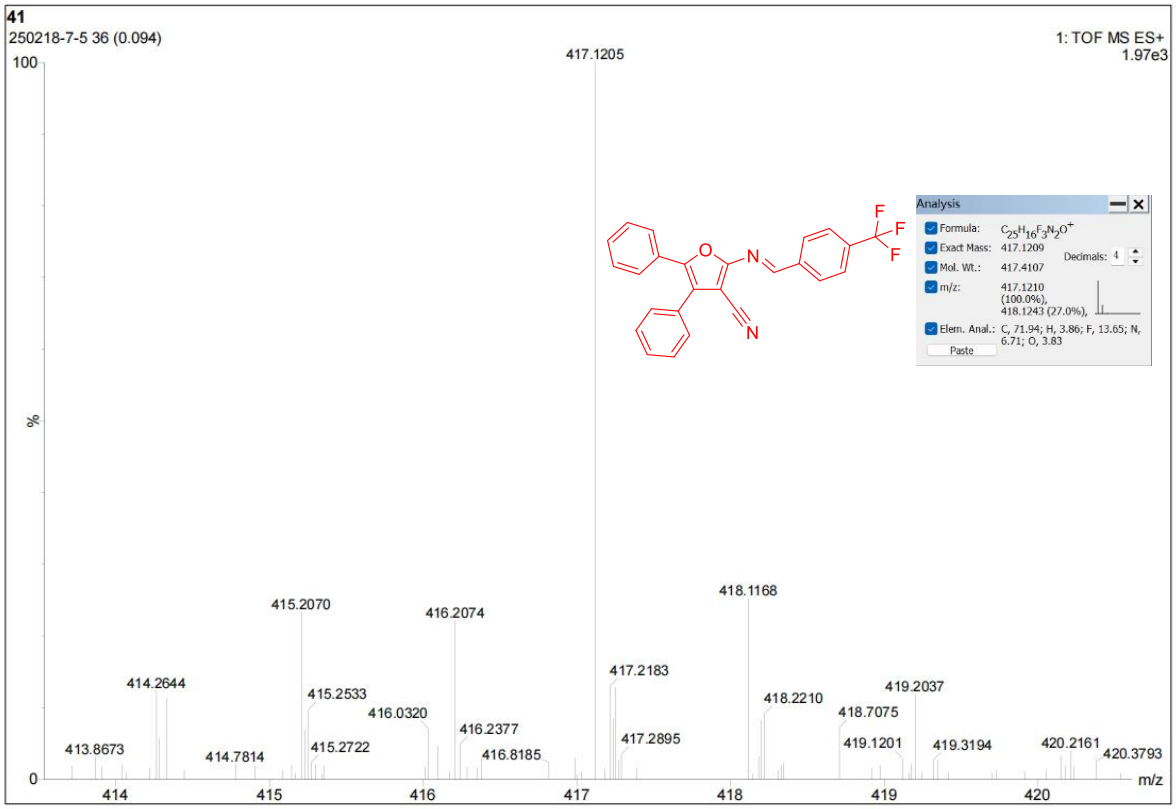
^{1}H NMR spectrum of compound **4q**



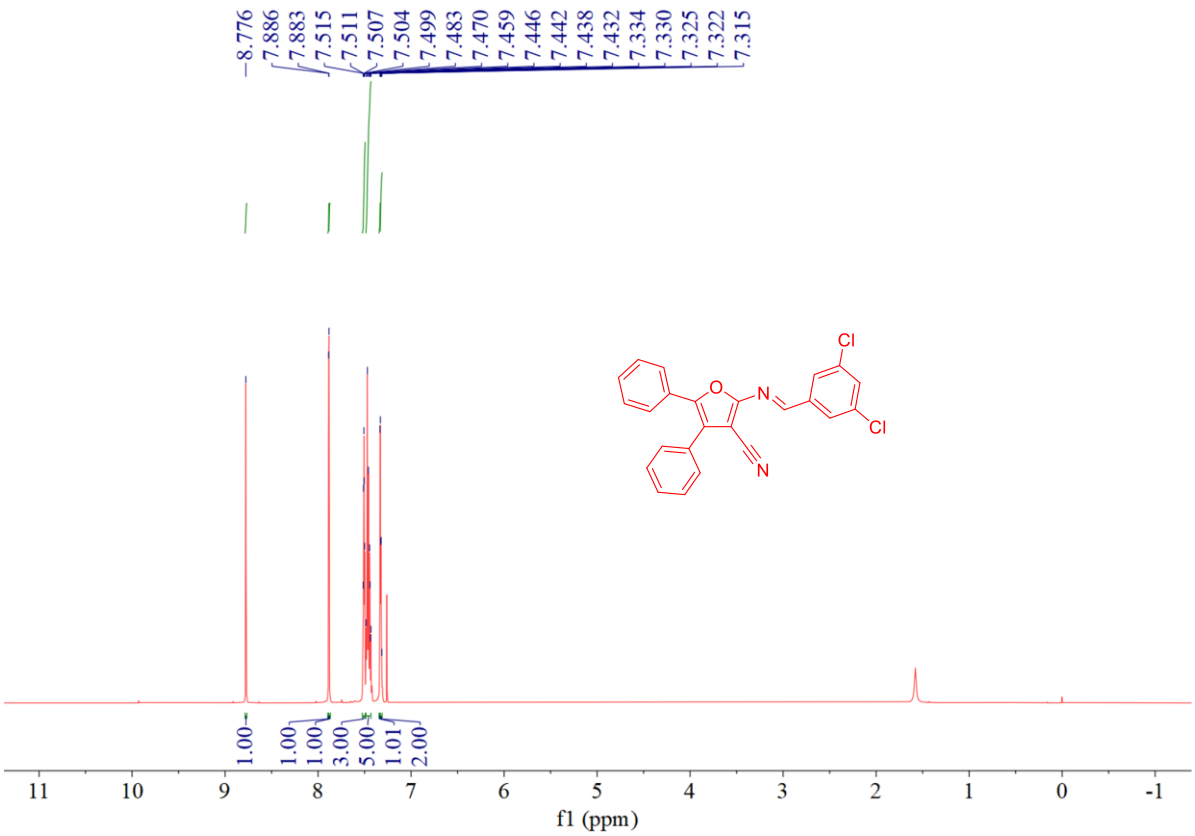
^{13}C NMR spectrum of compound **4q**



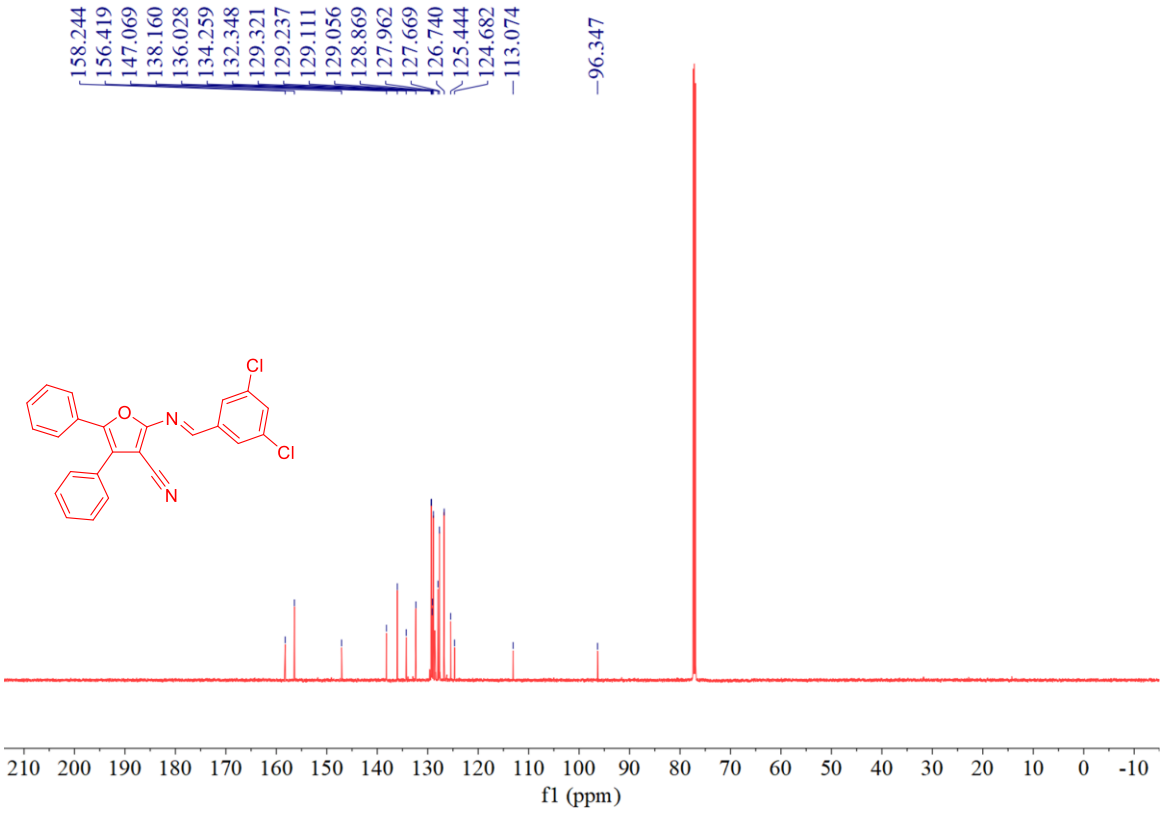
^{19}F NMR spectrum of compound **4q**



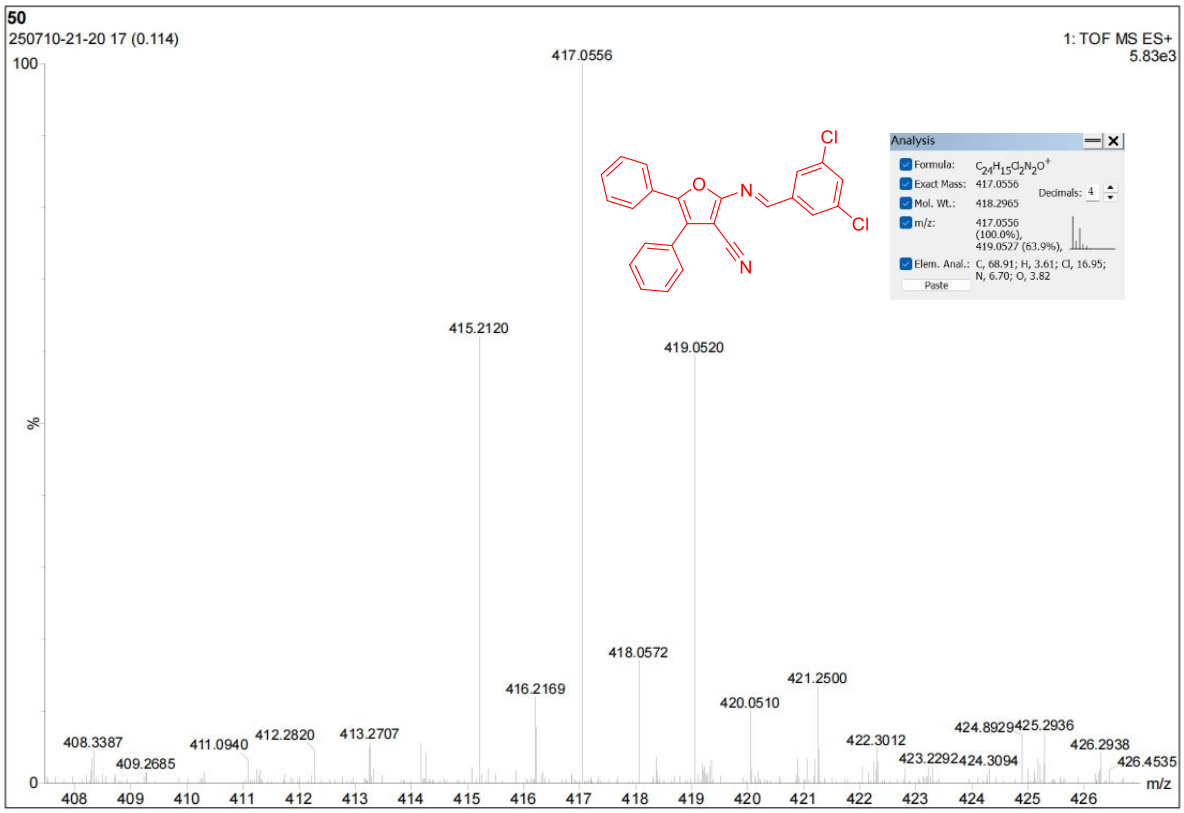
HR-MS spectrum of compound **4q**



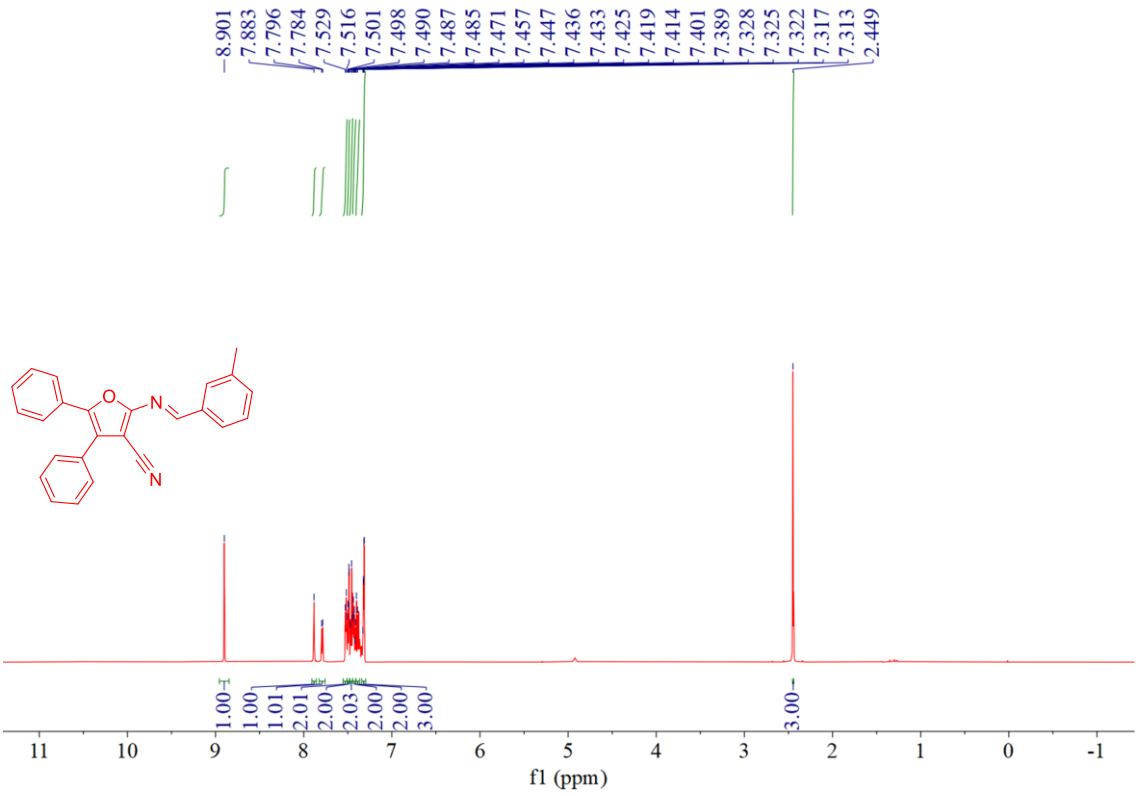
^{1}H NMR spectrum of compound **4r**



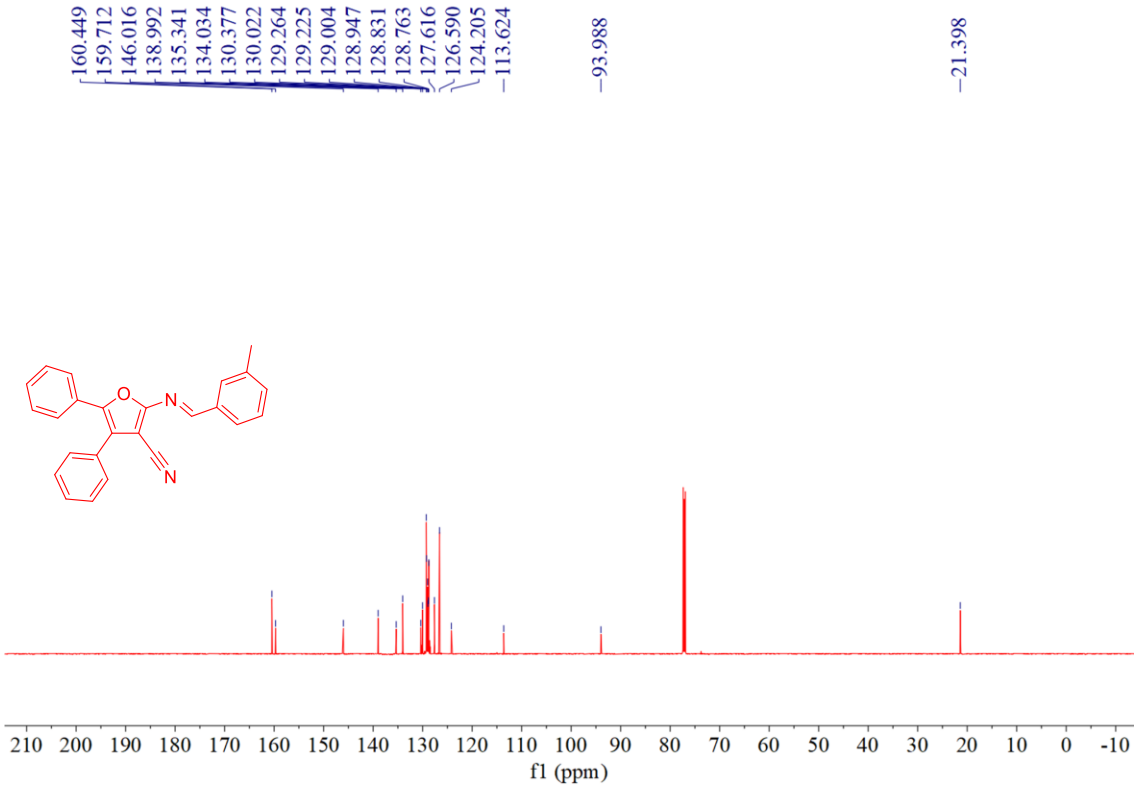
^{13}C NMR spectrum of compound **4r**



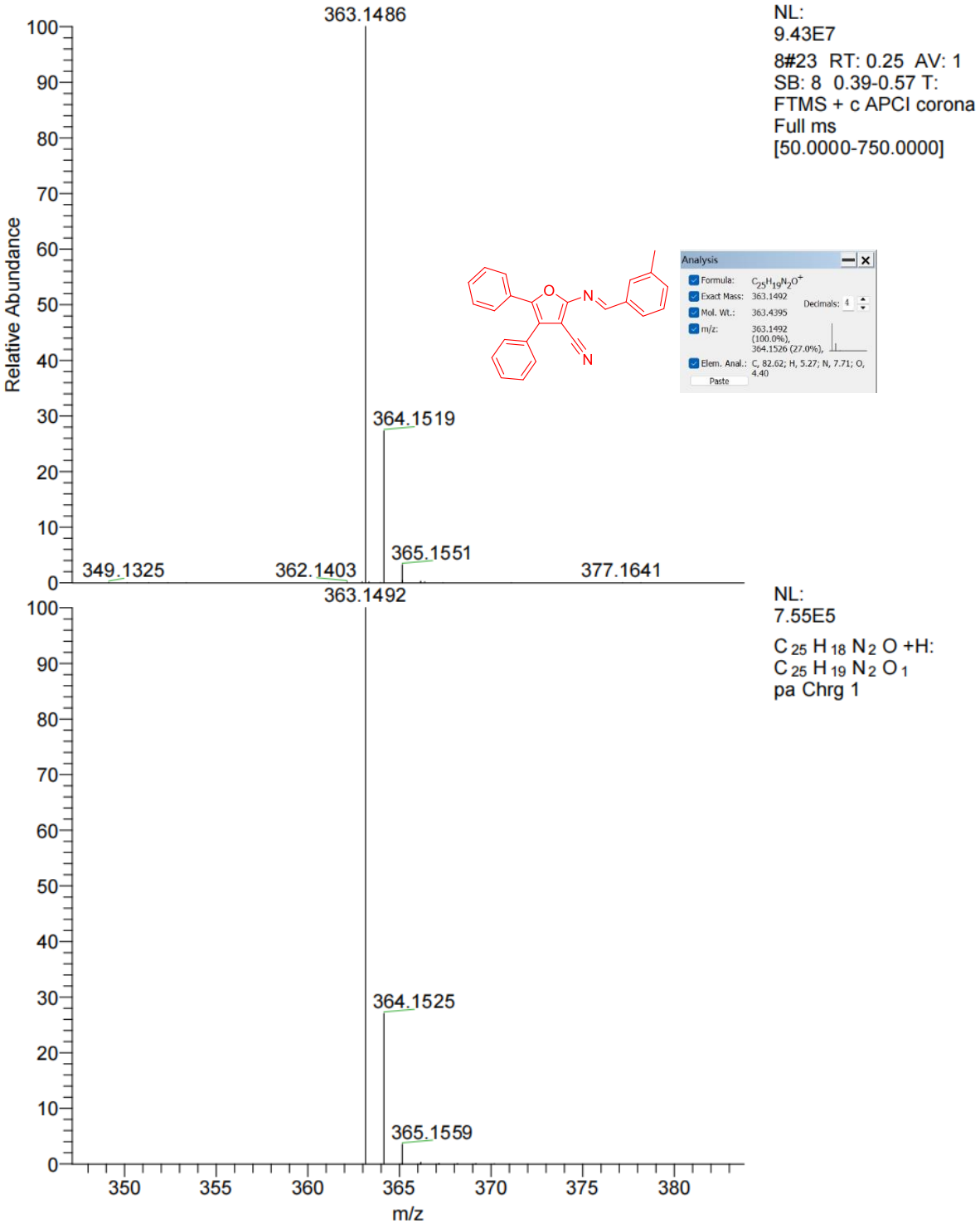
HR-MS spectrum of compound **4r**



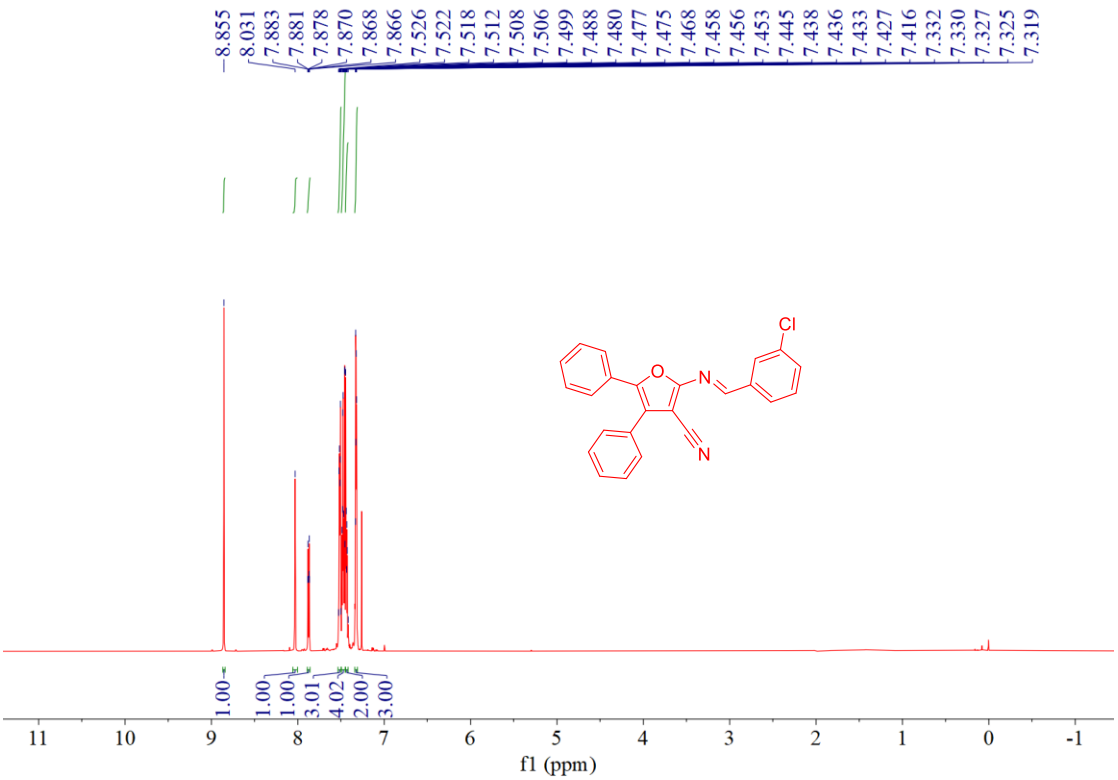
^{1}H NMR spectrum of compound **4s**



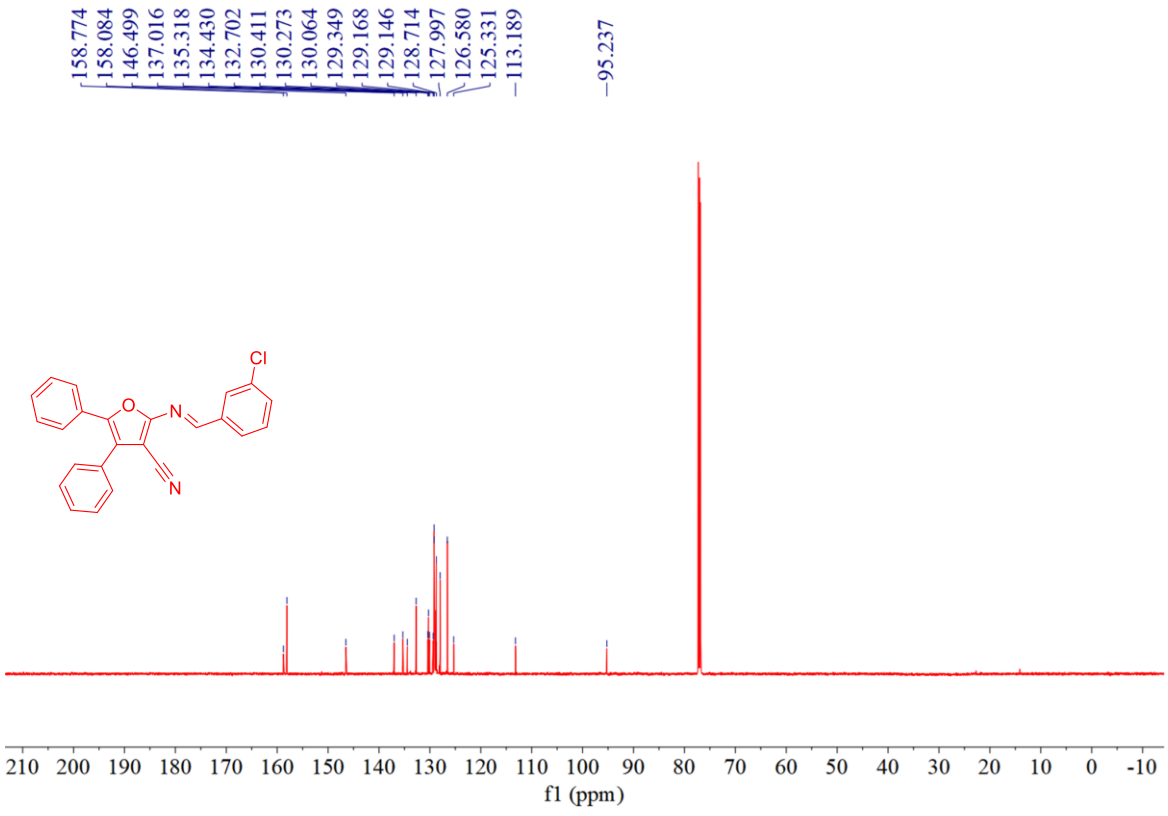
^{13}C NMR spectrum of compound **4s**



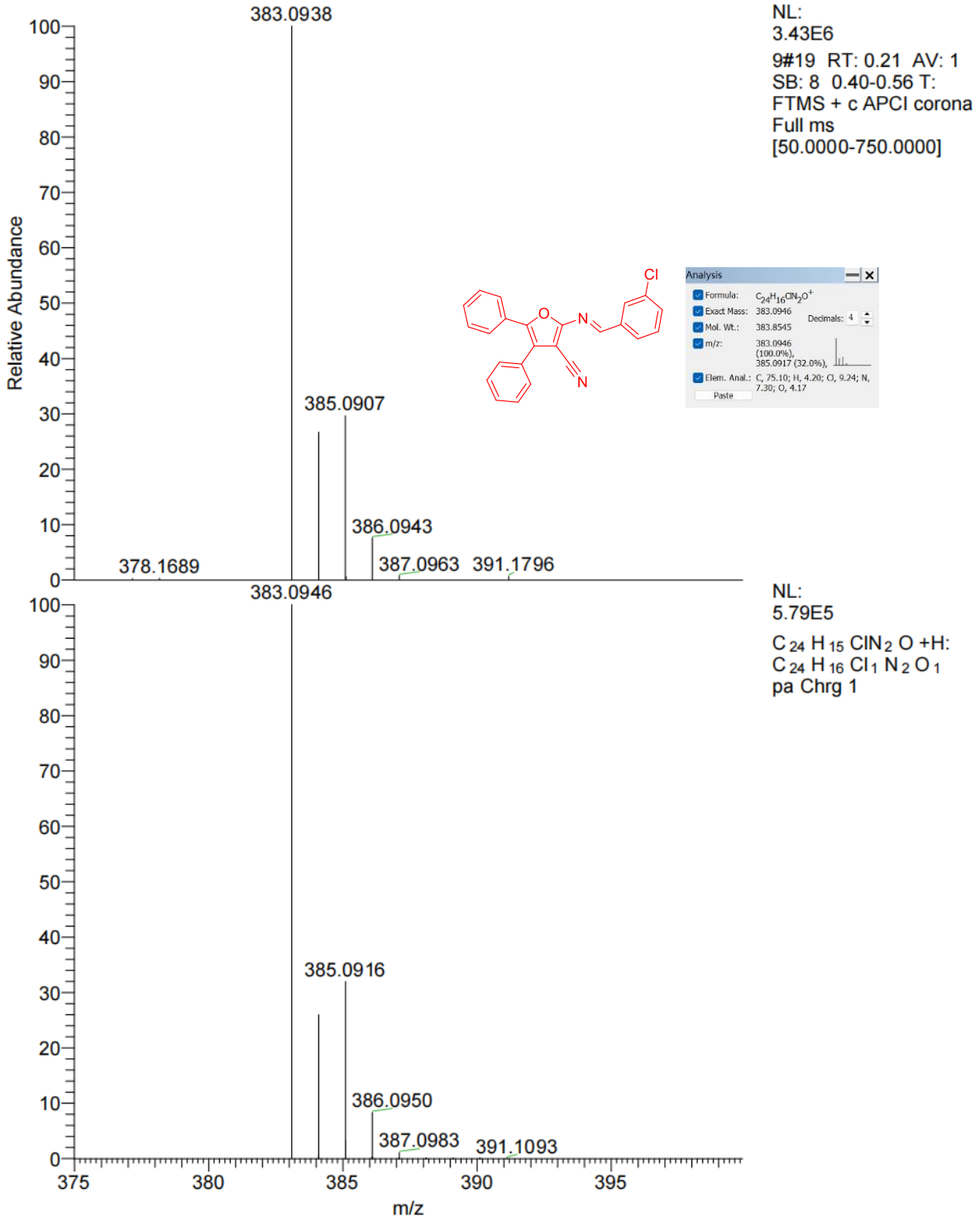
HR-MS spectrum of compound **4s**



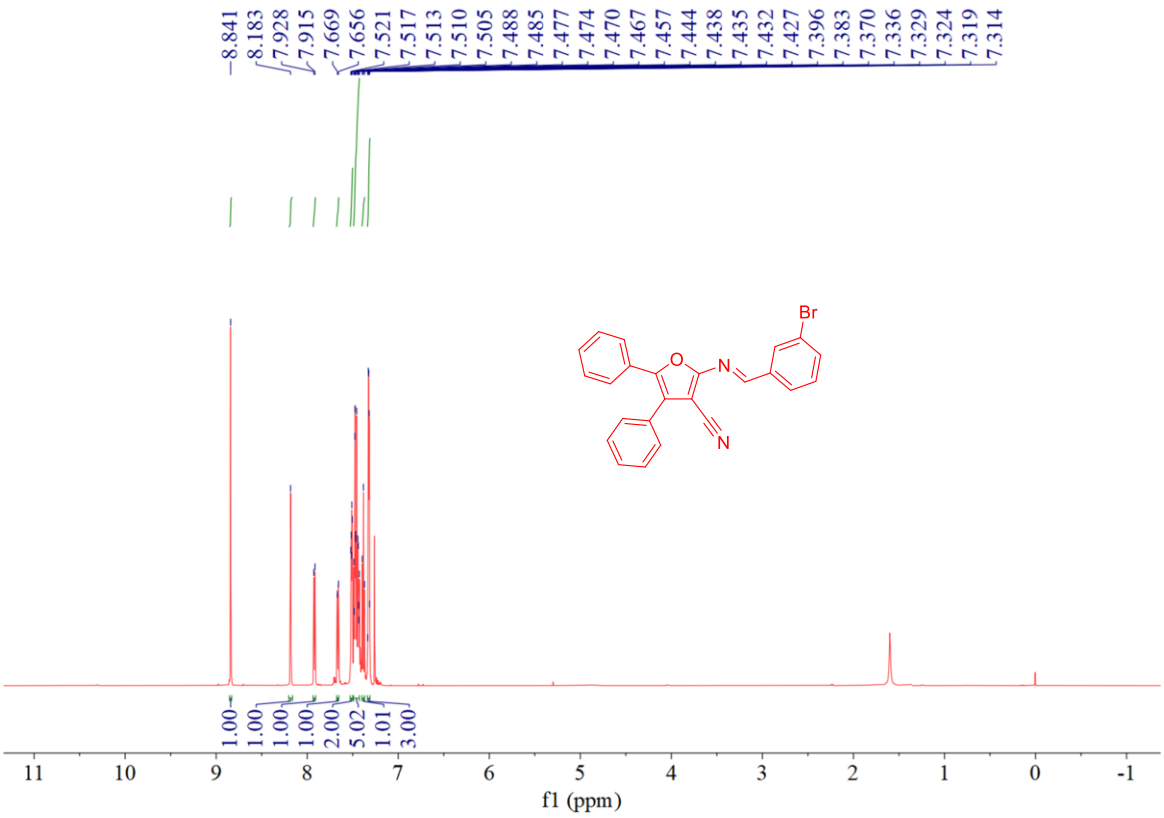
^{1}H NMR spectrum of compound **4t**



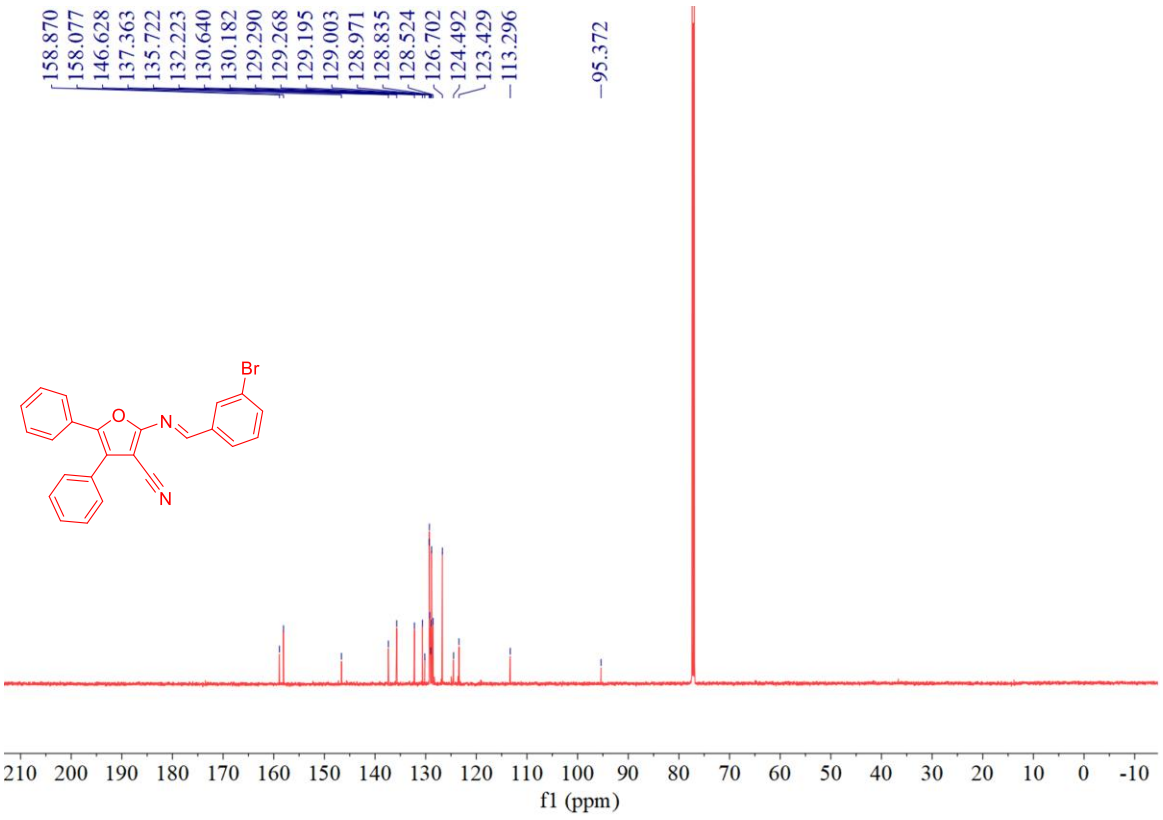
^{13}C NMR spectrum of compound **4t**



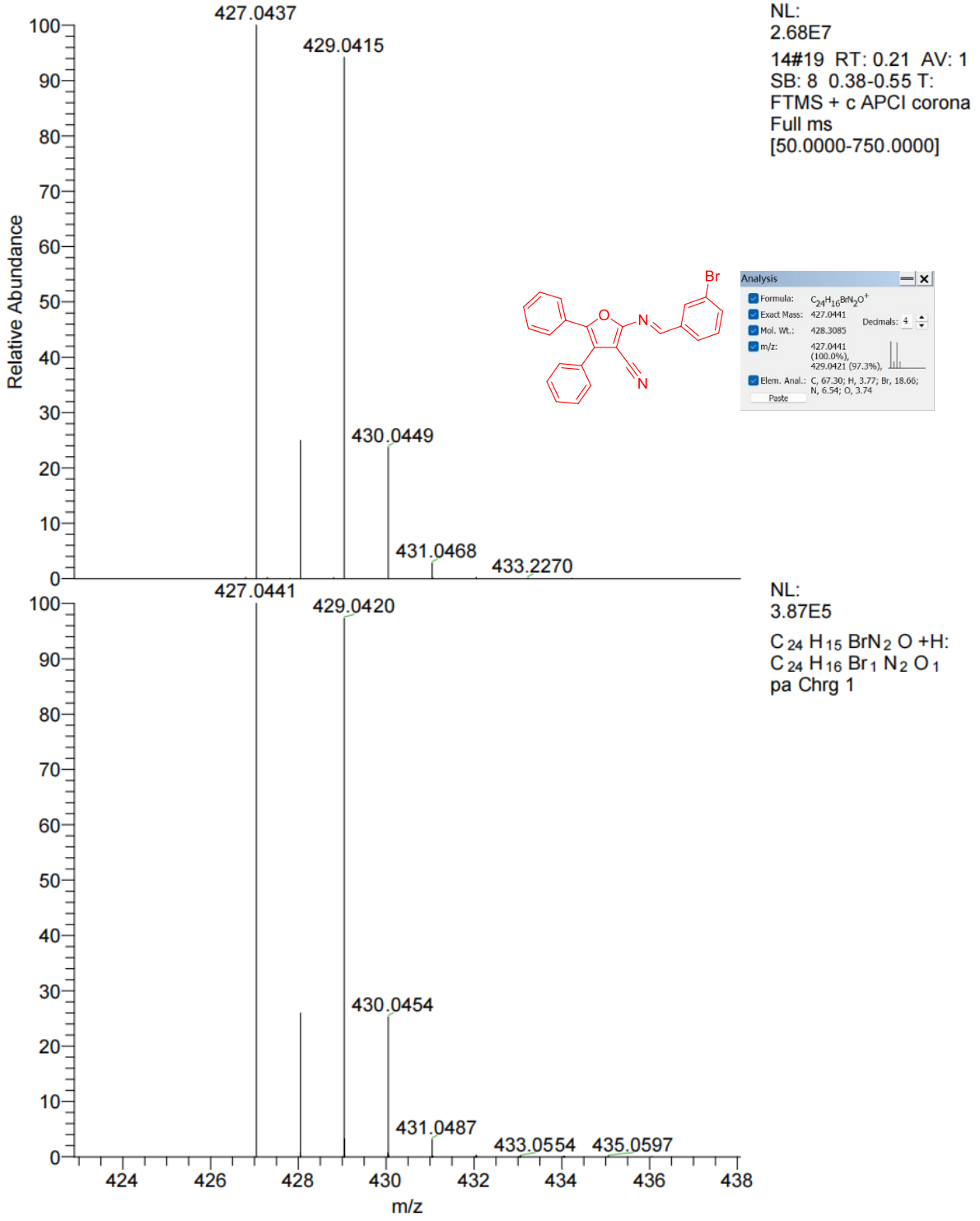
HR-MS spectrum of compound **4t**



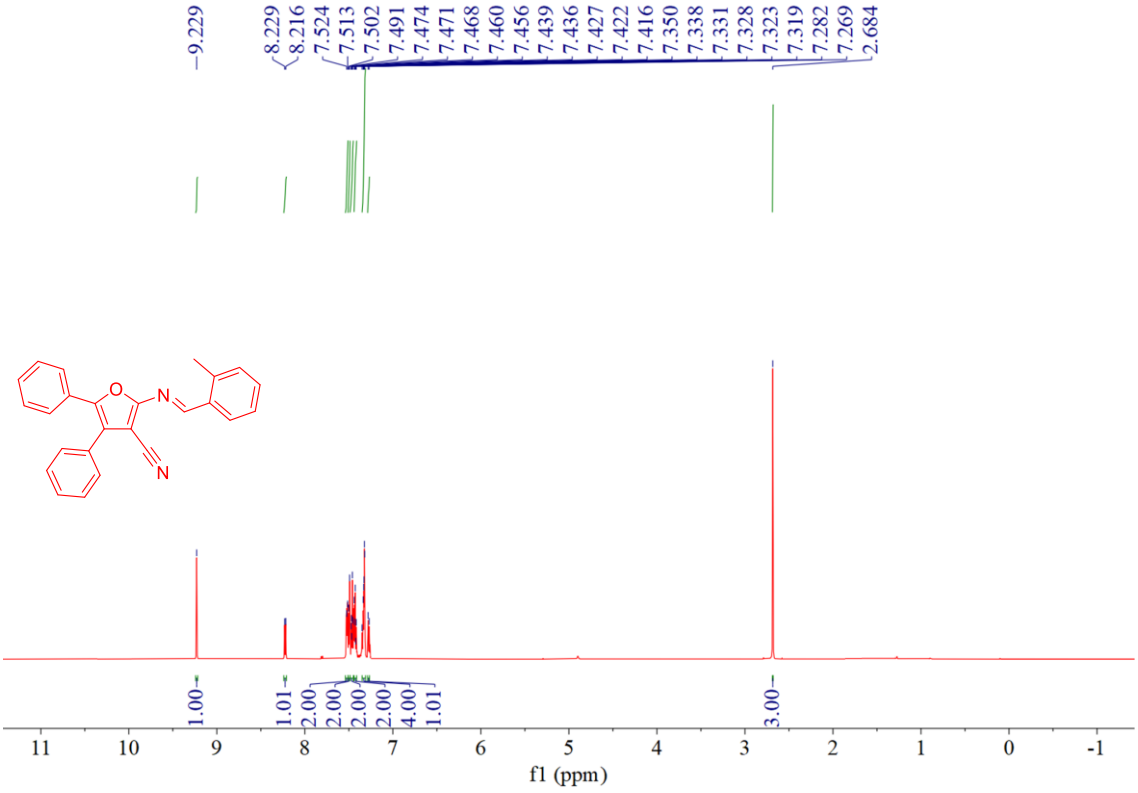
^{1}H NMR spectrum of compound **4u**



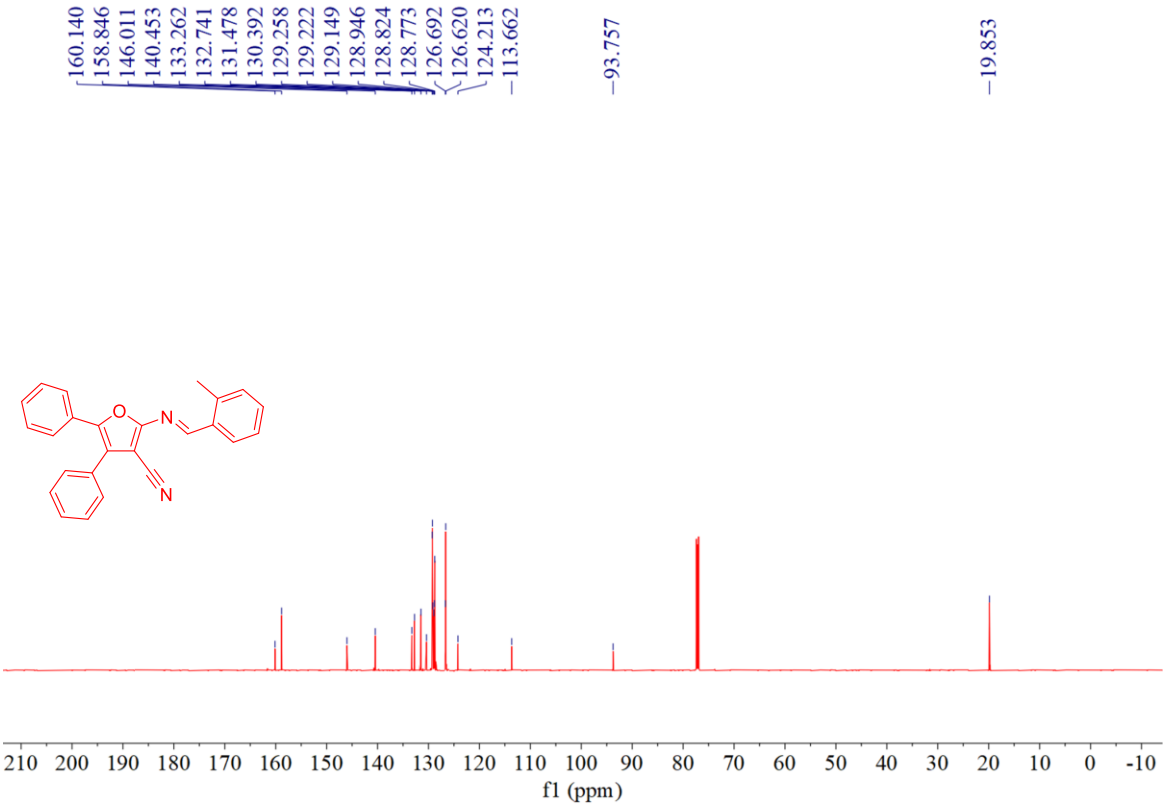
^{13}C NMR spectrum of compound **4u**



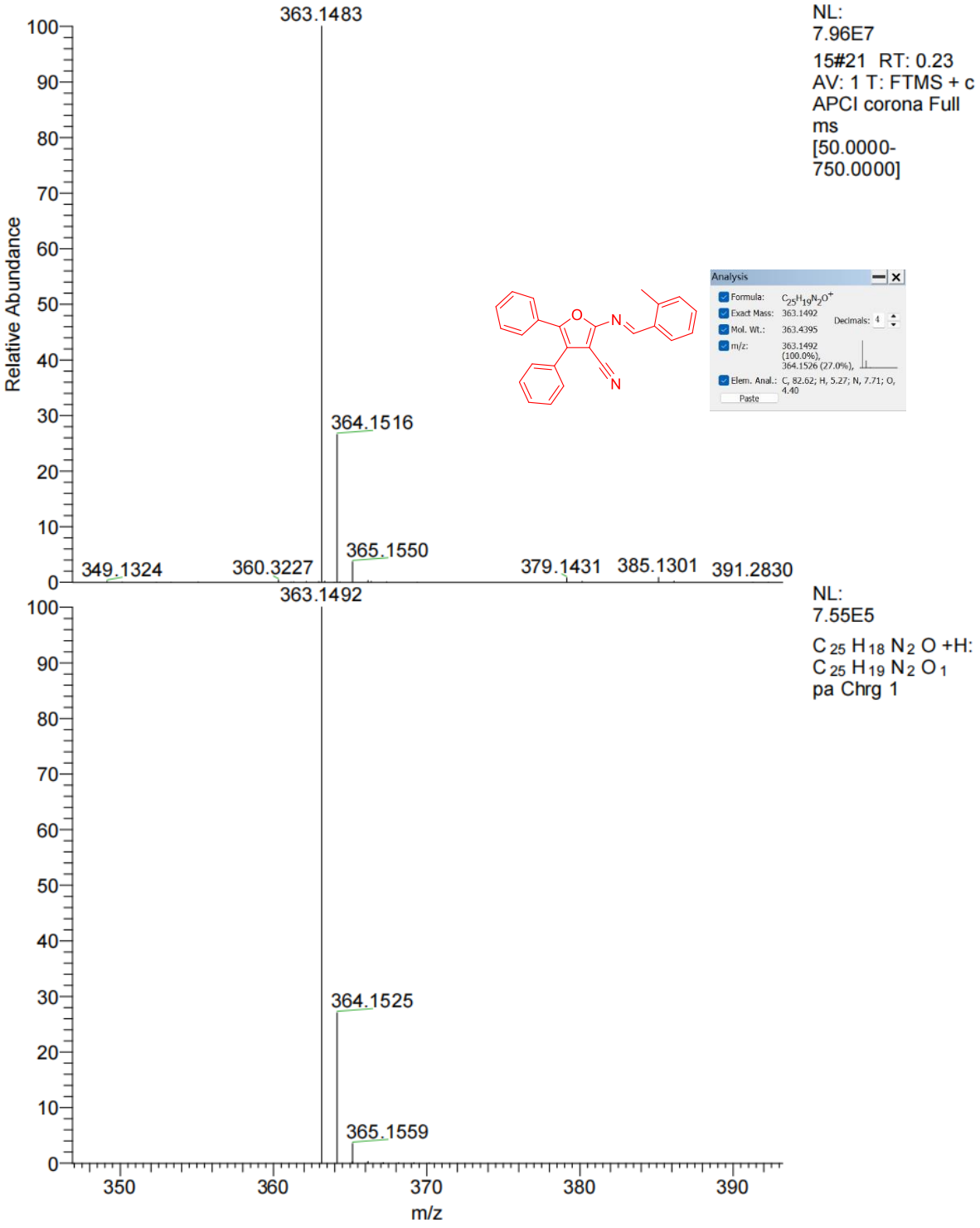
HR-MS spectrum of compound **4u**



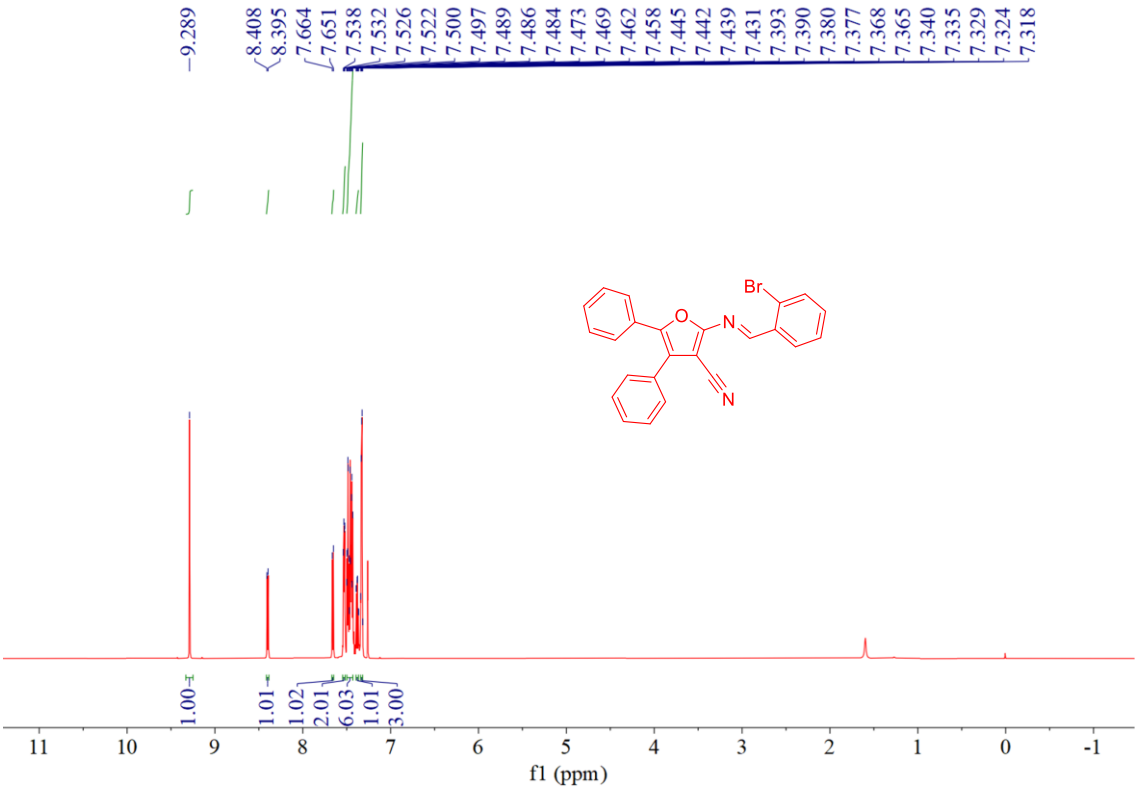
^{1}H NMR spectrum of compound **4v**



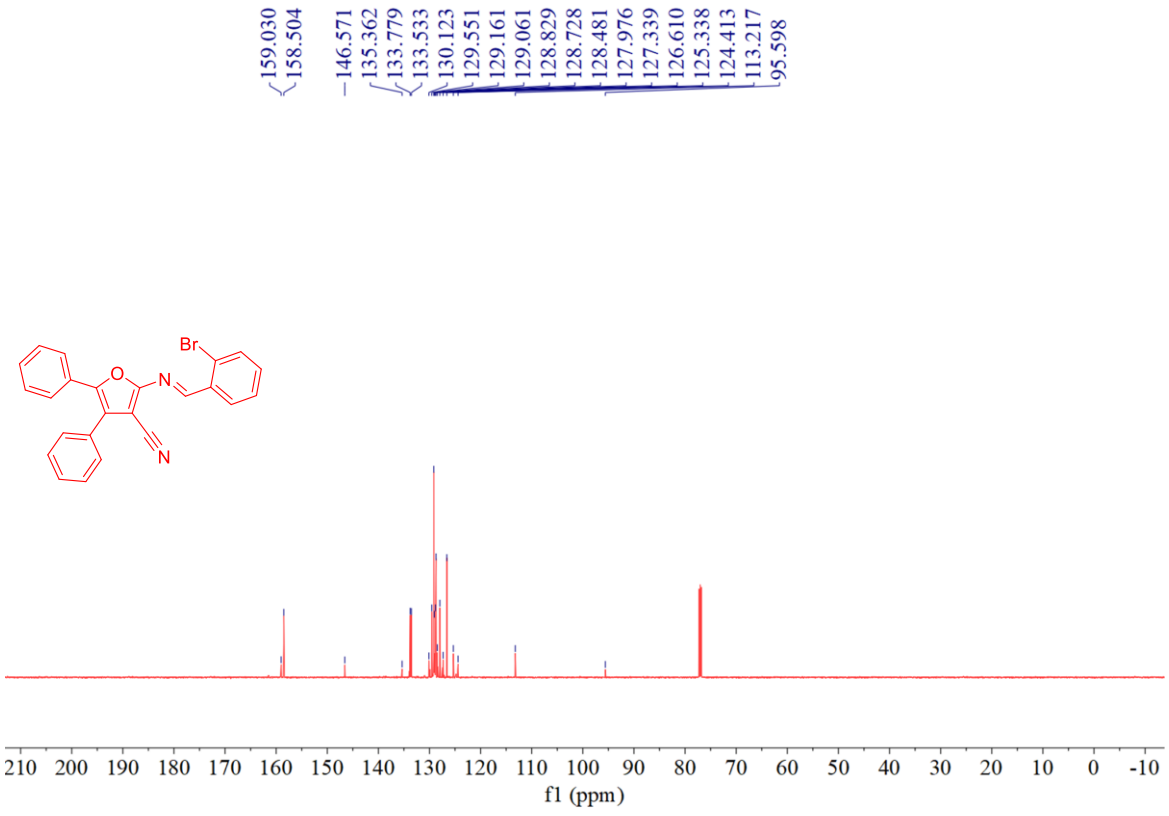
^{13}C NMR spectrum of compound **4v**



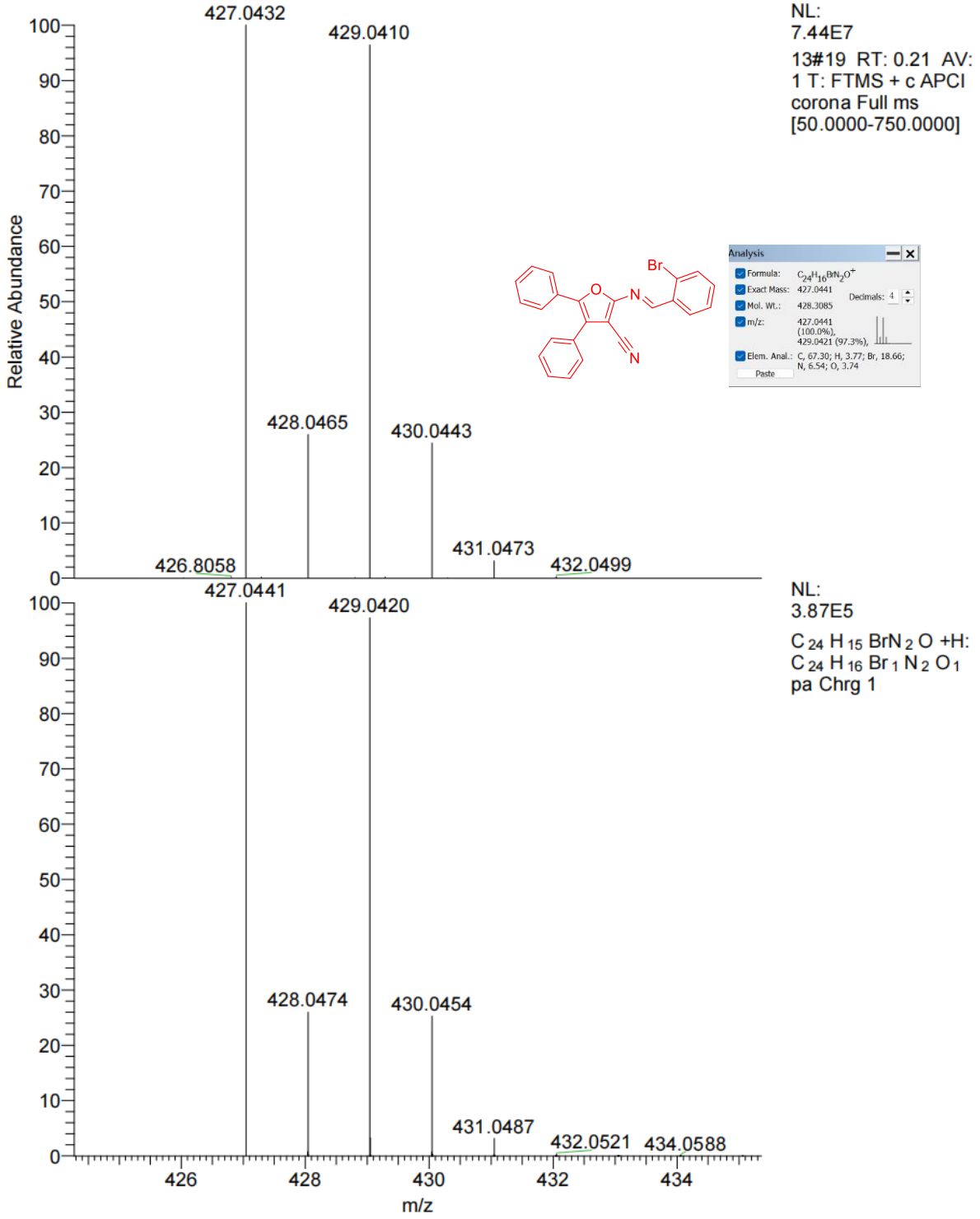
HR-MS spectrum of compound **4v**



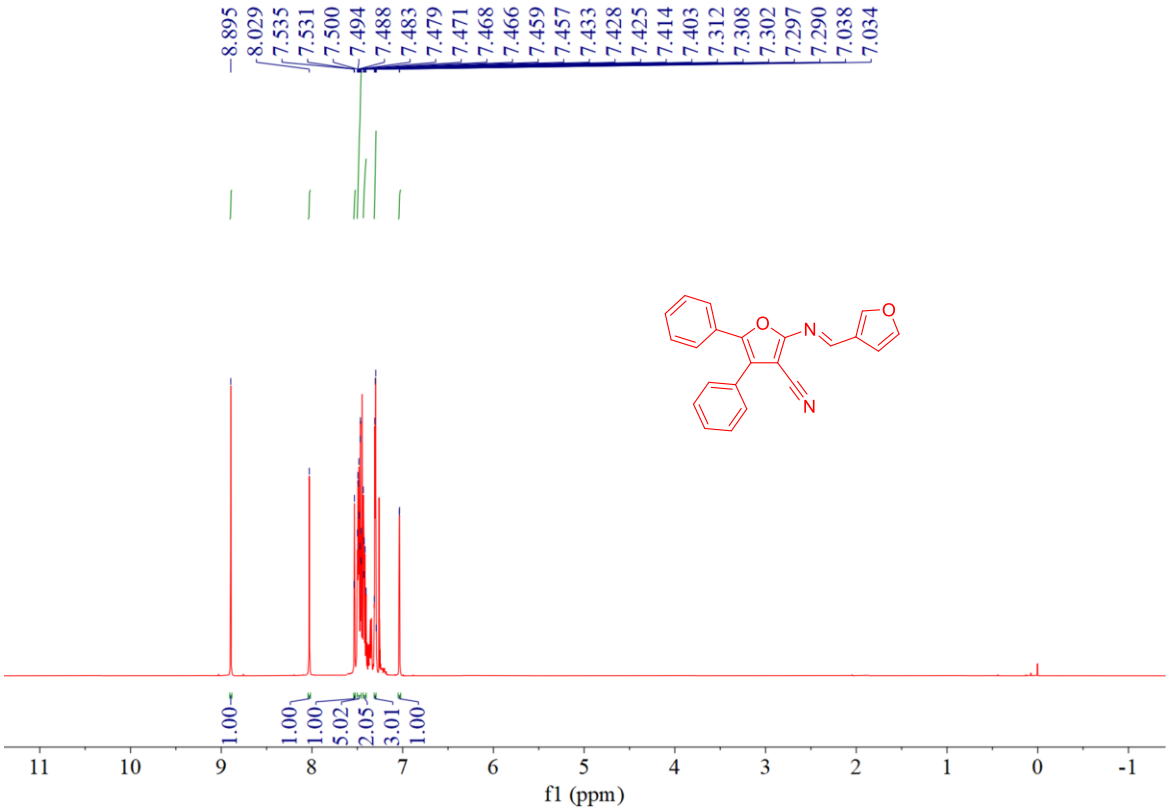
^{1}H NMR spectrum of compound **4w**



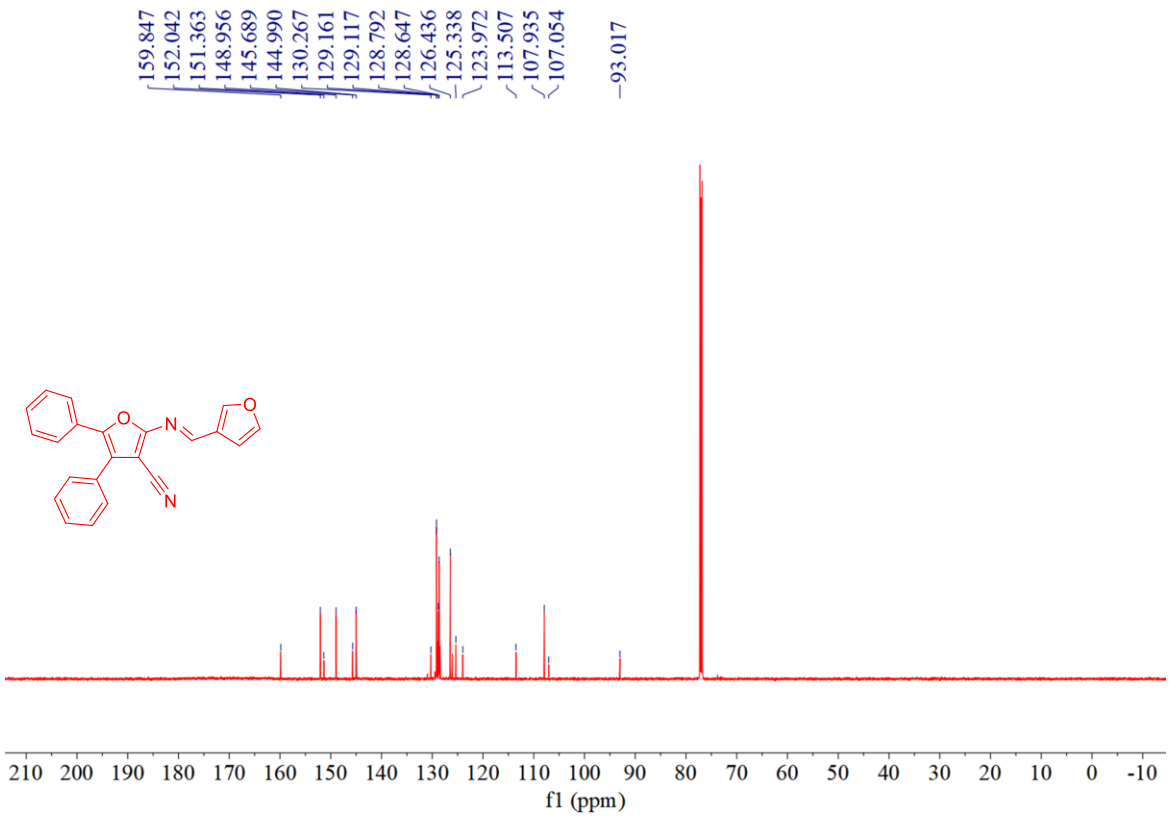
^{13}C NMR spectrum of compound **4w**



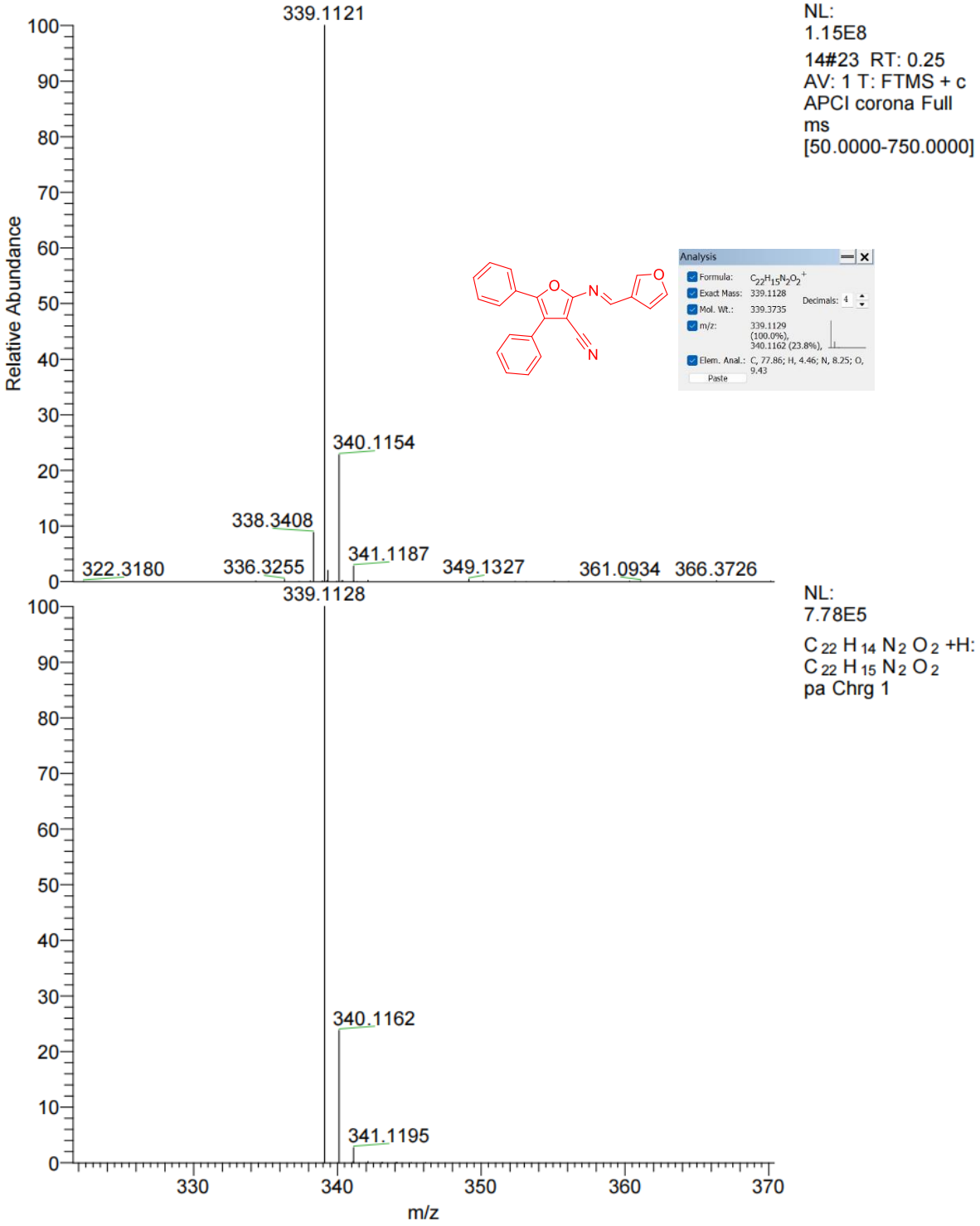
HR-MS spectrum of compound **4w**



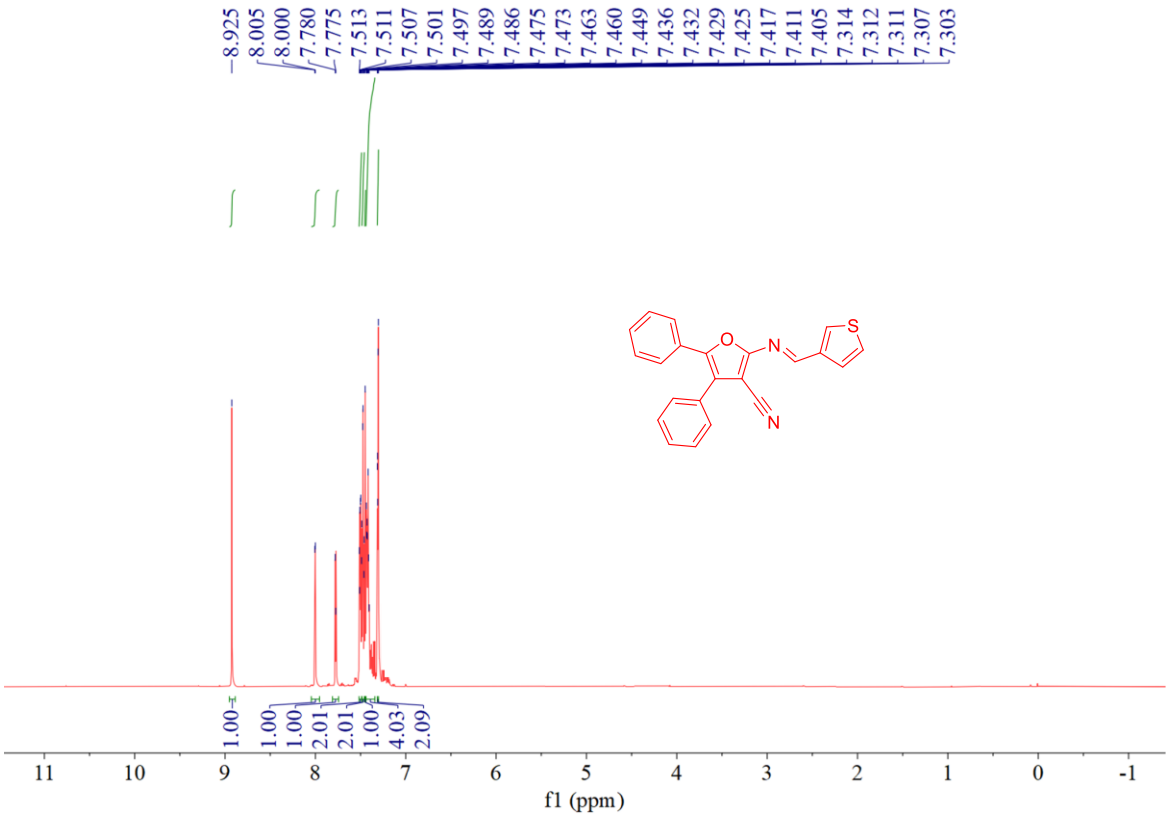
^{1}H NMR spectrum of compound **4x**



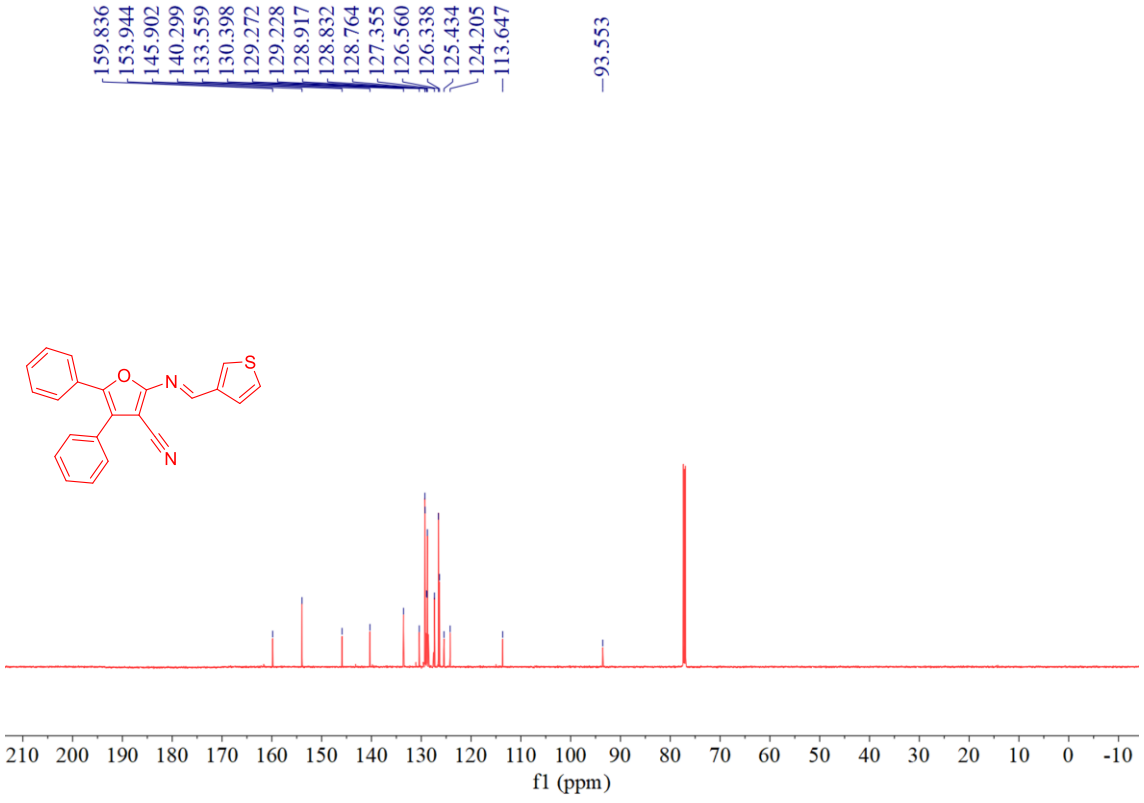
^{13}C NMR spectrum of compound **4x**



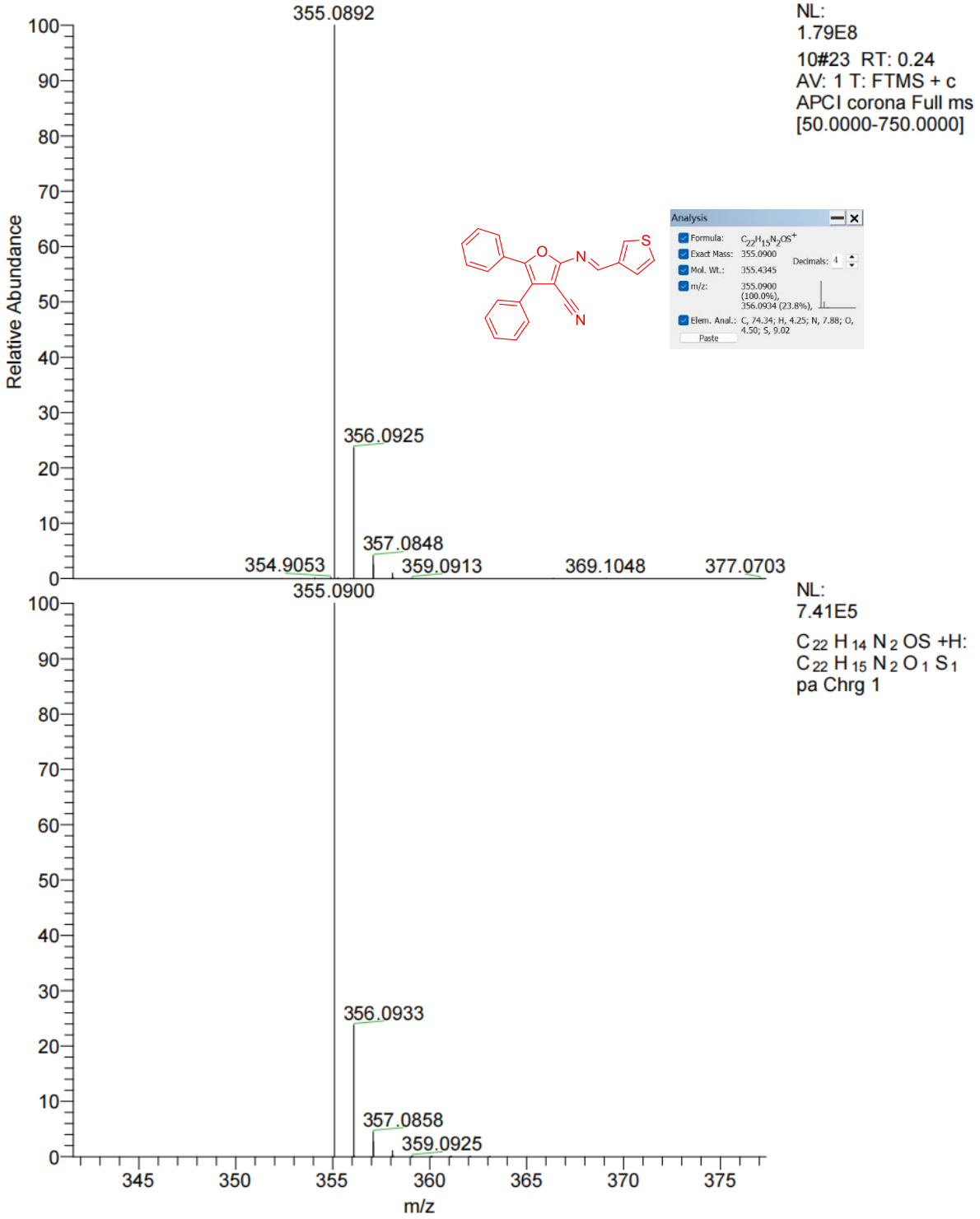
HR-MS spectrum of compound **4x**



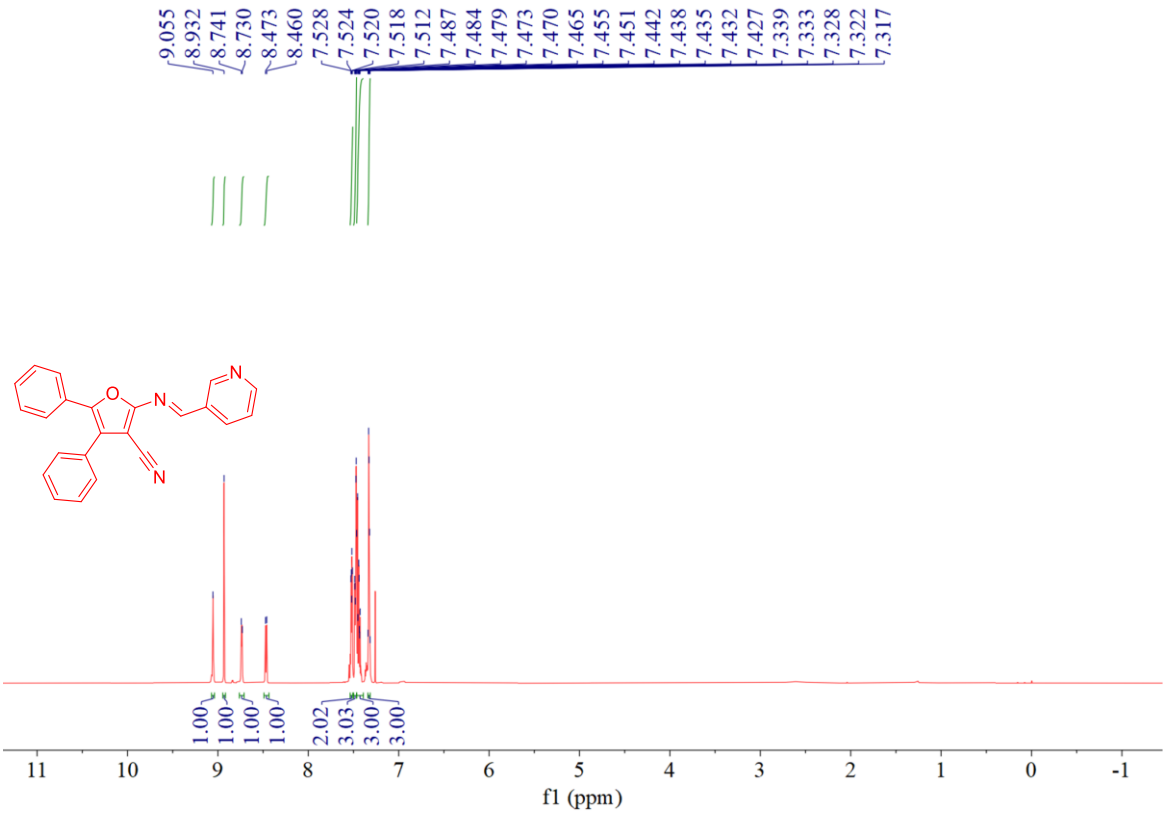
^{1}H NMR spectrum of compound **4y**



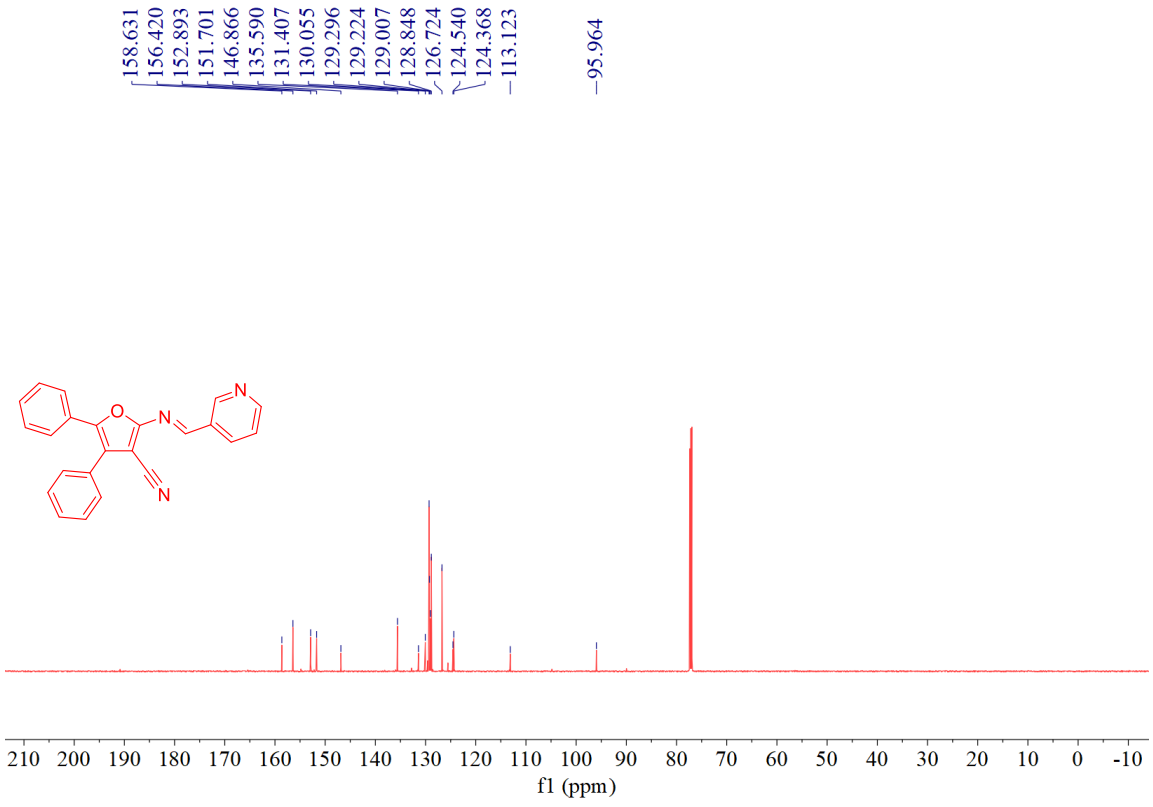
^{13}C NMR spectrum of compound **4y**



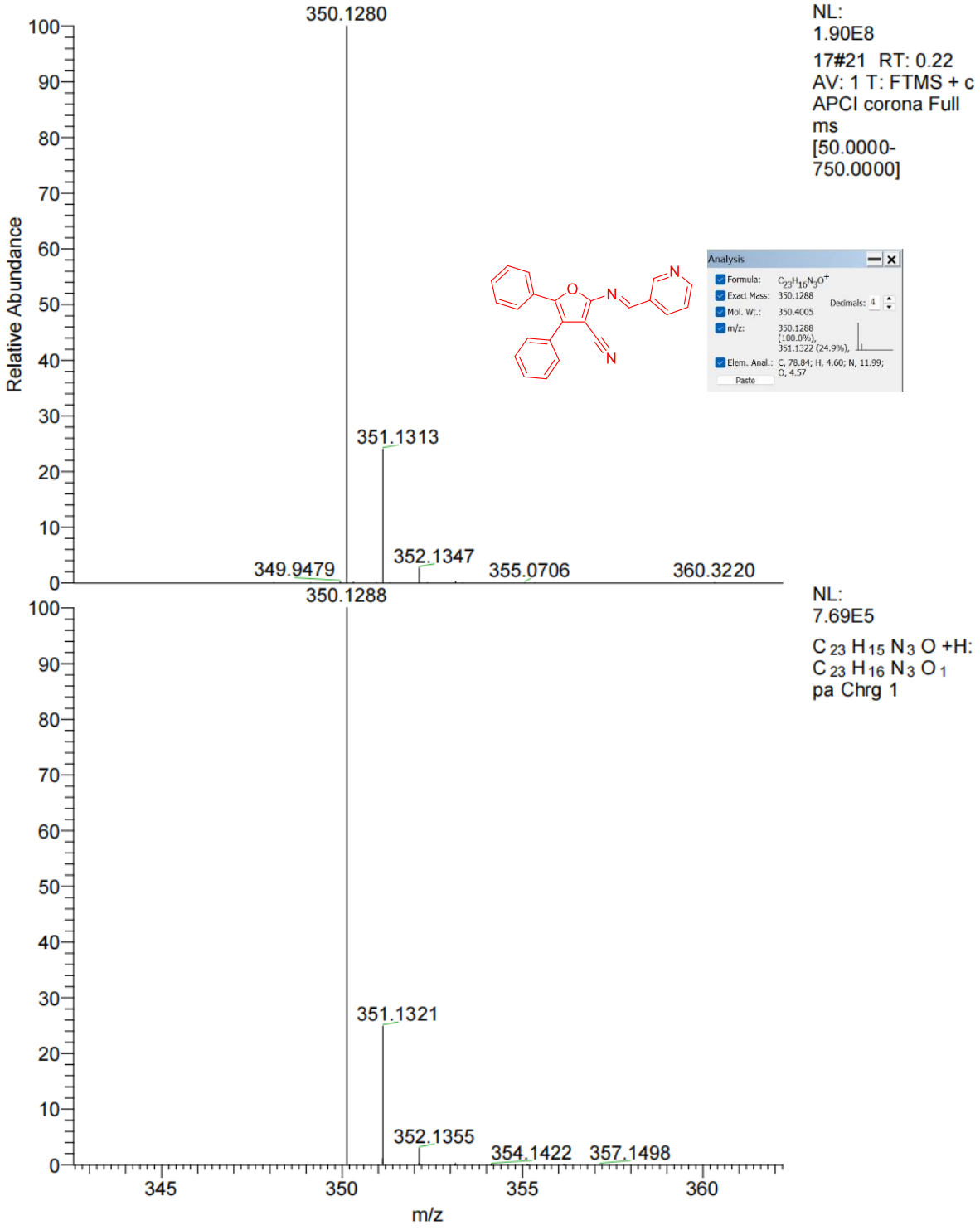
HR-MS spectrum of compound **4y**



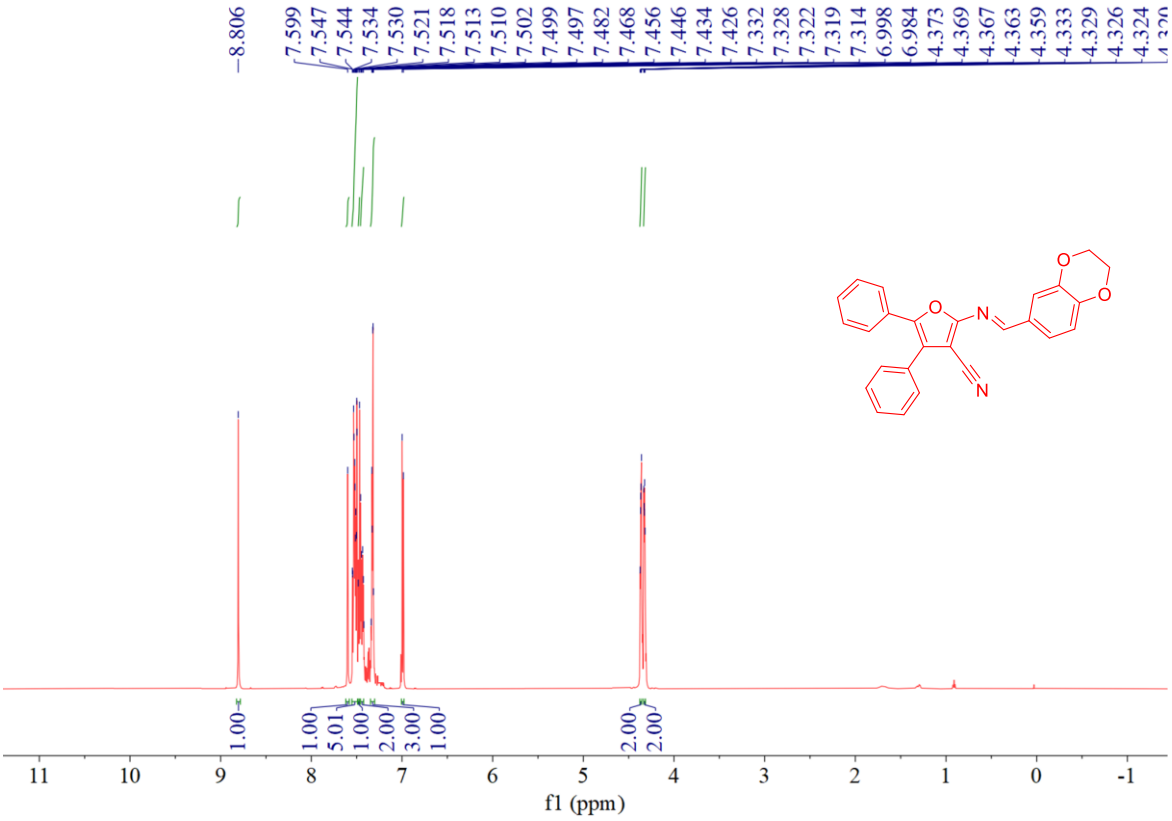
^{1}H NMR spectrum of compound **4z**



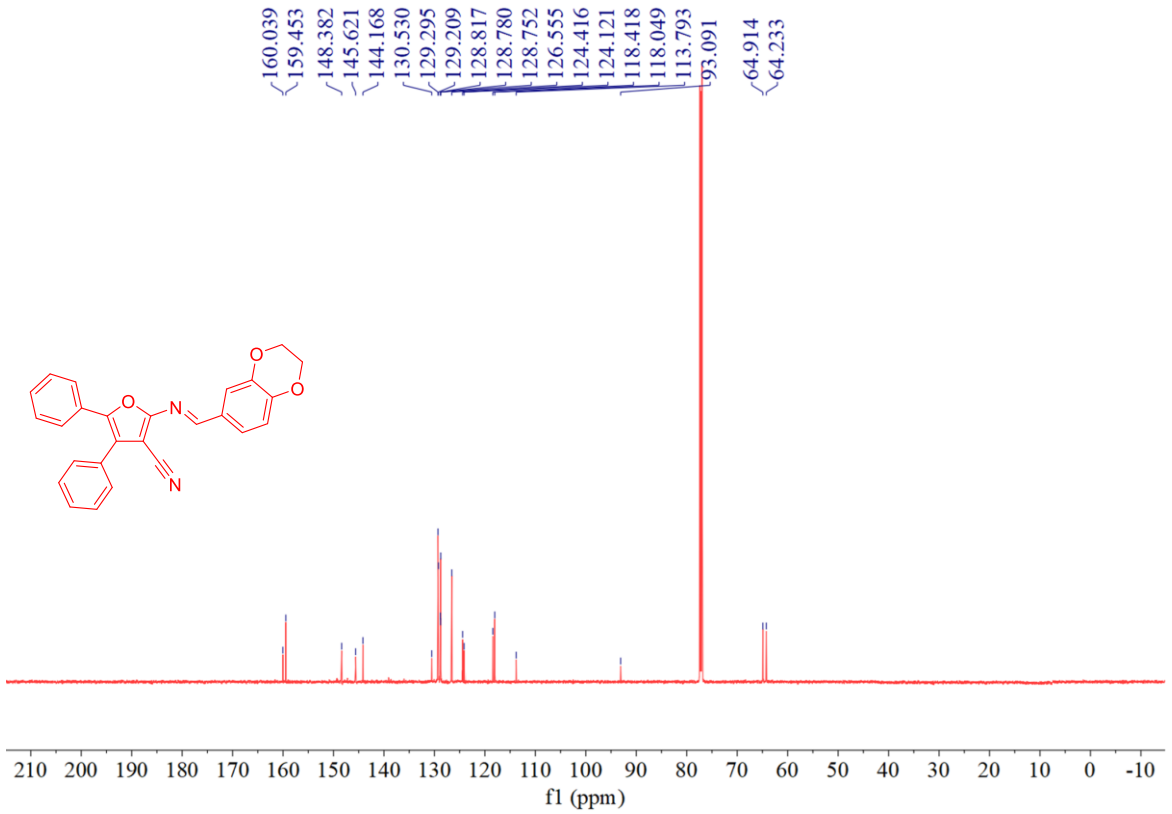
^{13}C NMR spectrum of compound **4z**



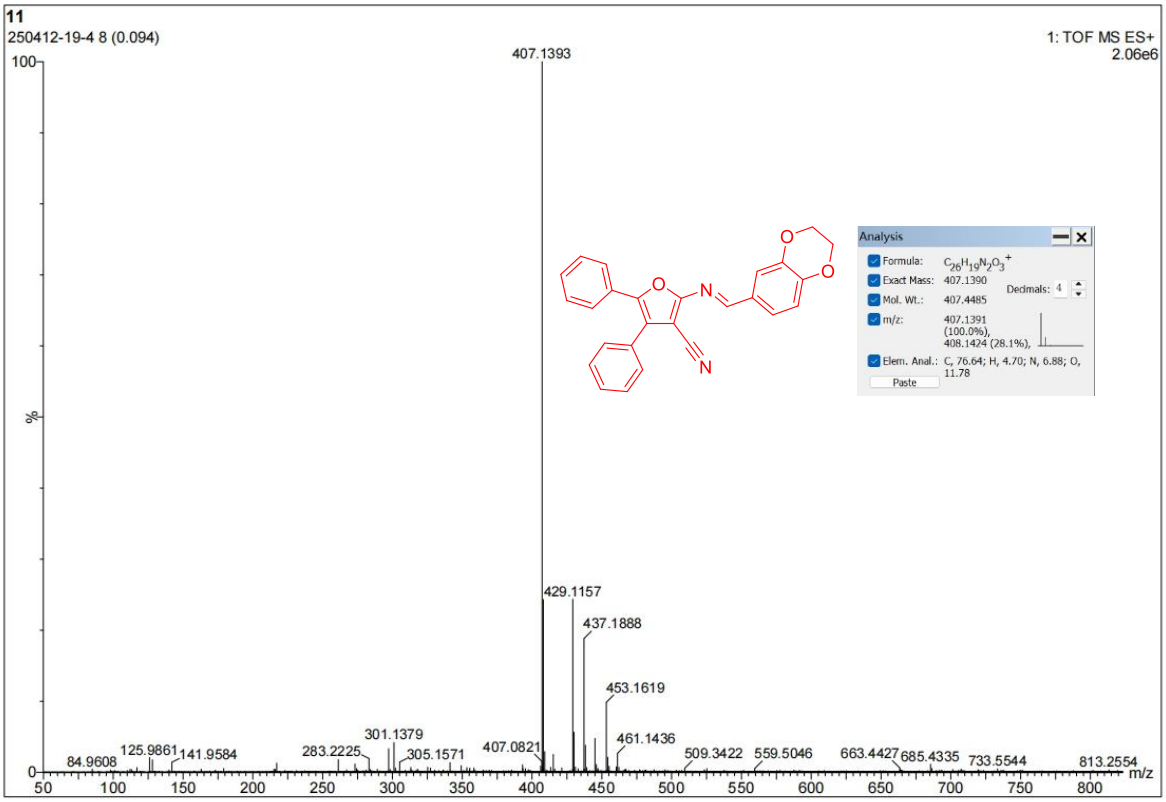
HR-MS spectrum of compound **4z**



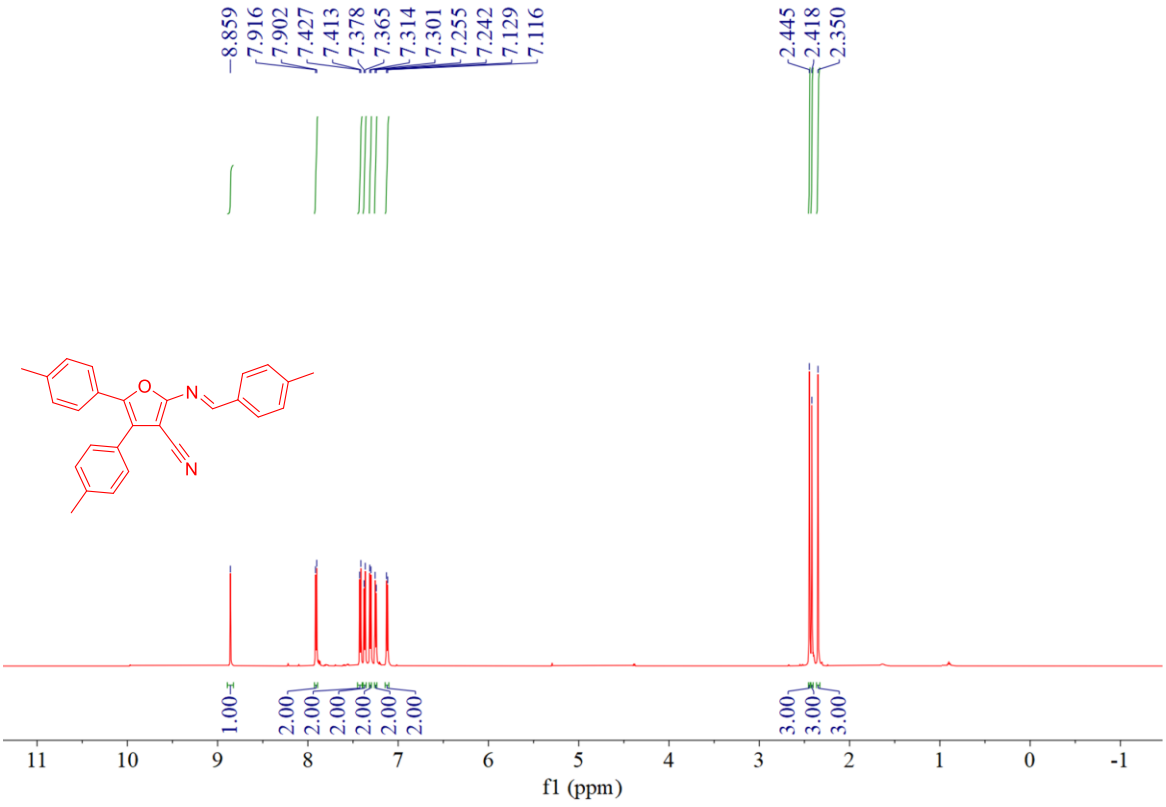
^{1}H NMR spectrum of compound **4aa**



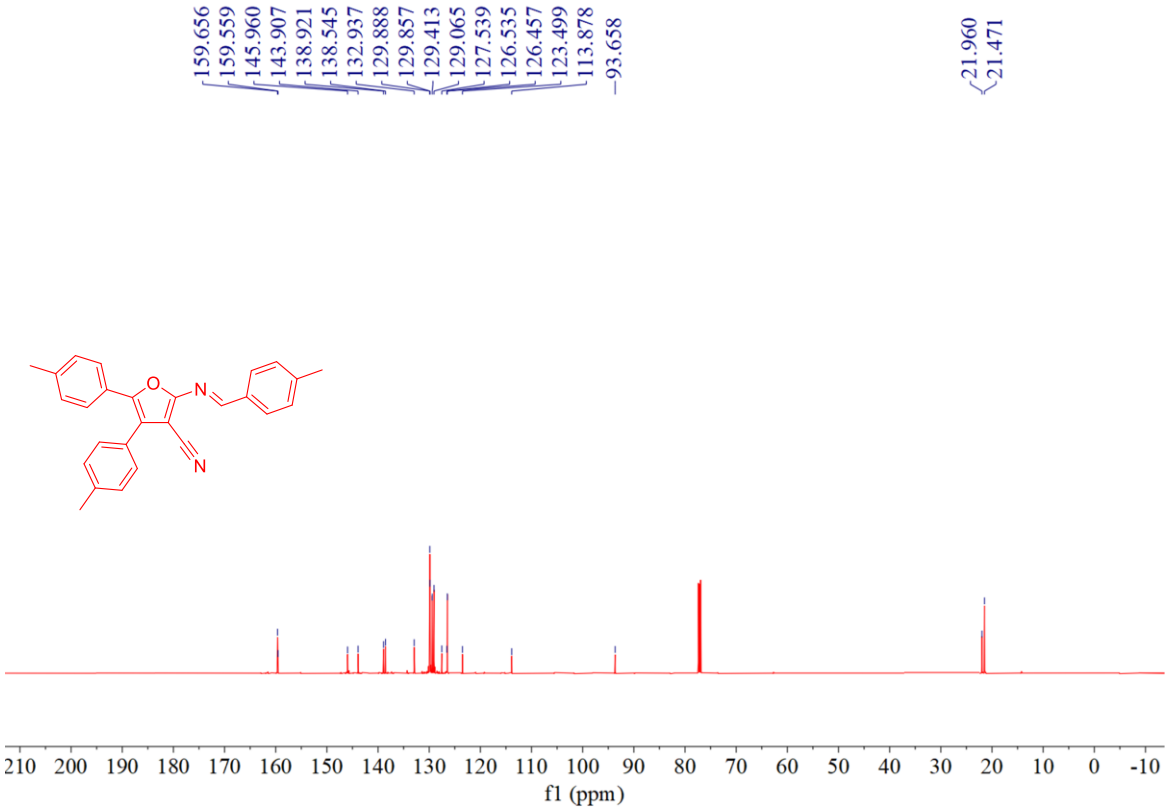
^{13}C NMR spectrum of compound **4aa**



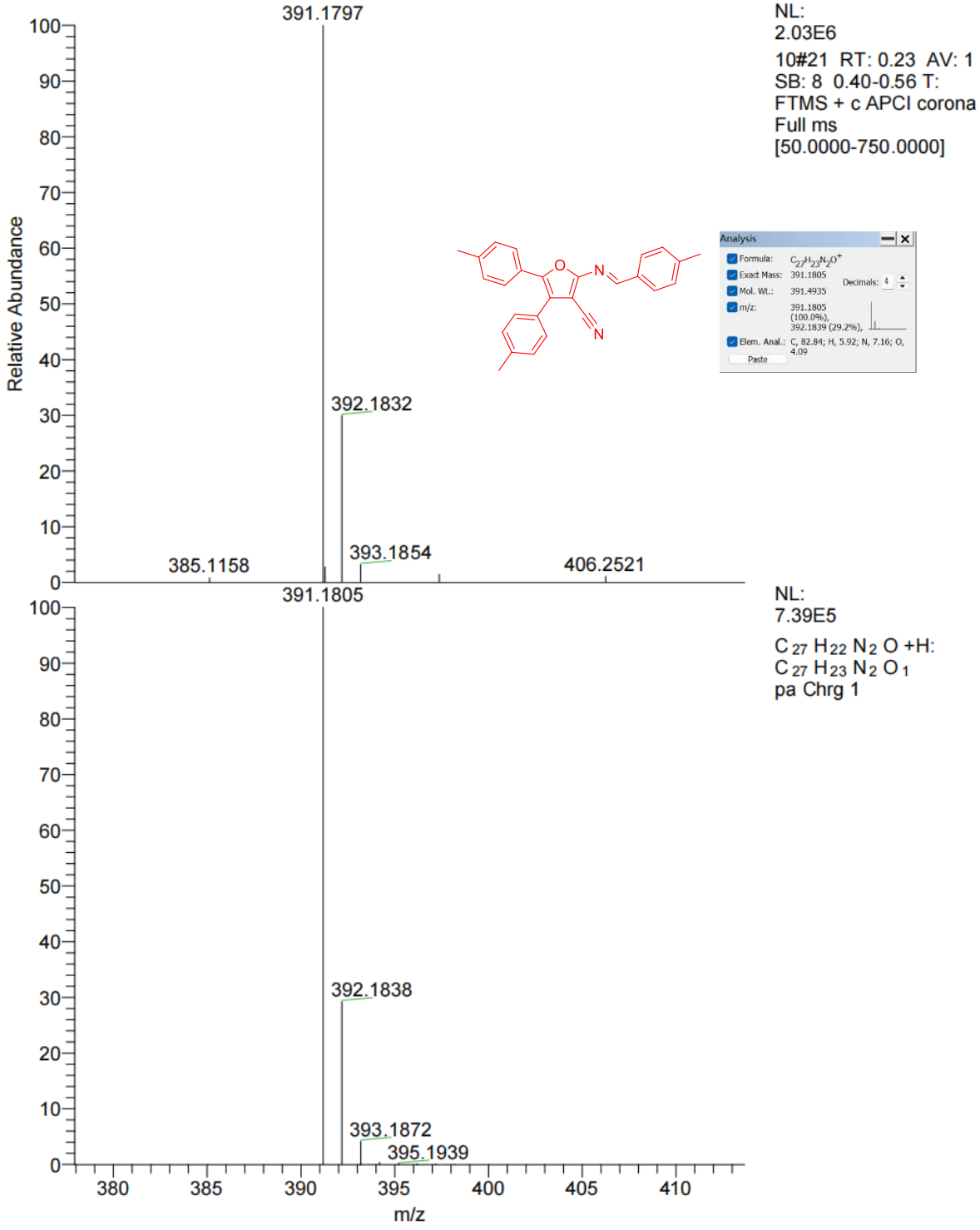
HR-MS spectrum of compound **4aa**



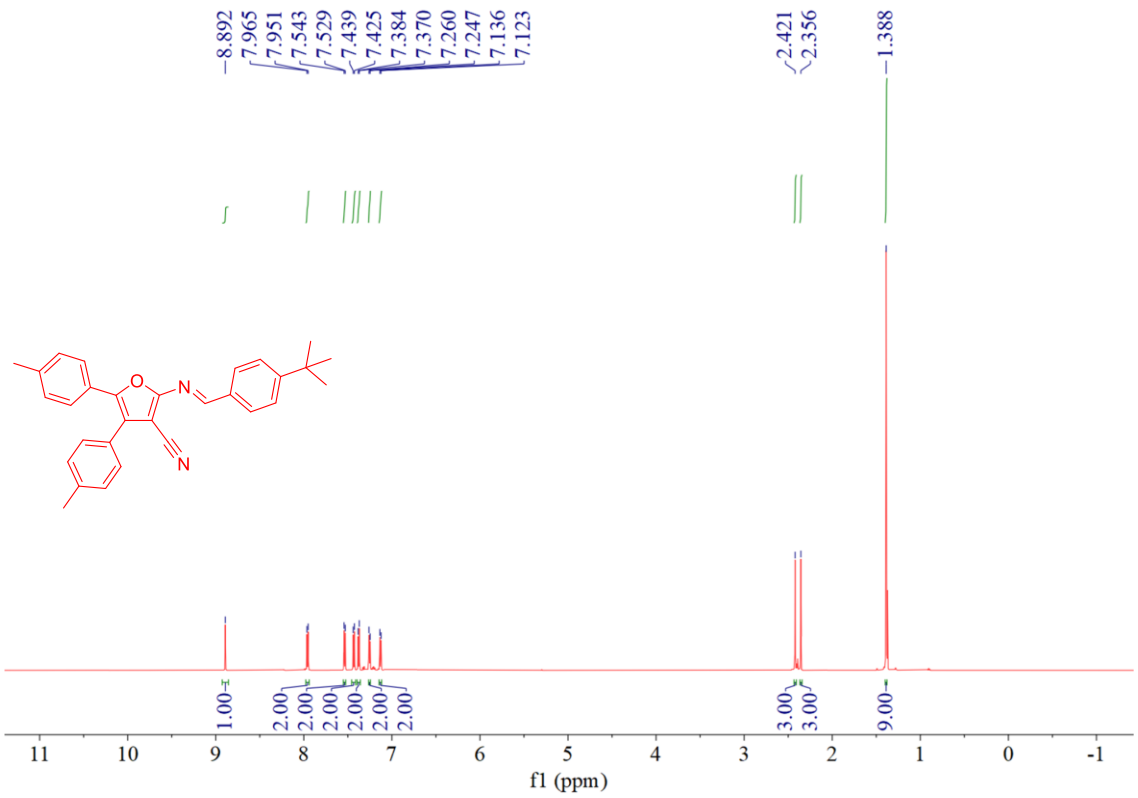
^{1}H NMR spectrum of compound **4ab**



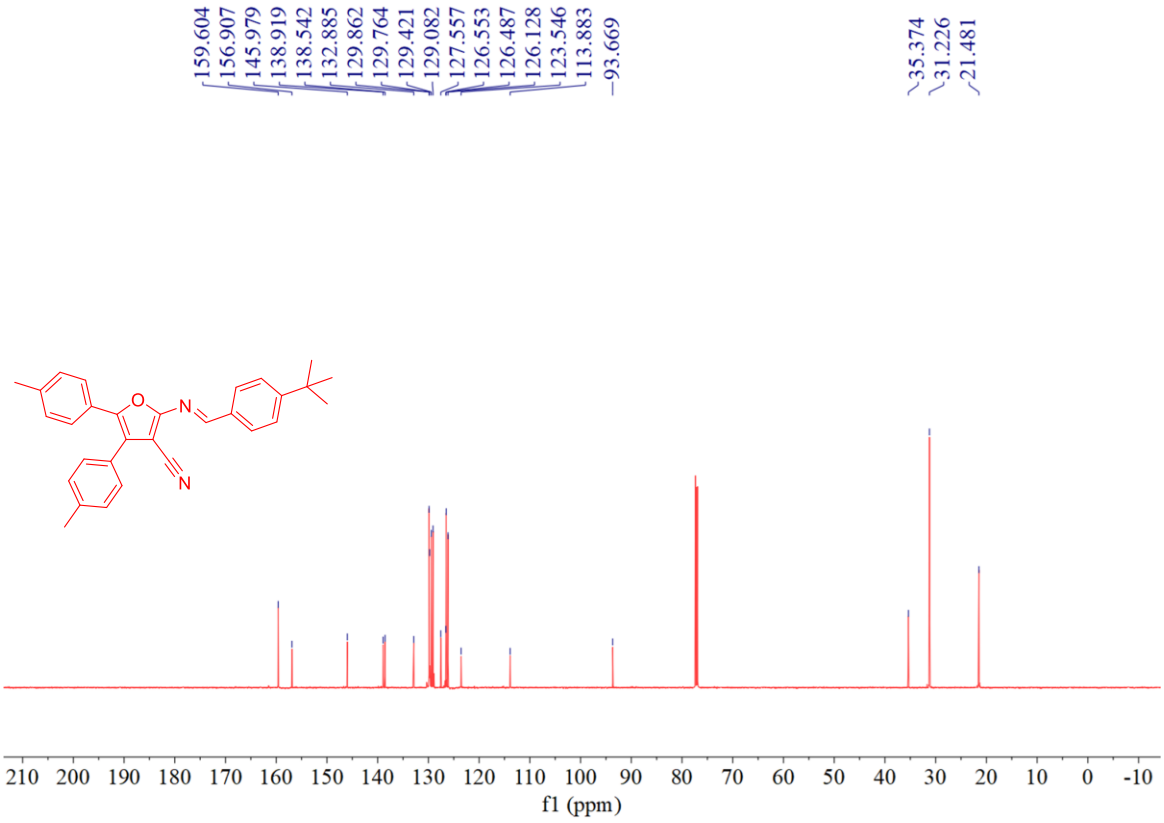
^{13}C NMR spectrum of compound **4ab**



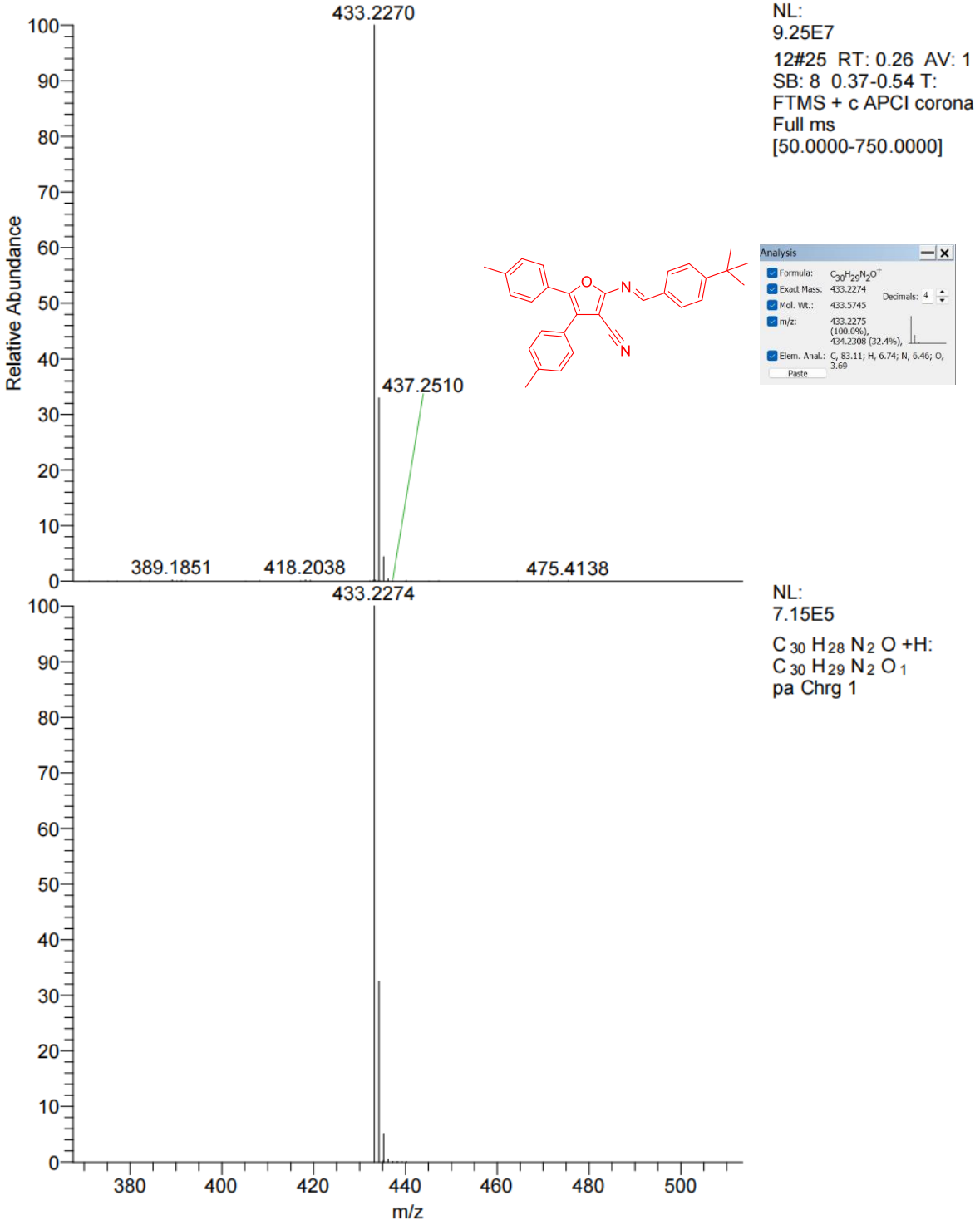
HR-MS spectrum of compound **4ab**



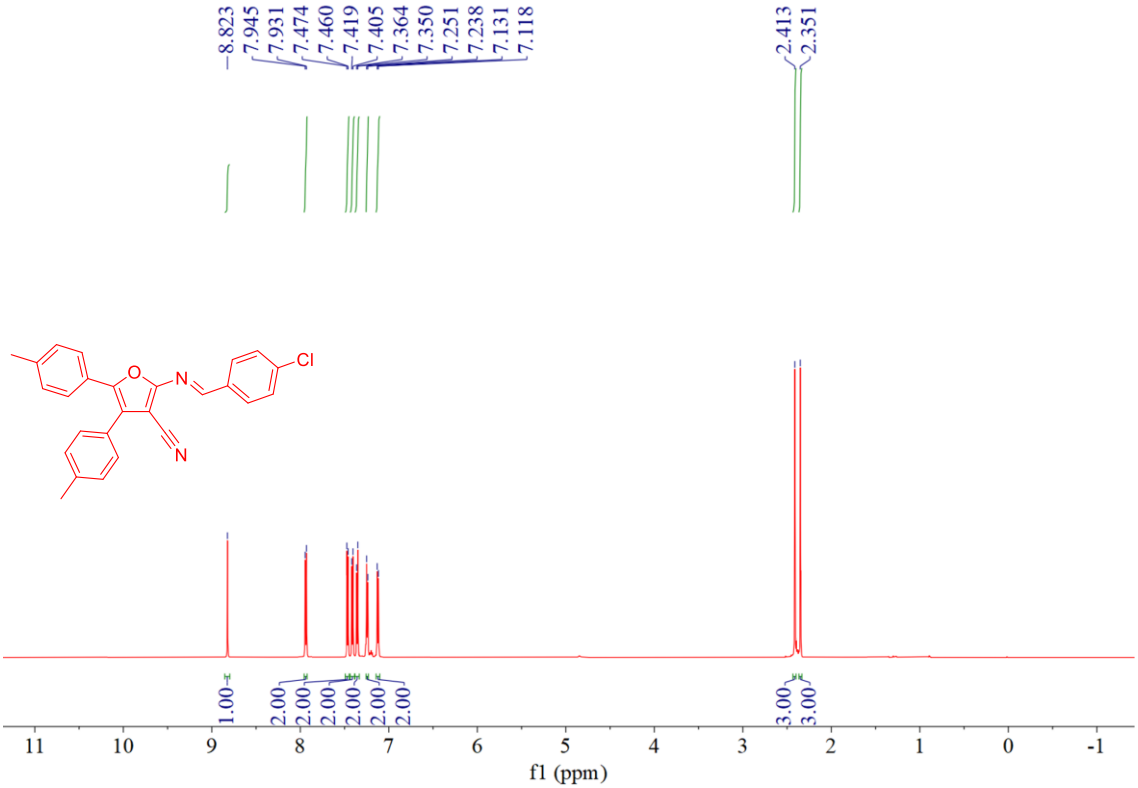
^{1}H NMR spectrum of compound **4ac**



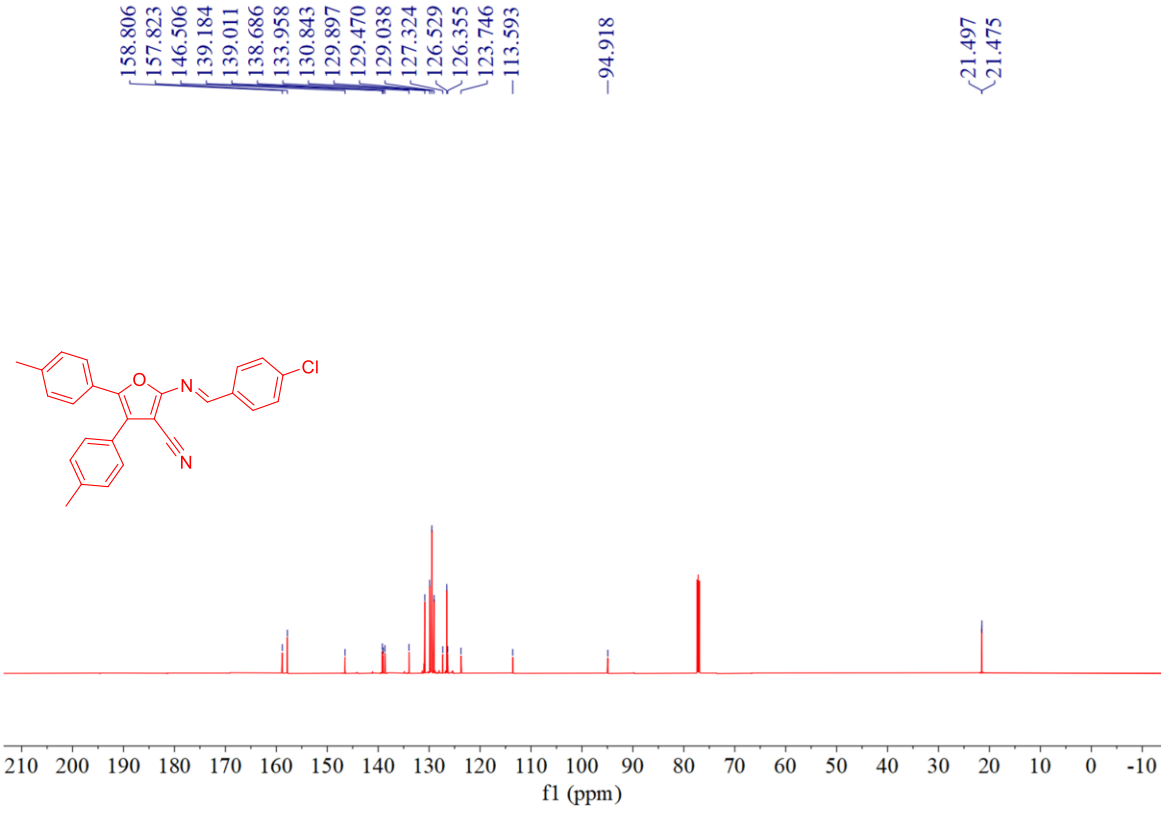
^{13}C NMR spectrum of compound **4ac**



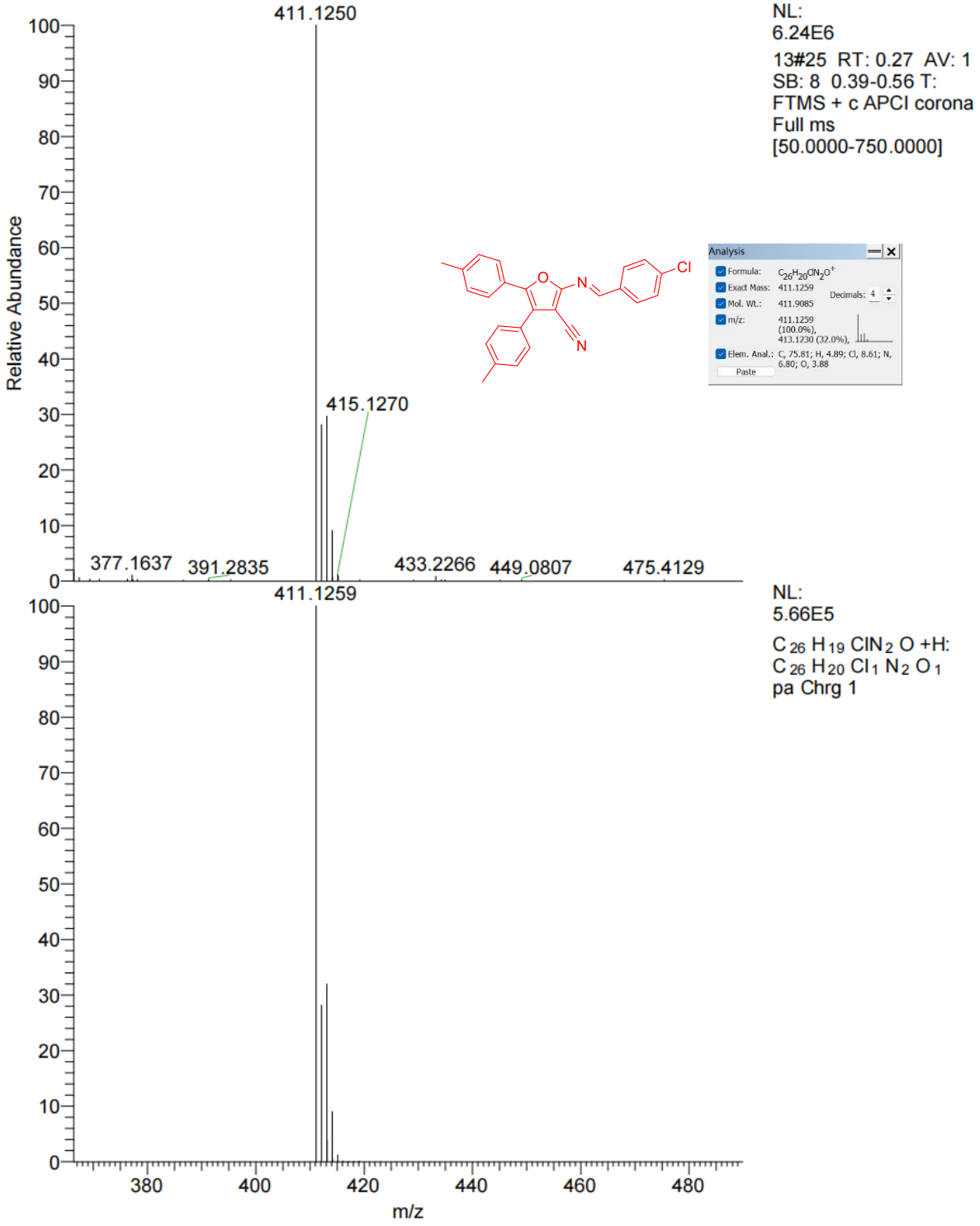
HR-MS spectrum of compound **4ac**



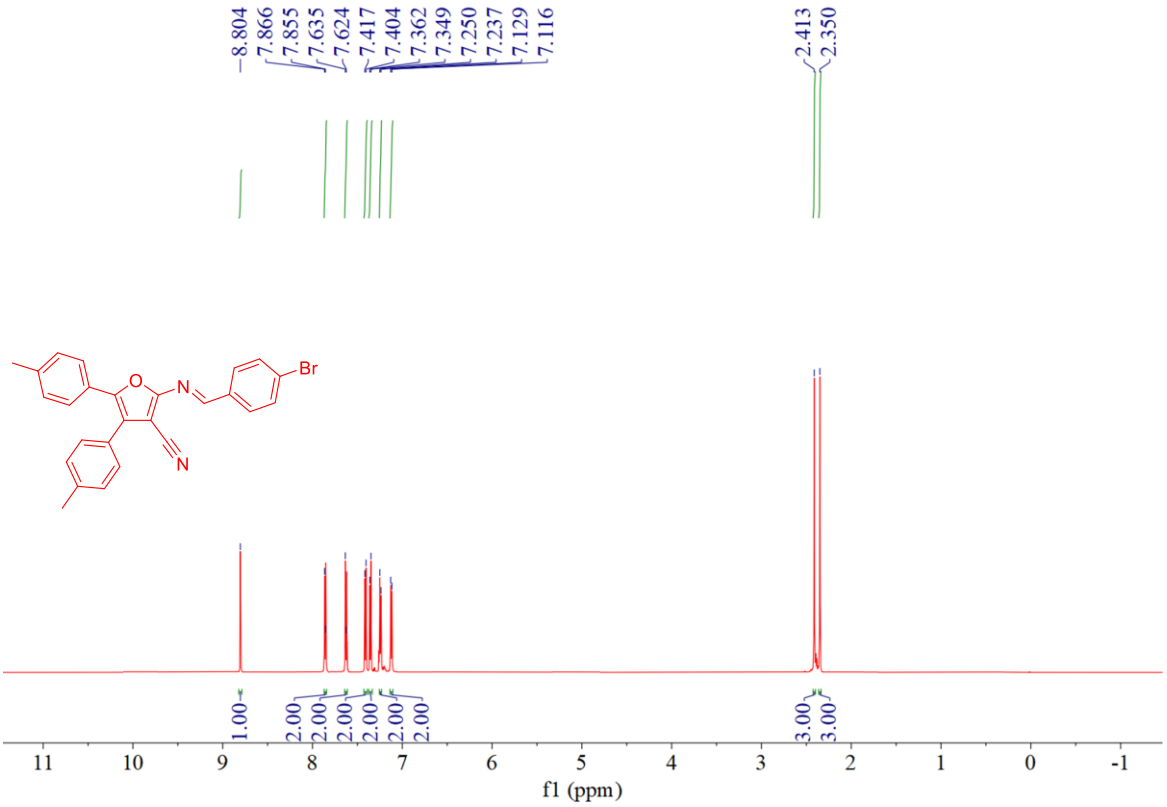
^{1}H NMR spectrum of compound **4ad**



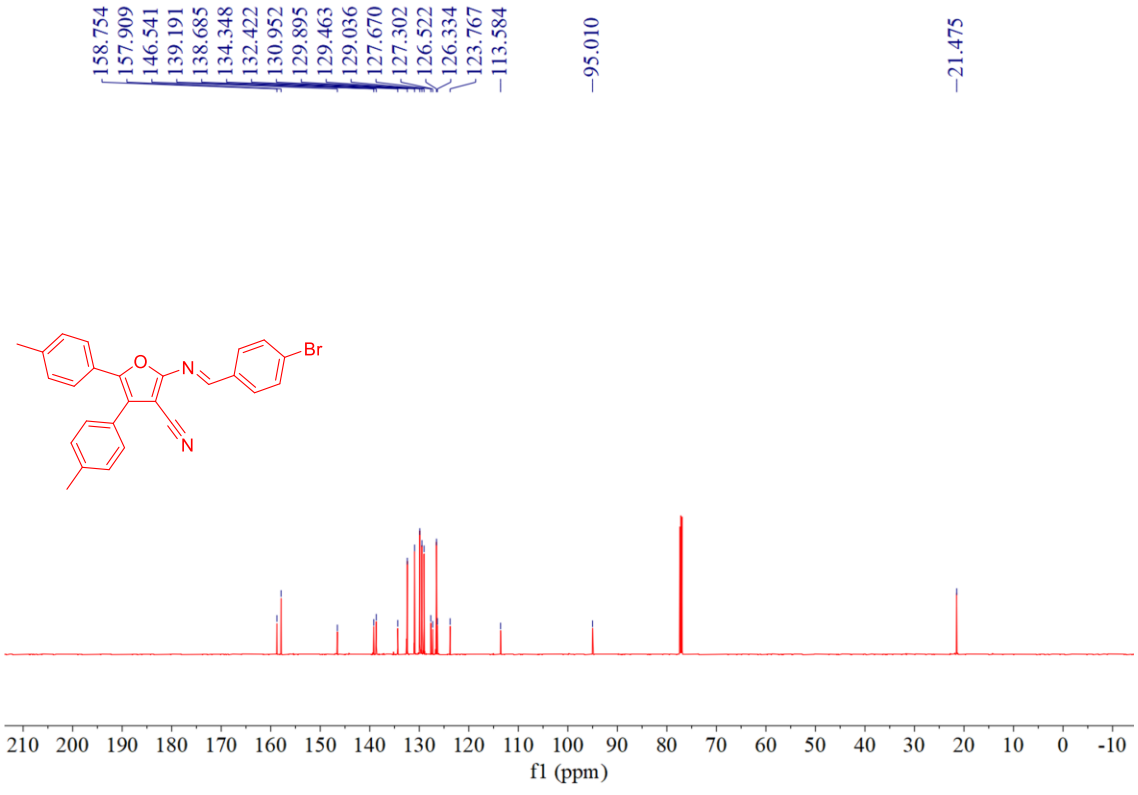
^{13}C NMR spectrum of compound **4ad**



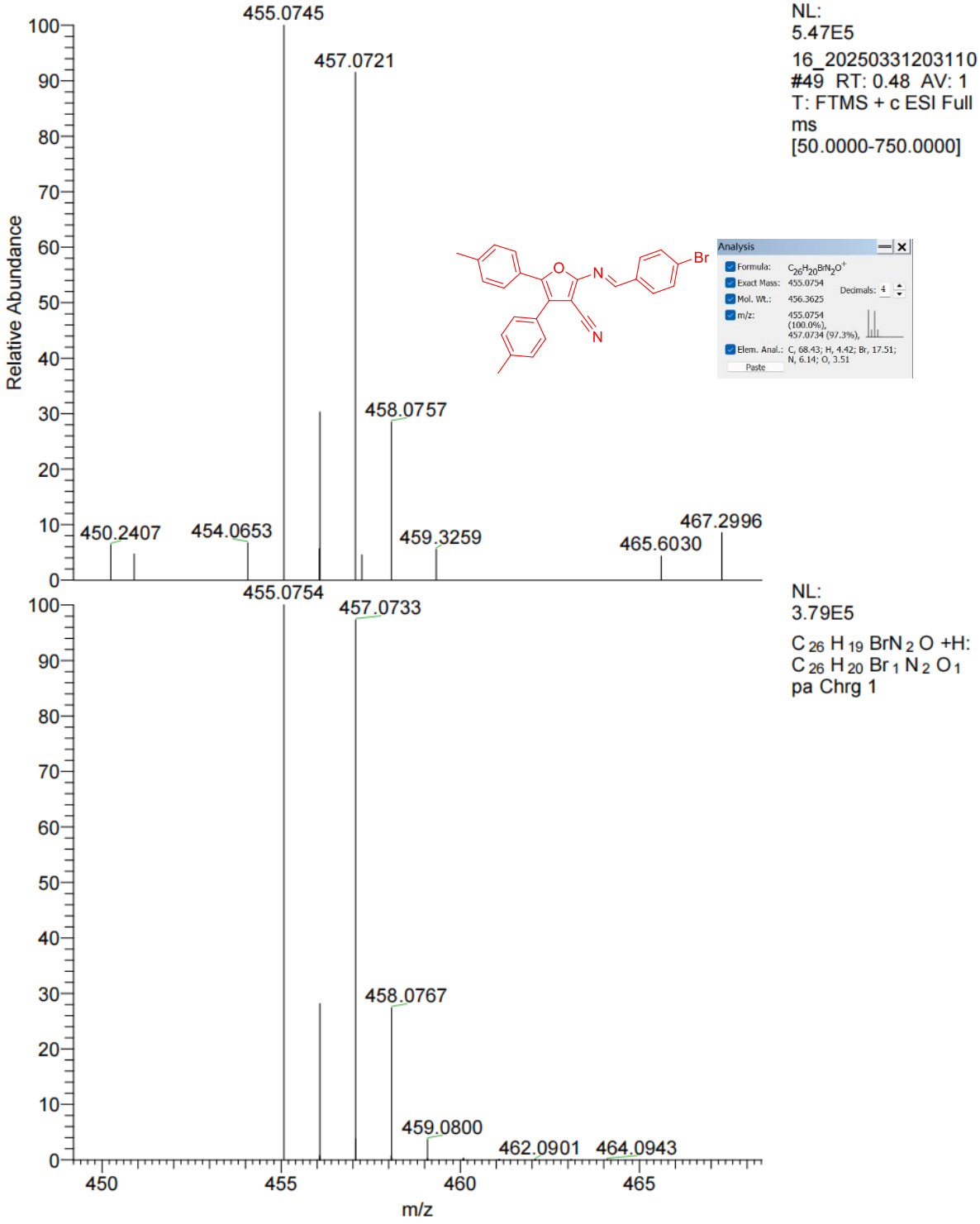
HR-MS spectrum of compound **4ad**



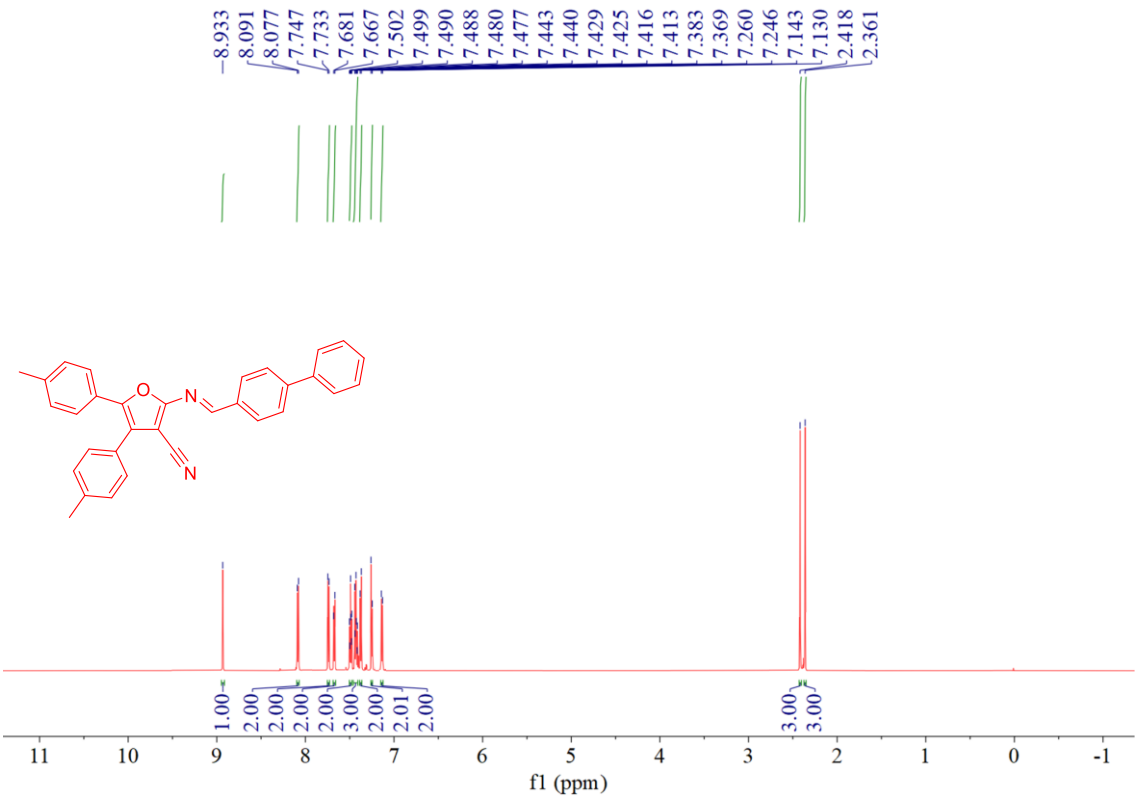
^{1}H NMR spectrum of compound **4ae**



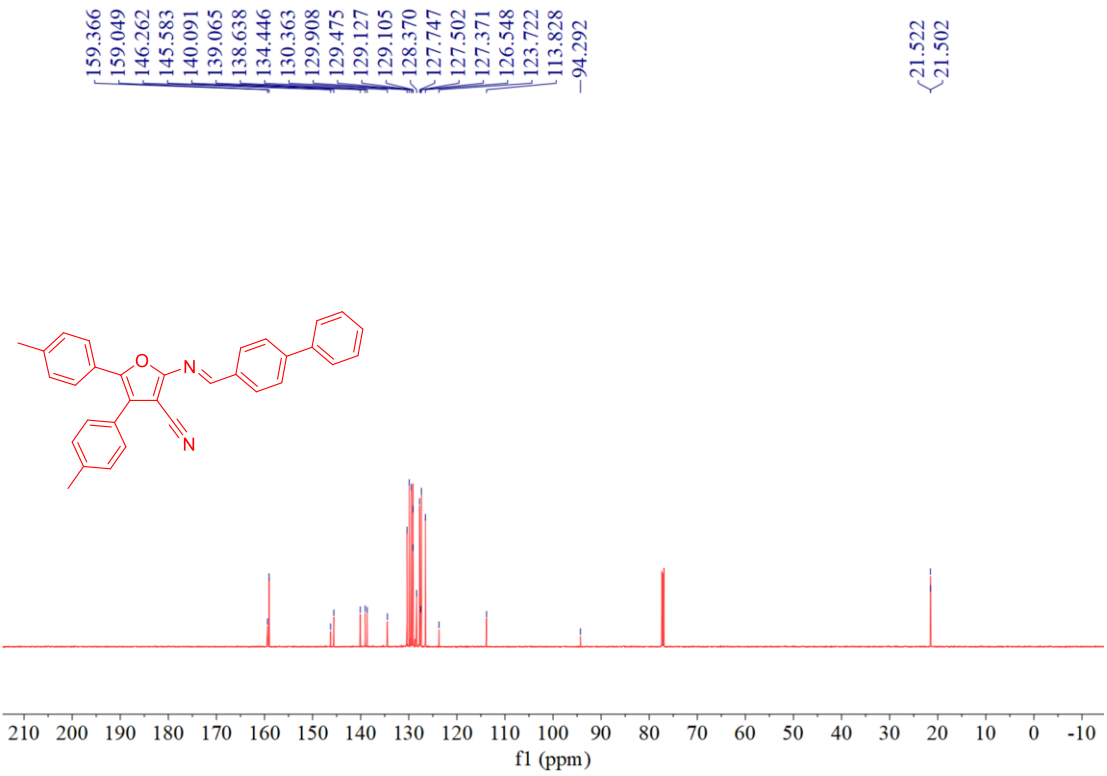
^{13}C NMR spectrum of compound **4ae**



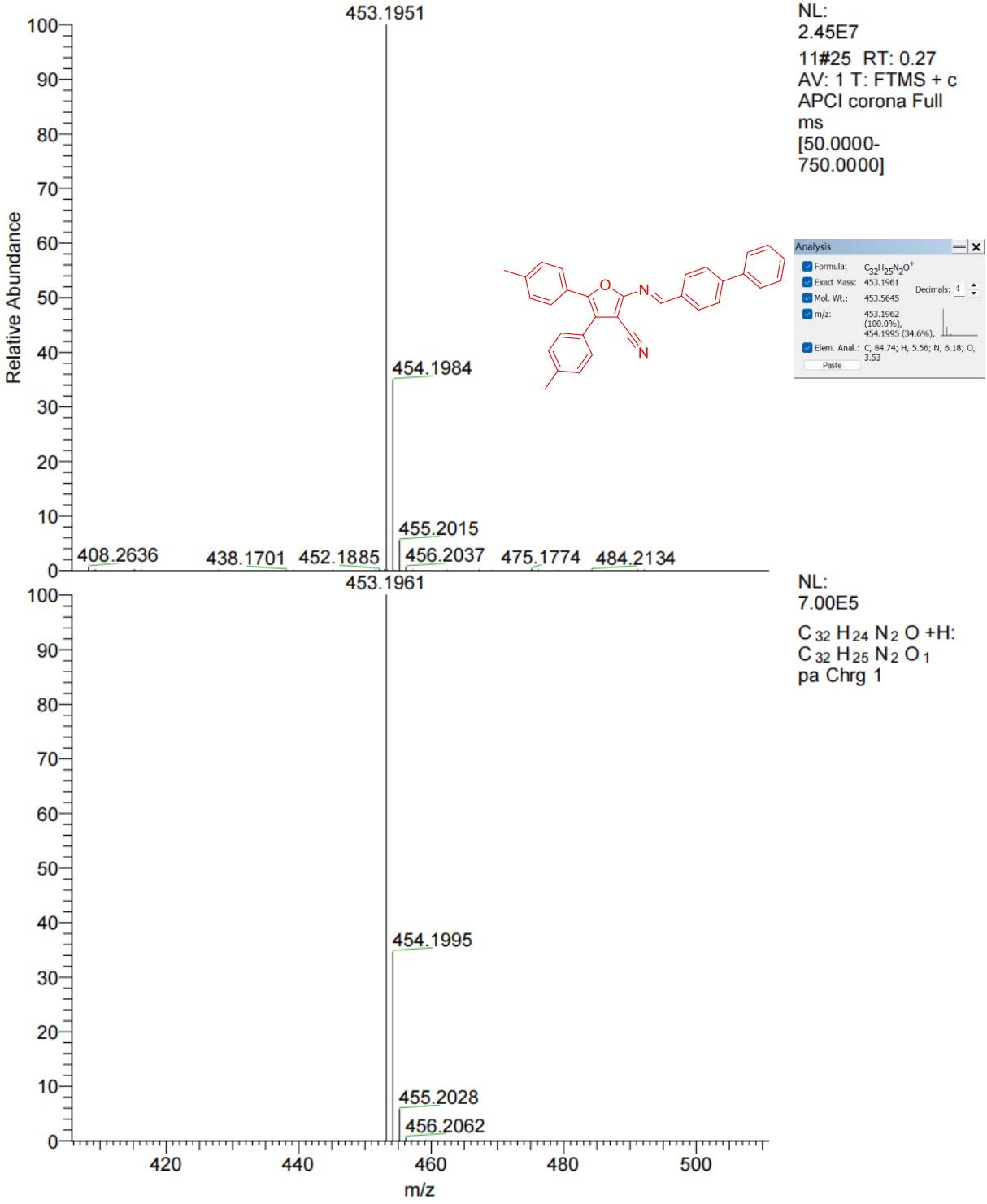
HR-MS spectrum of compound **4ae**



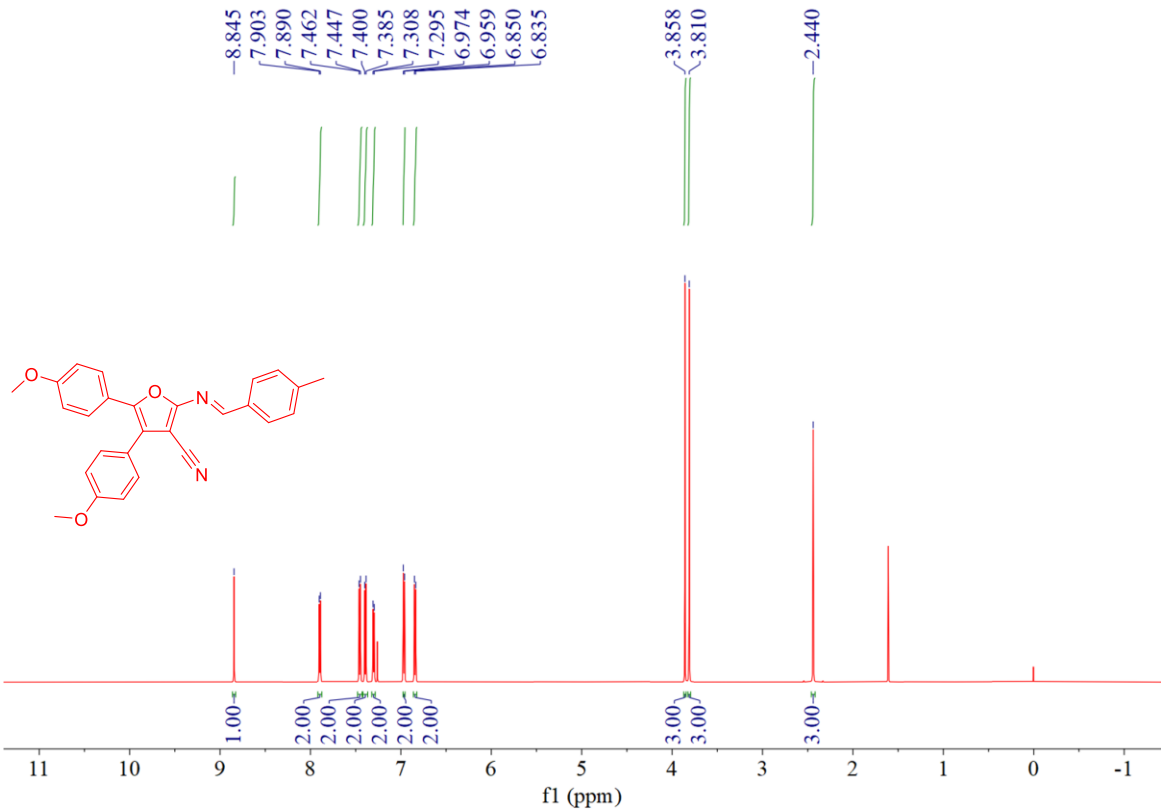
^{1}H NMR spectrum of compound **4af**



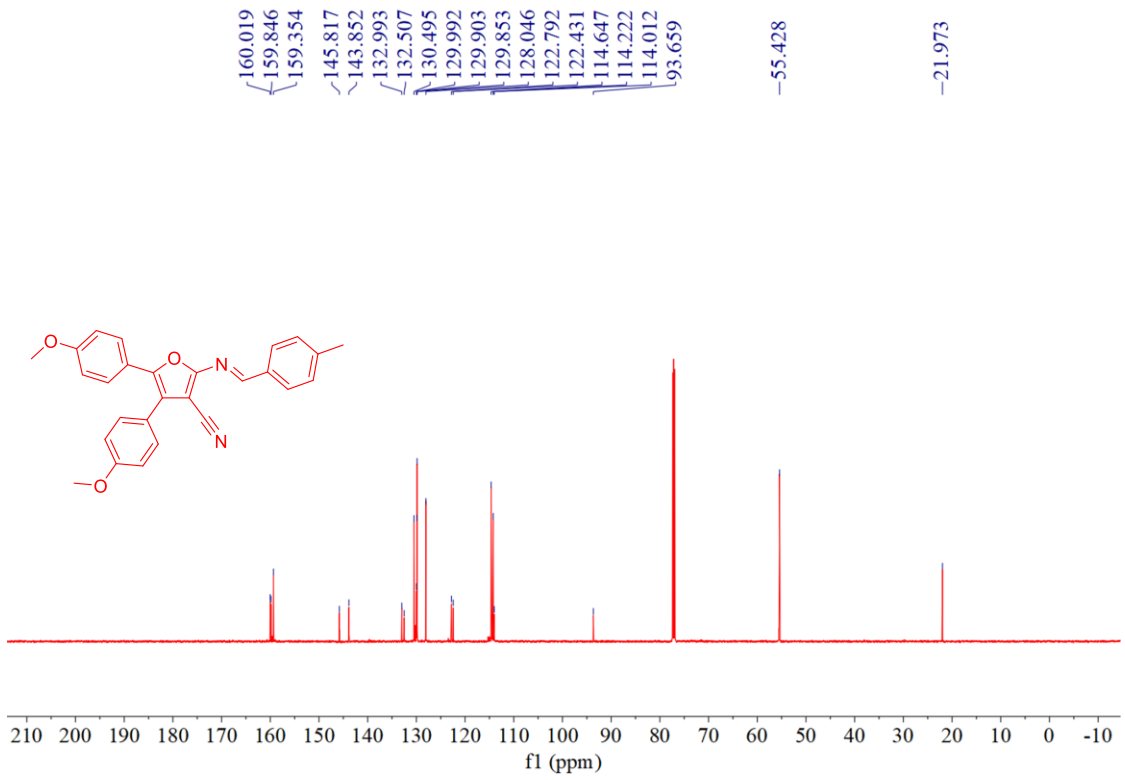
^{13}C NMR spectrum of compound **4af**



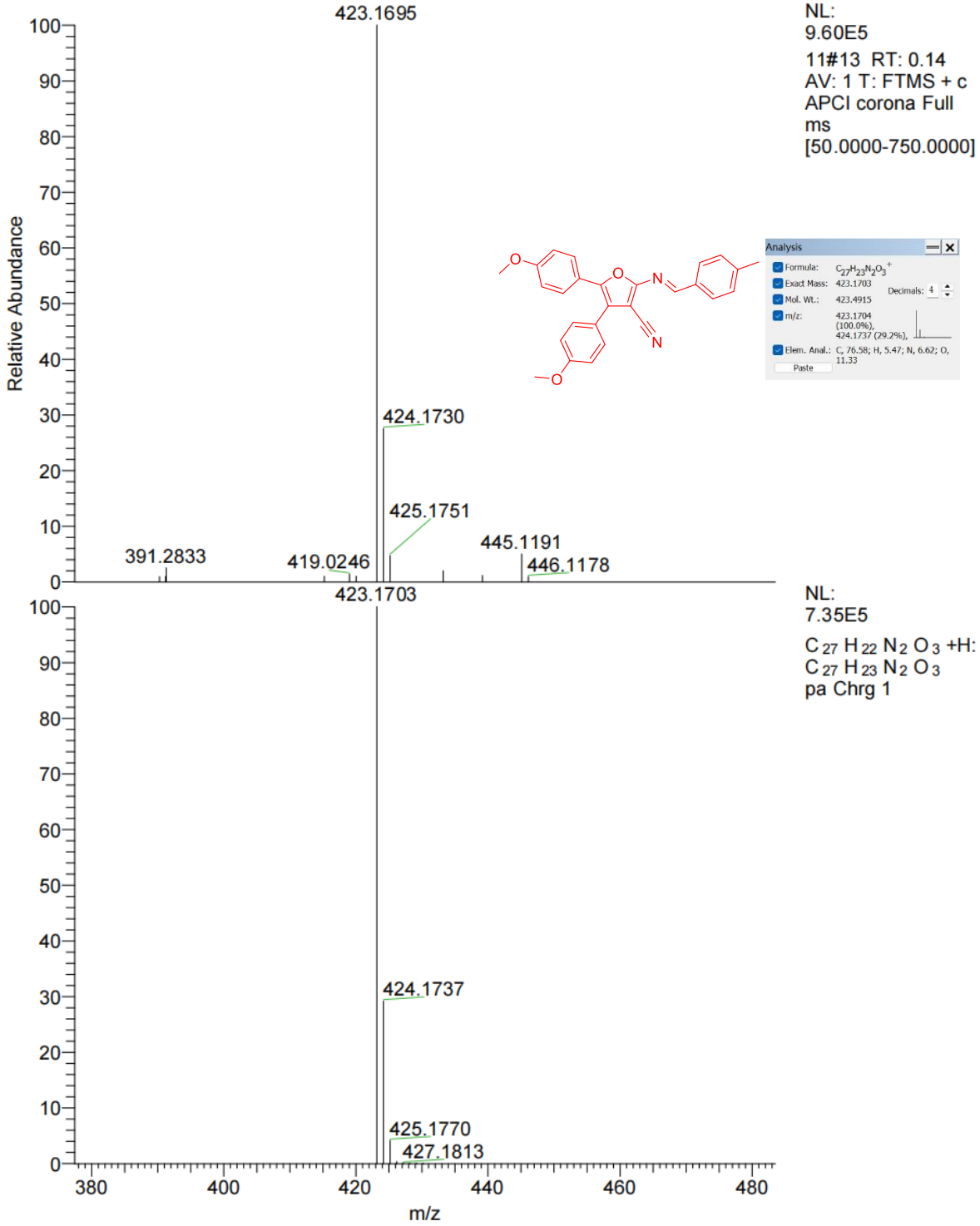
HR-MS spectrum of compound **4af**



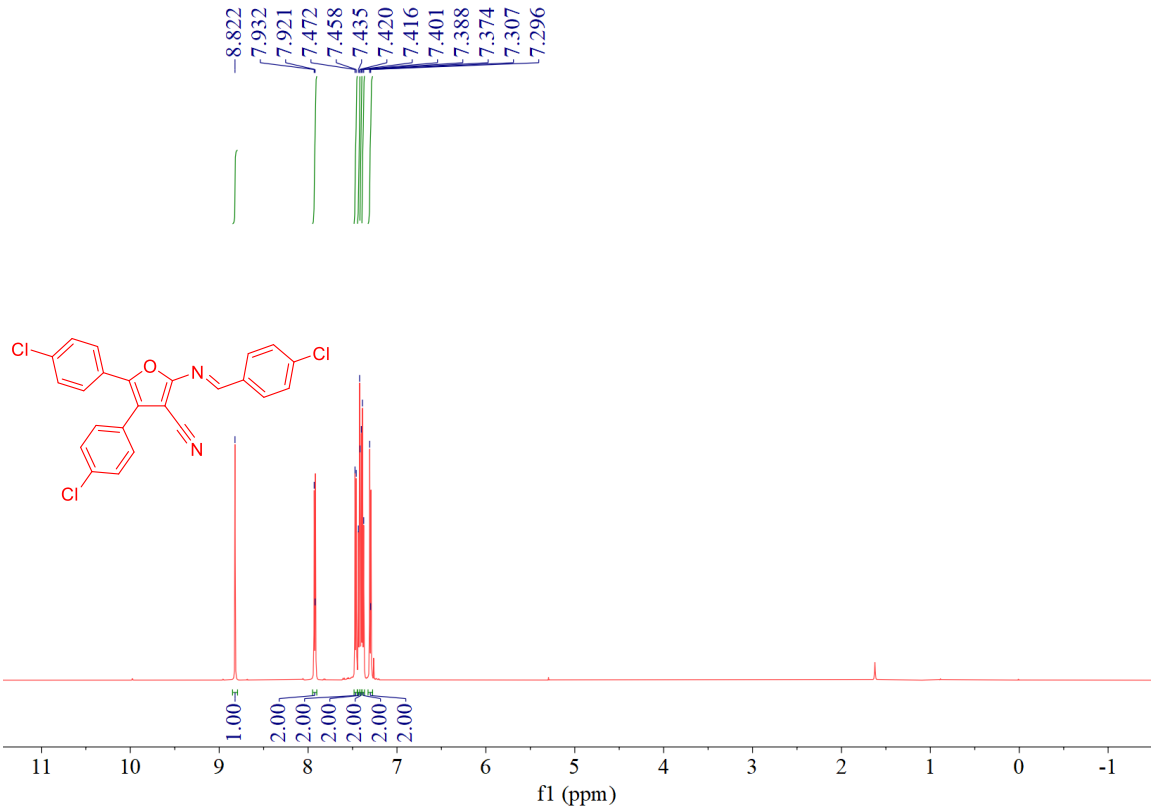
^{1}H NMR spectrum of compound **4ag**



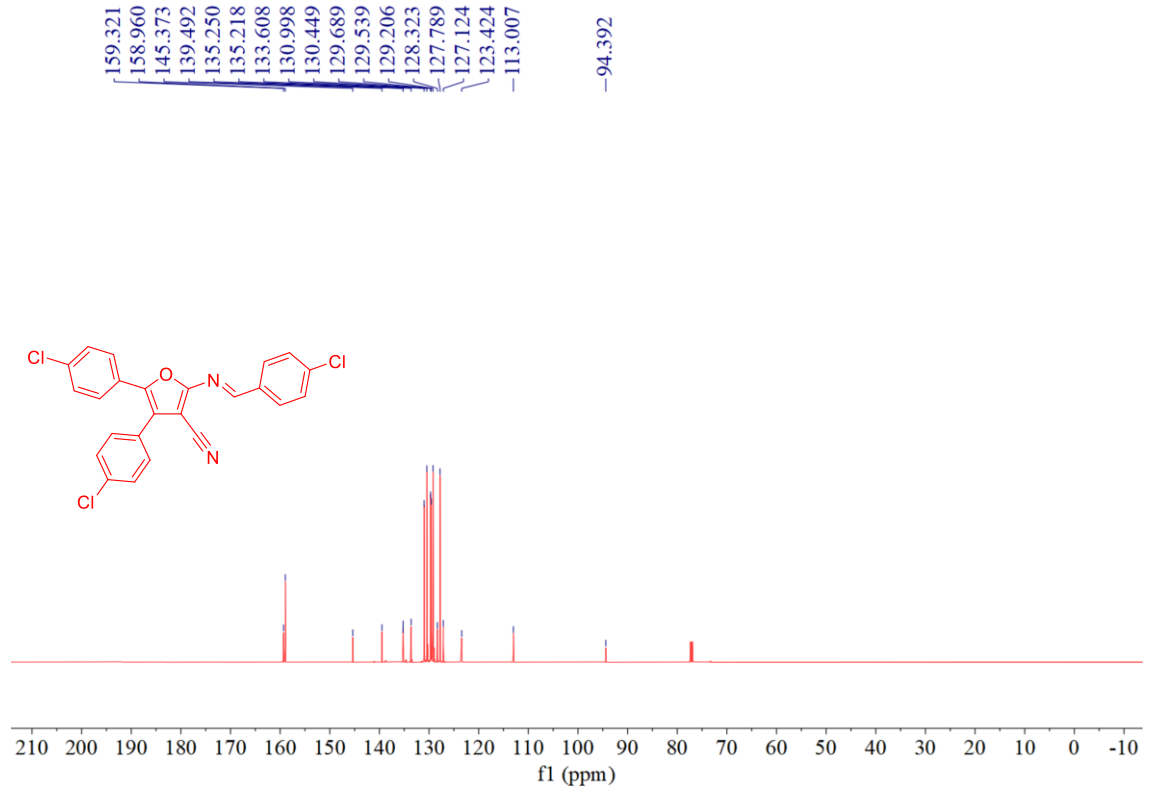
^{13}C NMR spectrum of compound **4ag**



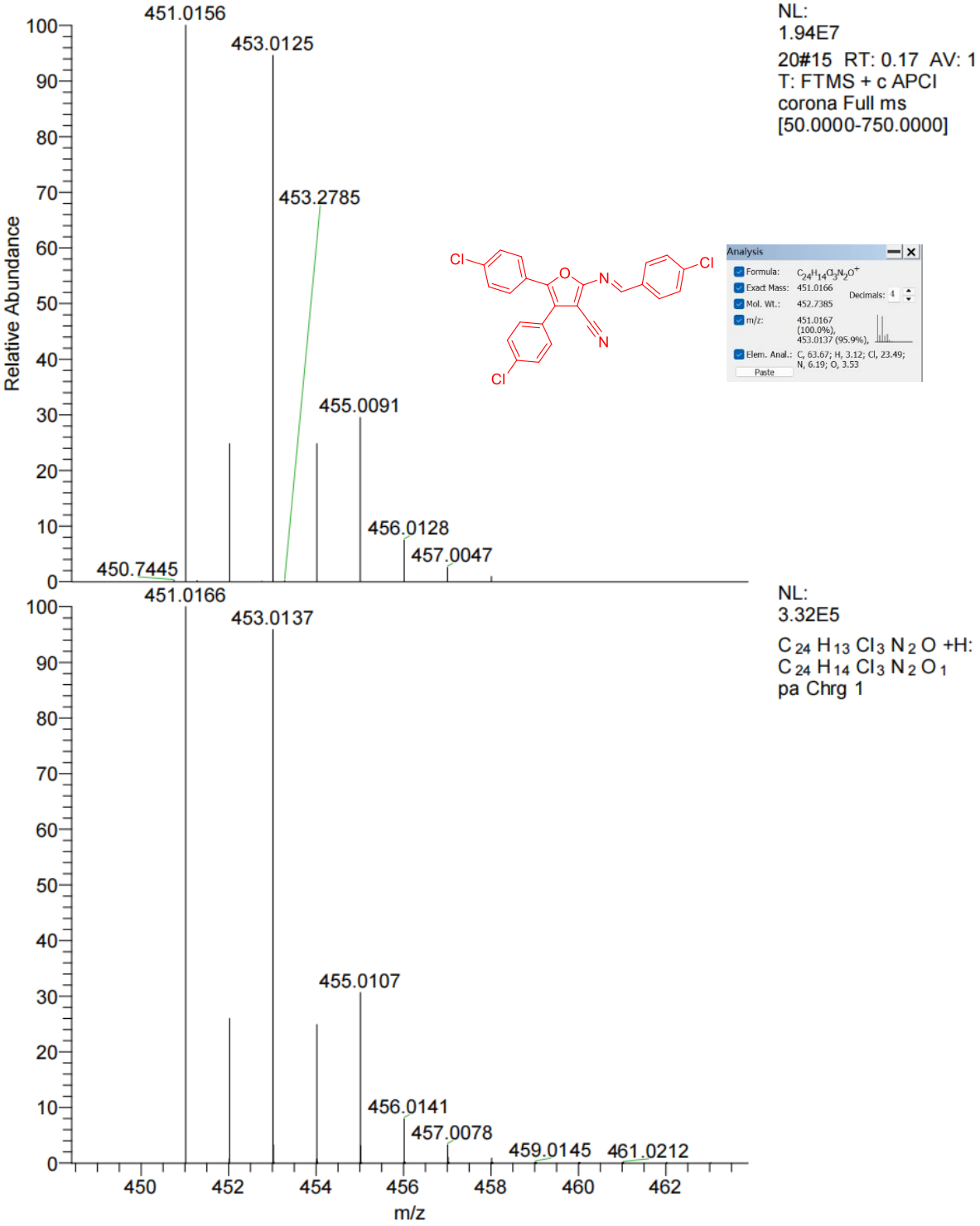
HR-MS spectrum of compound **4ag**



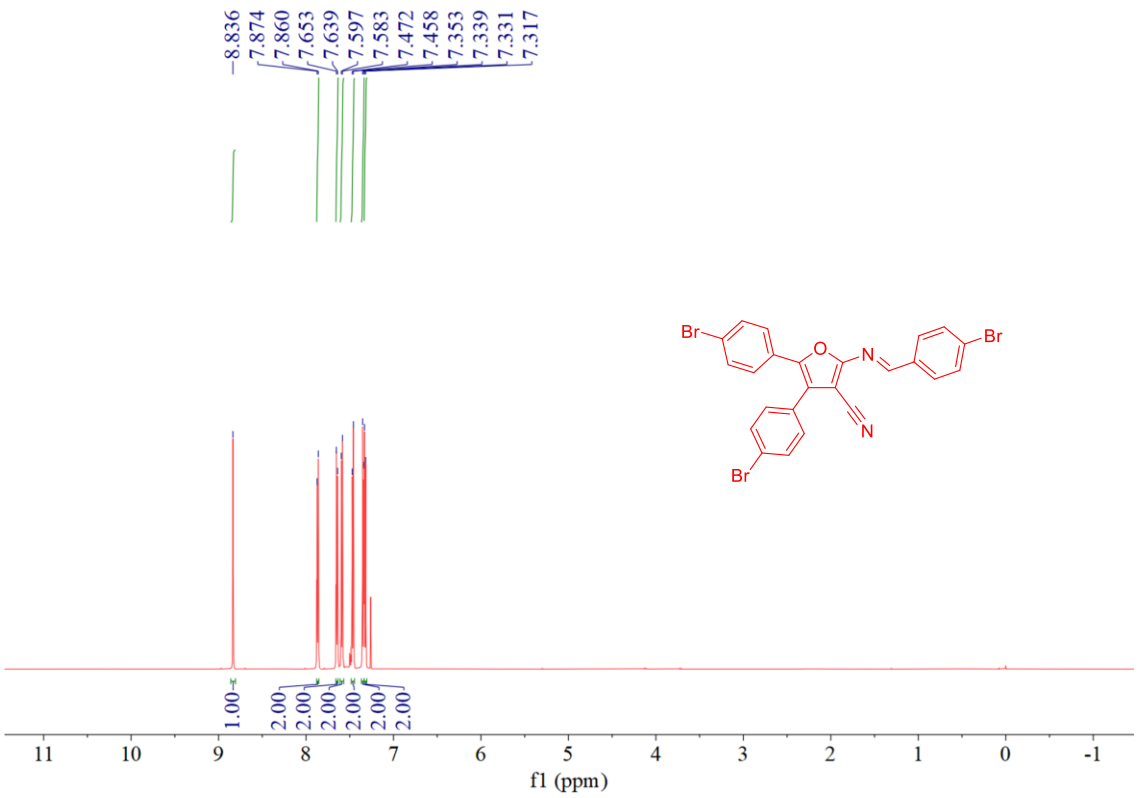
^{1}H NMR spectrum of compound **4ah**



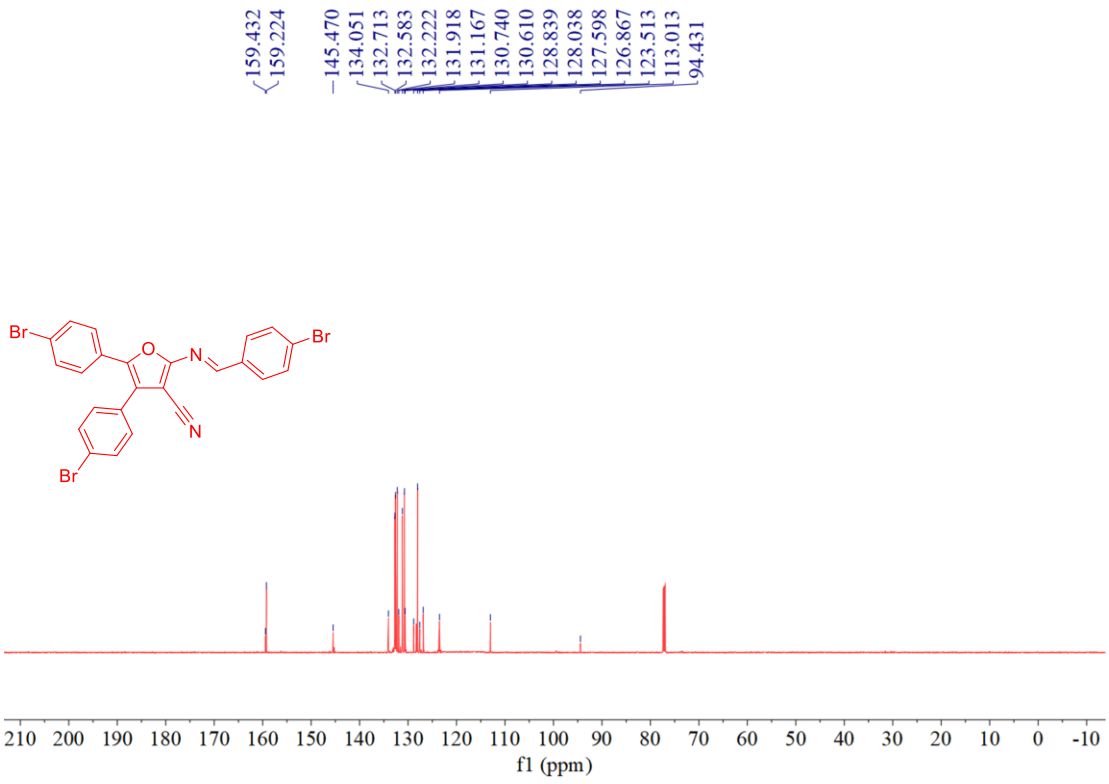
^{13}C NMR spectrum of compound **4ah**



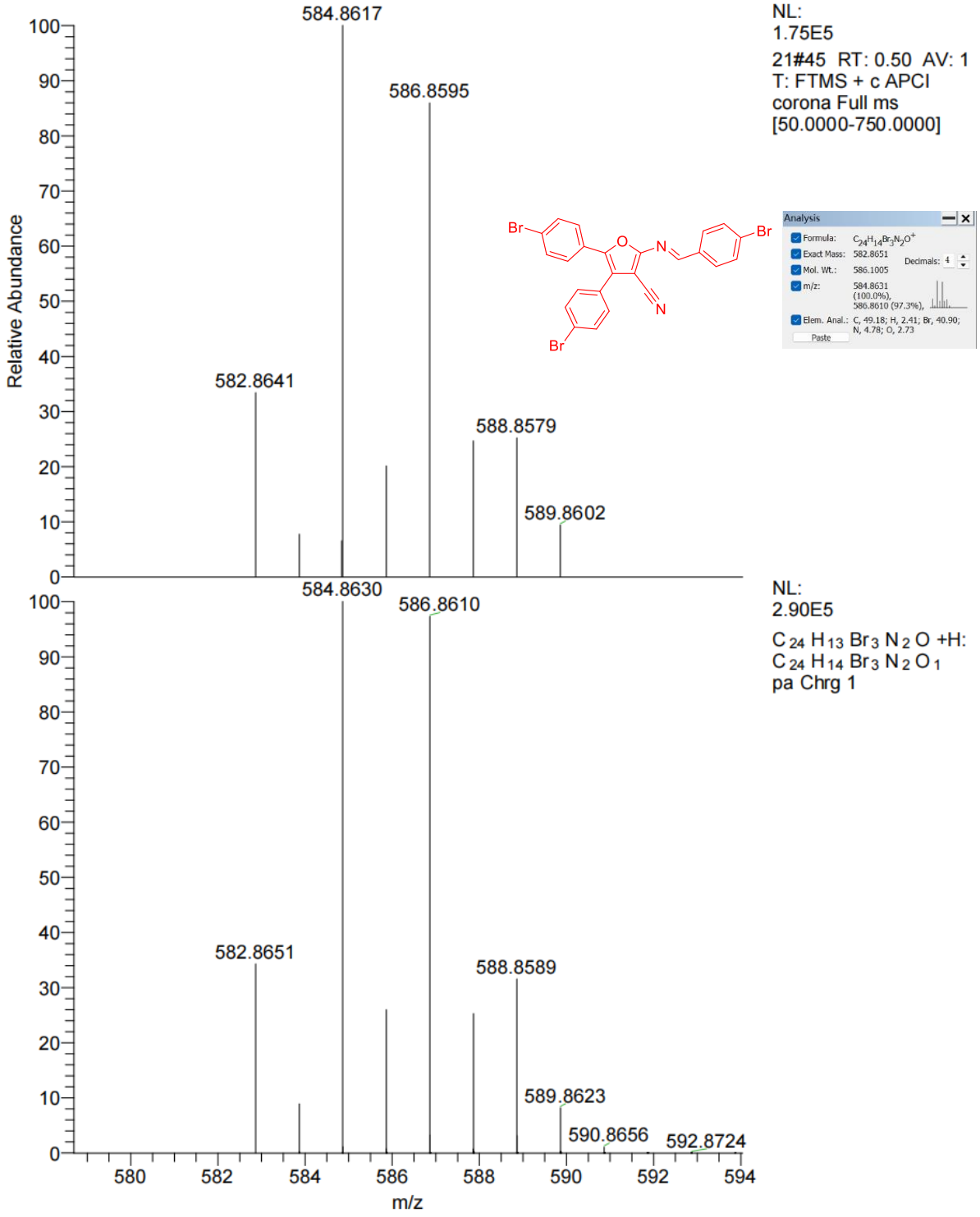
HR-MS spectrum of compound **4ah**



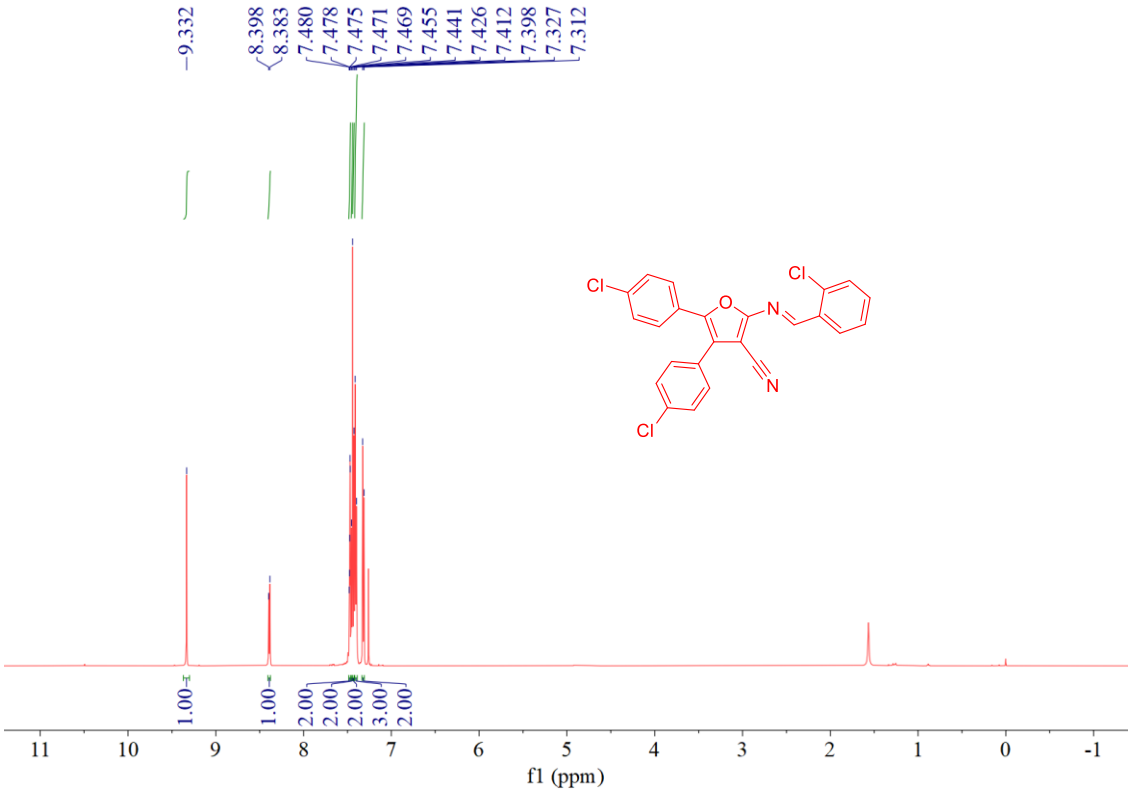
^{1}H NMR spectrum of compound **4ai**



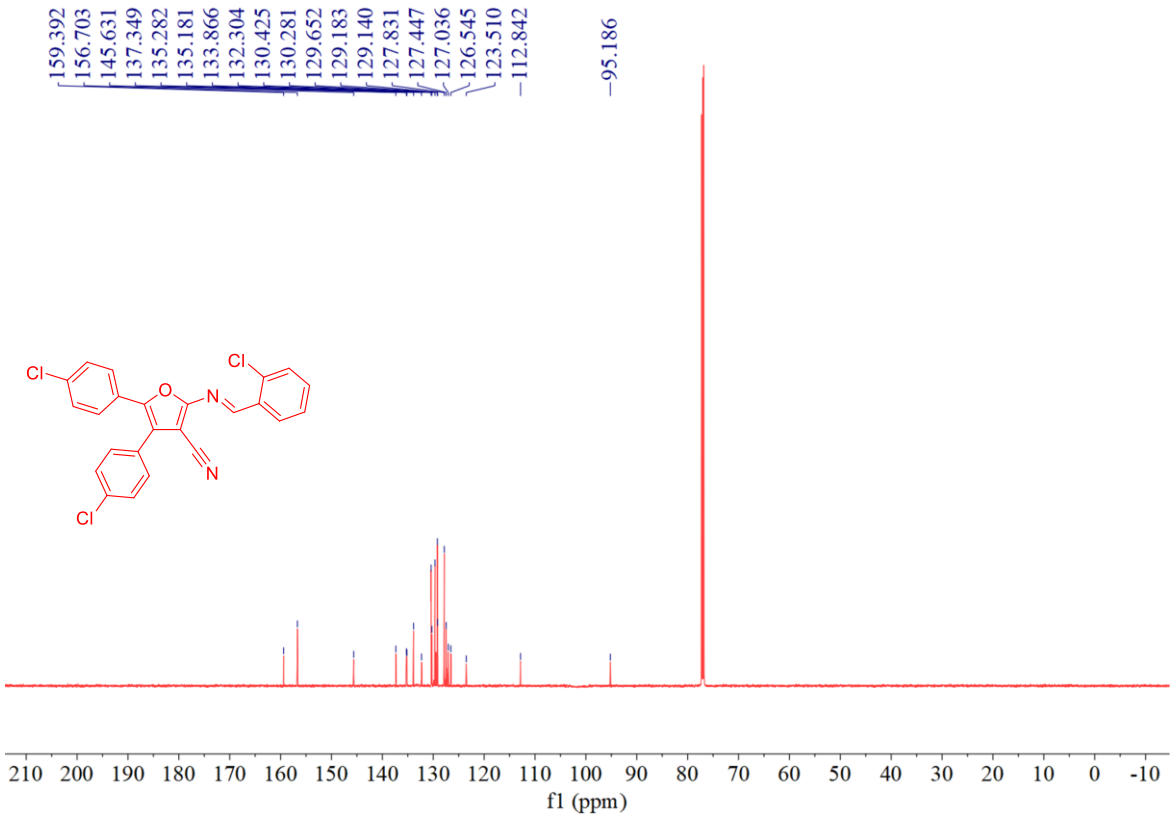
^{13}C NMR spectrum of compound **4ai**



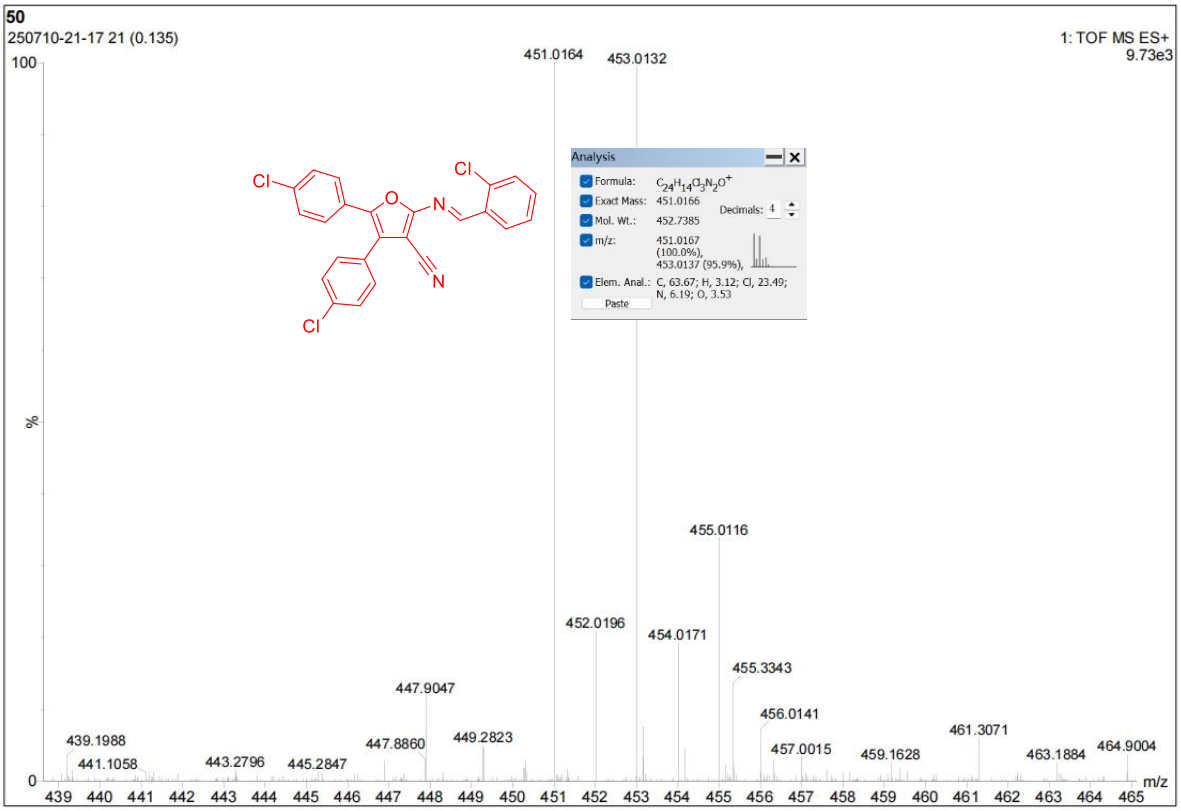
HR-MS spectrum of compound **4ai**



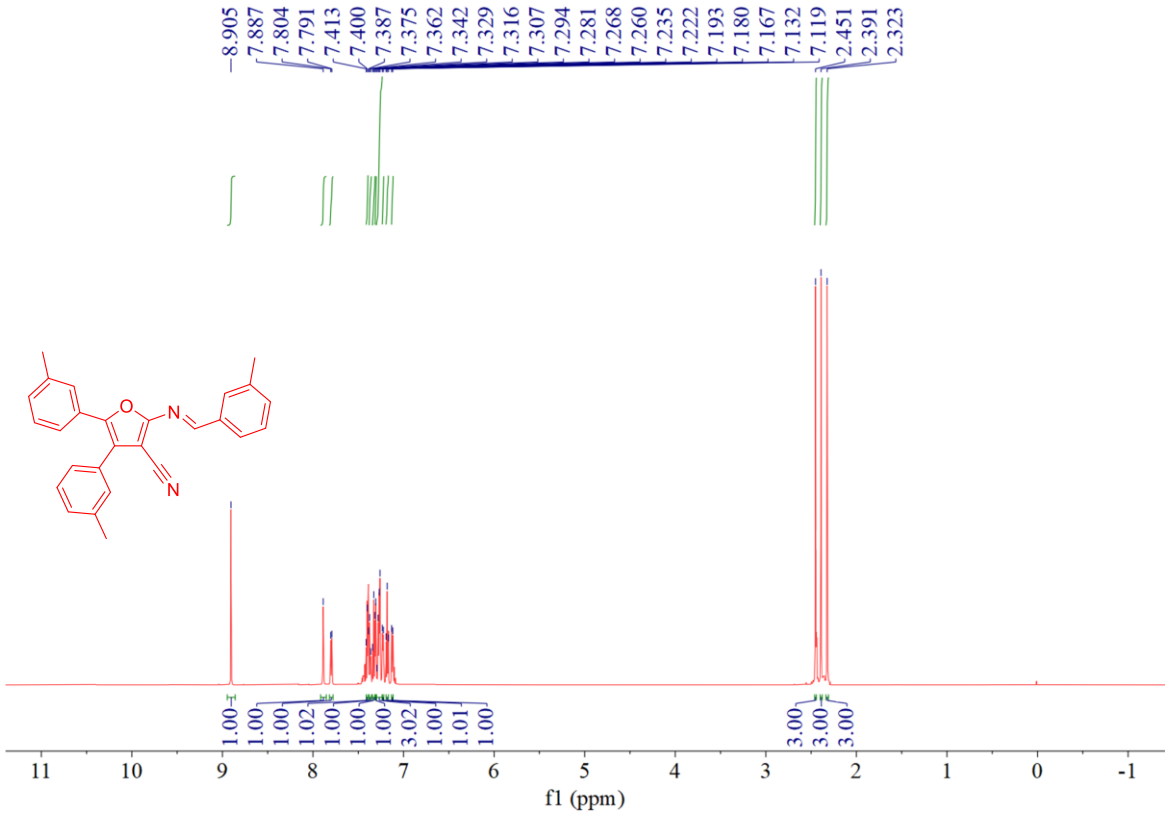
^{1}H NMR spectrum of compound **4aj**



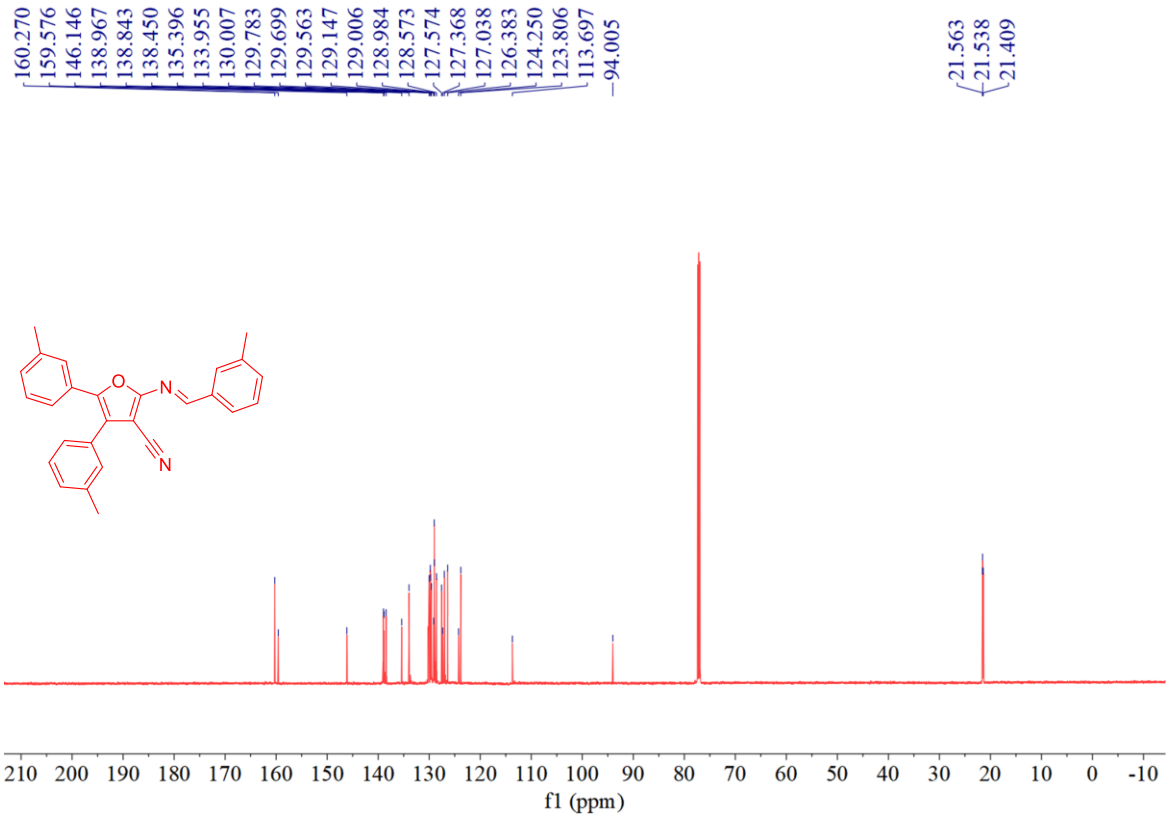
^{13}C NMR spectrum of compound **4aj**



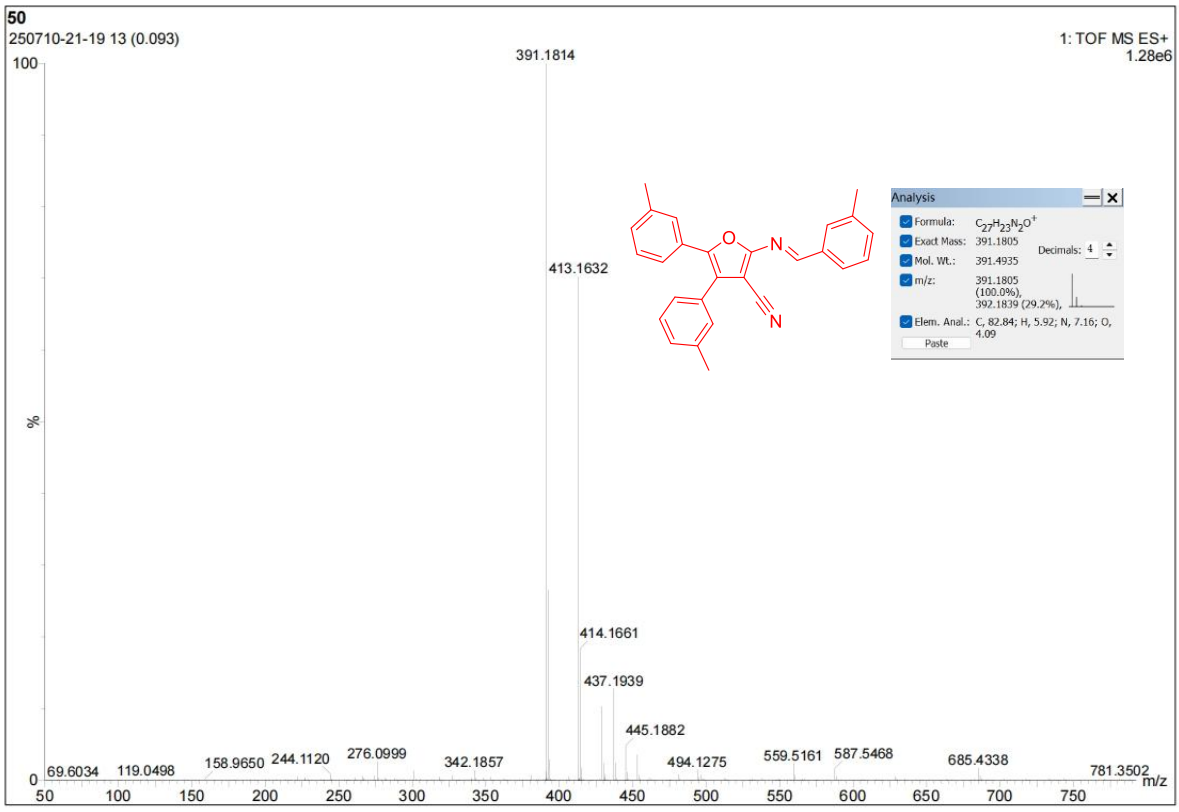
HR-MS spectrum of compound **4aj**



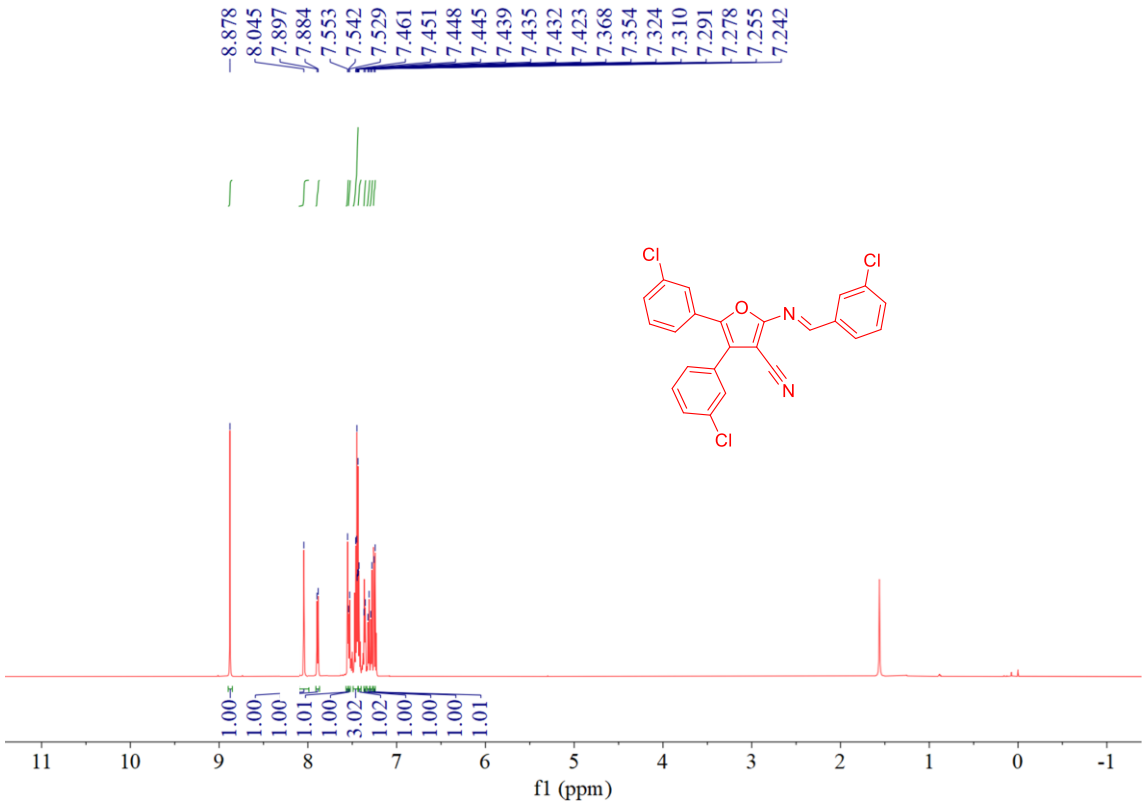
^{1}H NMR spectrum of compound **4ak**



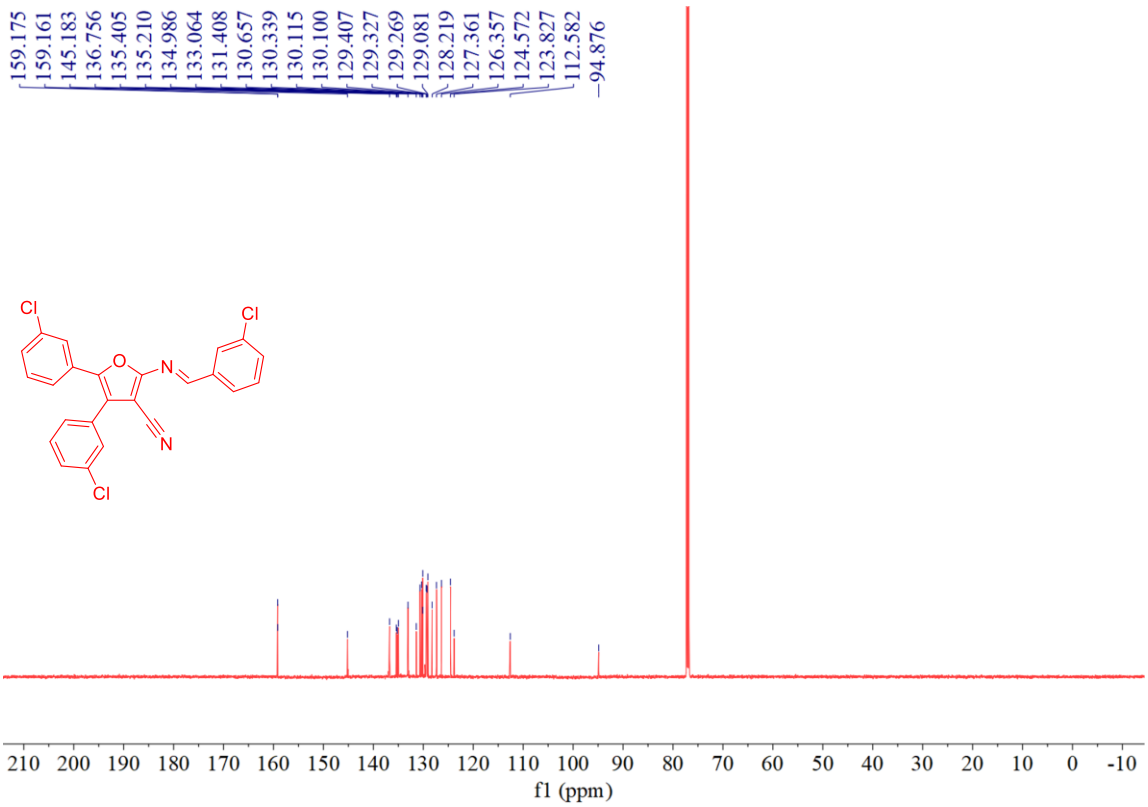
^{13}C NMR spectrum of compound **4ak**



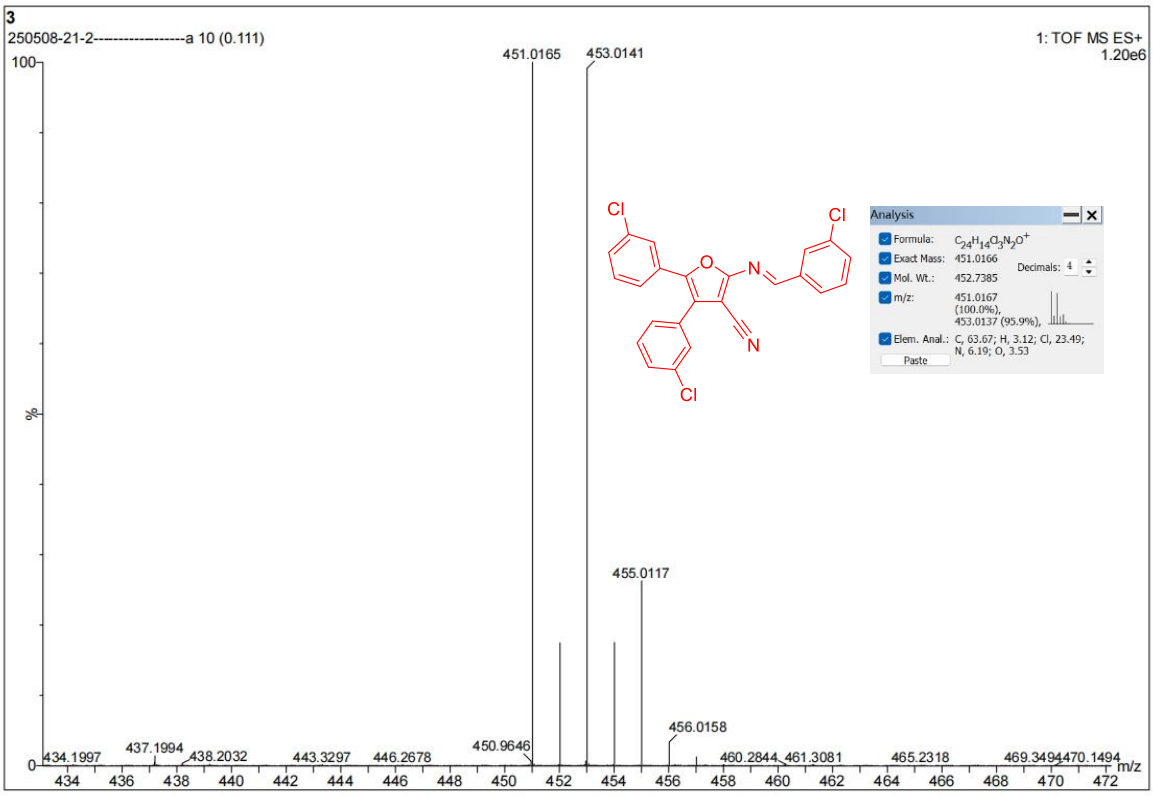
HR-MS spectrum of compound **4ak**



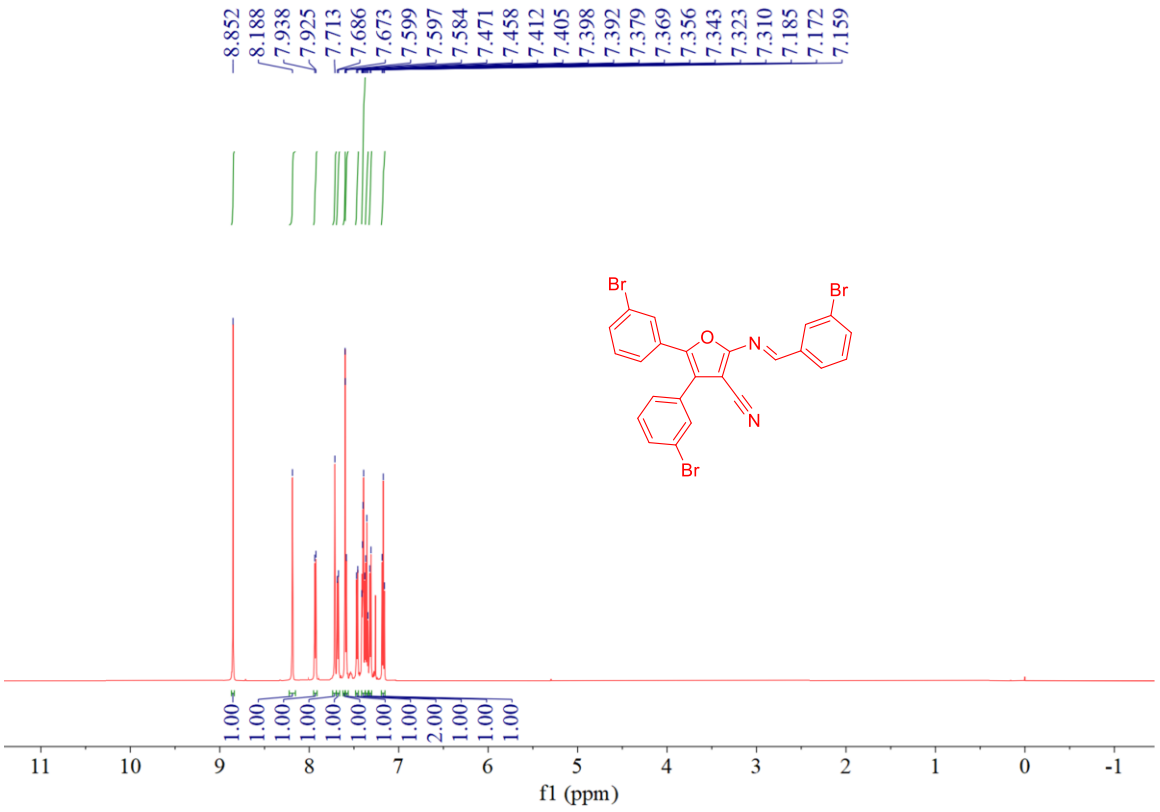
^{1}H NMR spectrum of compound **4al**



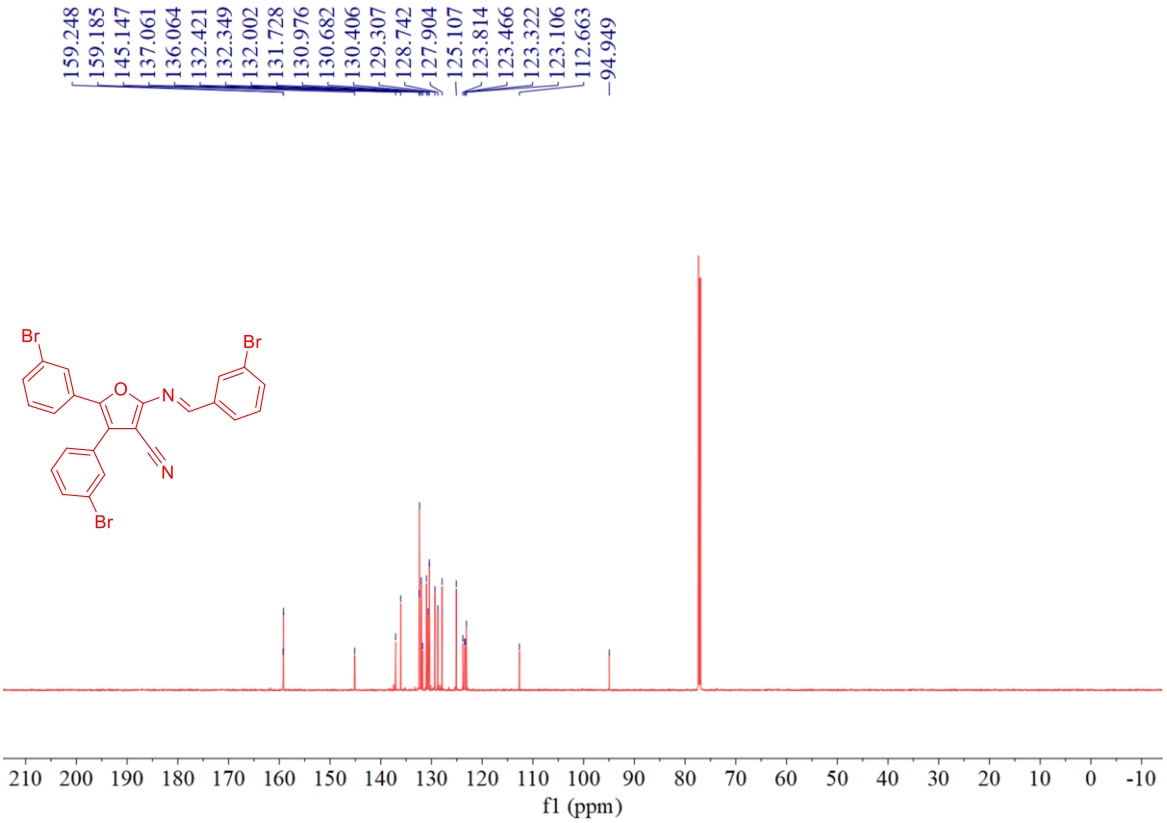
^{13}C NMR spectrum of compound **4al**



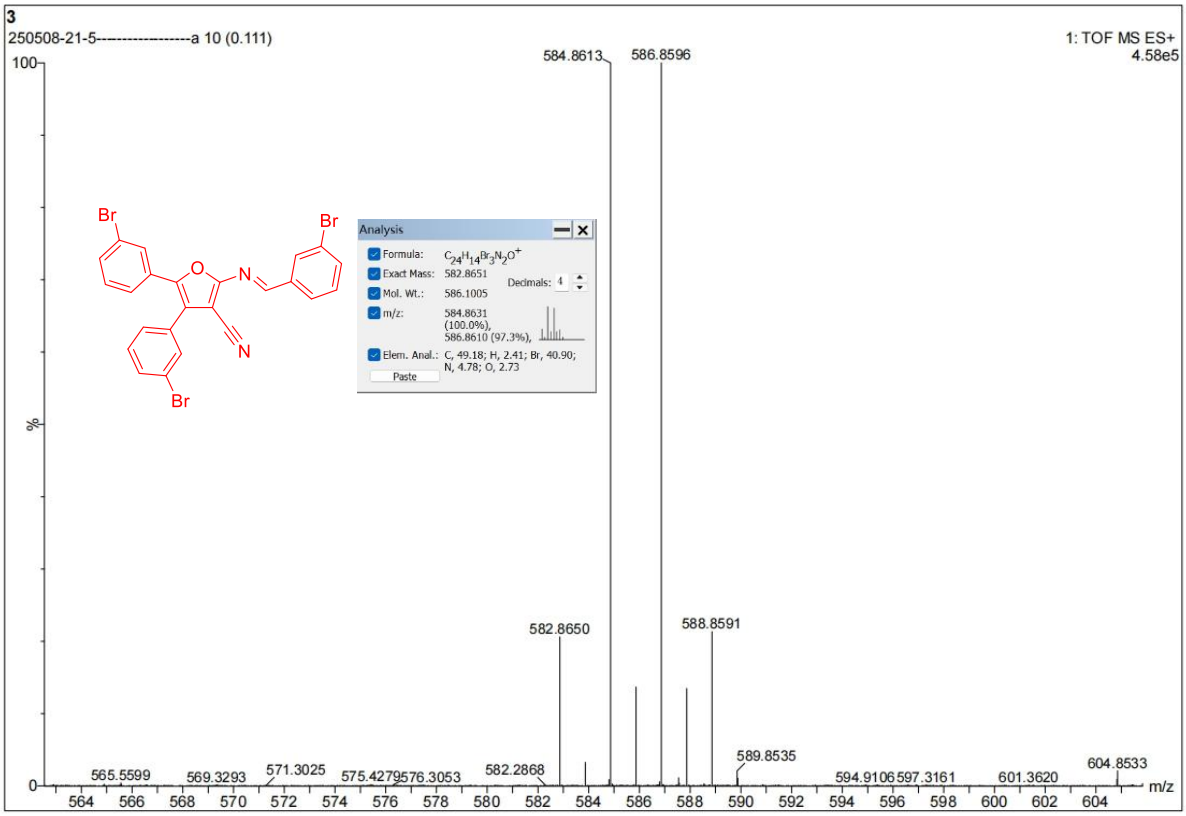
HR-MS spectrum of compound **4al**



^{1}H NMR spectrum of compound **4am**



^{13}C NMR spectrum of compound **4am**



HR-MS spectrum of compound **4am**

2.4. Results of Single-crystal X-ray Analysis for 4m

Table S1. Data of Single-crystal X-ray Analysis for **4m**.

Compound	**4m**
Empirical formula	$C_{25}H_{18}N_2O$
Formula weight	362.41
Temperature (K)	297 K
Crystal system	orthorhombic
Space group	$Pca2_1$
Unit cell dimensions (Å, °)	a = 18.8420(12), b = 6.2924(3), c = 16.2912(11) $\alpha = 90$, $\beta = 90$, $\gamma = 90$
Volume ($Å^3$)	1931.5(2)
Z	4
Density (calculated) (g/cm^3)	1.246
Absorption coefficient (mm^{-1})	0.077
F(000)	760.0
Radiation	Mo Kα (λ = 0.71073)
Theta range for data collection	4.324 to 58.646
Index ranges	$-25 \le h \le 14$, $-8 \le k \le 8$, $-22 \le l \le 20$
Reflections collected	16130
Independent reflections	4639 [R_{int} = 0.0437, R_{sigma} = 0.0525]
Absorption correction	Multi-Scan
Refinement method	Least Squares minimisation
Data / restraints / parameters	4639/1/254
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R_1 = 0.0596, wR_2 = 0.1065
R indices (all data)	R_1 = 0.0923, wR_2 = 0.1199
Largest diff. peak and hole	e $Å^{-3}$ 0.13/-0.18

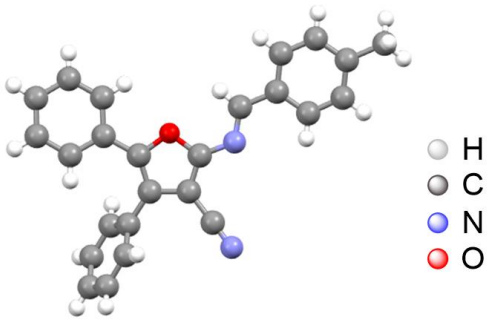


Figure S1. The molecular structure of **4m**

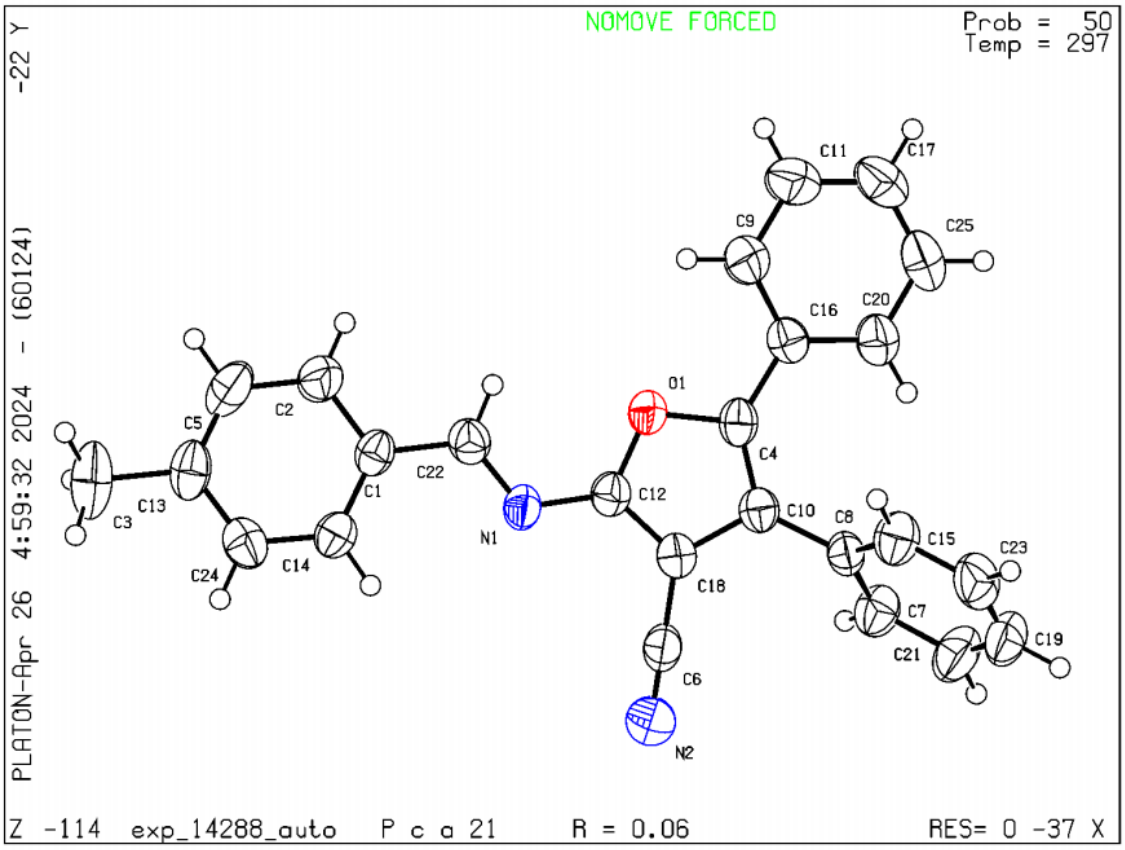


Figure S2. The ORTEP structural diagram of **4m**

3. Antimicrobial Activity Assays

Table S2. Antibacterial activity of tetrasubstituted furan-based Schiff base compounds **4**.

Compounds	*Escherichia coli*		*Staphylococcus aureus*	
	MIC (μg/mL)	MBC (μg/mL)	MIC (μg/mL)	MBC (μg/mL)
4a	1000	>1000	1000	>1000
4b	500	>1000	250	500
4c	>1000	>1000	>1000	>1000
4d	1000	>1000	**15.625**	**31.25**
4e	>1000	>1000	1000	>1000
4f	500	1000	**15.625**	**31.25**
4g	1000	>1000	250	500
4h	1000	>1000	500	>1000
4i	>1000	>1000	> 1000	>1000
4j	>1000	>1000	> 1000	>1000
4k	250	1000	1000	>1000
4l	>1000	>1000	>1000	>1000
4m	1000	>1000	1000	>1000
4n	1000	>1000	1000	>1000
4o	>1000	>1000	>1000	>1000
4p	1000	>1000	1000	>1000
4q	1000	>1000	125	500
4r	250	500	500	1000
4s	250	1000	500	1000
4t	1000	>1000	62.5	250
4u	1000	>1000	1000	>1000
4v	1000	>1000	1000	>1000
4w	1000	>1000	1000	>1000
4x	250	500	500	1000

4y	250	500	500	1000
4z	500	1000	500	1000
4aa	>1000	>1000	>1000	>1000
4ab	1000	>1000	1000	>1000
4ac	1000	>1000	1000	>1000
4ad	500	1000	500	1000
4ae	>1000	>1000	>1000	>1000
4af	>1000	>1000	>1000	>1000
4ag	>1000	>1000	>1000	>1000
4ah	1000	>1000	**62.5**	**125**
4ai	250	500	500	1000
4aj	500	>1000	**31.25**	**62.5**
4ak	500	1000	125	500
4al	500	1000	**15.625**	**31.25**
4am	1000	>1000	**31.25**	**62.5**

4. References

[1] Y. Zeng, S.-H. Yang, J.-L. Guo, Y. Li, T. Lin and Z.-Y. Wang, Metal-free Catalytic Synthesis of Tetrasubstituted Furans from α-Hydroxy Ketones and Cyano Compounds, *Molecules*, 2025, **30**, 1832.

[2] C. M. Pang, Y. X. Tan, J. H. Ling and L. Z. Hong, Synergetic Antibacterial Nanosheet Based on Ti_3C_2Tx Photothermal Therapy and Cationic Polymer to Eradicate Drug-resistant Bacterial Biofilms, *Nanoscale*, 2024, **16**, 21856-21868.

[3] C. M. Pang, B. Li, Z. S. Tu, J. H. Ling, Y. X. Tan, S. G. Chen and L. Z. Hong, Self-assembled Borneol-guanidine-based Amphiphilic Polymers as an Efficient Antibiofilm Agent, *ACS Appl. Mater. Interfaces*, 2024, **16**, 38429-38441.

[4] X.-Y. Cao, Z.-H. Li, X.-H. Cao, Z. Li, C.-M. Pang, Z.-Q. Zhang and Z.-Y. Wang, Multi-functional 3-Cyanopyridine Compounds: Synthesis Based on a Tandem Reaction with 100% Atom Economy and Their Applications, *Green Chem.*, 2025, **27**, 7300-7306.