**Supporting information**

# Green synthesis and characterisation of novel [1,3,4]thiadiazolo/benzo[4,5]thiazolo[3,2-*a*]pyrimidines *via* multicomponent reaction using vanadium oxide loaded on fluorapatite as a robust sustainable catalyst

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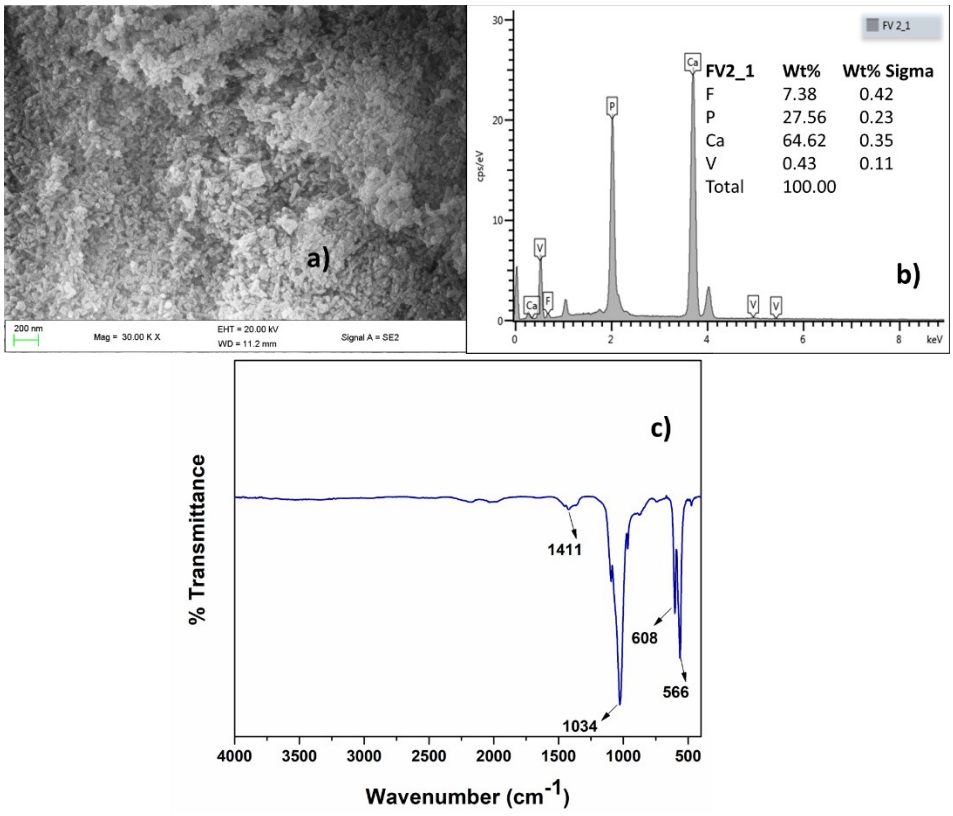


**Figure S1**: Recovered 2.5% $V_2O_5$/FAp catalyst of SEM (**a**), EDX (**b**) and FT-IR spectrum (**c**).

For illustration, 4-methoxy substituted derivative (4a) exhibited three sets of singlets in the $^1$H NMR spectrum, the most prominent singlet was seemed at $\delta$ 8.30 ppm due to the one proton of pyrimidine moiety. Another two singlets were observed at $\delta$ 3.87 and 12.69 ppm, which belong to the $OCH_3$ and $NH_2$ groups, respectively. Additionally, one quartet at 4.29 ppm and triplet at 1.29 ppm corresponds to the $-COOCH_2CH_3$ group. The remaining aromatic protons appeared at the respective aromatic region. The most characteristic peak seemed at $\delta$ 168.74 ppm due to the ester moiety carbonyl carbon (C=O) in $^{13}$C NMR. Further, two vibrational bands found at 3146 cm$^{-1}$ and 1695 cm$^{-1}$ in the FT-IR spectrum belong to the $NH_2$ and C=O groups, respectively. The molecular-ion peak was found at *m/z* = 427.0618 in the HRMS spectrum, which was further confirmed the formation of compound 4a.

## EXPERIMENTAL SECTION

### General Remarks

All the chemicals and reagents used for the reaction were of analytical grade and utilized without any further purification. $V_2O_5$, $Ca(NO_3)_3.4H_2O$, $Na_3PO_4.12H_2O$ and NaF were purchased from Alfa Aesar, Merck and Sigma−Aldrich. For the synthesized compounds, the structural elucidation was done by Bruker AMX 400 MHz NMR spectrometer and recording the spectral values of $^1H$ and $^{13}C$ NMR spectrum. Chemical shift values are reported in $\delta$ (ppm), with TMS assisted as the internal standard and DMSO−$d_6$ as a solvent. TLC−aluminum plates coated with silica gel (Merck Kieselgel 60 F254) were used for the initial conforming of reaction completion. Bruker micro TOF−Q II ESI instrument functioning at ambient temperature was used for High−resolution mass data (HRMS). FT-IR spectrum was recorded at the 400 $cm^{-1}$ to 4000 $cm^{-1}$ range and using Perkin Elmer Precisely 100 FT-IR spectrometer. JEOL JSM−6100 microscopes and Jeol JEM−1010 electron microscope was employed for the SEM, EDX and TEM morphology data. X−ray diffraction data associated with the structural phases of the material was obtained by using the Bruker D8 Advance instrument (Cu K radiation source with a wavelength of 1.5406 Å). Materials were degassed by passing nitrogen overnight at 200 $^oC$ and BJH adsorption and desorption curves were attained at −196 $^oC$. Surface area, pore size and pore volume of the material were established by using Micromeritics Tristar−II porosity and surface area analyzer.

### $V_2O_5$/FAp catalyst preparation

Different weight percentages loading of vanadium oxide on fluorapatite (1, 2.5 and 5 wt%) were synthesized by the co-precipitation method according to the literature reported method [42]. 1.5 mmol of trisodium phosphate dodecahydrate ($Na_3PO_4.12H_2O$) was suspended in deionized water (25 mL) in a 50 mL of the beaker. Next, 0.5 mmol of sodium fluoride (NaF) was gradually added

to that solution under constant stirring for 30 min at room temperature. Then, 2.5 mmol of calcium nitrate tetrahydrate was added into this solution mixture and continue stirring for further 15 min. Finally, the necessary calculated volume of 99.9% vanadium oxide (0.5 mmol) was added slowly and the solution mixture was more stirring for 6 h. The subsequent suspensions were divided by centrifugation and the number of runs rinsed with deionized water. The afforded composite material systems were dried in the heating oven at 120 $^{o}$C for 10h. Although, these catalyst materials were calcinated at 350$^{o}$C for 4 h under continuous airflow, to get the vanadium oxide loaded fluorapatite ($V_2O_5$/FAp) catalyst materials.

**General procedure for the synthesis of [1,3,4]thiadiazolo[3,2-*a*]pyrimidine and benzo[4,5]thiazolo[3,2-*a*]pyrimidine derivatives (4a-q)**

A mixture of different substituted 1,3,4-thiadiazole-amine (**1a-h**, 1 mmol) or 2-amino-benzathiazole (**5**, 1 mmol), varieties of selected benzaldehydes (**2a-f**, 1 mmol), active methylene compounds (**3a-c**, 1 mmol) and 30 mg of heterogeneous catalyst (2.5% $V_2O_5$/FAp) in solvent ethanol (5 mL) were added in a round bottom flask. The reaction mixture was constantly stirred at room temperature for 25 to 30 min. The progress of the reaction monitored by TLC. After finishing the reaction mixture, the catalyst was separated from the reaction mixture by filtration through the addition of excess ethyl acetate. The recovered catalyst material was further reused for the next cycles. The filtrate was concentrated by rotatory evaporation with vacuum pressure. Then the furnished the solid products and which were recrystallized by using hot ethanol to facilitate the corresponding pure products. The structural elucidation of all the synthesized novel compounds were established and interpreted by different spectroscopic methods (FT-IR, HRMS, $^{1}$H and $^{13}$C NMR).

*Ethyl-7-amino-2-(3-fluorophenyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4a**)

White solid; m.p. 176-178 $^{o}$C; IR cm$^{-1}$: 3146 ($NH_2$), 2906 (CH), 1695 (C=O), 1601 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.69 (s, 2H, $NH_2$), 8.30 (s, 1H, CH), 8.08 (d, $J$ = 8.6 Hz, 2H, Ar-H), 7.98 (t, $J$ = 10.3 Hz, 1H, Ar-H), 7.82 (d, $J$ = 8.0 Hz, 1H, Ar-H), 7.57 (dd, $J$ = 13.6, 7.5 Hz, 1H, Ar-H), 7.36 (t, $J$ = 8.8 Hz, 1H, Ar-H), 7.15 (d, $J$ = 8.6 Hz, 2H, Ar-H), 4.29 (q, $J$ = 6.9 Hz, 2H, $CH_2$), 3.87 (s, 3H, $OCH_3$), 1.29 (t, $J$ = 7.0 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 168.74, 163.52, 162.33, 161.12, 154.43, 133.48, 131.54, 131.46, 123.93, 123.26, 117.41, 117.20, 116.20, 114.94, 113.35, 113.11, 98.54, 62.04, 55.73, 22.38, 13.99; HRMS of $[C_{21}H_{19}N_4O_3FS + H]^+$ (*m/z*) 427.0618; Calcd: 427.0621.

*Ethyl-7-amino-2-(3-bromophenyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4b**)

Cream white solid; m.p. 182-184 $^{o}$C; IR cm$^{-1}$: 3147 ($NH_2$), 2906 (CH), 1695 (C=O), 1609 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.87 (s, 2H, $NH_2$), 8.29 (s, 1H, CH), 8.07 (d, $J$ = 8.6 Hz, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 7.73 (d, $J$ = 7.8 Hz, 1H, Ar-H), 7.61 (d, $J$ = 7.8 Hz, 1H, Ar-H), 7.42 (t, $J$ = 7.8 Hz, 1H, Ar-H), 7.14 (d, $J$ = 8.5 Hz, 2H, Ar-H), 4.30 (q, $J$ = 6.9 Hz, 2H, $CH_2$), 3.87 (s, 3H, OCH3), 1.30 (t, $J$ = 7.0 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 164.02, 162.83, 154.89, 133.98, 133.64, 133.61, 132.58, 131.73, 128.68, 125.92, 124.43, 122.74, 116.68, 115.42, 115.34, 99.04, 62.53, 56.22, 14.48; HRMS of $[C_{21}H_{19}N_4O_3BrS + H]^+$ (*m/z*) 487.9764; Calcd: 487.9777.

*Ethyl-7-amino-2-(p-tolyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4c**)

White solid; m.p. 189-181 $^{o}$C; IR cm$^{-1}$: 3146 ($NH_2$), 2905 (CH), 1695 (C=O), 1609 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.59 (s, 2H, $NH_2$), 8.31 (s, 1H, CH), 8.09 (d, $J$ = 9.0 Hz, 2H, Ar-

H), 7.82 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.63 (d, *J* = 7.9 Hz, 1H, Ar-H), 7.34 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.14 (d, *J* = 8.9 Hz, 2H, Ar-H), 4.30 (q, *J* = 7.1 Hz, 2H, $CH_2$), 3.87 (s, 3H, OCH3), 2.21 (s, 3H, CH3), 1.30 (t, *J* = 7.1 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.08, 164.03, 162.84, 154.93, 133.99, 133.71, 130.34, 127.27, 124.44, 116.71, 115.45, 115.38, 99.06, 62.54, 56.24, 22.89, 21.42, 14.50; HRMS of $[C_{22}H_{22}N_4O_3S + H]^+$ (*m/z*) 423.1623; Calcd: 423.1617.

*Ethyl-7-amino-2-(3-nitrophenyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4d**)

Pale yellow solid; m.p. 192-194 $^{o}$C; IR cm$^{-1}$: 3146 ($NH_2$), 2912 (CH), 1697 (C=O), 1608 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.80 (s, 2H, $NH_2$), 8.49 (s, 1H, CH), 8.29 (s, 1H, Ar-H), 8.25 (d, *J* = 7.1 Hz, 1H, Ar-H), 8.15 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.08 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.75 (t, *J* = 7.9 Hz, 1H, Ar-H), 7.15 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.30 (dd, *J* = 13.8, 6.8 Hz, 2H, $CH_2$), 3.87 (s, 3H, $OCH_3$), 1.30 (t, *J* = 6.9 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 164.02, 162.83, 154.90, 148.70, 133.98, 132.99, 132.89, 131.55, 131.34, 124.43, 124.25, 120.53, 116.69, 115.43, 99.05, 62.54, 56.23, 22.89, 14.49; HRMS of $[C_{21}H_{19}N_5O_5S + H]^+$ (*m/z*) 454.1720; Calcd: 454.1723.

*Ethyl-7-amino-2-(3-fluorophenyl)-5-(4-fluorophenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4e**)

Cream white solid; m.p. 174-176 $^{o}$C; IR cm$^{-1}$: 3158 ($NH_2$), 2904 (CH), 1696 (C=O), 1610 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.70 (s, 2H, $NH_2$), 8.42 (s, 1H, CH), 8.16 (dd, *J* = 8.7, 5.6 Hz, 2H, Ar-H), 7.78 (d, *J* = 7.5 Hz, 2H, Ar-H), 7.60 (t, *J* = 4.6 Hz, 1H, Ar-H), 7.46 (t, *J* = 4.9 Hz, 1H, Ar-H), 7.36 (dd, *J* = 12.1, 8.2 Hz, 1H, Ar-H), 7.27 (t, *J* = 8.6 Hz, 1H, Ar-H), 4.32 (q, *J* = 7.1 Hz, 2H, $CH_2$), 1.31 (t, *J* = 7.1 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.25, 164.07, 162.24, 161.64, 159.32, 154.27, 134.22, 134.12, 132.05, 131.96, 128.59, 123.76, 117.91, 117.70, 117.21,

117.14, 116.99, 116.92, 113.86, 113.62, 113.13, 112.89, 102.72, 62.86, 22.89, 14.45; HRMS of $[C_{20}H_{16}N_4O_2F_2S + H]^+$ (*m/z*) 415.1115; Calcd: 415.1109.

*Ethyl-7-amino-2-(3-bromophenyl)-5-(4-fluorophenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4f**)

White solid; m.p. 202-204 $^oC$; IR $cm^{-1}$: 3276 ($NH_2$), 2911 (CH), 1715 (C=O), 1610 (C=C); $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.70 (s, 2H, $NH_2$), 8.41 (s, 1H, CH), 8.15 (dd, $J$ = 8.5, 5.6 Hz, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 7.73 (d, $J$ = 7.8 Hz, 1H, Ar-H), 7.62 (d, $J$ = 7.9 Hz, 1H, Ar-H), 7.52 (s, 1H, Ar-H), 7.46 (t, $J$ = 8.8 Hz, 2H, Ar-H), 4.32 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 1.31 (t, $J$ = 7.1 Hz, 3H, $CH_3$); $^{13}C$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 166.40, 163.88, 162.23, 154.24, 134.21, 134.12, 133.61, 132.59, 131.74, 128.68, 128.58, 128.55, 125.93, 122.74, 117.20, 116.98, 116.02, 102.72, 102.70, 62.85, 22.86, 14.44; HRMS of $[C_{20}H_{16}N_4O_2FBrS + H]^+$ (*m/z*) 475.9894; Calcd: 475.9892.

*Ethyl-7-amino-2-(m-tolyl)-5-(4-fluorophenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4g**)

White solid; m.p. 194-196 $^oC$; IR $cm^{-1}$: 3141 ($NH_2$), 2913 (CH), 1692 (C=O), 1611 (C=C); $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.78 (s, 2H, $NH_2$), 8.49 (s, 1H, Ar-H), 8.39 (s, 1H, CH), 8.24 (d, $J$ = 7.9 Hz, 1H, Ar-H), 8.15 (d, $J$ = 7.7 Hz, 2H, Ar-H), 7.75 (t, $J$ = 8.0 Hz, 1H, Ar-H), 7.63 (s, 1H, Ar-H), 7.44 (t, $J$ = 8.6 Hz, 2H, Ar-H), 4.32 (q, $J$ = 7.0 Hz, 2H, $CH_2$), 2.24 (s, 3H, $CH_3$), 1.31 (t, $J$ = 7.0 Hz, 3H, $CH_3$); $^{13}C$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 166.39, 163.87, 162.22, 154.22, 148.69, 134.20, 134.11, 132.97, 132.89, 131.32, 128.56, 128.53, 124.22, 120.51, 117.19, 116.97, 116.01, 102.69, 102.67, 62.85, 48.12, 22.87, 14.43; HRMS of $[C_{21}H_{19}N_4O_2FS + H]^+$ (*m/z*) 411.0676; Calcd: 411.0671.

*Ethyl-7-amino-2-(4-chlorophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate* (**4h**)

Cream white solid; m.p. 206-208 $^{o}$C; IR cm$^{-1}$: 3138 ($NH_2$), 2914 (CH), 1692 (C=O), 1611 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.67 (s, 2H, $NH_2$), 8.29 (s, 1H, CH), 8.14 (d, $J$ = 8.6 Hz, 1H, Ar-H), 7.96 (d, $J$ = 8.6 Hz, 1H, Ar-H), 7.70 (d, $J$ = 8.6 Hz, 2H, Ar-H), 7.58 (d, $J$ = 8.6 Hz, 2H, Ar-H), 7.17 (d, $J$ = 8.5 Hz, 1H, Ar-H), 4.30 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 3.88 (s, 3H, $OCH_3$), 3.81 (s, 3H, $OCH_3$), 1.30 (t, $J$ = 7.1 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.24, 162.87, 155.28, 154.01, 149.19, 134.45, 129.85, 129.63, 129.03, 128.38, 124.47, 122.59, 113.44, 112.37, 98.98, 62.55, 56.39, 55.99, 22.88, 14.51; HRMS of $[C_{22}H_{21}N_4O_4ClS + H]^+$ (*m/z*) 473.1340; Calcd: 473.1338.

*Ethyl-7-amino-2-phenyl-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4i**)

White solid; m.p. 176-178 $^{o}$C; IR cm$^{-1}$: 3156 ($NH_2$), 2912 (CH), 1713 (C=O), 1589 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.63 (s, 2H, $NH_2$), 8.28 (s, 1H, CH), 8.02 – 7.86 (m, 2H, Ar-H), 7.80 – 7.70 (m, 2H, Ar-H), 7.63 – 7.38 (m, 3H, Ar-H), 7.17 (d, $J$ = 8.5 Hz, 1H, Ar-H), 4.30 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 3.88 (s, 3H, $OCH_3$), 3.81 (s, 3H, $OCH_3$), 1.30 (t, $J$ = 7.1 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.14, 162.86, 158.84, 155.26, 154.01, 149.19, 130.99, 130.69, 129.80, 127.35, 127.25, 126.77, 124.48, 116.85, 113.44, 112.36, 98.95, 62.53, 56.38, 55.98, 22.89, 14.50; HRMS of $[C_{22}H_{22}N_4O_4S + H]^+$ (*m/z*) 439.0523; Calcd: 439.0511.

*Ethyl-7-amino-2-(4-fluorophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate* (**4j**)

White solid; m.p. 191-193 $^{o}$C; IR cm$^{-1}$: 3139 ($NH_2$), 2912 (CH), 1692 (C=O), 1589 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.64 (s, 2H, $NH_2$), 8.30 (s, 1H, CH), 8.20 (dd, $J$ = 8.5, 5.4 Hz, 2H, Ar-H), 8.00 (d, $J$ = 3.0 Hz, 1H, Ar-H), 7.75 (t, $J$ = 8.4 Hz, 2H, Ar-H), 7.49 (t, $J$ = 8.8 Hz, 1H, Ar-H), 7.18 (d, $J$ = 8.4 Hz, 1H, Ar-H), 4.31 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 3.88 (s, 3H, $OCH_3$), 3.81 (s, 3H,

$OCH_3$), 1.31 (t, $J$ = 7.1 Hz, 3H, $CH_3$); $^{13}C$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.17, 162.87, 155.28, 154.02, 149.19, 129.95, 129.86, 129.72, 129.64, 127.23, 124.49, 120.50, 117.26, 117.04, 116.98, 116.76, 113.48, 112.39, 98.97, 62.53, 56.39, 55.99, 22.88, 14.51; HRMS of $[C_{22}H_{21}N_4O_4FS + H]^+$ (*m/z*) 457.0515; Calcd: 457.0522.

*Ethyl-7-amino-2-(3-fluorophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate* (**4k**)

White solid; m.p. 184-186 $^oC$; IR $cm^{-1}$: 3158 ($NH_2$), 2914 (CH), 1712 (C=O), 1588 (C=C); $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.64 (s, 2H, $NH_2$), 8.27 (s, 1H, CH), 7.74 (m, 3H, Ar-H), 7.53 (t, $J$ = 12.6 Hz, 2H, Ar-H), 7.36 (t, $J$ = 8.7 Hz, 1H, Ar-H), 7.16 (d, $J$ = 7.9 Hz, 1H, Ar-H), 4.29 (q, $J$ = 6.7 Hz, 2H, $CH_2$), 3.87 (s, 3H, $OCH_3$), 3.80 (s, 3H, $OCH_3$), 1.30 (d, $J$ = 6.3 Hz, 3H, $CH_3$); $^{13}C$ NMR (151 MHz, DMSO-$d_6$) $\delta$ 168.74, 165.47, 162.36, 161.25, 154.73, 153.55, 148.73, 131.50, 126.74, 124.00, 123.24, 117.33, 117.19, 116.32, 113.29, 113.13, 113.00, 111.89, 98.52, 62.02, 55.89, 55.51, 22.37, 13.99; HRMS of $[C_{22}H_{21}N_4O_4FS + H]^+$ (*m/z*) 457.1714; Calcd: 457.1723.

*Ethyl-7-amino-2-(3-bromophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate* (**4l**)

Pale yellow solid; m.p. 183-185 $^oC$; IR $cm^{-1}$: 3159 ($NH_2$), 2942 (CH), 1712 (C=O), 1588 (C=C); $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.69 (s, 2H, $NH_2$), 8.27 (s, 1H, CH), 8.23 (s, 1H, Ar-H), 8.10 (t, $J$ = 1.7 Hz, 1H, Ar-H), 7.91 (dd, $J$ = 4.4, 1.6 Hz, 1H, Ar-H), 7.74 (dd, $J$ = 10.0, 1.9 Hz, 2H, Ar-H), 7.51 (t, $J$ = 8.1 Hz, 1H, Ar-H), 7.16 (d, $J$ = 8.5 Hz, 2H, Ar-H), 4.29 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 3.87 (s, 3H, $OCH_3$), 3.80 (s, 3H, $OCH_3$), 1.30 (t, $J$ = 7.1 Hz, 3H, $CH_3$); $^{13}C$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 168.73, 162.36, 154.74, 153.50, 148.67, 133.10, 132.32, 131.43, 131.23, 126.74, 126.44, 123.96, 116.35, 112.90, 112.71, 111.84, 98.41, 62.02, 55.87, 55.45, 22.37, 14.00; HRMS of $[C_{22}H_{21}N_4O_4BrS + H]^+$ (*m/z*) 517.9402; Calcd: 517.9399.

*Ethyl-7-amino-2-(p-tolyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4m**)

White solid; m.p. 201-203 $^{o}$C; IR cm$^{-1}$: 3160 ($NH_2$), 2942 (CH), 1698 (C=O), 1588 (C=C); $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 13.02 (s, 2H, $NH_2$), 8.29 (s, 1H, CH), 8.05 (d, $J$ = 8.1 Hz, 2H, Ar-H), 7.85 (d, $J$ = 8.1 Hz, 2H, Ar-H), 7.73 (dd, $J$ = 12.9, 4.4 Hz, 1H, Ar-H), 7.36 (dd, $J$ = 8.0, 4.9 Hz, 2H, 1H, Ar-H), 7.17 (d, $J$ = 8.5 Hz, 1H, Ar-H), 4.30 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 3.87 (s, 3H, $OCH_3$), 3.80 (s, 3H, $OCH_3$), 2.36 (s, 3H, $CH_3$), 1.29 (t, $J$ = 7.1 Hz, 3H, $CH_3$); $^{13}$C NMR (151 MHz, DMSO-$d_6$) $\delta$ 168.57, 162.37, 154.77, 153.56, 148.75, 143.36, 140.48, 129.87, 128.43, 126.83, 124.02, 116.34, 113.08, 111.94, 98.56, 62.03, 55.92, 55.55, 21.09, 20.94, 14.02; HRMS of $[C_{23}H_{24}N_4O_4S + H]^+$ (*m/z*) 453.0276; Calcd: 453.0282.

*Ethyl-2-phenyl-5-(4-bromophenyl)-7-methyl-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4n**)

White solid; m.p. 158-160 $^{o}$C; $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.67 (d, $J$ = 7.7 Hz, 2H, Ar-H), 7.60-7.47 (m, 5H, Ar-H), 7.35 (d, $J$ = 7.9 Hz, 2H, Ar-H), 6.61 (s, 1H, CH), 3.89 (q, $J$ = 7.1 Hz, 2H, $CH_2$), 2.30 (s, 3H, $CH_3$), 1.07 (t, $J$ = 7.2 Hz, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 166.04, 160.65, 151.39, 144.23, 140.69, 139.42, 132.22, 129.87, 129.79, 129.07, 126.60, 120.09, 109.65, 61.54, 55.37, 31.15, 22.06; HRMS of $[C_{21}H_{18}N_3O_2SBr + Na]^+$ (*m/z*) 478.9894; Calcd: 478.9892.

*1-(2-phenyl-5-(4-Bromophenyl)-7-methyl-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidin-6-yl)ethenone* (**4o**)

White solid; m.p. 164-166 $^{o}$C; $^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.30 (s, 1H, CH), 7.94 (d, $J$ = 8.4 Hz, 2H, Ar-H), 7.68 (d, $J$ = 8.4 Hz, 2H, Ar-H), 7.31 (d, $J$ = 8.2 Hz, 2H, Ar-H), 7.04 (dd, $J$ = 38.2, 8.2 Hz, 3H, Ar-H), 3.24 (s, 3H, $CH_3$), 3.18 (s, 3H, $CH_3$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 192.52,

161.89, 153.84, 137.52, 136.10, 134.09, 133.57, 131.80, 129.78, 128.69, 122.77, 115.70, 104.80, 63.01, 21.65, 14.43; HRMS of $[C_{21}H_{16}N_3O_2SBr + Na]^+$ (*m/z*) 448.0921; Calcd: 448.0920.

*Ethyl-2-amino-4-(4-ethylphenyl)-4H-benzo[4,5]thiazolo[3,2-a]pyrimidine-3-carboxylate* (**4p**)

White solid; m.p. 206-208 $^oC$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.35 (s, 2H, $NH_2$), 8.33 (s, 1H, CH), 7.99 – 7.93 (m, 2H, Ar-H), 7.73 (d, $J$ = 7.9 Hz, 2H, Ar-H), 7.41 (d, $J$ = 7.0 Hz, 2H, Ar-H), 7.28 (t, $J$ = 7.4 Hz, 2H, Ar-H), 4.30 (q, $J$ = 6.9 Hz, 2H, $CH_2$), 2.67 (q, $J$ = 7.3 Hz, 2H, $CH_2$), 1.30 (t, $J$ = 6.9 Hz, 3H, $CH_3$), 1.19 (t, $J$ = 7.3 Hz, 3H, $CH_3$); $^{13}C$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.87, 162.47, 158.40, 155.42, 150.84, 148.98, 131.55, 129.24, 126.49, 123.88, 122.09, 120.93, 116.27, 101.66, 62.74, 28.79, 23.22, 15.46, 14.44; HRMS of $[C_{21}H_{21}N_3O_2S + H]^+$ (*m/z*) 380.0484; Calcd: 380.0481.

*Ethyl-2-amino-4-(2,4-dichlorophenyl)-4H-benzo[4,5]thiazolo[3,2-a]pyrimidine-3-carboxylate* (**4q**)

White solid; m.p. 210-212 $^oC$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 10.15 (s, 2H, $NH_2$), 8.55 (s, 1H, Ar-H), 8.49 (s, 1H, CH), 8.19 (d, $J$ = 8.5 Hz, 1H, Ar-H), 8.07 (d, $J$ = 8.6 Hz, 1H, Ar-H), 8.01 (t, $J$ = 7.4 Hz, 2H, Ar-H), 7.68 (d, $J$ = 7.5 Hz, 1H, Ar-H), 7.64 (d, $J$ = 7.4 Hz, 1H, Ar-H), 4.33 (q, $J$ = 6.7 Hz, 2H, $CH_2$), 1.33 (t, $J$ = 6.9 Hz, 3H, $CH_3$); $^{13}C$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 162.39, 155.34, 135.27, 134.92, 132.79, 129.76, 129.71, 129.60, 129.51, 129.43, 129.39, 128.30, 127.87, 124.97, 116.24, 102.74, 62.85, 55.35, 14.46; HRMS of $[C_{19}H_{15}N_3O_2SCl_2 + Na]^+$ (*m/z*) 442.2028; Calcd: 442.2018.

## Spectras

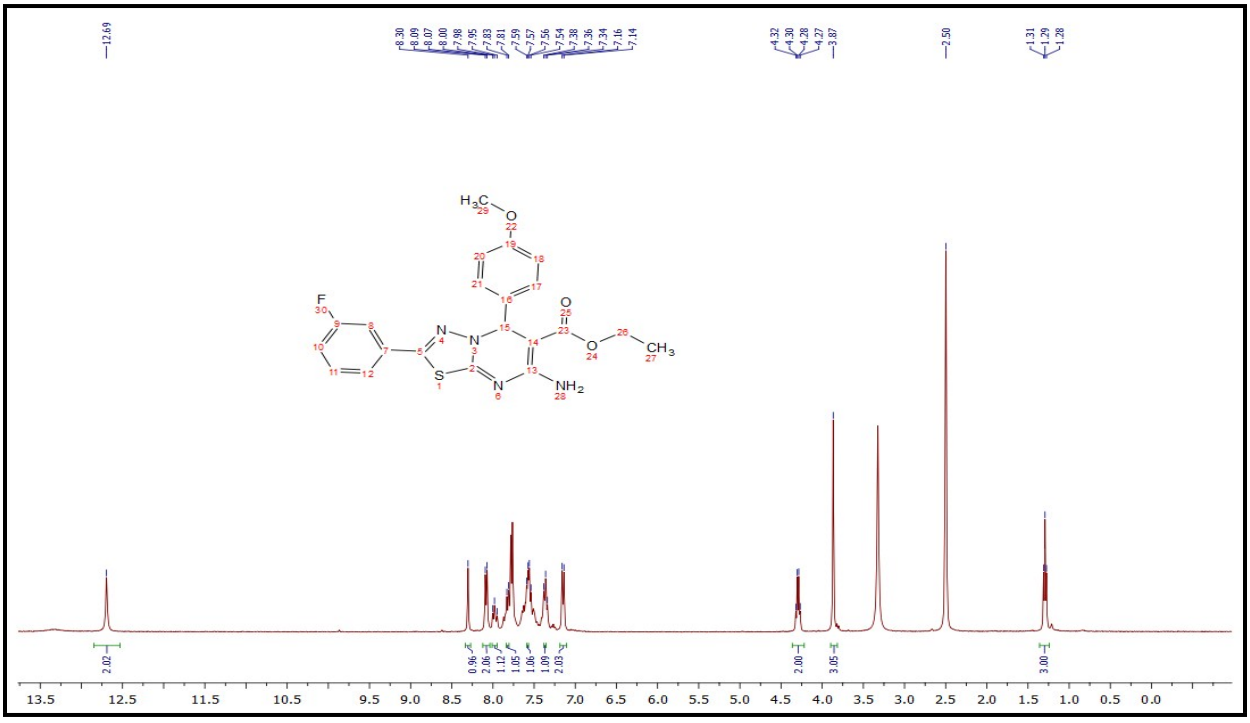

**Figure S2**. $^{1}$H-NMR spectra of compound **4a**

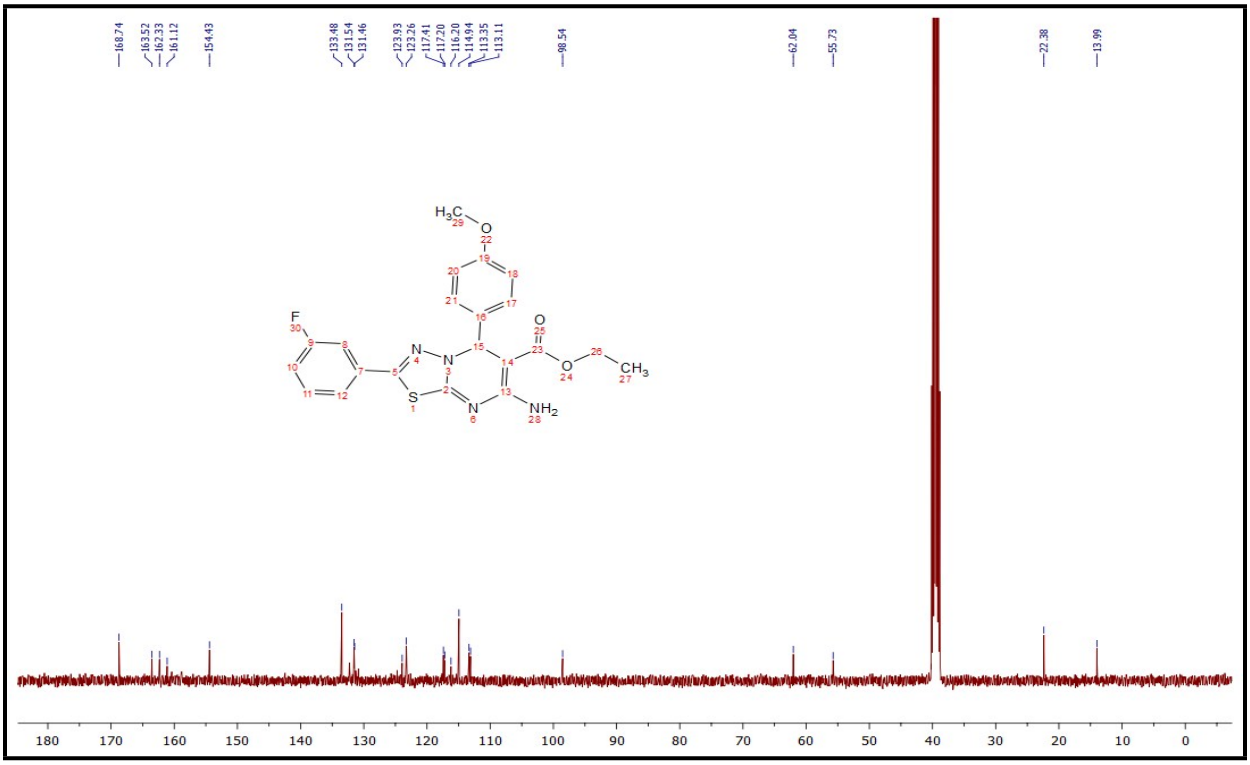

**Figure S3**. $^{13}$C-NMR spectra of compound **4a**

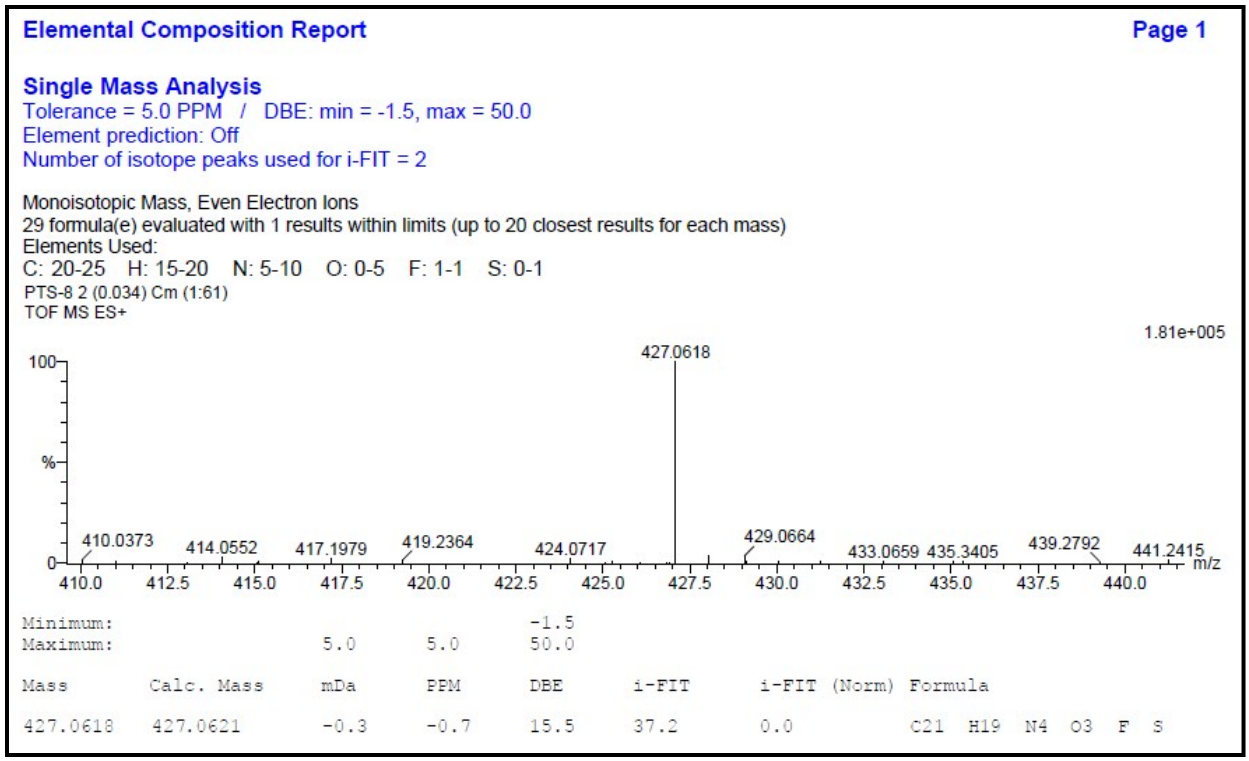


**Figure S4**. HRMS-spectra of compound **4a**

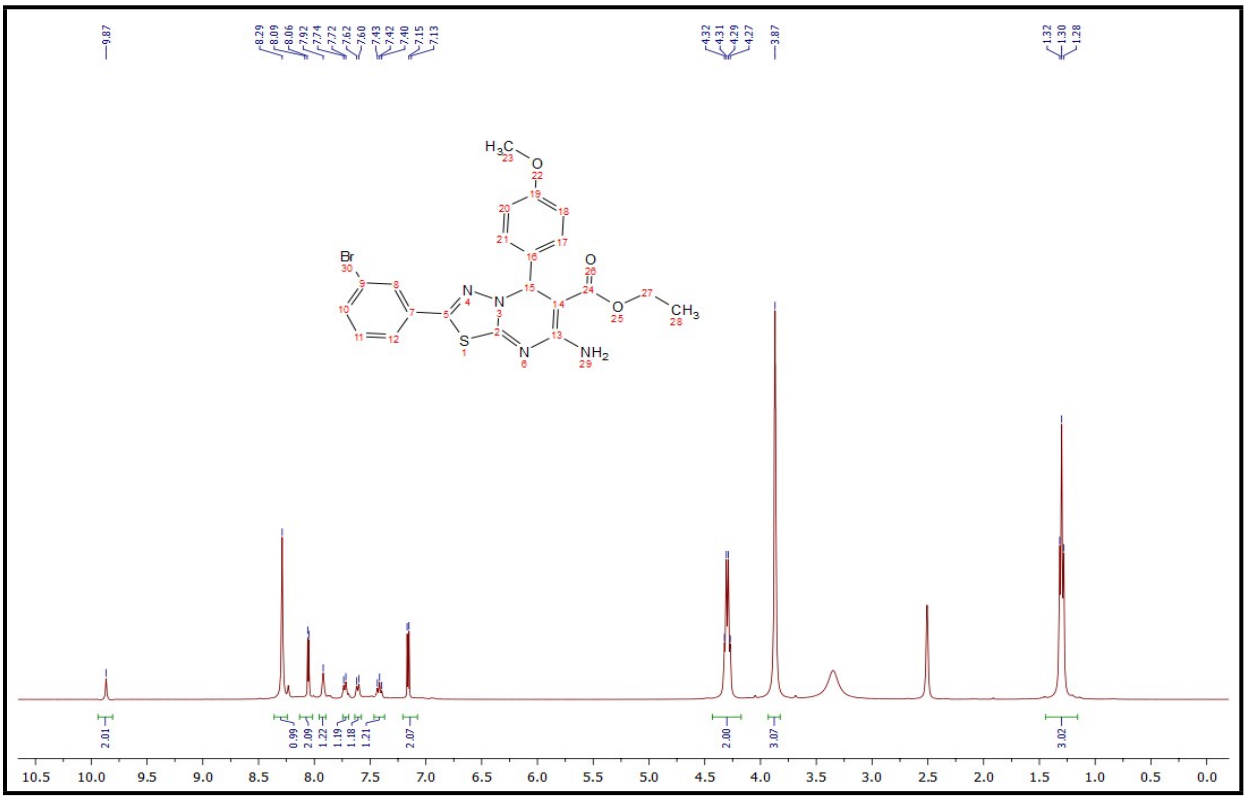

**Figure S5**. [1]H-NMR spectra of compound **4b**

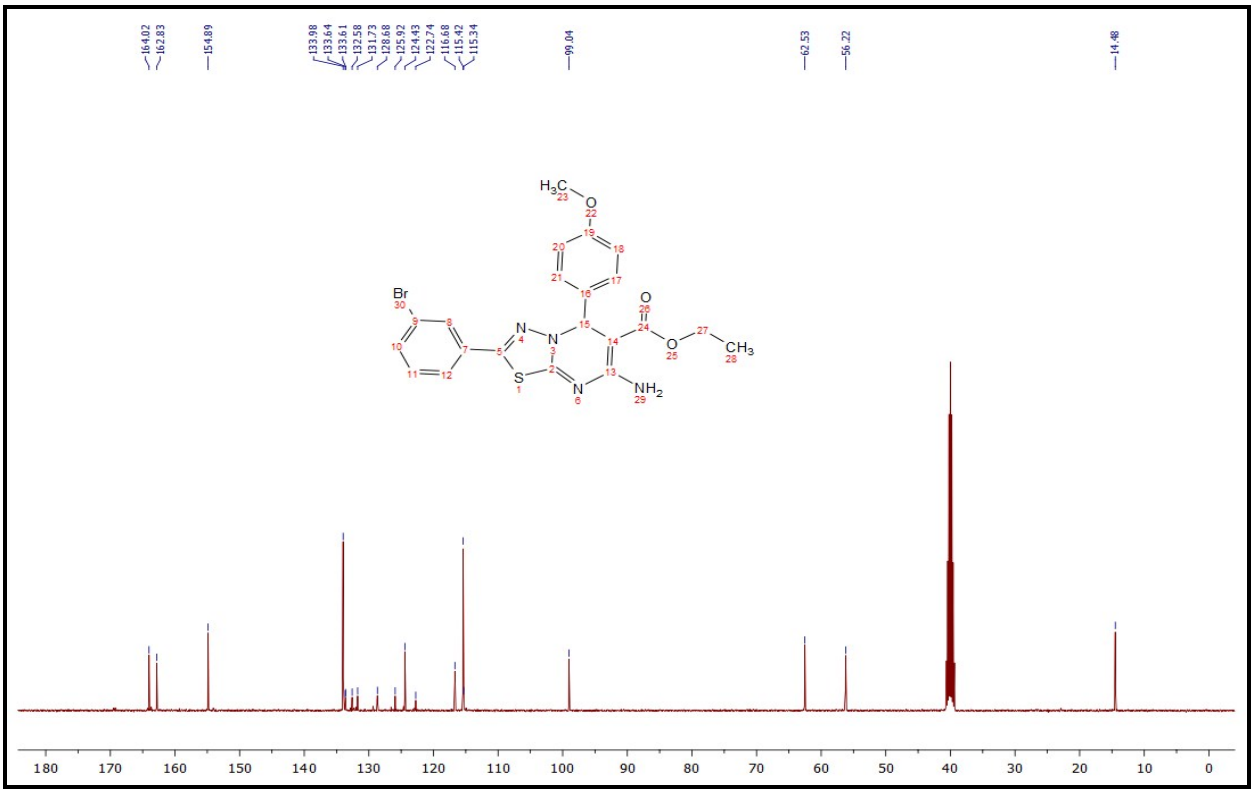


**Figure S6**. $^{13}$C-NMR spectra of compound **4b**

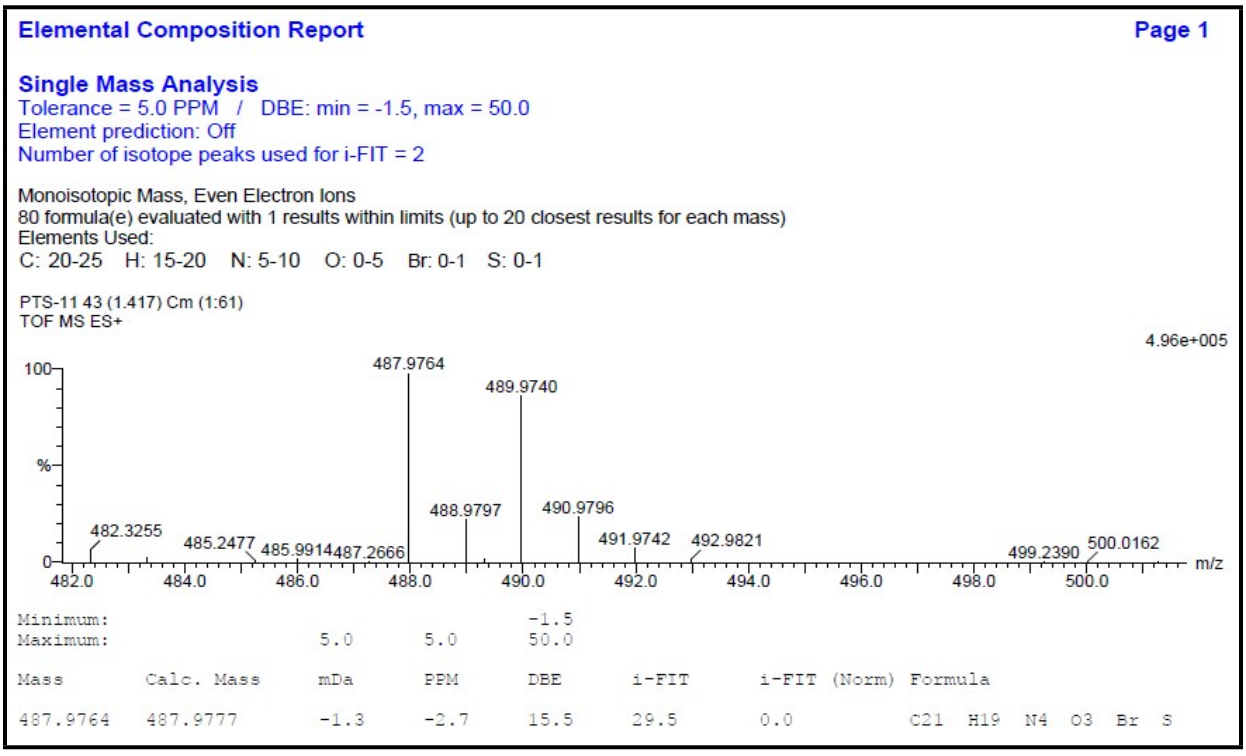


**Figure S7**. HRMS-spectra of compound **4b**

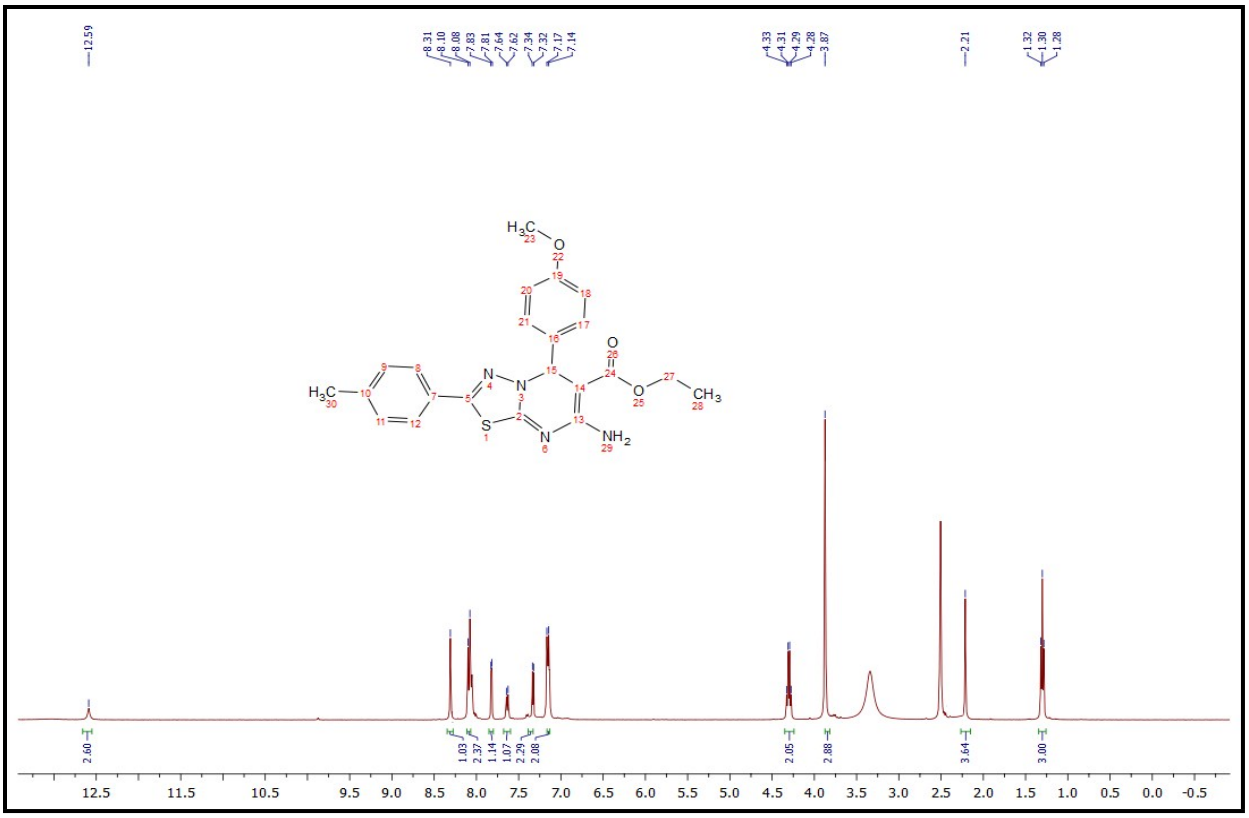

**Figure S8**. $^{1}$H-NMR spectra of compound **4c**

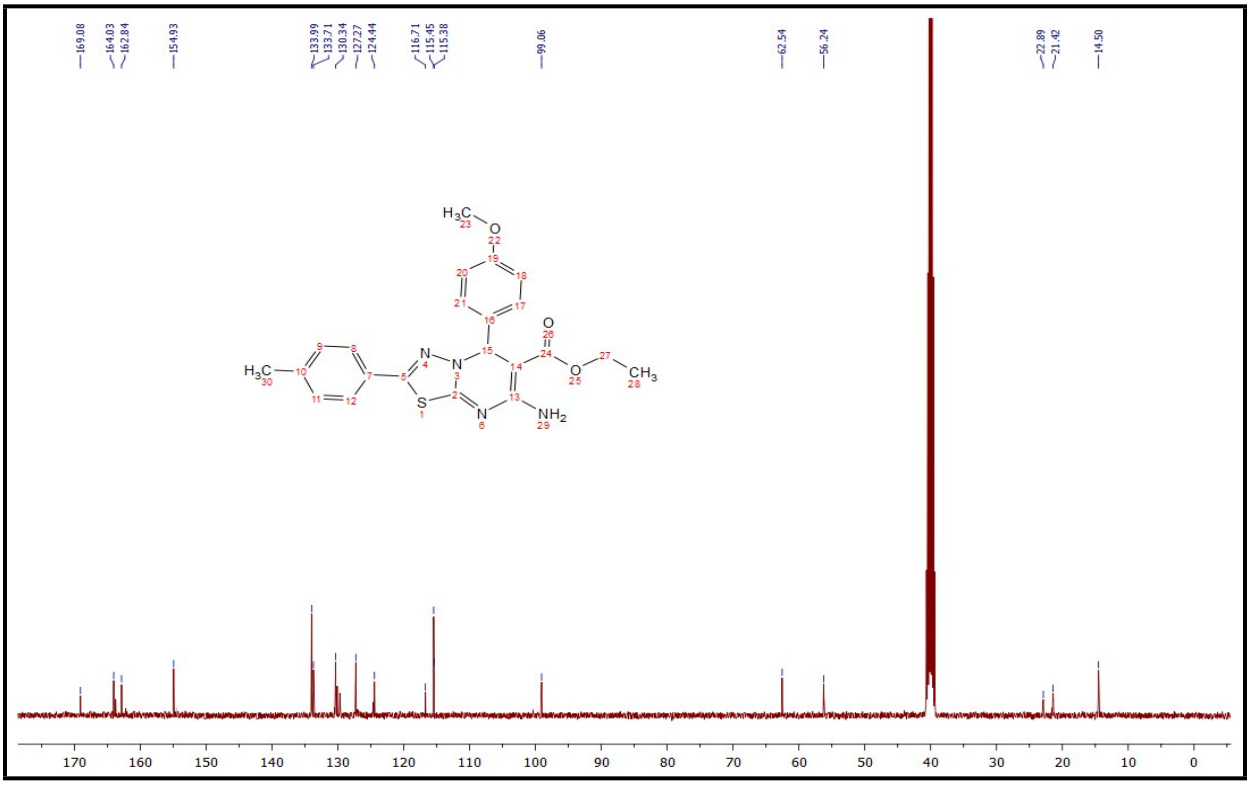

**Figure S9**. $^{13}$C-NMR spectra of compound **4c**

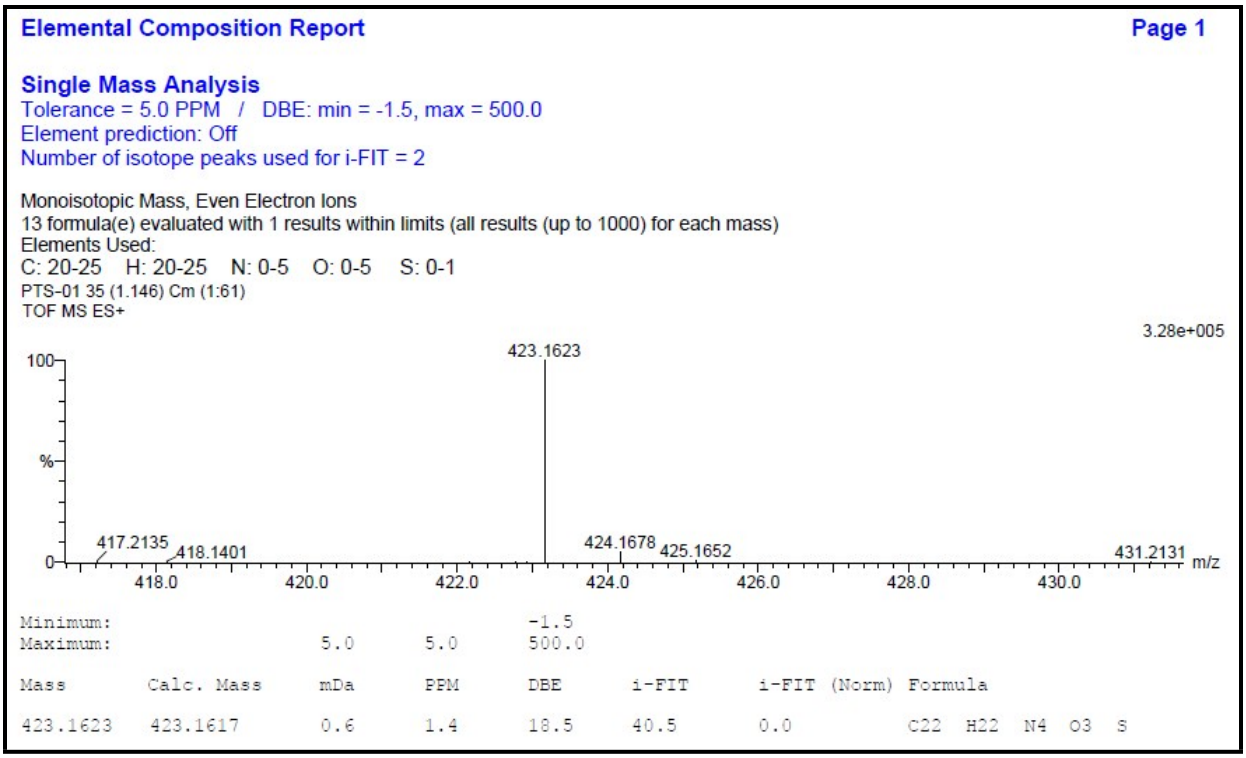


**Figure S10**. HRMS-spectra of compound **4c**

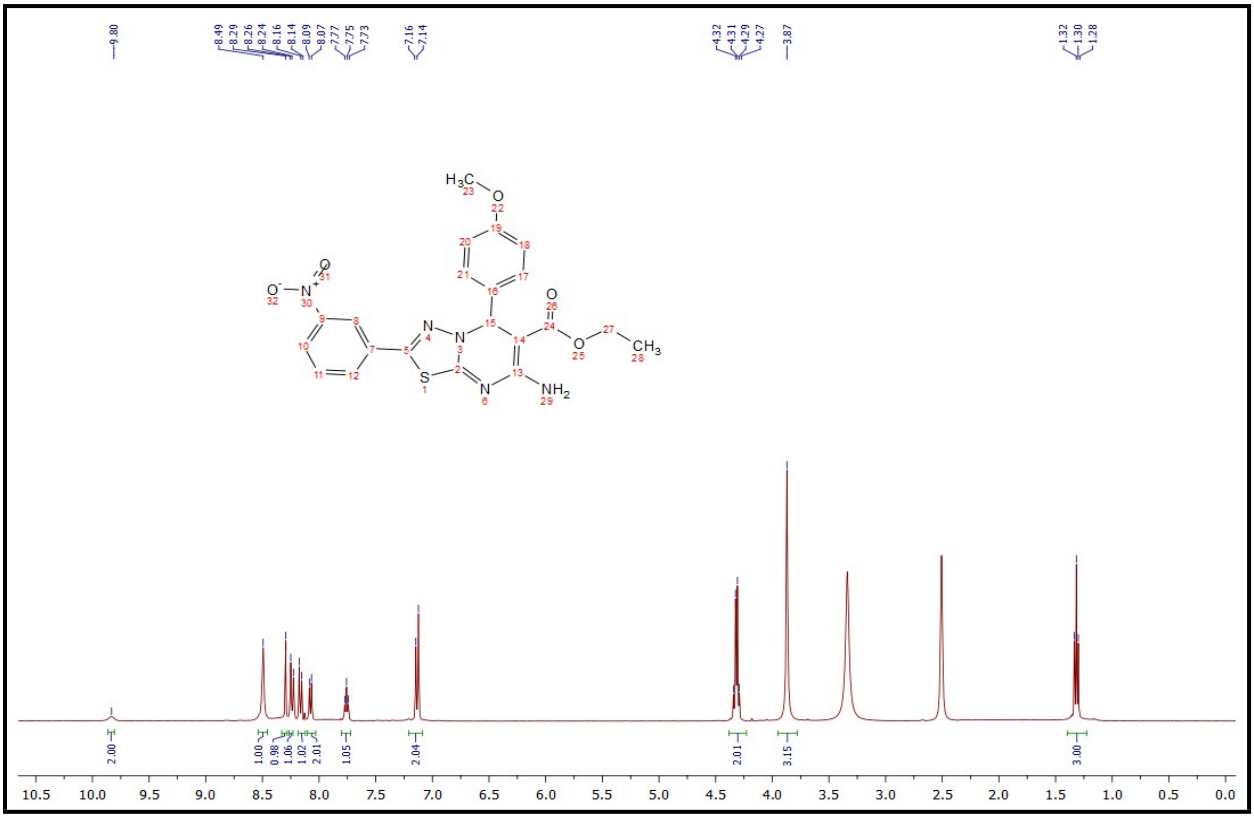

**Figure S11**. [1]H-NMR spectra of compound **4d**

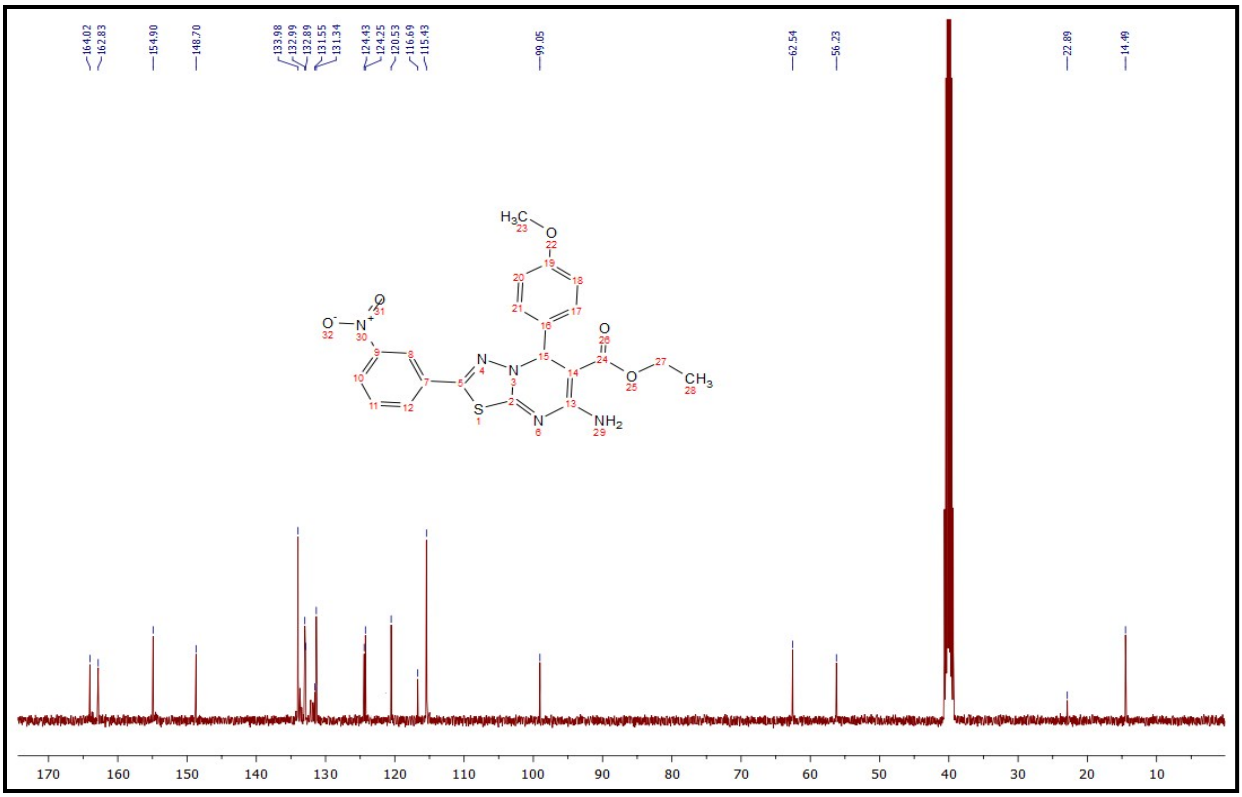


**Figure S12**. $^{13}$C-NMR spectra of compound **4d**

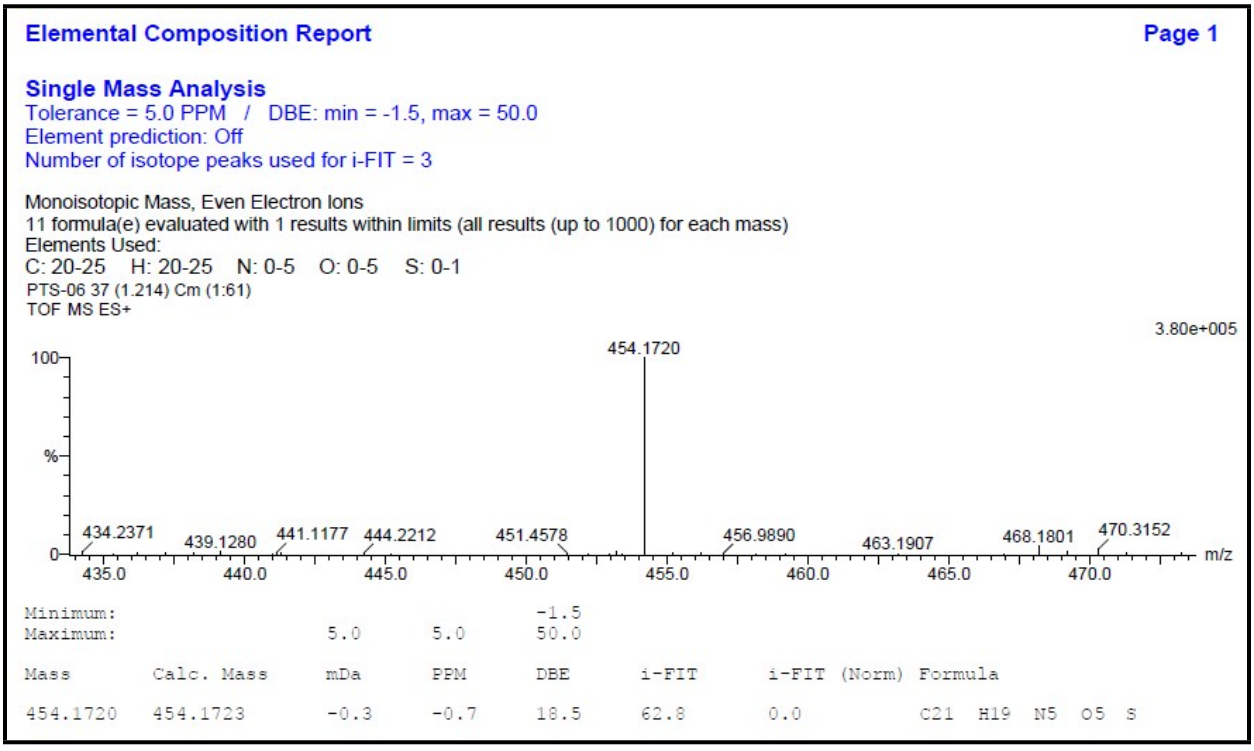


**Figure S13**. HRMS-spectra of compound **4d**

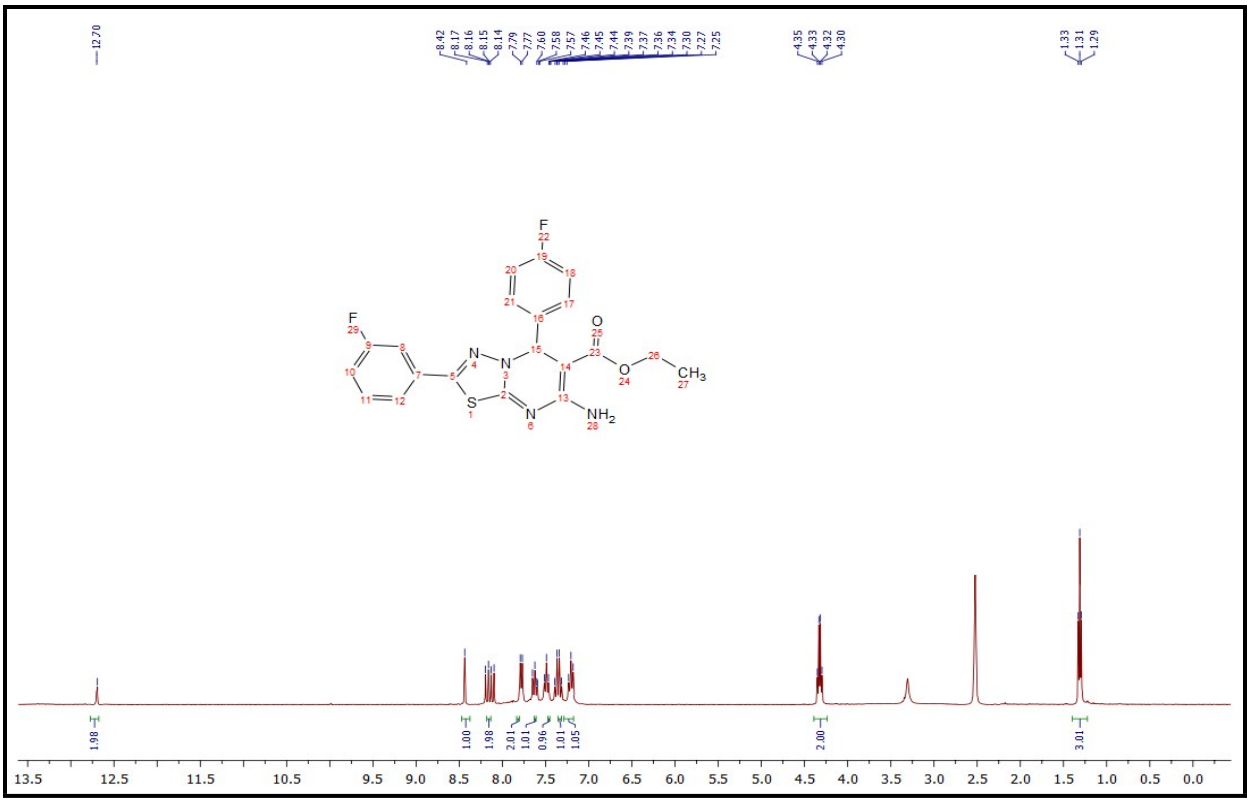

**Figure S14**. $^{1}$H-NMR spectra of compound **4e**

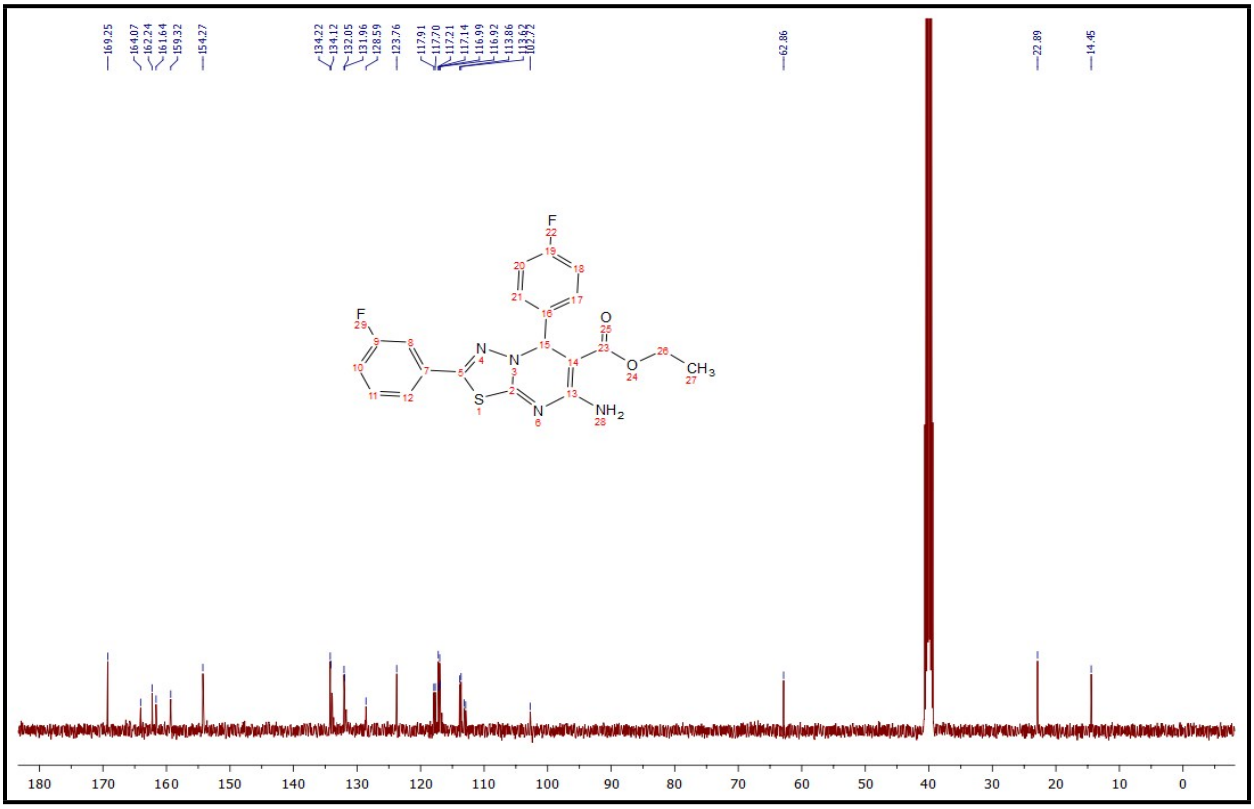

**Figure S15**. $^{13}$C-NMR spectra of compound **4e**

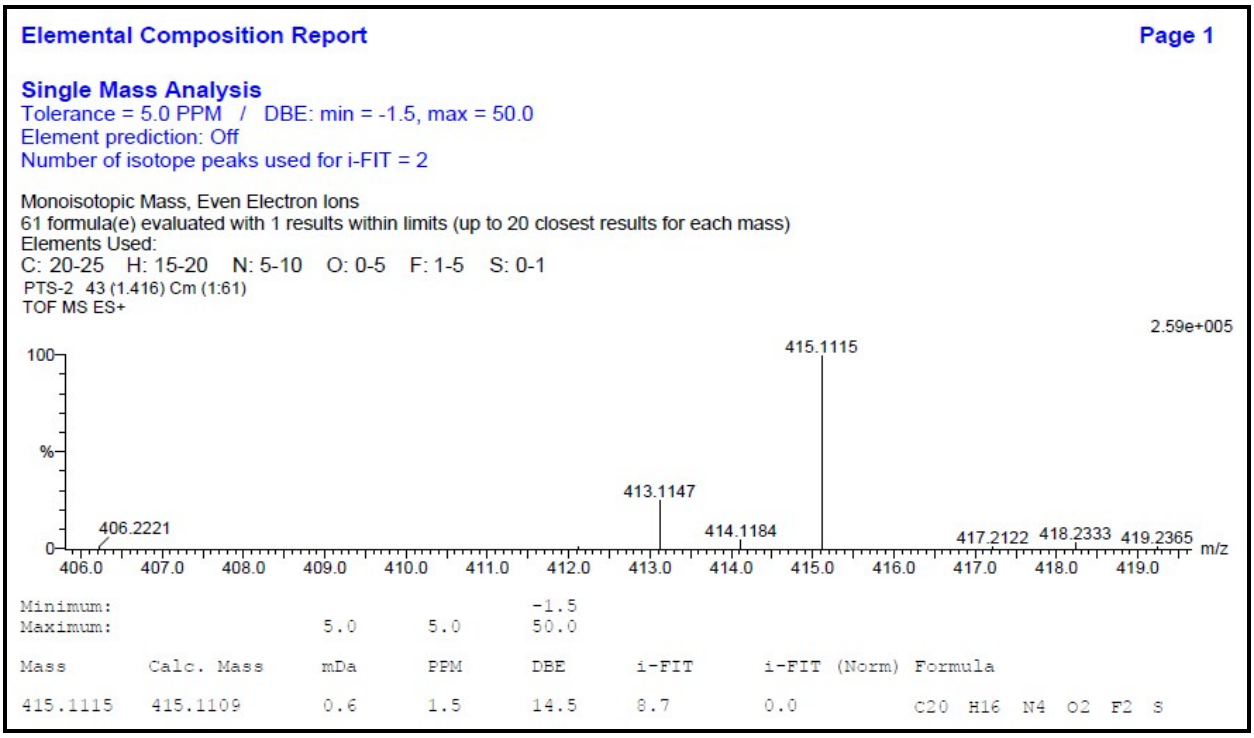


**Figure S16**. HRMS-spectra of compound **4e**

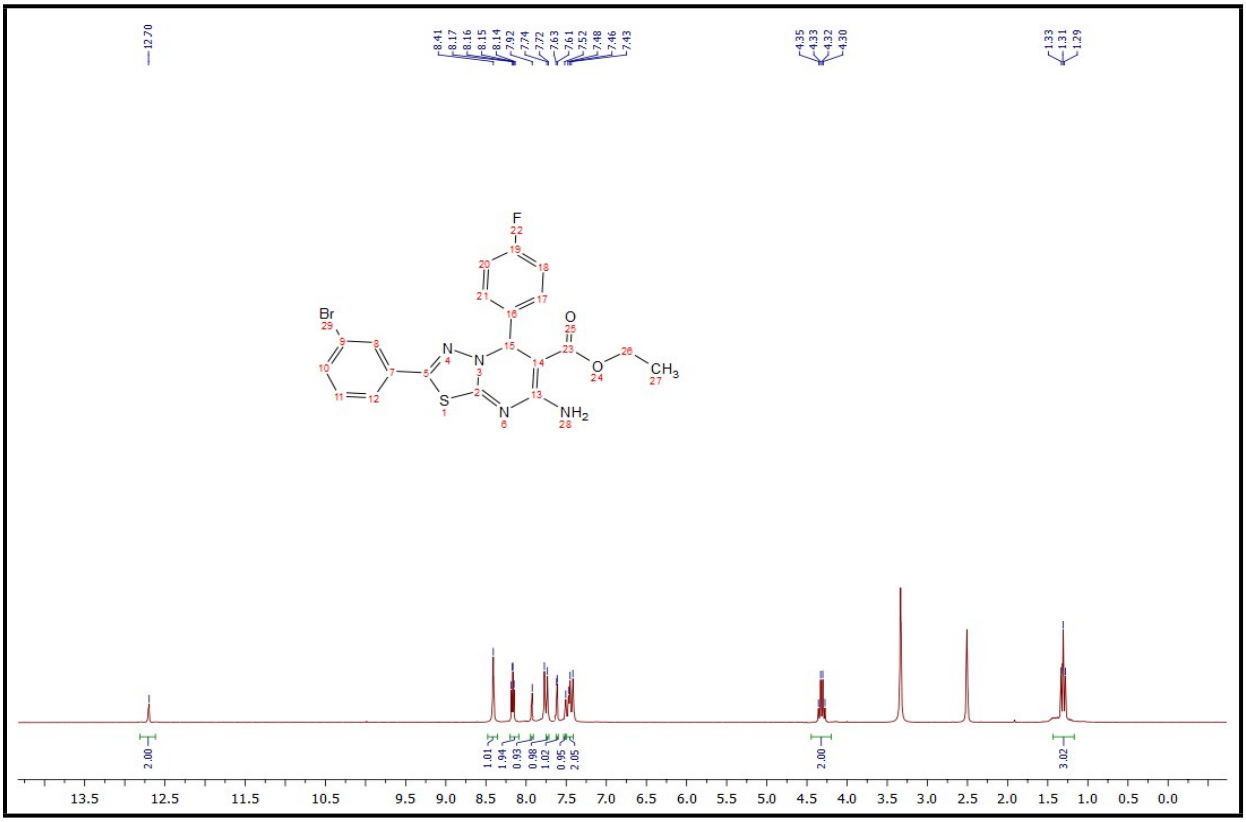

**Figure S17**. $^{1}$H-NMR spectra of compound **4f**

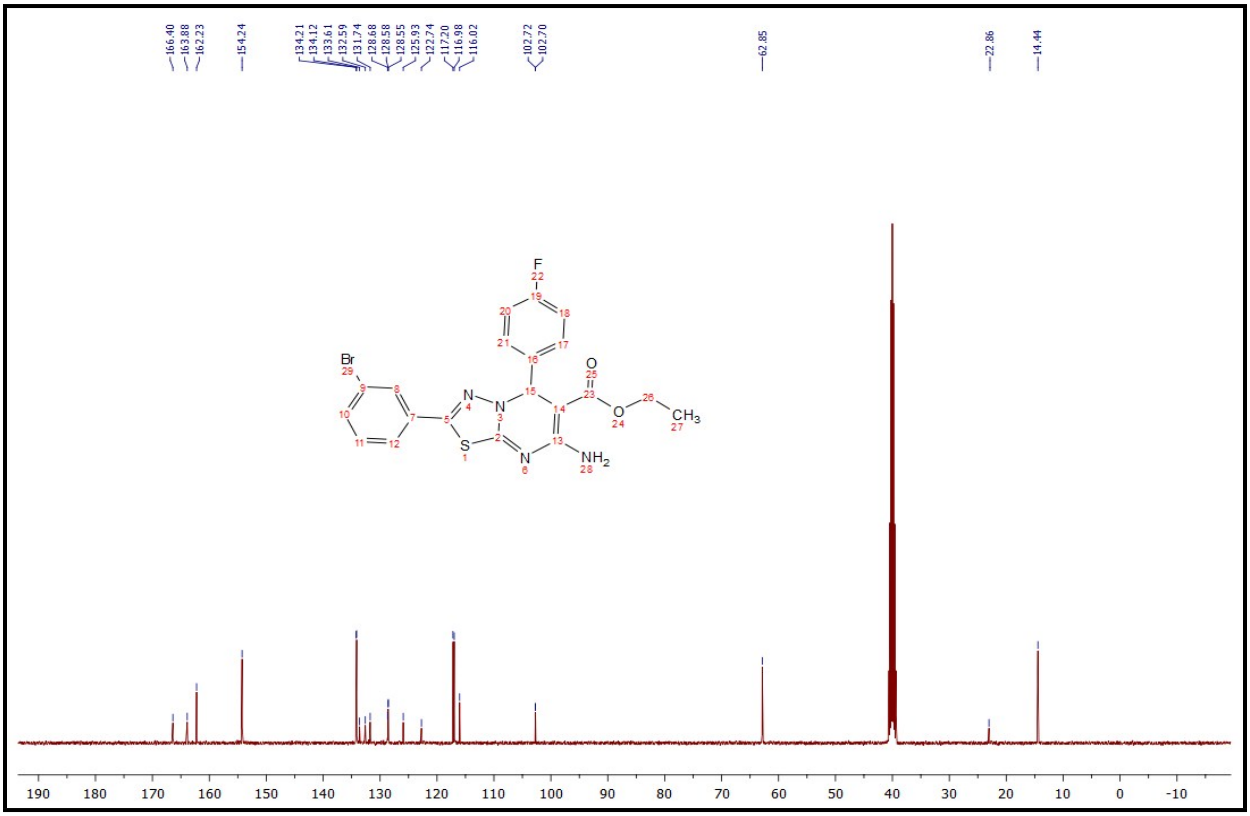


**Figure S18**. $^{13}$C-NMR spectra of compound **4f**

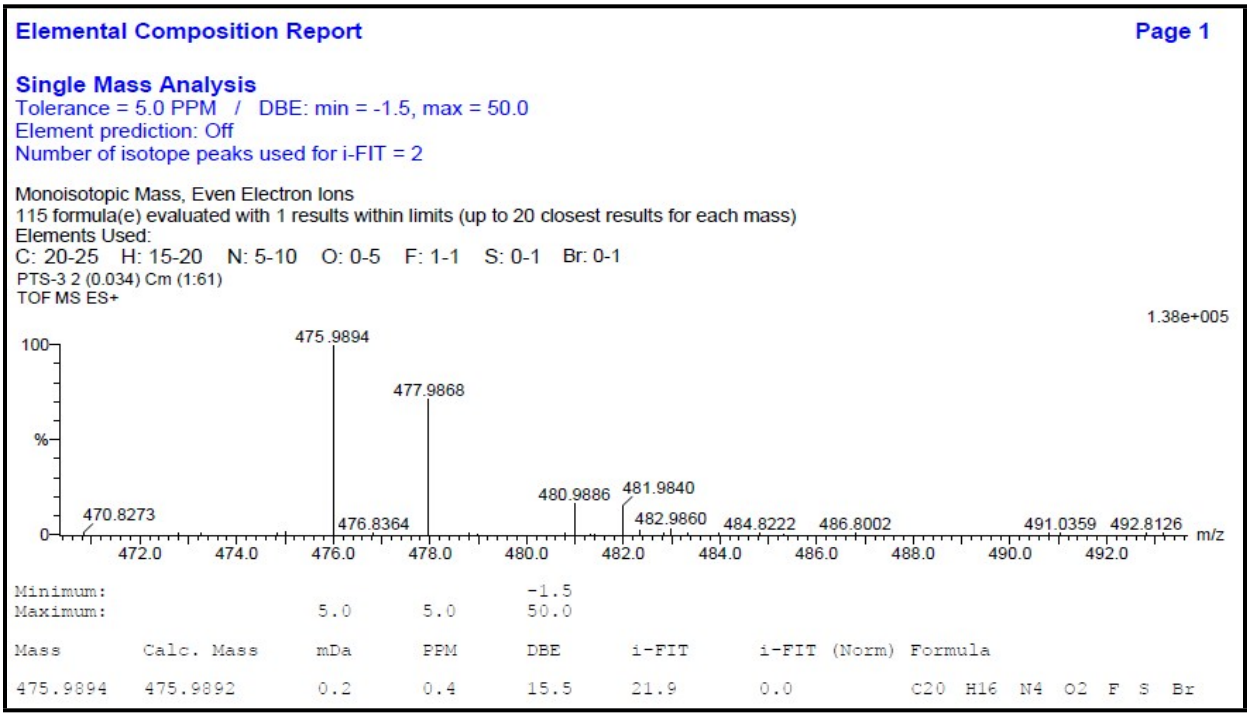


**Figure S19**. HRMS-spectra of compound **4f**

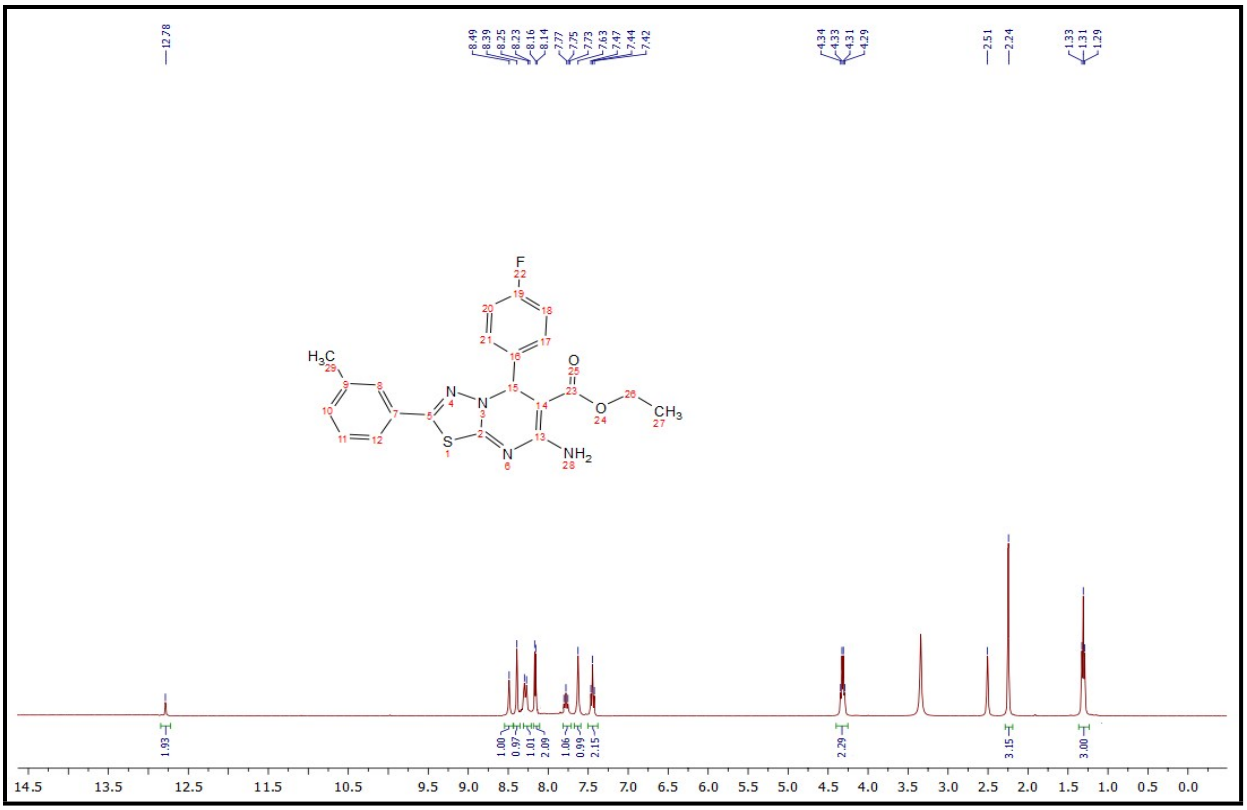

**Figure S20**. [1]H-NMR spectra of compound **4g**

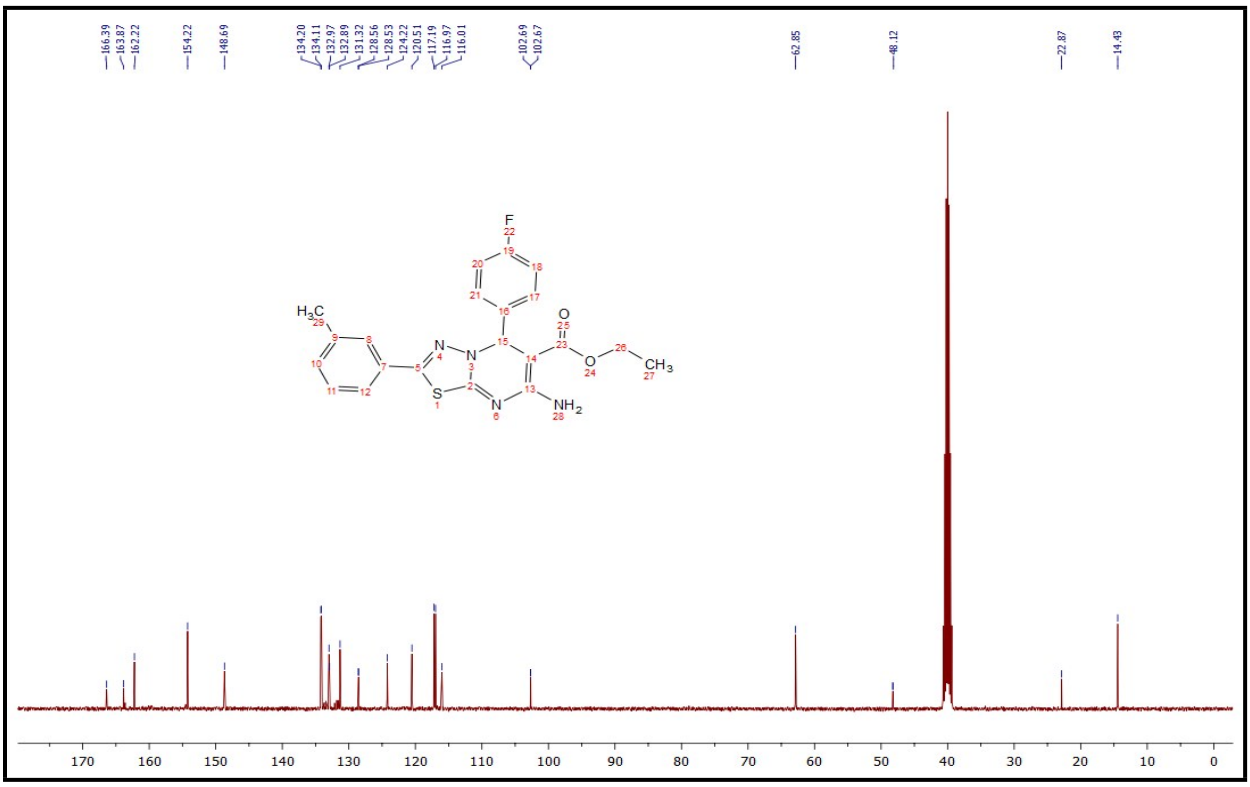

**Figure S21**. [13]C-NMR spectra of compound **4g**

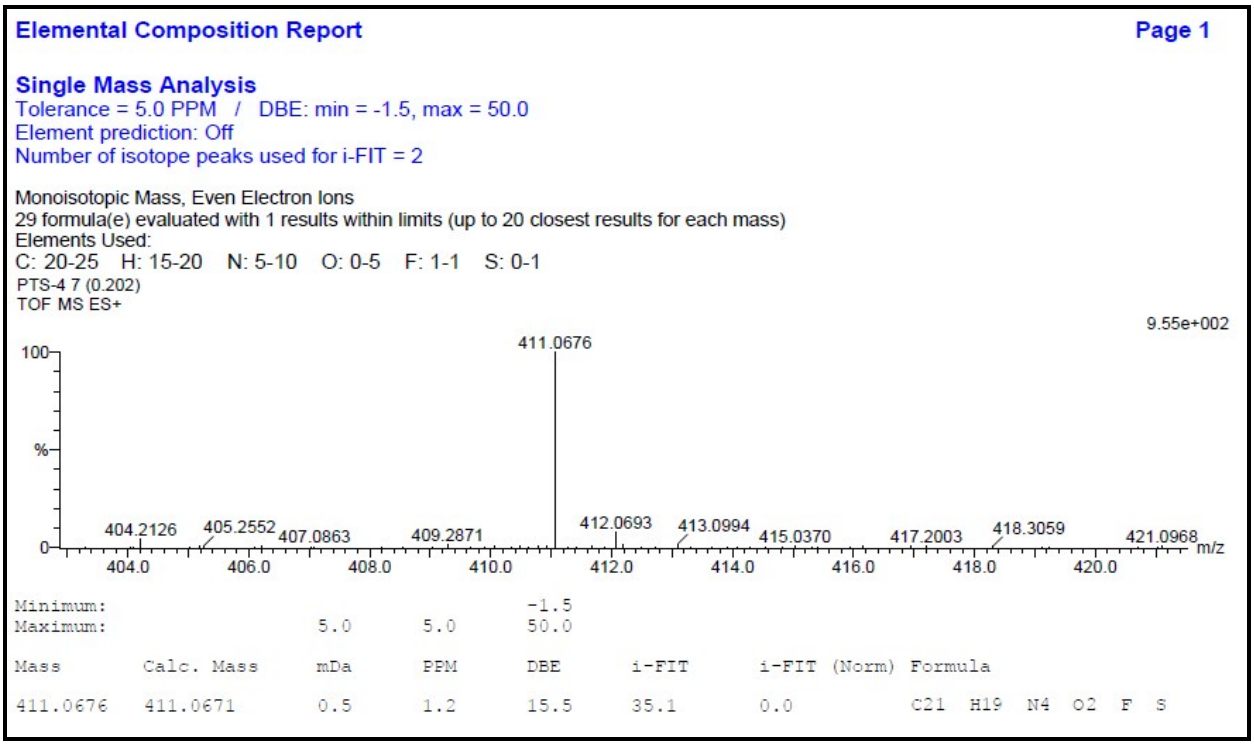


**Figure S22**. HRMS-spectra of compound **4g**

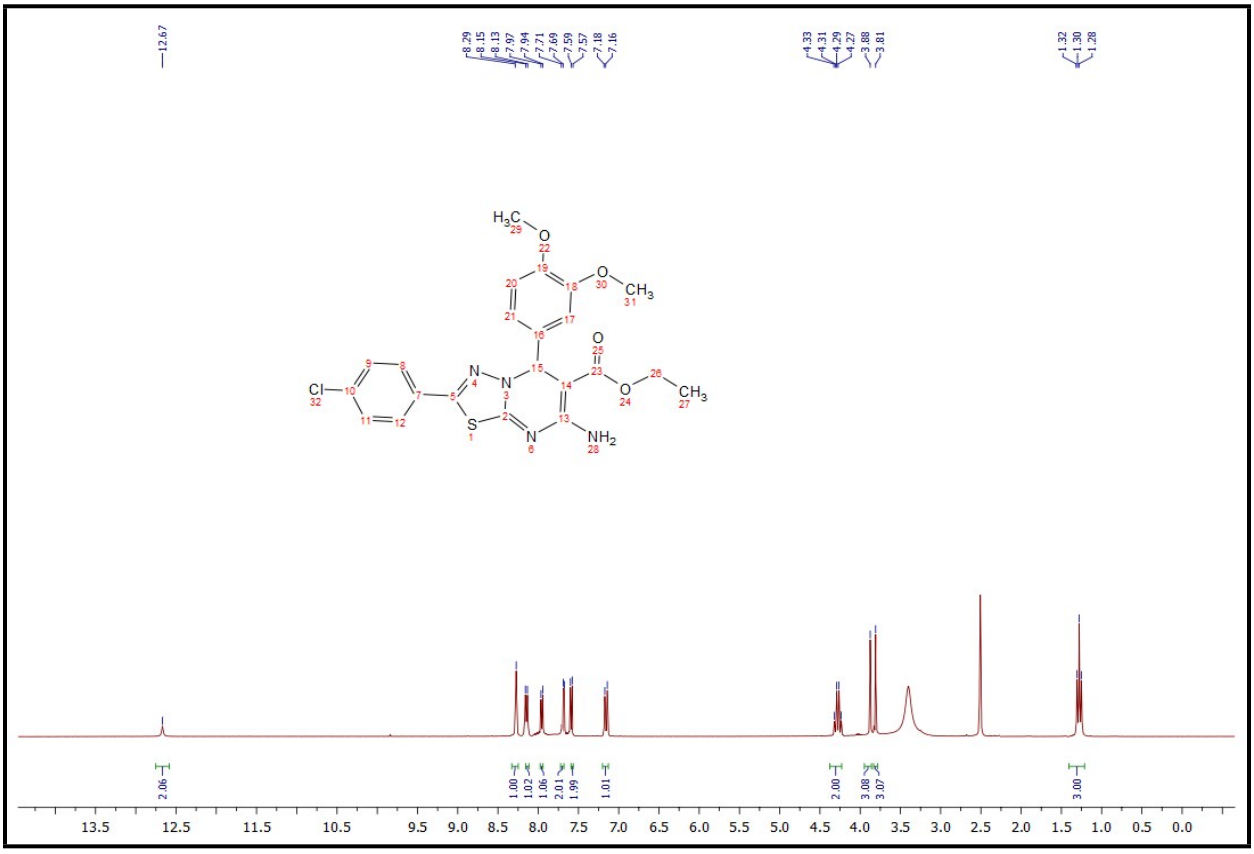

**Figure S23**. [1]H-NMR spectra of compound **4h**

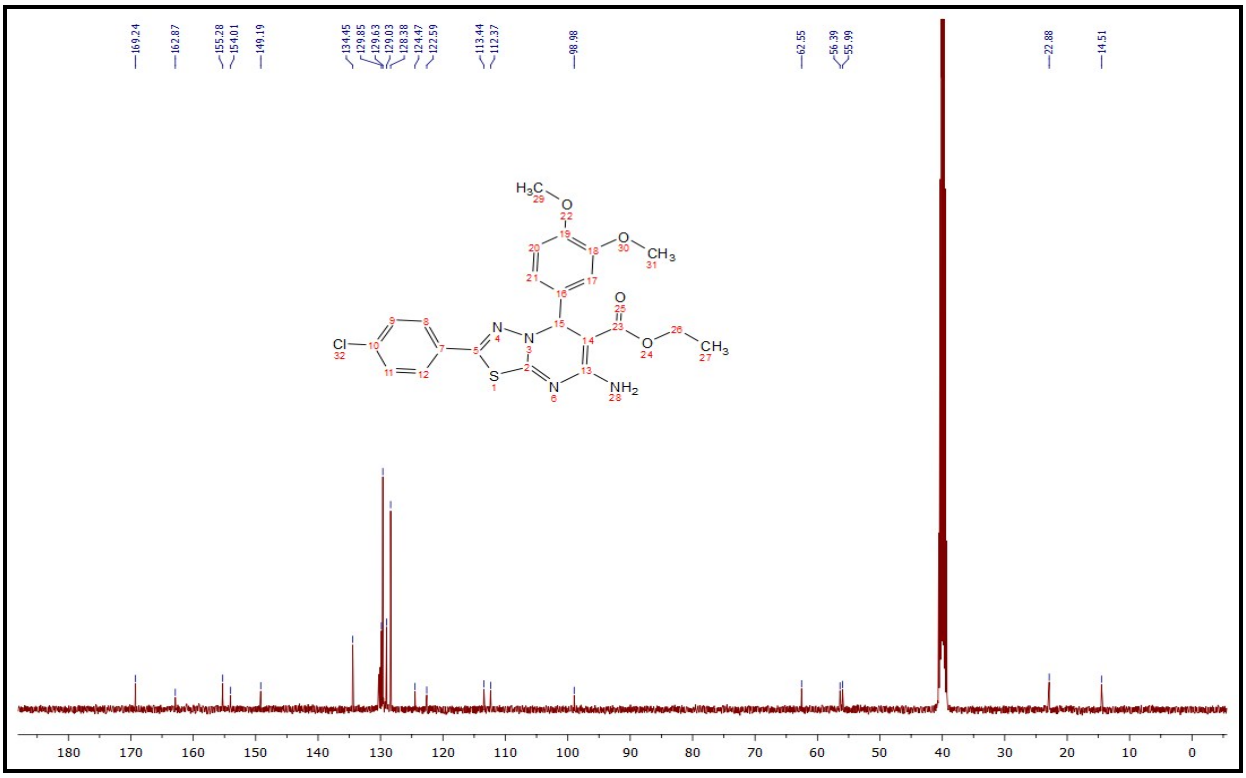


**Figure S24**. $^{13}$C-NMR spectra of compound **4h**

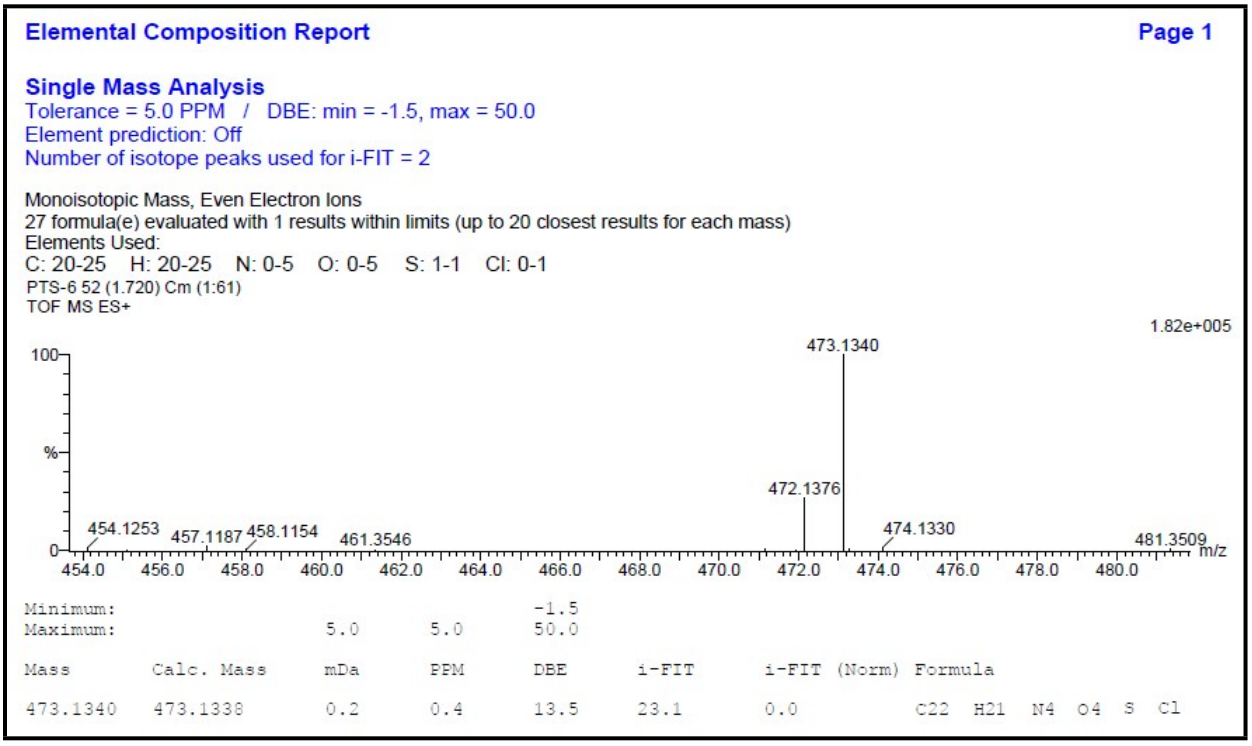


**Figure S25**. HRMS-spectra of compound **4h**

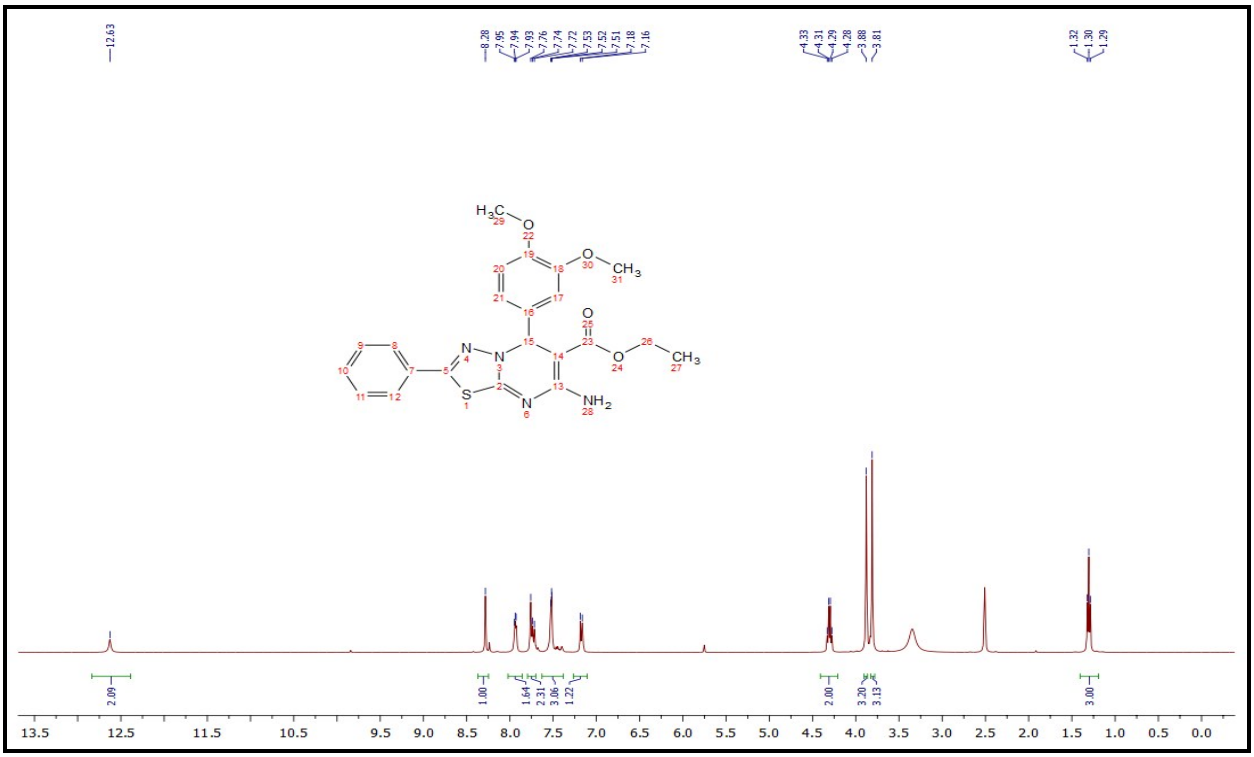

**Figure S26**. [1]H-NMR spectra of compound **4i**

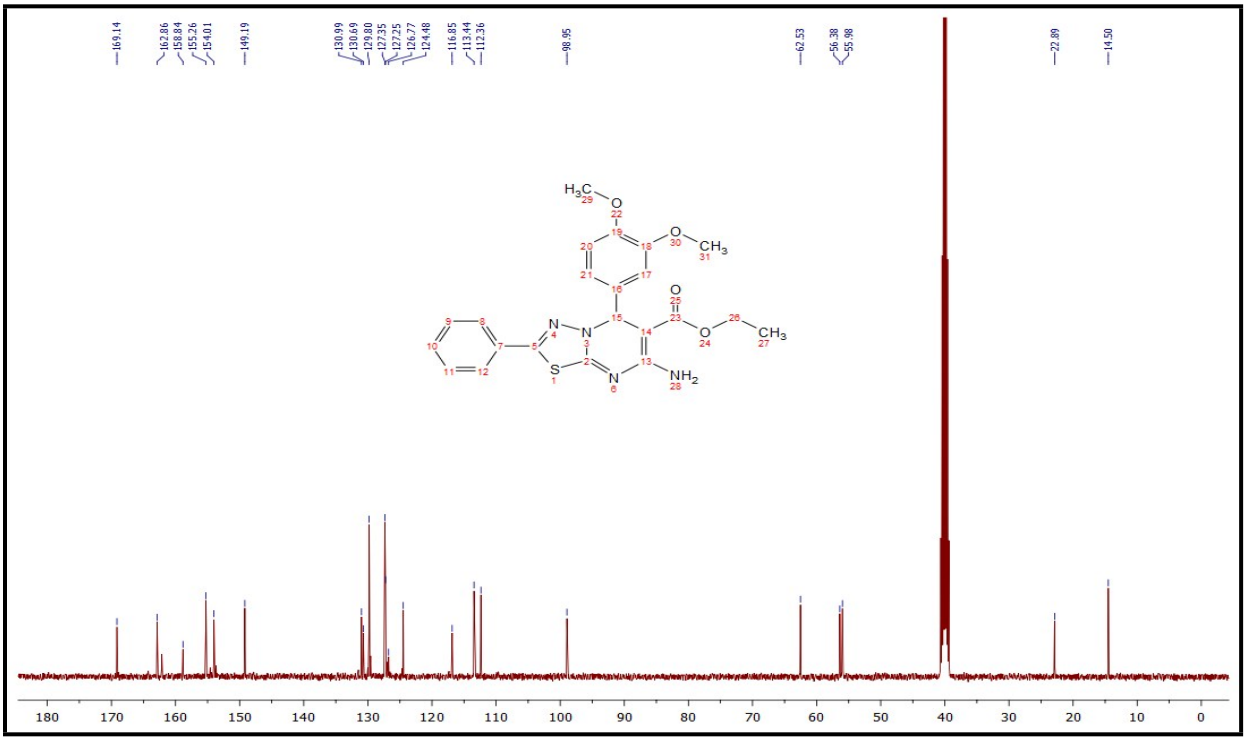

**Figure S27**. [13]C-NMR spectra of compound **4i**

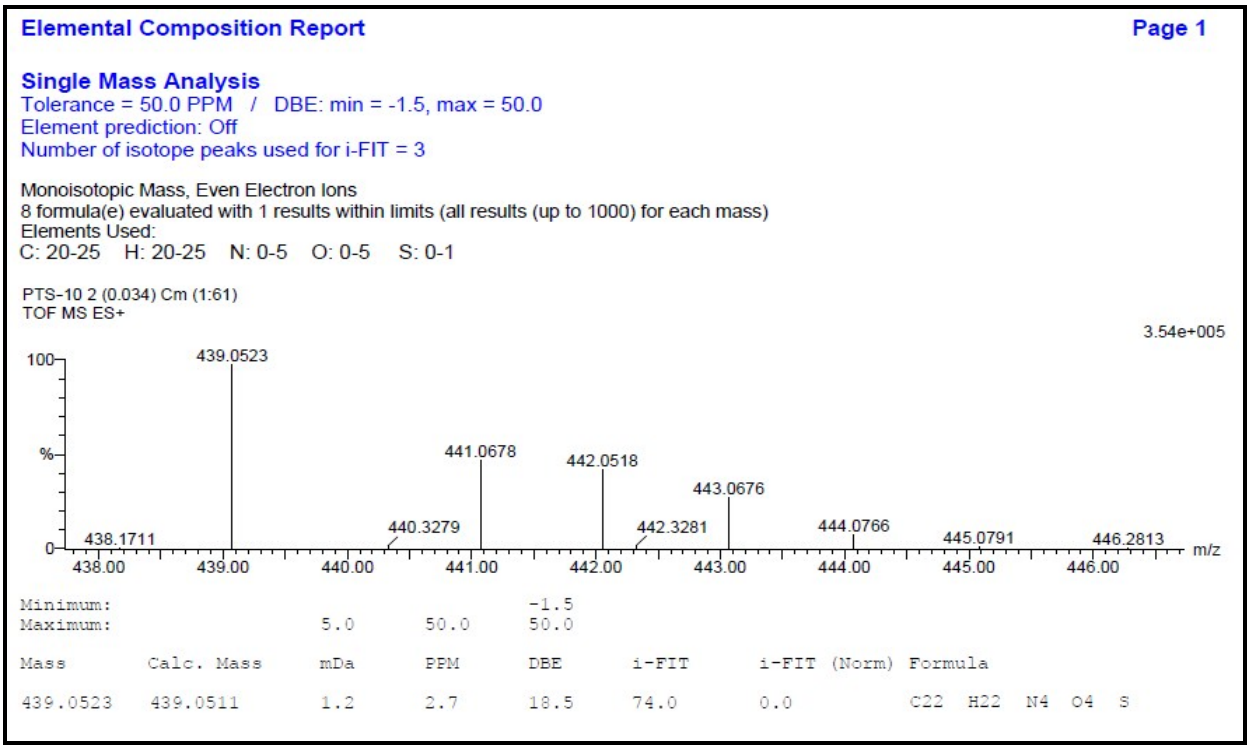


**Figure S28**. HRMS-spectra of compound **4i**

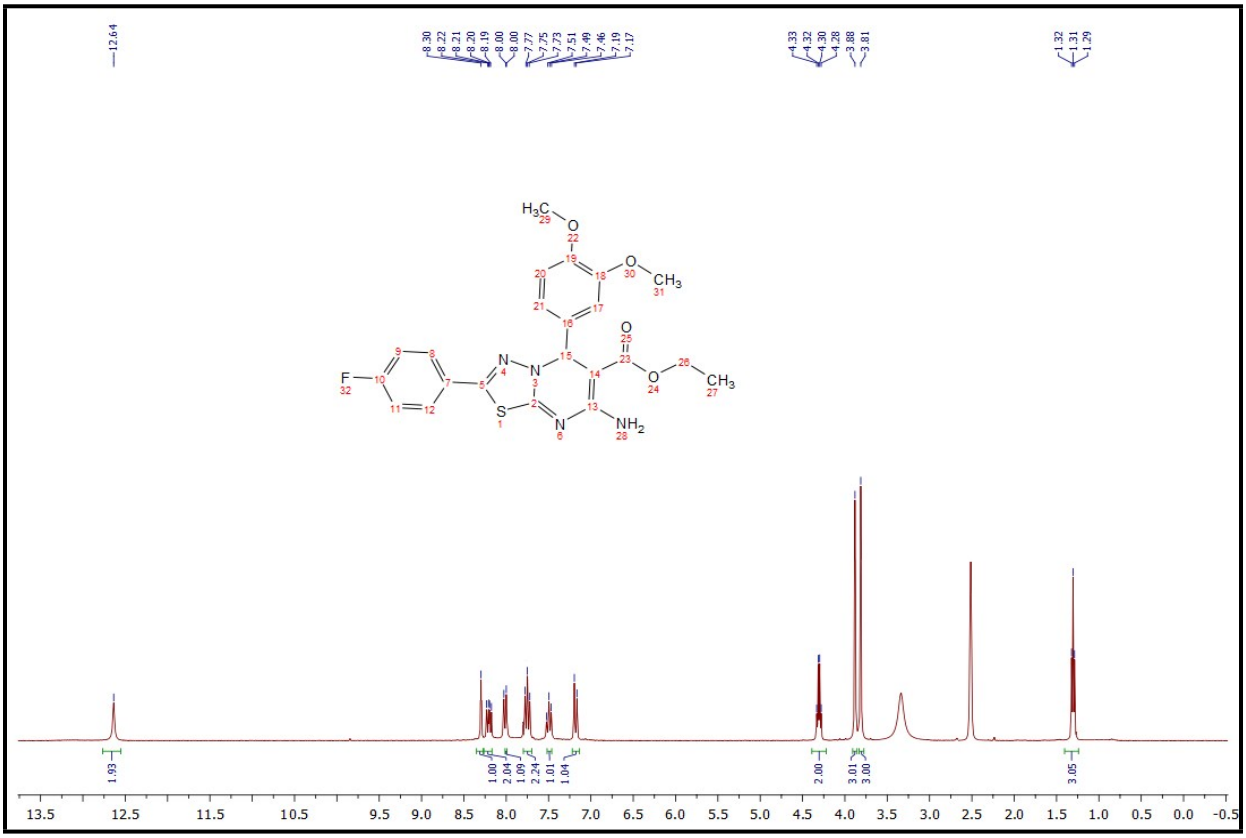

**Figure S29**. [1]H-NMR spectra of compound **4j**

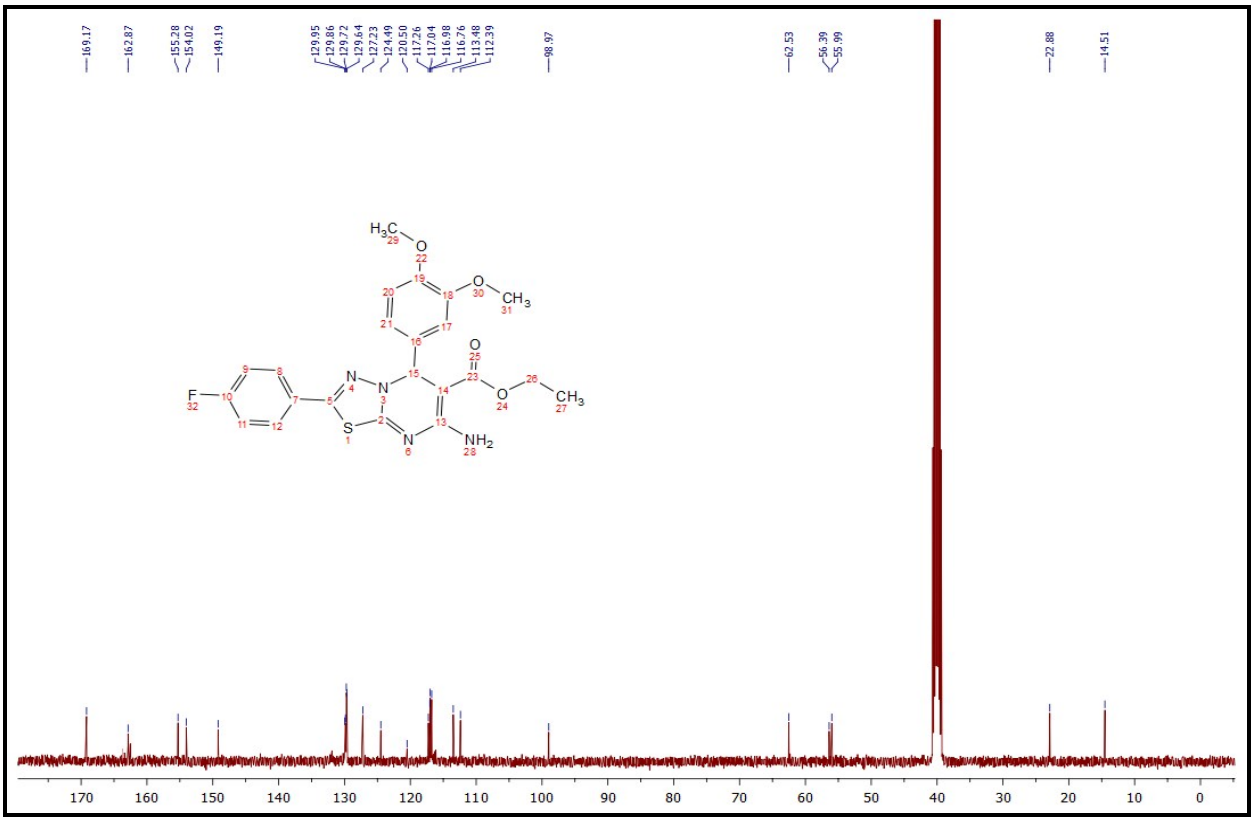


**Figure S30**. $^{13}$C-NMR spectra of compound **4j**

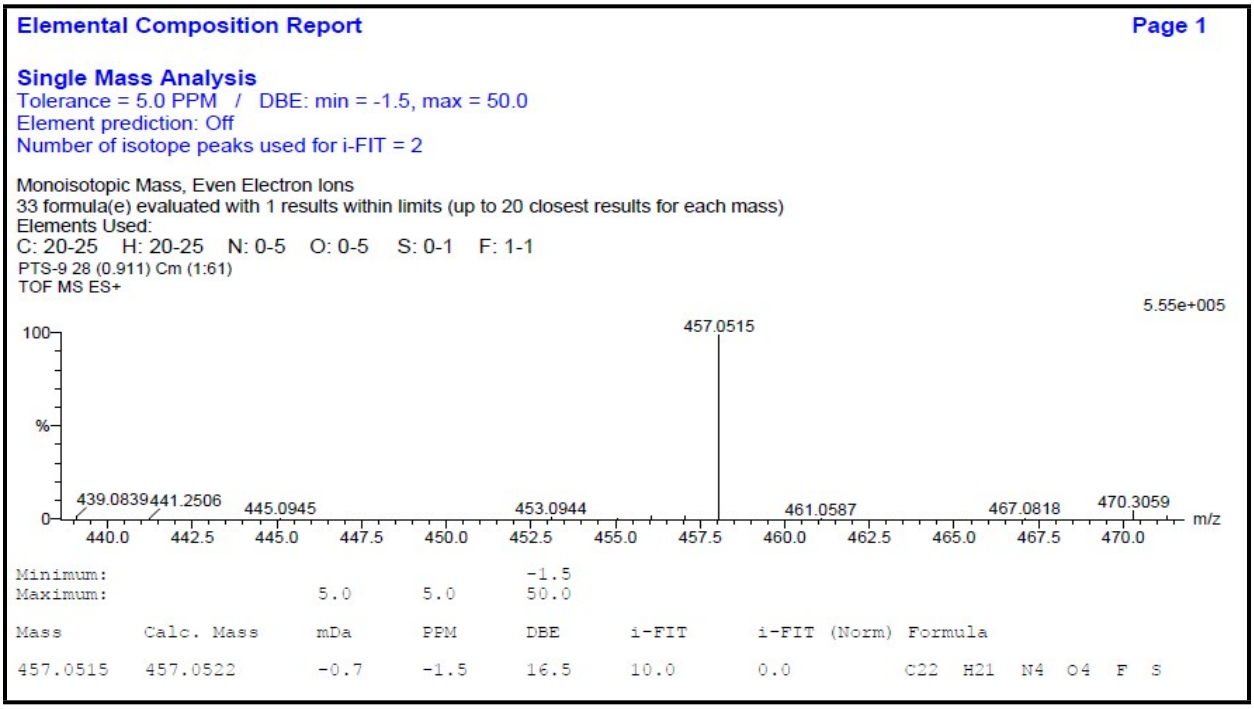


**Figure S31**. HRMS-spectra of compound **4j**

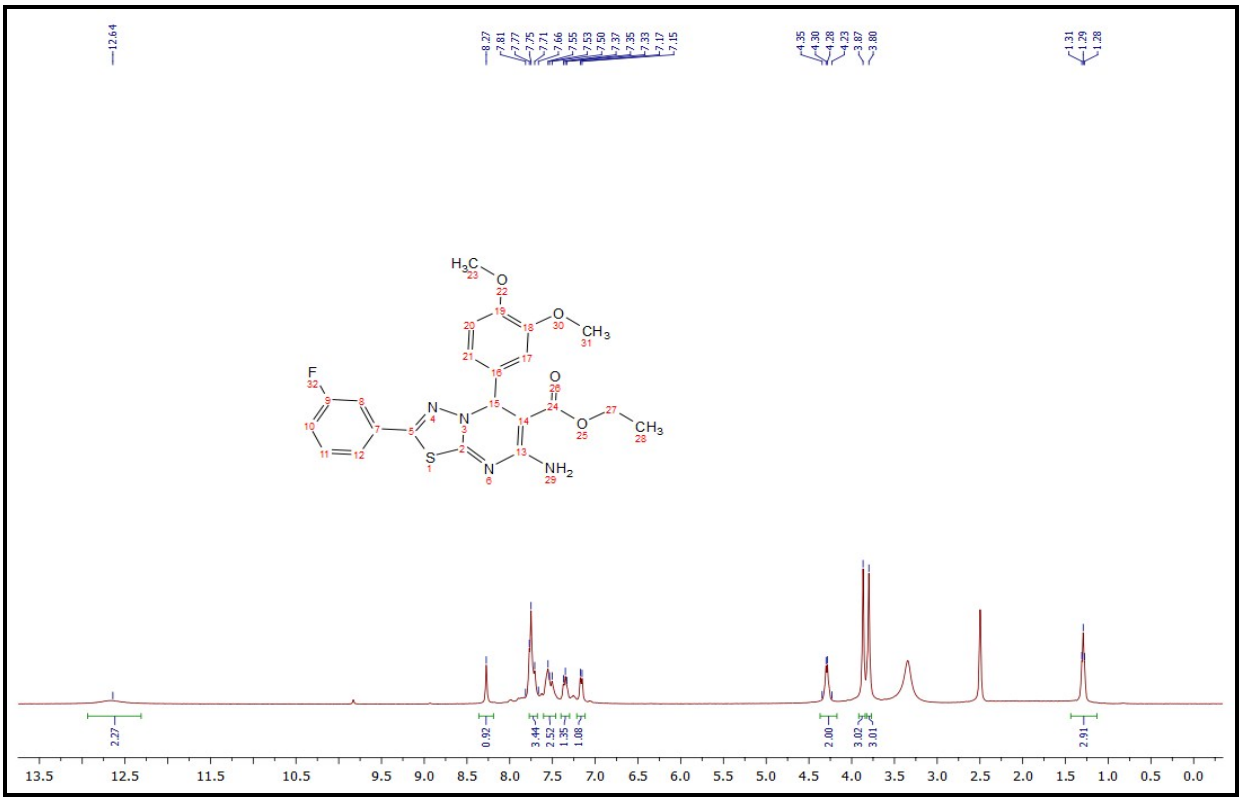

**Figure S32**. [1]H-NMR spectra of compound **4k**

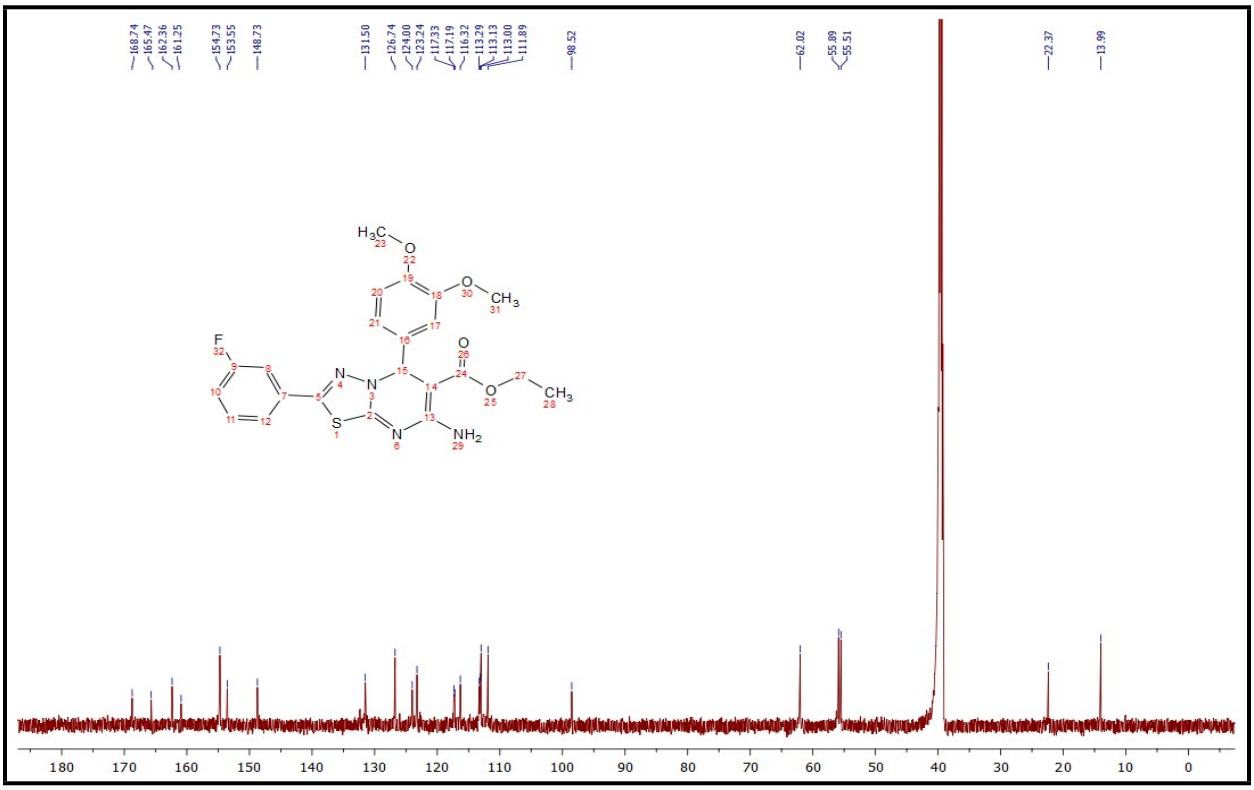

**Figure S33**. [13]C-NMR spectra of compound **4k**

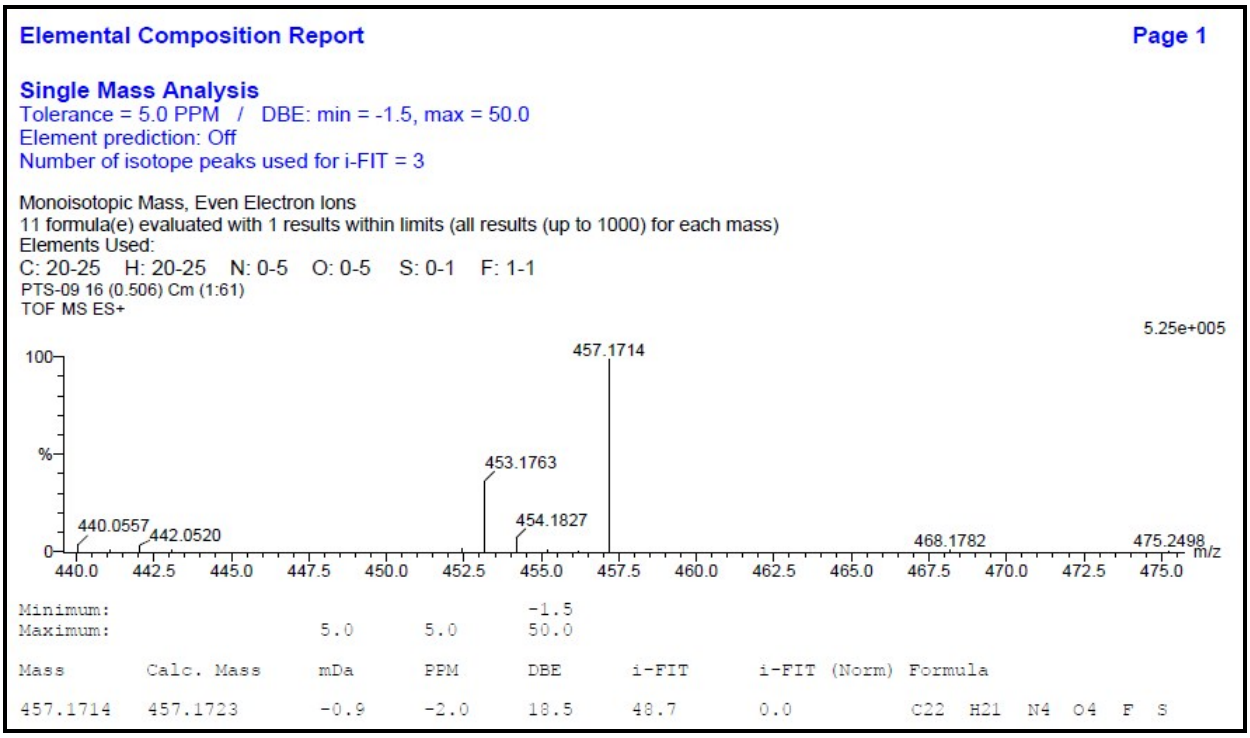


**Figure S34**. HRMS-spectra of compound **4k**

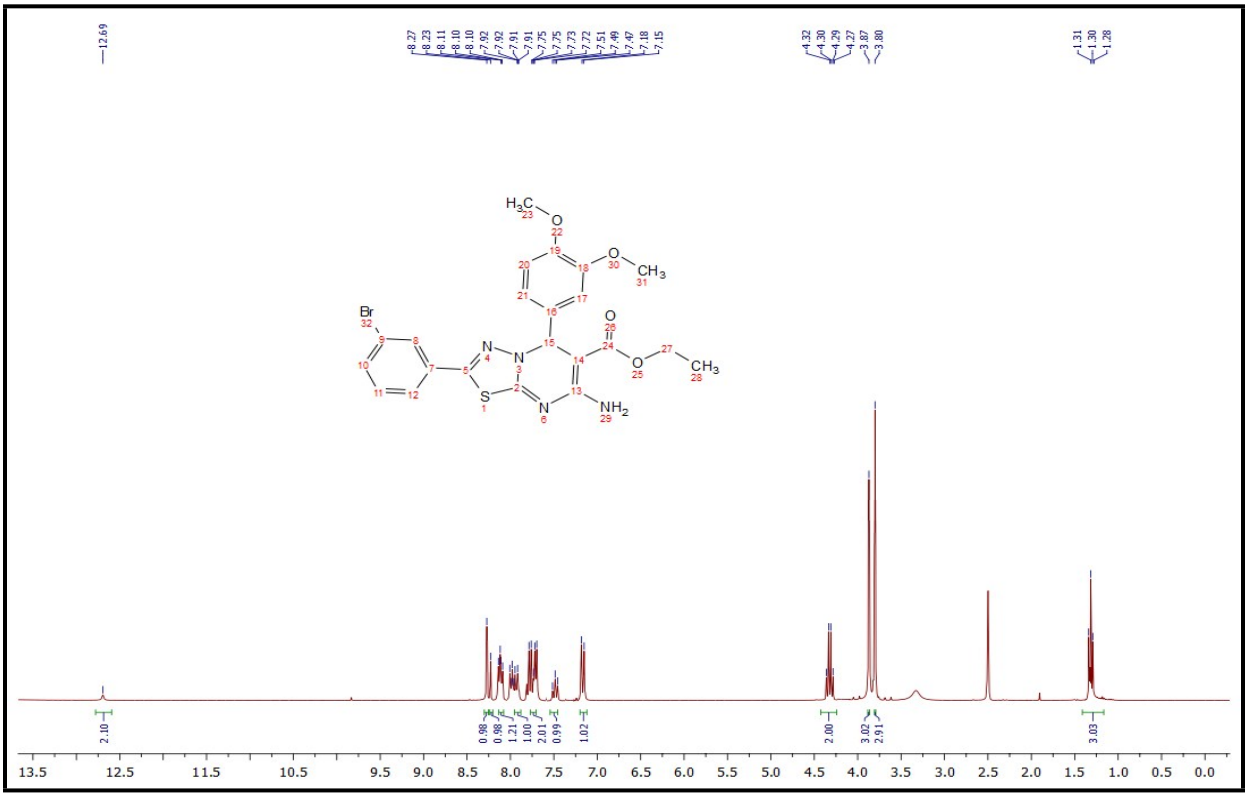

**Figure S35**. [1]H-NMR spectra of compound **4l**

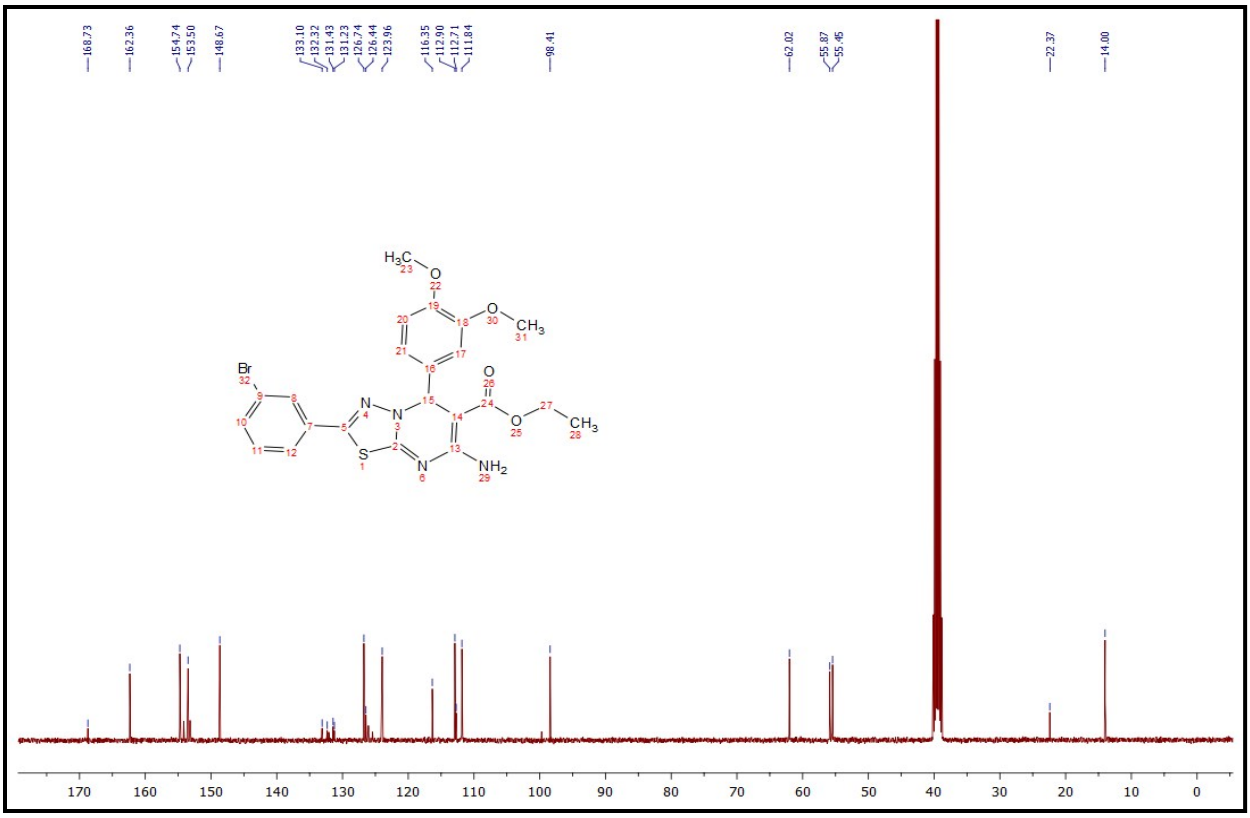


**Figure S36**. $^{13}$C-NMR spectra of compound **4l**

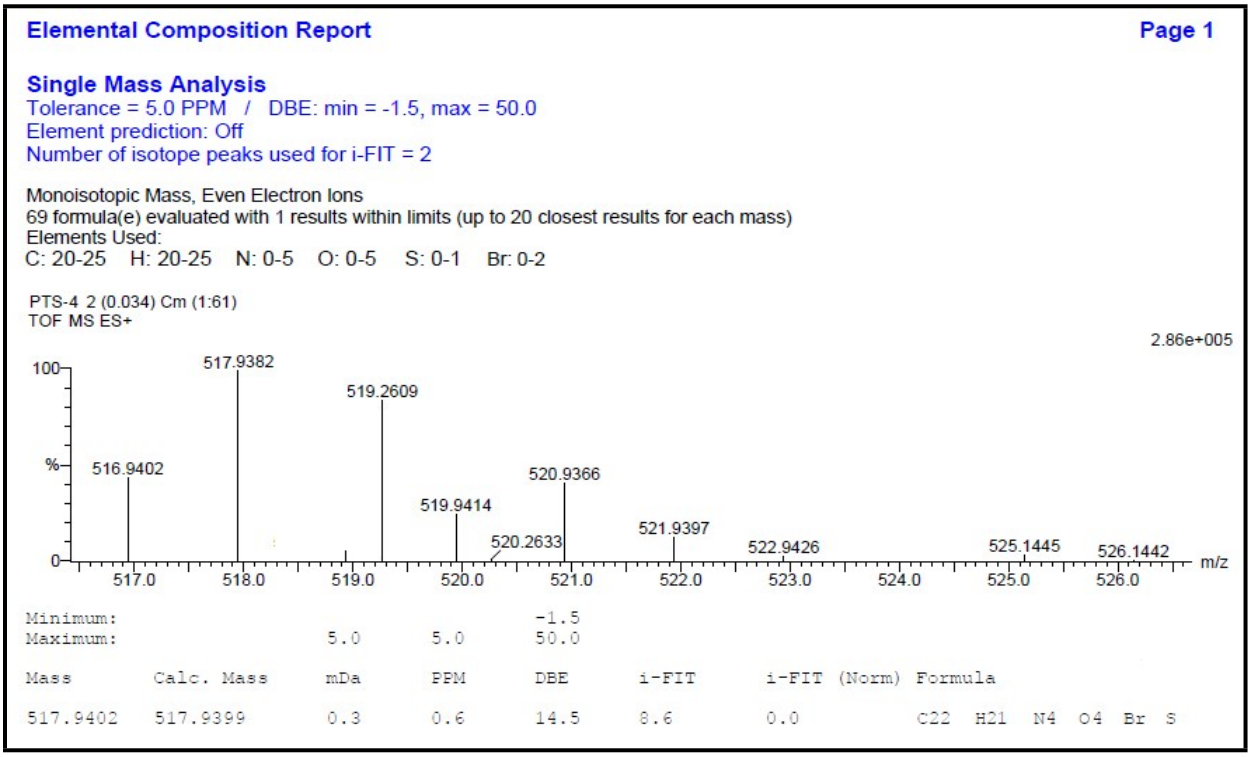


**Figure S37**. HRMS-spectra of compound **4l**

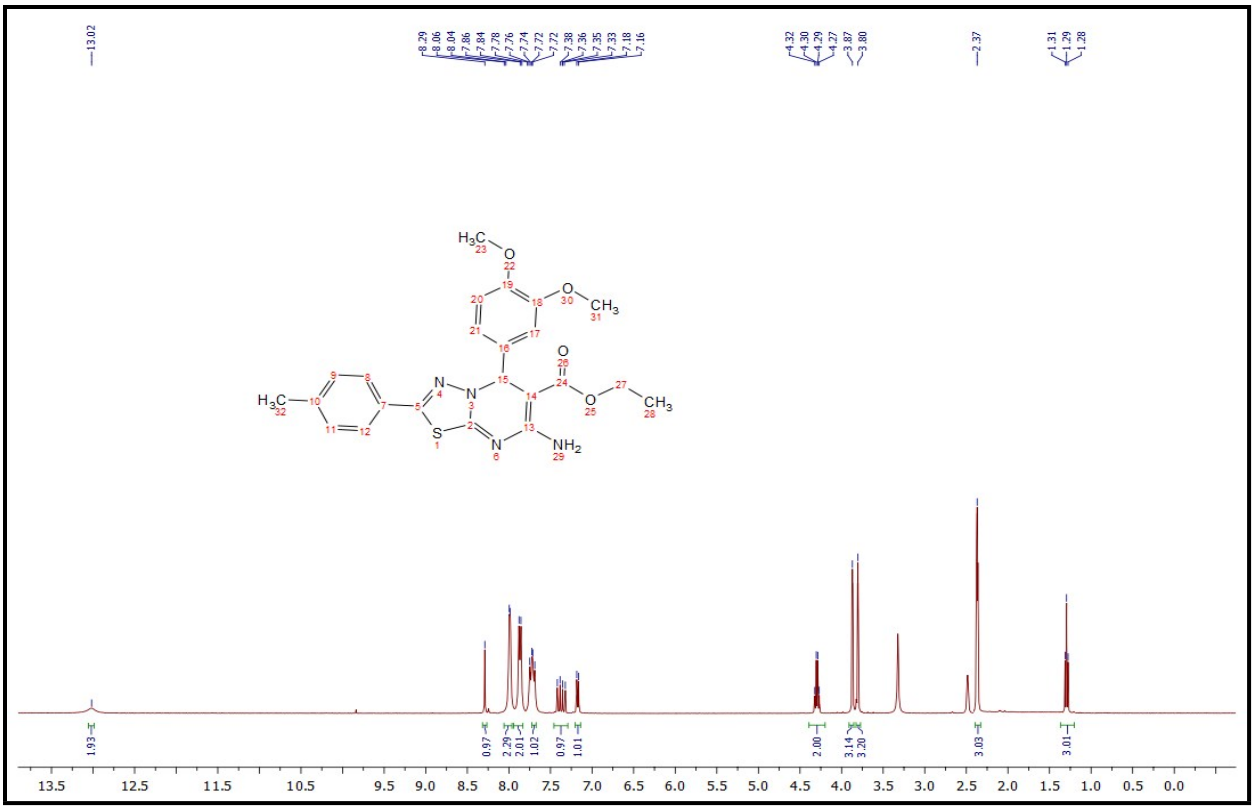

**Figure S38**. [1]H-NMR spectra of compound **4m**

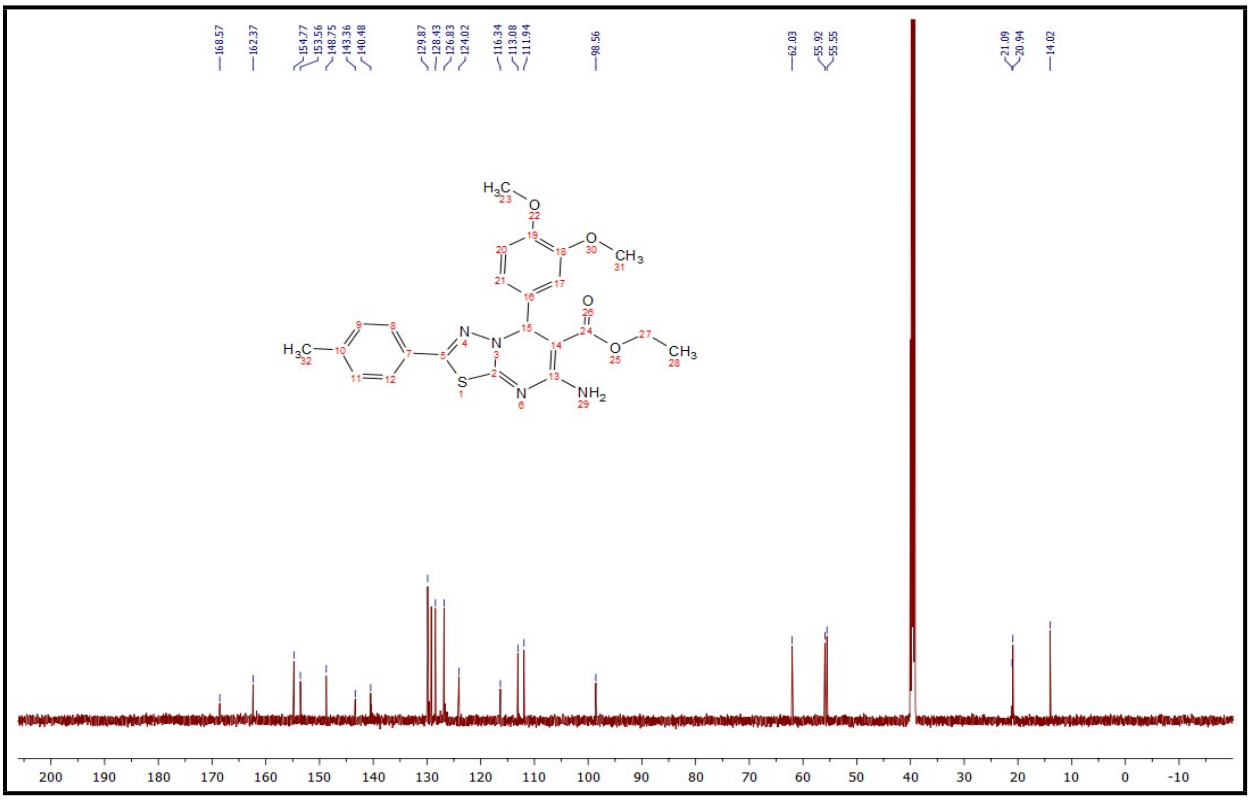

**Figure S39**. [13]C-NMR spectra of compound **4m**

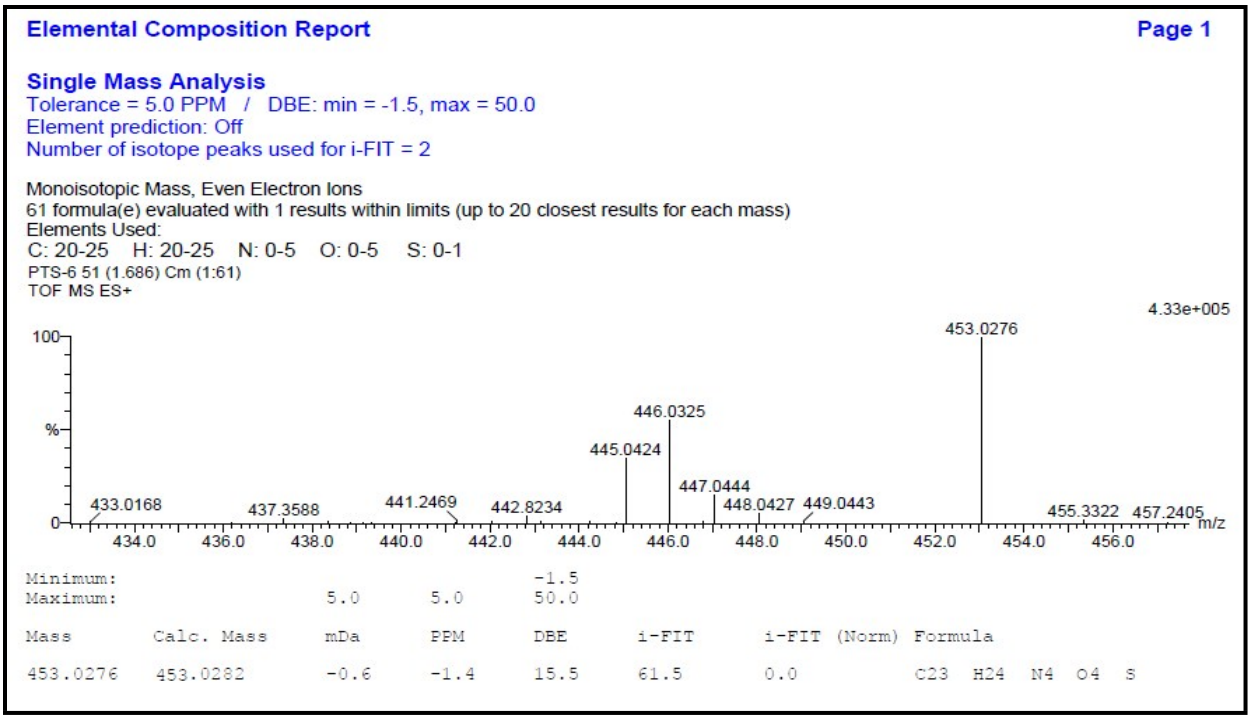


**Figure S40**. HRMS-spectra of compound **4m**

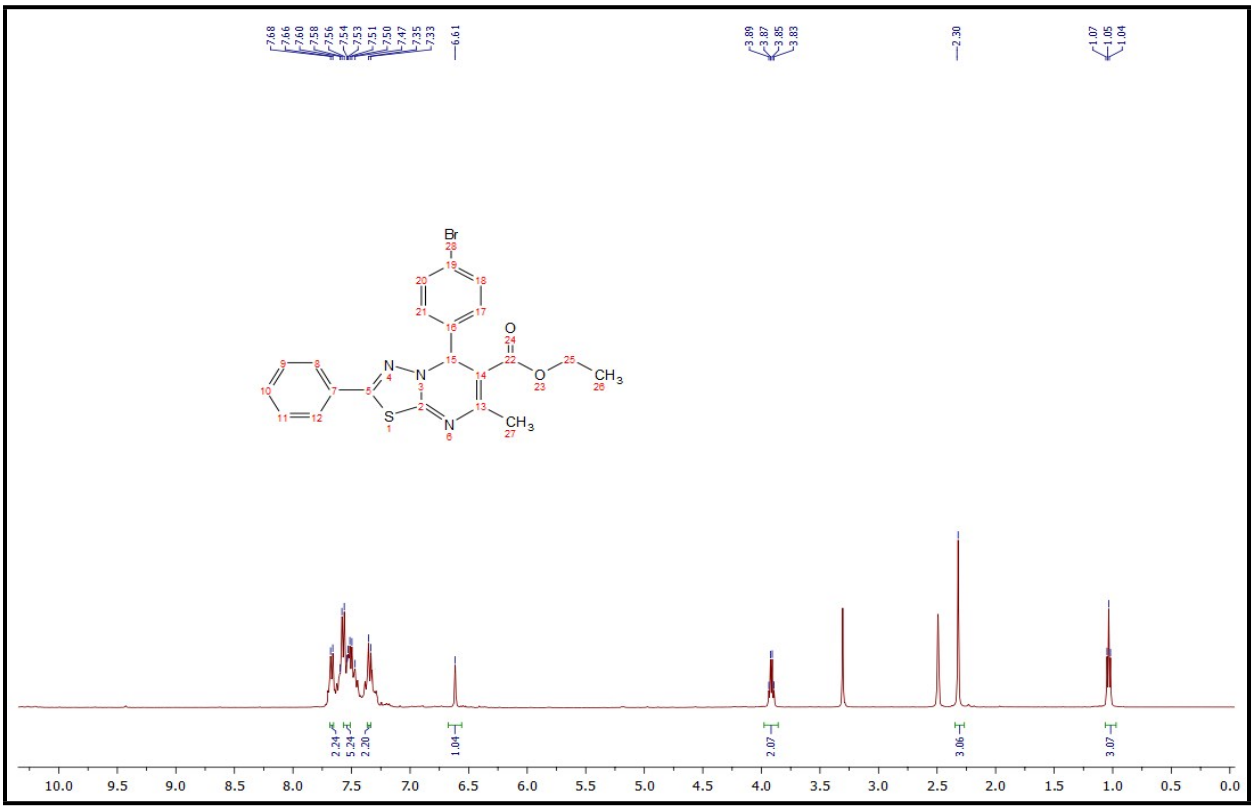


**Figure S41**. $^{1}$H-NMR spectra of compound **4n**

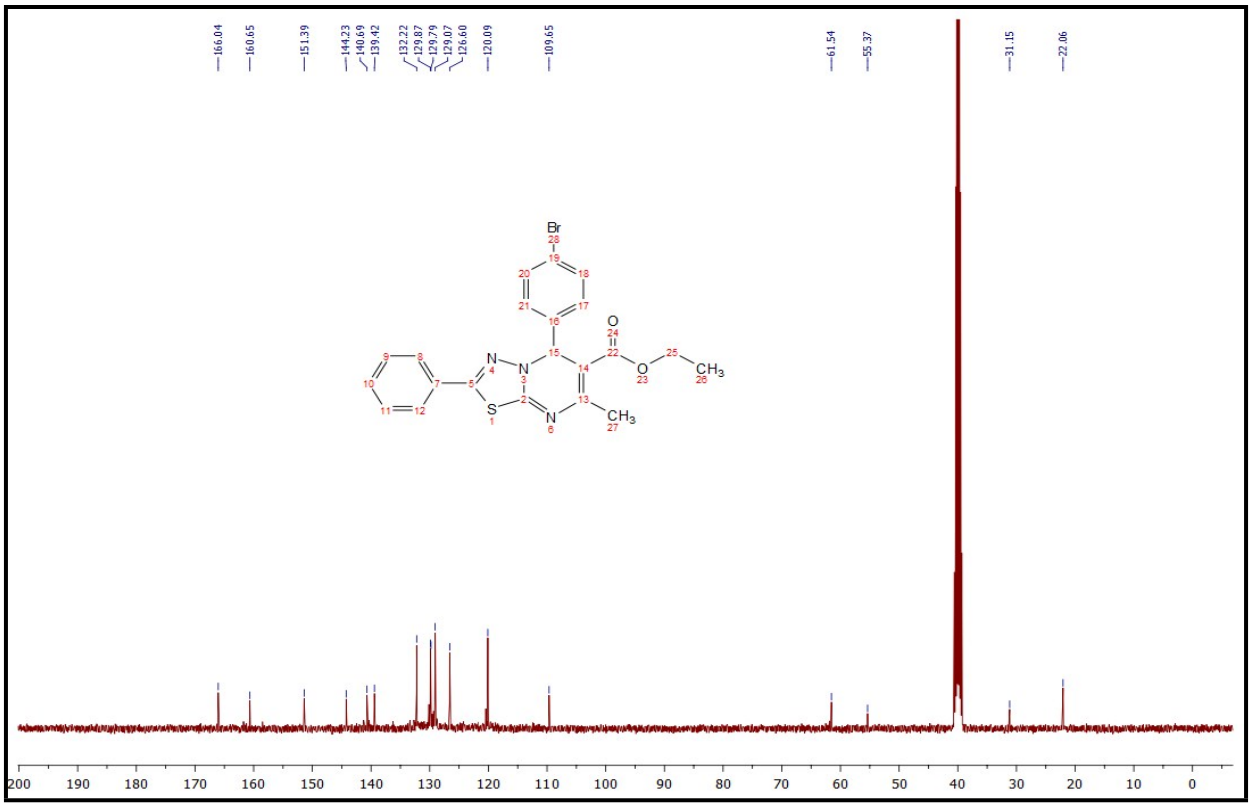


**Figure S42**. $^{13}$C-NMR spectra of compound **4n**

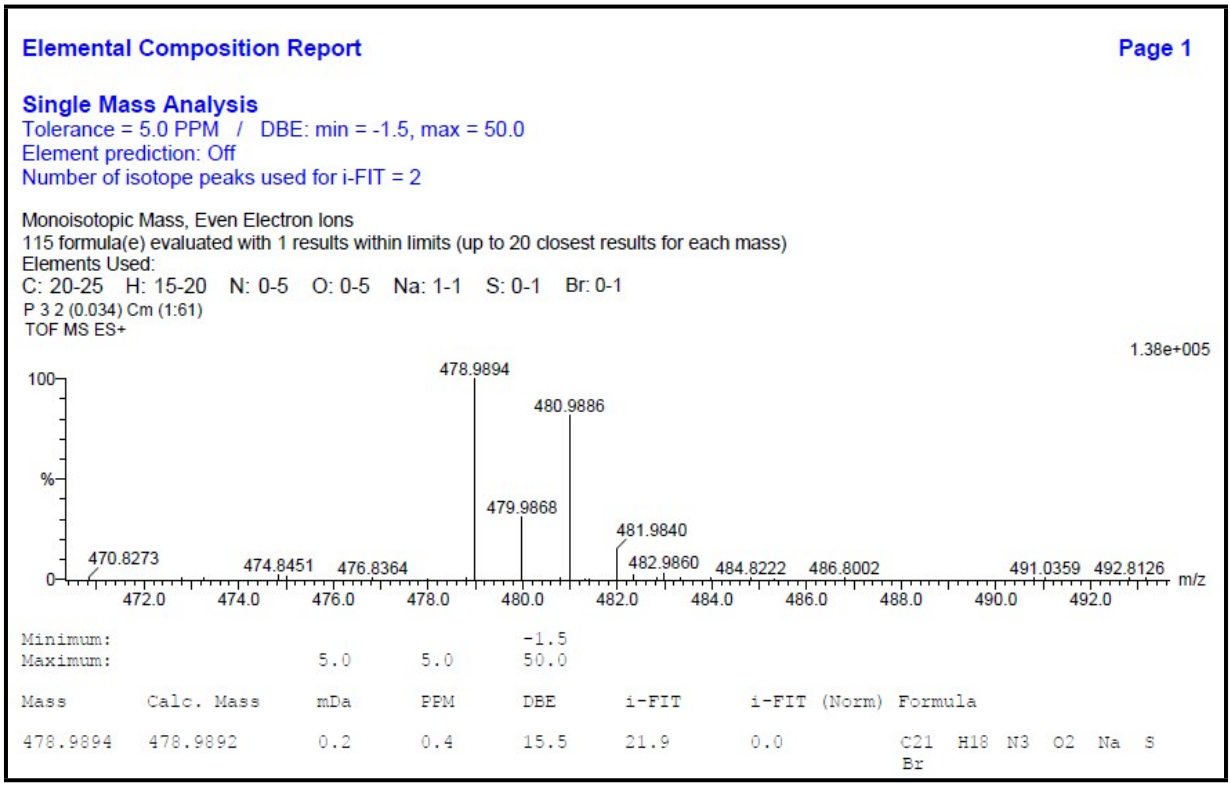


**Figure S43**. HRMS-spectra of compound **4n**

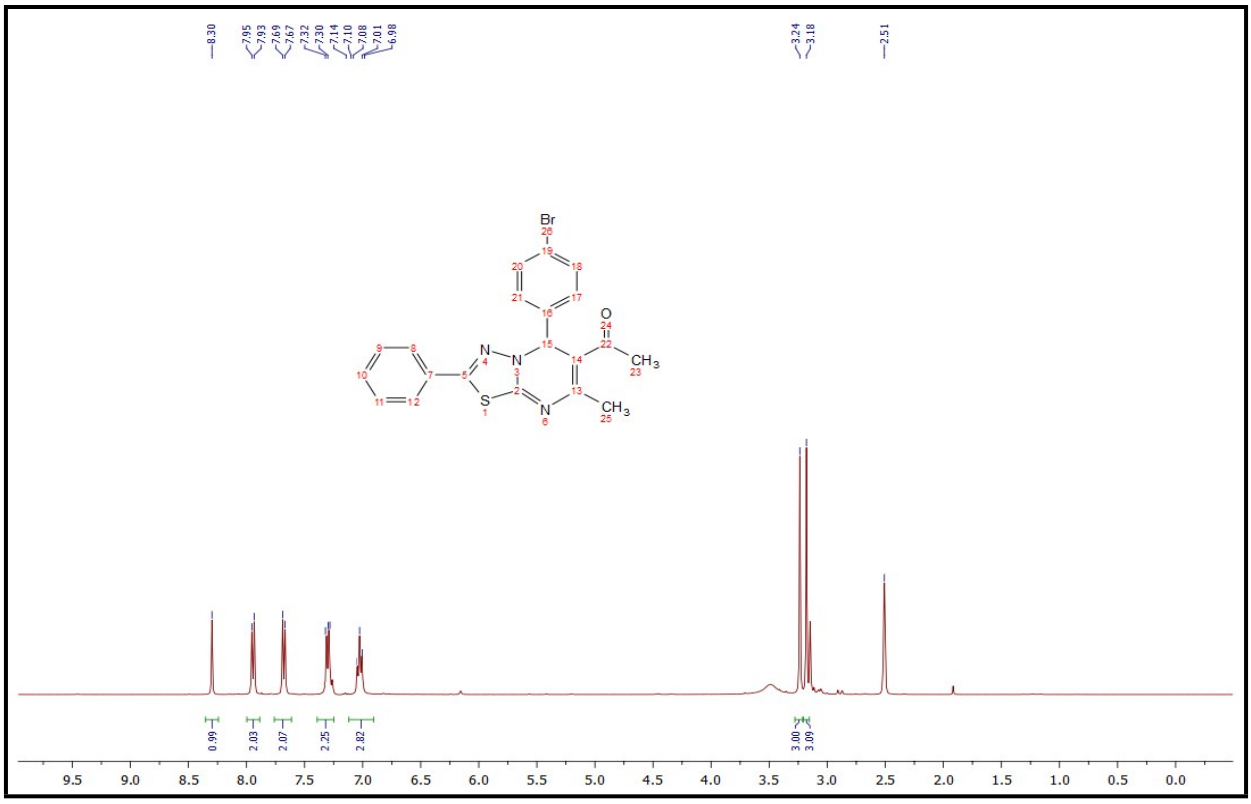

**Figure S44**. $^{1}$H-NMR spectra of compound **4o**

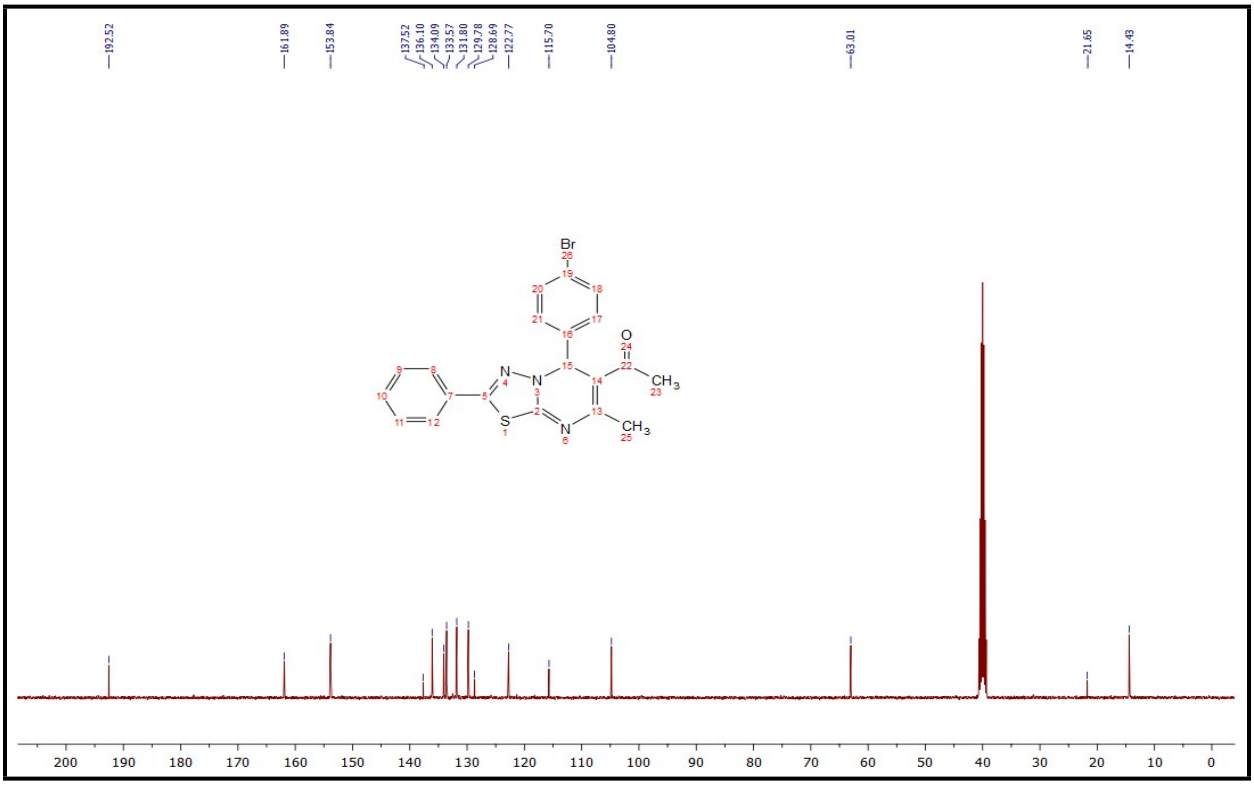

**Figure S45**. $^{13}$C-NMR spectra of compound **4o**

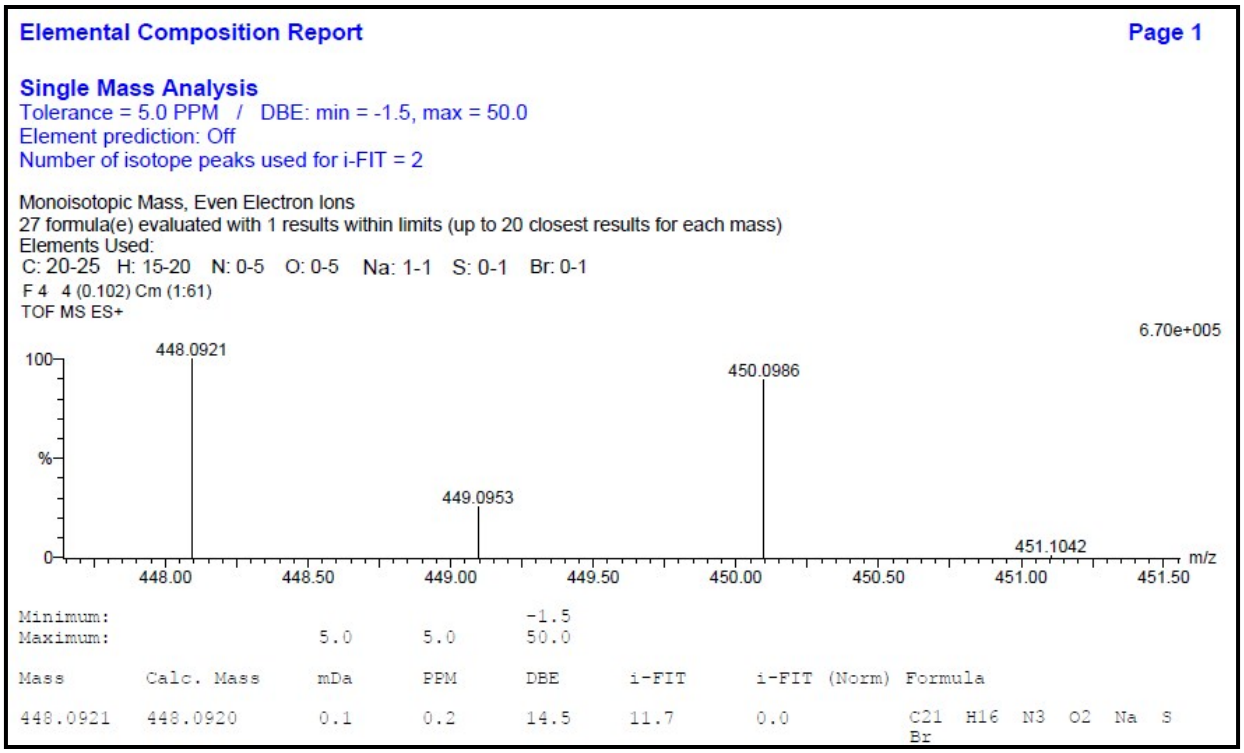


**Figure S46**. HRMS-spectra of compound **4o**

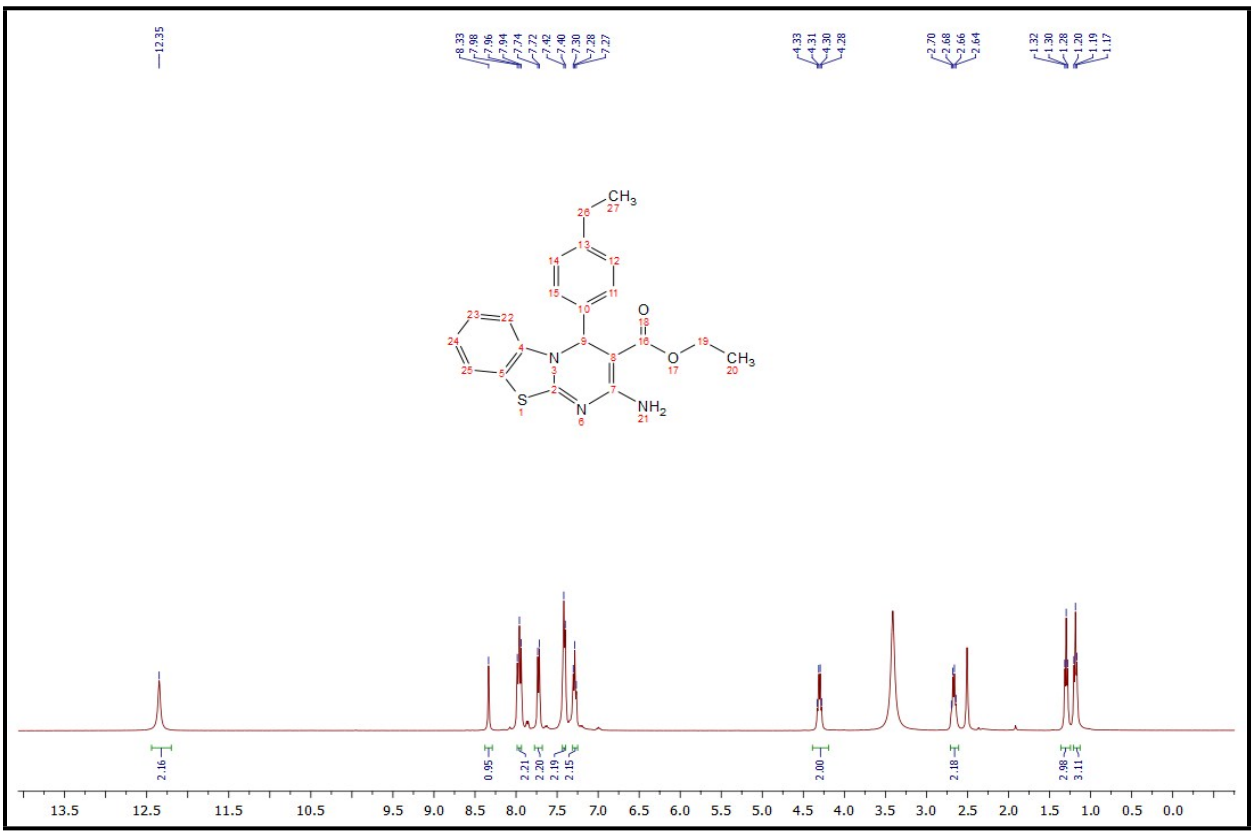

**Figure S47**. $^{1}$H-NMR spectra of compound **4p**

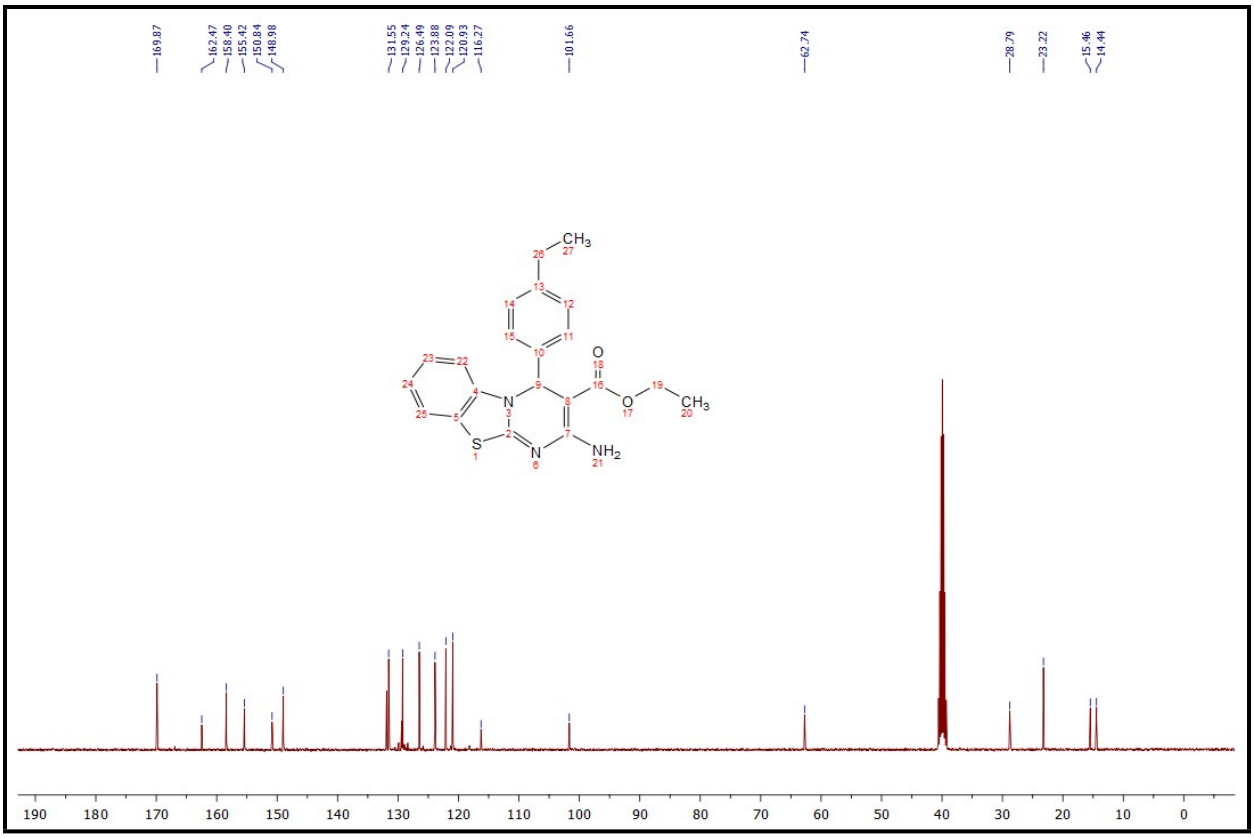


**Figure S48**. $^{13}$C-NMR spectra of compound **4p**

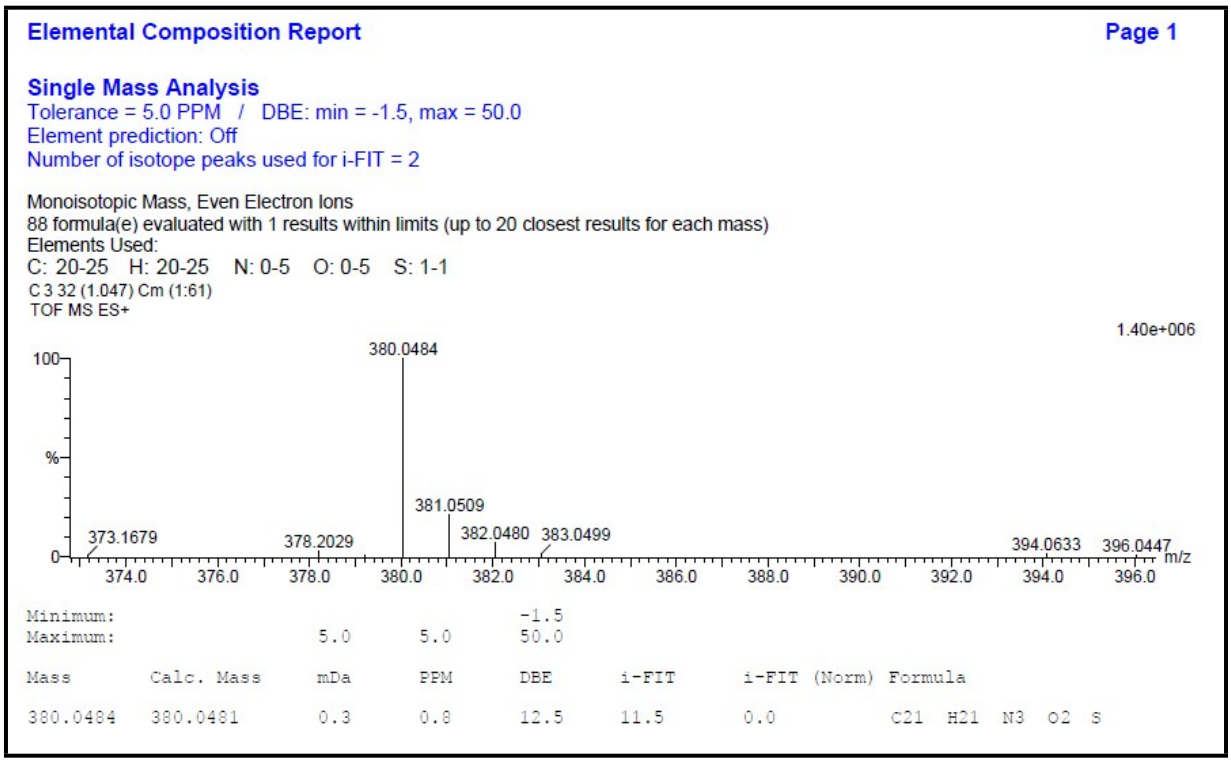


**Figure S49**. HRMS-spectra of compound **4p**

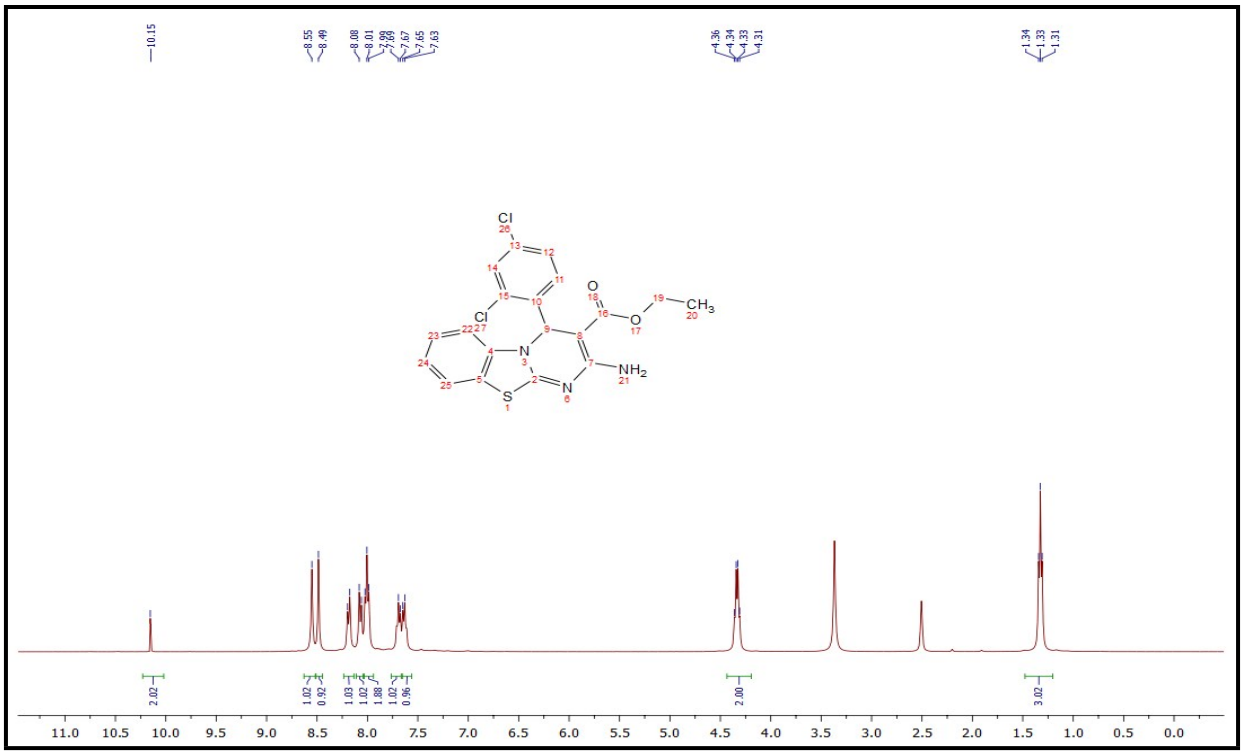

**Figure S50**. [1]H-NMR spectra of compound **4q**

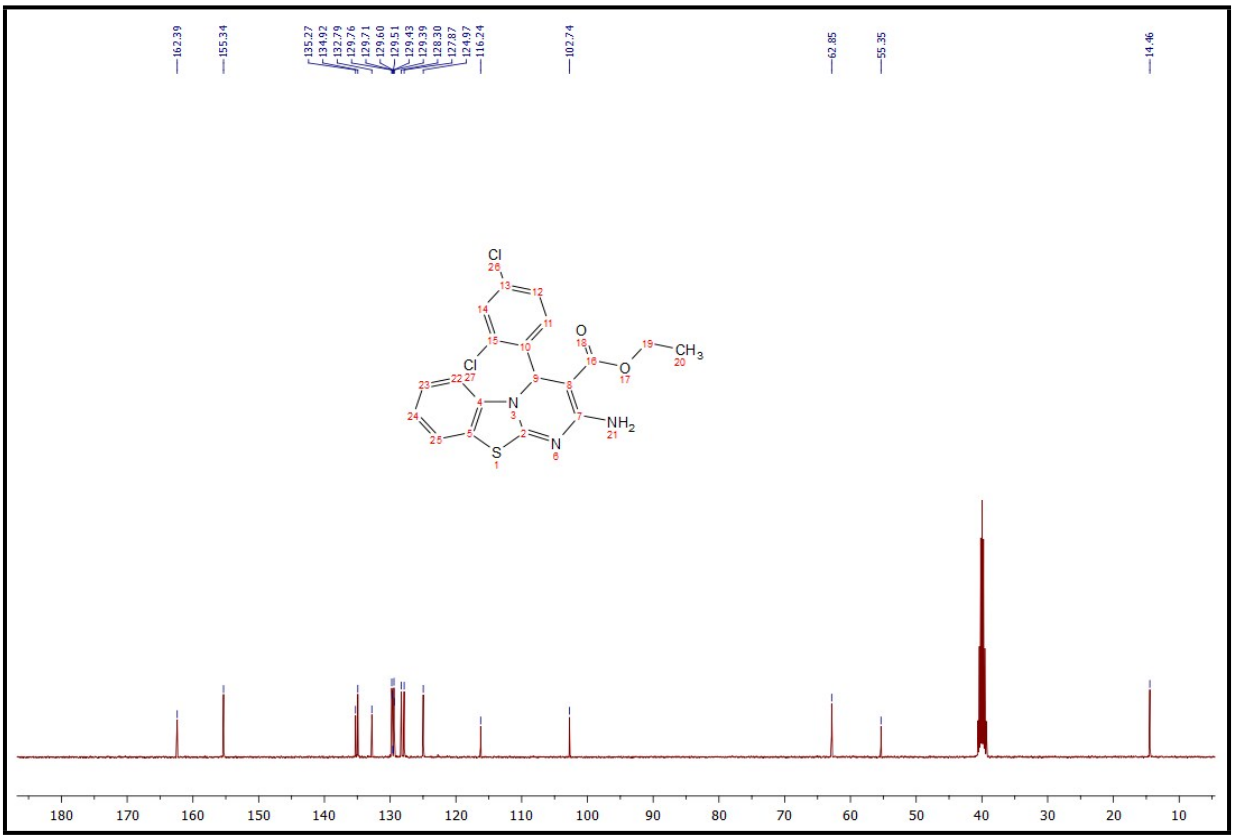

**Figure S51**. [13]C-NMR spectra of compound **4q**

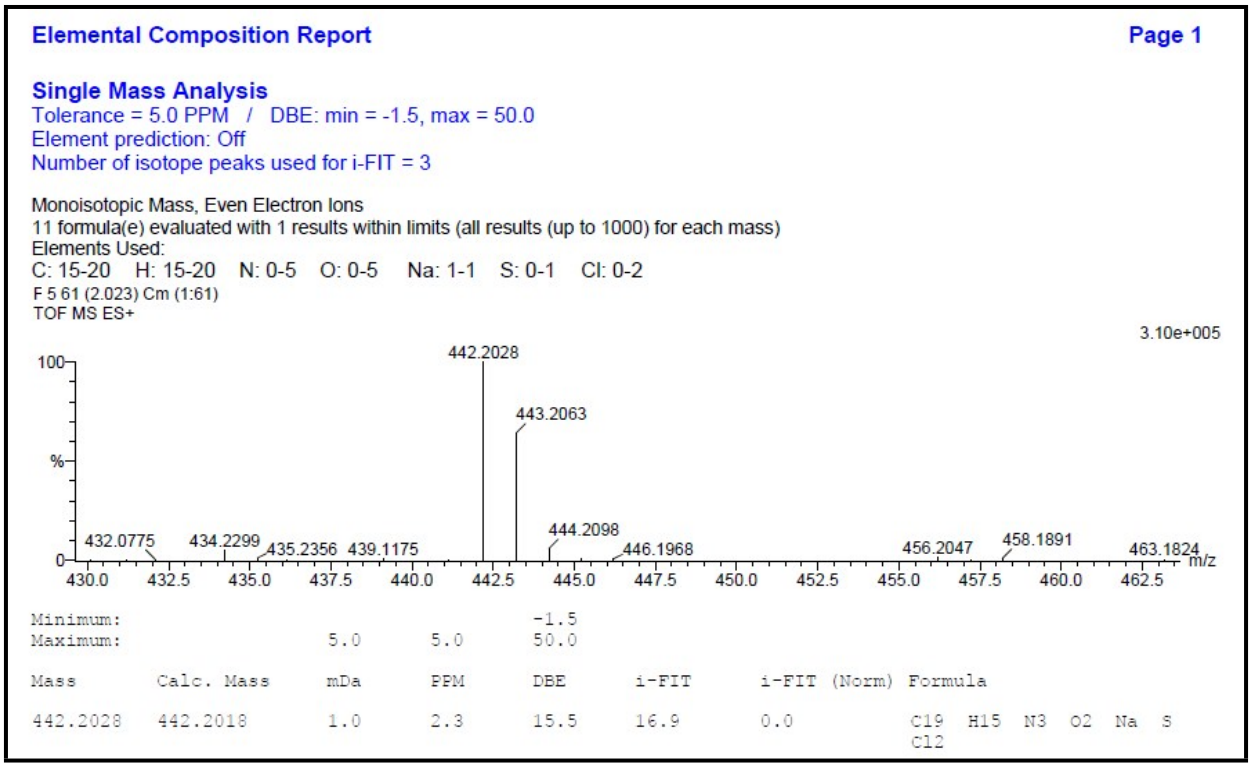


**Figure S52**. HRMS-spectra of compound **4q**