Supporting Information-

Scandium Triflate-Catalyzed Synthesis of Novel Azo-Fused Benzo[4,5]thiazolo[2,3-b]quinazolin-1-ones: Bridging Molecular Docking, DFT Insights, and Anticancer Applications

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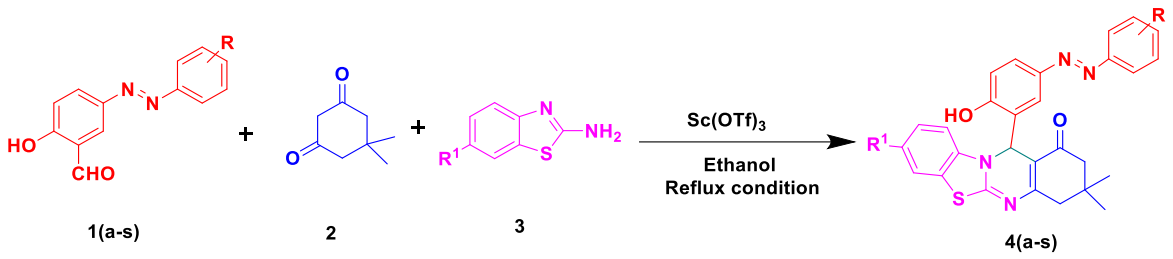
General Remarks

All the reagents and common solvents were procured from different commercial sources (Sigma-Aldrich, Merck and Loba-Chemie) and were used as received. Doubly distilled water was used for the entire experimentation. Reactions were monitored by TLC using silica gel 60 F^{254} coated aluminium sheets with ethyl acetate-hexane (1:1) mixture as the mobile phase. Melting points are uncorrected and were determined using electro-thermal apparatus by open capillary method. FT-IR spectra were recorded on Perkin Elmer FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Multiprobe Nuclear Magnetic Resonance Spectrometer-400 MHz (Bruker) in DMSO-d_6 and $CDCl_3$ solvents and δ values are expressed in ppm using TMS as an internal standard. Mass spectra were recorded on maXis 10138 mass spectrometer operating at 70 eV.

General procedure for the synthesis of aryl azo-salicylaldehydes (1a-s)

Aryl azo-salicylaldehydes were prepared according to the well-known literature procedure.[1,2] In a 250 mL beaker containing substituted aromatic anilines (9 mmol) in a small quantity of water, 10 mL of 37% aq. HCl solution was added and the mixture was magnetically stirred at 200-300 rpm at 0-5°C for 30 min. To this reaction mixture, 20 mL of 20% aq. NaNO2 solution was added and continued the stirring for about 1 h at the same temperature providing a dark yellow colored solution (diazonium chloride). On the other hand, salicylaldehyde (9 mmol) was dissolved in a solution of 20% aqueous sodium hydroxide that resulted in the formation of bright yellow solution. Eventually, the cold mixture of diazotized solution was added to the mixture of salicylaldehyde solution at cold condition (below 5°C) and magnetically stirred for 1 h. Simultaneously, the reaction was monitored by TLC technique. After the completion of the reaction, the obtained solid product was washed with 10% NaOH solution to neutralize the pH level. Finally, the resultant mass of aryl azo-salicylaldehydes (1a-s) was filtered with Whatman no.1 filter paper and washed with distilled water for several times to remove the impurities and dried at room temperature and recrystallized using ethanol.

General procedure for the synthesis of azo fused tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one derivatives:



In a 25 ml round bottom flask, a mixture of 5-((4-chlorophenyl)diazenyl)-2-hydroxybenzaldehyde (1d) (1.0 mmol, 0.2606g) and dimedone (1.0 mmol, 0.1401g) was taken with 30 mol% of Scandium(Ⅲ) triflate (0.1476g) as catalyst in ethanol (5.0 mL) and refluxed for 1 hour to form the intermediate. Then 2- amino 6-methyl benzothiazole (1.0 mmol, 0.1642g) was added into the mixture and refluxed. The progress of the reaction was monitored by TLC (Hexane:Ethylacetate 1:1). After completion of the reaction, the mixture was cooled to room temperature and the obtained solid was filtered. Finally, the solid product was washed with ethanol twice to remove the catalyst and impurities and then the catalyst was recovered by using extraction. The same procedure was followed for other derivatives of azoaldehydes. The formations of the targeted compounds were confirmed by ^{1}H NMR, ^{13}C NMR, ESI-MS, FT-IR and melting points.

Experimental

Procedure for Molecular Docking

Ligand Preparation

The chemical structures of all the synthesized compounds were drawn using ChemDraw 12.0 and the structures were saved in Mol file format using chem 3D after which the Mol files of compounds were converted into PDB (protein data bank) format. All the PDB ligands were optimized by energy minimization using MM2 method.

Receptor Preparation

For molecular docking analysis, the three-dimensional crystal structure of the Epidermal Growth Factor Receptor (EGFR) tyrosine kinase domain, with a resolution of 2.60 Å (PDB code: 1M17), was downloaded from the Protein Data Bank (PDB: 1M17). The ligand was separated from the receptor 1M17.pdb by using Discovery Studio 4.0 Client.

Molecular Docking

Docking studies of all the compounds were performed using a AutoDock Vina software. AutoDock Vina software was employed for all docking calculations. The docking input files were used to generate by Autodock tools program. In all docking, a grid box size of 100×100×100 points in x, y, and z directions was built. Grid box plays a central role in the process of docking as it is made to cover all the amino acids present in active sites necessary for binding other than those present in receptor. A grid spacing of 0.375 Å (carbon–carbon covalent bond has approximately one forth of the lengths) and a dielectric constant that is distances-dependent function and energetic map were used for the calculation. Ten runs were generated by using Lamarckian genetic algorithm searches. Default settings were used with an initial population of 50 randomly placed individuals, a maximum number of 2.5 ×106 energy evaluations, and a maximum number of 27000 generations. A crossover rate of 0.8 was chosen and mutation rate of 0.02. Results varied from positional root–mean–square deviation (RMSD) were clustered together by less than 0.5 Å and a resultant complex structure of the favorable free energy was selected for binding. Further, the Discovery Studio 4.0 Client was used for visualization and determining the mode of interaction between the receptor and ligands.[3]

Spectral characterization:

(E)-12-(2-hydroxy-5-(phenyldiazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4a):

Color: Orange-yellowish solid; M.P: 230 ˚C; FT- IR (KBr) (ϑmax/cm^{-1})**:** 3058, 2963, 1595, 1578, 1489, 1468, 1352, 1328, 1220; ^{1}H NMR (400 MHz, DMSO): δ (ppm): 10.96 (s, 1H, OH), 8.04 (d, *J*=1.6Hz, 1H, ArH), 7.82 (d, *J*=7.2Hz, 2H, ArH), 7.66 (dd, *J*=8.4Hz, 2.4Hz, 1H, ArH), 7.55 (m, 4H, ArH), 7.41 (d, *J*=8.4Hz, 1H, ArH), 7.14 (dd, *J*=8.4Hz, 0.8Hz 1H, ArH), 6.92 (d, *J*=8.4Hz, 1H, ArH), 6.71 (s, 1H, CH), 2.50-2.41 (d, 2H, CH_2), 2.27 (s, 3H, A-CH_3), 2.24-2.05 (m, 2H, CH_2), 1.05 (s, 3H, CH_3), 0.94 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.49, 165.15, 159.48, 158.58, 152.46, 145.45, 136.63, 134.16, 131.11, 129.82, 128.14, 123.16, 116.91, 112.35, 108.76, 56.52, 50.87, 32.78, 29.54, 27.07, 21.07, 19.07; ESI-MS: m/z Calcd for $C_{29}H_{26}N_4O_2S$: 494.6130; Found: 495.2174 (M+).

(E)-12-(5-((2-chlorophenyl)diazenyl)-2-hydroxyphenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4b):

Color: Yellow colour solid; M.P: 208 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3062, 2947, 1604, 1489, 1378, 1279, 1112, 753; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 11.08 (s, 1H, OH), 8.04 (d, *J*=2Hz, 1H, ArH), 7.66 (m, 2H, ArH), 7.58 (dd, *J*=9.6Hz, 1.6Hz, 1H, ArH), 7.46 (m, 4H, ArH), 7.12 (d, 1H, ArH), 6.94 (d, *J*=8.8Hz, 1H, ArH), 6.70 (s, 1H, CH), 2.48 (m, 2H, CH_2), 2.25 (s, 3H, A-CH_3), 2.07-2.23 (m, 2H, CH_2), 1.04 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):194.48, 165.13, 159.49, 158.97, 148.48, 145.94, 136.59, 134.21, 133.66, 132.15, 131.01, 128.41, 128.30, 123.59, 121.26, 117.98, 112.24, 108.90, 56.53, 52.03, 50.87, 45.20, 32.74, 29.57, 27.10, 21.05, 19.04; ESI-MS: m/z Calcd for $C_{29}H_{25}ClN_4O_2S$: 529.0550; Found: 529.1743 (M+).

(E)-12-(5-((3-chlorophenyl)diazenyl)-2-hydroxyphenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4c):

Color: Yellow colour solid; M.P: 208 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3136, 2964, 1593, 1468, 1352, 1278, 1114, 815; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 11.05 (s, 1H, OH), 8.03 (s, 1H, ArH), 7.76 (t, *J*=10 Hz, 2H, ArH), 7.64 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.55 (m, 3H, ArH), 7.36 (d, *J*=8.4Hz, 1H, ArH), 7.11 (d, *J*=8.4Hz, 1H, ArH), 6.91 (d, *J*=8.8Hz, 1H, ArH), 6.68 (s, 1H, CH), 2.44 (d, 2H, CH_2), 2.25 (s, 3H, A-CH_3), 2.01-2.20 (m, 2H, CH_2), 1.02 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):194.46, 165.16, 159.48, 159.20, 153.54, 145.25, 136.61, 134.53, 134.17, 131.56, 130.53, 128.13, 123.61, 120.97, 117.01, 112.33, 108.67, 56.51, 50.88, 45.17, 32.75, 29.48, 27.09, 21.05; ESI-MS: m/z Calcd for $C_{29}H_{25}ClN_4O_2S$: 529.0550; Found: 529.1696 (M+).

(E)-12-(5-((4-chlorophenyl)diazenyl)-2-hydroxyphenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4d):

Color: Yellow color solid; M.P: 218 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3060, 2956, 1581, 1467, 1386, 1276, 1117, 753; ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 10.40 (s, 1H, OH), 7.70 (t, *J*=8.4Hz, 3H, ArH), 7.47 (d, *J*=2.4Hz,1H, ArH), 7.39 (d, *J*=8.4Hz, 2H, ArH), 7.32 (s, 1H, ArH), 7.10 (d, *J*=8.8Hz, 1H, ArH), 7.03 (d, J=8.4Hz, 1H, ArH), 6.84 (d, *J*=8.4Hz, 1H, ArH), 6.72 (s, 1H, CH), 2.36 (d, 2H, CH_2), 2.31 (s, 3H, A-CH_3), 1.24 (d, 2H, CH_2), 1.11 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 198.16, 167.02, 163.20, 156.12, 150.86, 147.39, 136.28, 135.61, 129.19, 128.56, 124.12, 122.53, 120.23, 111.96, 108.65, 50.62, 50.15, 45.69, 32.80, 29.71, 28.88, 27.61, 21.21; ESI-MS: m/z Calcd for $C_{29}H_{25}ClN_4O_2S$: 529.0550; Found: 529.1743 (M+).

(E)-12-(2-hydroxy-5-((2-nitrophenyl)diazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4e):

Color: Yellow color solid; M.P: 242 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3077, 2962, 1576, 1485, 1363, 1267, 1115; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 11.29 (s, 1H, OH), 8.04 (t, *J*=6.4Hz, 2H, ArH), 7.66 (m, 5H, ArH), 7.37 (s, 1H, ArH), 7.20 (s, 1H, ArH), 6.90 (d, *J*=7.6Hz, 1H, ArH), 6.69 (s, 1H, CH), 2.25 (s, 3H, A-CH_3), 2.40-2.01 (m, 4H, 2×CH_2), 1.02 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.47, 165.11, 159.66, 159.49, 147.31, 145.59, 136.57, 134.23, 133.98, 128.27, 124.49, 123.06, 118.99, 112.26, 55.37, 50.85, 45.15, 40.61, 32.73, 29.54, 27.07, 21.05; ESI-MS: m/z Calcd for $C_{29}H_{25}N_5O_4S$: 539.6100; Found: 538.3000 (M-).

(E)-12-(2-hydroxy-5-((3-nitrophenyl)diazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4f):

Color: Orange colour solid; M.P: 230 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3106, 2962, 1620, 1556, 1329, 1266, 1118; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 11.12 (s, 1H, OH), 8.45 (s, 1H, ArH), 8.33 (dd, *J*=8Hz, 0.8Hz, 1H, ArH), 8.23 (d, *J*=0.8Hz, 1H, ArH), 8.10 (d, *J*=2Hz, 1H, ArH), 7.84 (t, *J*=8Hz, 1H, ArH), 7.70 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.53 (s, 1H, ArH), 7.37 (d, *J*=8Hz, 1H, ArH), 7.11 (d, *J*=8.4Hz, 1H, ArH), 6.91 (d, *J*=8.8Hz, 1H, ArH), 6.69 (s, 1H, CH), 2.46- 2.42 (m, 2H, CH_2), 2.25 (s, 3H, A-CH_3), 2.21-2.06 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):194.45, 165.20, 159.75, 152.85, 149.09, 145.11, 136.60, 131.44, 129.83, 128.14, 127.80, 124.97, 123.94, 117.10, 115.68, 112.37, 108.56, 52.66, 50.88, 45.19, 32.75, 29.49, 27.08, 21.05; ESI-MS: m/z Calcd for $C_{29}H_{25}N_5O_4S$: 539.6100; Found: 540.2010 (M+).

(E)-12-(2-hydroxy-5-((4-nitrophenyl)diazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4g):

Color: Orange solid; M.P: 238 ˚C; FT- IR (KBr) (ϑmax/cm-1): 3051, 2914, 1580, 1470, 1387, 1275, 1112; ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 10.60 (s, 1H, OH), 8.30 (d, *J*=8.8Hz, 2H, ArH), 7.87 (d, *J*=9.2Hz, 2H, ArH), 7.77 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.52 (d, *J*=2Hz, 1H, ArH), 7.35 (s, 1H, ArH), 7.13 (d, *J*=8.8Hz, 1H, ArH), 7.06 (d, *J*=8Hz, 1H, ArH), 6.84 (d, 1H, ArH), 6.73 (s, 1H, CH), 2.60-2.48 (m, 2H, CH_2), 2.33 (s, 3H, A-CH3), 1.25 (s, 2H, CH_2), 1.12 (s, 3H, CH_3), 0.97 (s, 3H, CH3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 198.25, 167.09, 163.43, 157.31, 155.75, 148.29, 147.40, 135.51, 135.47, 129.54, 128.63, 124.75, 123.68, 123.17, 122.81, 120.48, 111.90, 108.51, 50.57, 50.11, 45.69, 32.81, 29.71, 28.87, 27.58, 21.23; ESI-MS: m/z Calcd for $C_{29}H_{25}N_5O_4S$: 539.6100; Found: 540.2010 (M+).

(E)-12-(5-((3-bromophenyl)diazenyl)-2-hydroxyphenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4h):

Color: Yellow colour solid; M.P: 232 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3055, 2957, 1591, 1489, 1324, 1223, 1118, 682; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 11.22 (s, 1H, OH), 8.38 (s, 2H, ArH), 8.10 (s, 1H, ArH), 7.97 (s, 2H, ArH), 7.69 (d, *J*=1.6Hz, 1H, ArH), 7.55 (s, 1H, ArH), 7.36 (s, 1H, ArH), 6.91 (s, 1H, ArH), 6.70 (s, 1H, CH), 2.51 (s, 3H, A-CH_3), 2.25-2.202 (m, 4H, 2×CH_2), 1.03 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 197.63, 165.20, 159.35, 148.50, 145.91, 138.75, 133.64, 132.18, 131.03, 128.45, 123.28, 123.11, 118.01, 117.07, 112.50, 109.07, 50.87, 45.18, 32.76, 31.63, 29.54, 27.11, 26.17, 19.04; ESI-MS: m/z Calcd for $C_{29}H_{25}BrN_4O_2S$: 573.5090; Found: 575.1213 (M+2).

(**E)-12-(5-((4-bromophenyl)diazenyl)-2-hydroxyphenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4i):**

Color: Yellow colour solid; M.P: 232 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3085, 2916, 1612, 1587, 1473, 1353, 1278, 1114, 831; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 10.97 (s, 1H, OH), 8.00 (d, *J*=2Hz, 1H, ArH), 7.74 (m, 4H, ArH), 7.62 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.55 (s, 1H, ArH), 7.37 (d, *J*=8.4Hz, 2H, ArH), 7.12 (d, *J*=8.4Hz, 1H, ArH), 6.88 (d, *J*=8.8Hz, 1H, ArH), 6.69 (s, 1H, CH), 2.44 (d, 2H, CH_2), 2.26 (s, 3H, A-CH_3), 2.20-2.09 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):194.47, 165.17, 159.49, 158.95, 151.39, 145.33, 136.62, 134.17, 132.86, 128.15, 127.21, 124.30, 123.45, 123.05, 117.00, 112.35, 108.70, 50.87, 45.18, 32.76, 29.46, 27.10, 21.05, 19.03; ESI-MS: m/z Calcd for $C_{29}H_{25}BrN_4O_2S$: 573.5090; Found: 575.1213 (M+2).

(E)-12-(2-hydroxy-5-(3-tolyldiazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4j):

Color: Yellow colour solid; M.P: 229 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3043, 2963, 1577, 1485, 1376, 1272, 1115; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 10.84 (s, 1H, OH), 7.96 (s, 1H, ArH), 7.70 (d, *J*=8Hz, 2H, ArH), 7.59 (dd, *J*=8.4Hz, 2Hz, 1H, ArH), 7.55 (s, 1H, ArH), 7.37 (m, 3H, ArH), 7.12 (d, *J*=8Hz, 1H, ArH), 6.87 (d, *J*=8.8Hz, 1H, ArH), 6.69 (s, 1H, CH), 2.44 (d, 2H, CH_2), 2.38 (s, 3H, A-CH_3), 2.26 (s, 3H, -CH_3), 2.09 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.48, 165.14, 159.45, 150.55, 145.47, 141.17, 136.65, 134.16, 134.16, 130.32, 128.15, 127.86, 123.05, 122.62, 116.89, 112.35, 108.80, 56.50, 52.41, 45.18, 32.77, 29.47, 27.11, 21.43, 21.06, 19.03; ESI-MS: m/z Calcd for $C_{30}H_{28}N_4O2S$: 508.6400; Found: 509.2247 (M+).

(E)-12-(2-hydroxy-5-(4-tolyldiazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4k):

Color: Yellow colour solid; M.P: 242 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3108, 2917, 1614, 1584, 1472, 1381, 1278, 1112; ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 10.29 (s, 1H, OH), 7.68 (m, 3H, ArH), 7.46 (d, *J*=2.4Hz, 1H, ArH), 7.32 (s, 1H, ArH), 7.24 (d, *J*=8Hz, 2H, ArH), 7.09 (d, *J*=8.8Hz, 1H, ArH), 7.03 (d, *J*=8.4Hz, 1H, ArH), 6.83 (d, *J*=8.4Hz, 1H, ArH), 6.72 (s, 1H, CH), 2.53 (d, 2H, CH_2), 2.38 (s, 3H, A-CH3), 2.32 (s, 3H, -CH_3), 1.86 (m, 2H, CH_2), 1.11 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm):198.17, 167.02, 163.20, 155.49, 150.60, 147.69, 140.98, 135.65, 135.29, 129.64, 129.28, 128.54, 123.93, 123.93, 123.65, 122.56, 121.70, 120.18, 111.99, 108.69, 50.64, 50.16, 45.71, 32.80, 28.85, 27.65, 21.44, 21.20; ESI-MS: m/z Calcd for $C_{30}H_{28}N_4O2S$: 508.6400; Found: 509.2247 (M+).

(E)-12-(2-hydroxy-5-((3-methoxyphenyl)diazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4l):

Color: Yellow colour solid; M.P: 300 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3039, 2923, 1606, 1575, 1473, 1378, 1215, 1117; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 10.92 (s, 1H, OH), 8.02 (s,1H, ArH), 7.63 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.40 (m, 5H, ArH), 7.08 (m, 2H, ArH), 6.89 (d, *J*=8.4Hz, 1H, ArH), 6.69 (s, 1H, CH), 3.84 (s, 3H, -OCH_3), 2.47 (m, 2H, CH_2), 2.25 (s, 3H, A-CH_3), 2.02-2.21 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):194.46, 165.16, 160.50, 159.48, 158.72, 153.78, 153.78, 145.37, 136.64, 134.14, 130.56, 128.10, 127.80, 127.14, 123.11, 123.07, 117.34, 116.95, 112.34, 108.70, 106.12, 56.52, 55.79, 52.57, 50.89, 45.20, 32.74, 29.50, 27.09, 21.05, 19.04; ESI-MS: m/z Calcd for $C_{30}H_{28}N_4O_3S$: 524.6390; Found: 525.2175 (M+).

(E)-12-(2-hydroxy-5-((4-methoxyphenyl)diazenyl)phenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4m):

Color: Yellow colour solid; M.P: 300 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3092, 2960, 1603, 1573, 1489, 1380, 1274, 1114; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 10.90 (s, 1H, OH), 8.19 (s,1H, ArH), 7.63 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.55 (s, 1H, ArH), 7.42 (m, 4H,

ArH), 7.12 (m, 3H, ArH), 6.87 (d, *J*=8.4Hz, 1H, ArH), 6.69 (s, 1H, CH), 3.84 (s, 3H, -OCH_3), 2.26 (s, 3H, A-CH_3), 2.20 (d, 2H, CH_2), 2.04 (d, 2H, CH_2) 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):194.47, 165.17, 160.54, 159.48, 158.72, 153.64, 145.34, 145.05, 136.65, 134.15, 130.66, 128.13, 127.15, 126.37, 123.06, 121.27, 119.00, 117.87, 116.61, 112.38, 108.66, 106.34, 55.81, 52.59, 50.89, 45.18, 40.62, 32.75, 31.64, 29.64, 27.82, 27.10, 26.58, 21.21, 21.06; ESI-MS: m/z Calcd for $C_{30}H_{28}N_4O_3S$: 524.6390; Found: 523.0000 (M-).

(E)-12-(5-((4-acetylphenyl)diazenyl)-2-hydroxyphenyl)-3,3,8-trimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4n):

Color: Yellowish orange colour solid; M.P: 300 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3509, 2950, 1735, 1672, 1587, 1486, 1379, 1263, 1143; ^{1}H-NMR (400 MHz, DMSO): δ (ppm): 11.04 (s, 1H, OH), 8.06-8.12 (m, 3H, ArH), 7.88 (d, *J*=6.4Hz, 3H, ArH), 7.72 (t, *J*=7.2Hz, 2H, ArH), 7.56 (s, 1H, ArH), 7.37 (d, *J*=7.2Hz, 1H, ArH), 6.70 (s, 1H, CH), 2.64 (s, 3H, -$COCH_3$), 2.40 (d, 2H, CH_2), 2.26 (s, 3H, A-CH_3), 2.04 (d, 2H, CH_2) 1.03 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 197.82, 194.47, 165.18, 159.41, 154.92, 145.50, 138.54, 136.60, 130.02, 128.18, 127.64, 123.21, 123.05, 122.62, 117.04, 112.41, 50.85, 45.10, 40.58, 40.37, 32.78, 32.30, 32.10, 29.65, 29.46, 27.40, 27.07, 26.52, 21.06; ESI-MS: m/z Calcd for $C_{31}H_{28}N_4O_3S$: 536.1882; Found: 537.5000 (M+).

(E)-12-(2-hydroxy-5-(phenyldiazenyl)phenyl)-3,3-dimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4o):

Color: Dark Yellow Solid; M.P: 224 ˚C; FT-IR (KBr) (ϑmax/cm-1): 3067, 2958, 1652, 1586, 1438, 1379, 1237, 1117; ^{1}H NMR (400 MHz, DMSO): δ (ppm): 10.92 (s, 1H, OH), 8.02 (d, *J*=2Hz, 1H, ArH), 7.78 (t, *J*=7.6Hz, 3H, ArH), 7.63 (dd, *J*=8.4Hz, 2.4Hz, 1H, ArH), 7.52 (m, 4H, ArH), 7.33 (t, *J*=7.6Hz, 1H, ArH), 7.20 (t, *J*=7.6Hz, 1H, ArH), 6.88 (d, *J*=8.4Hz, 1H, ArH), 6.73 (s, 1H, CH), 2.43-2.25 (m, 2H, CH_2), 2.21-2.02 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.56, 165.24, 159.34, 152.50, 145.45, 138.78, 131.12, 129.83, 127.71, 127.37, 127.05, 124.52, 123.33, 123.09, 122.62, 116.94, 112.60, 108.93, 50.89, 45.16, 32.79, 29.47, 27.09, 27.83; ESI-MS: m/z Calcd for $C_{28}H_{24}N_4O_2S$: 480.1620; Found: 481.4037 (M+).

(E)-12-(2-hydroxy-5-((2-nitrophenyl)diazenyl)phenyl)-3,3-dimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4p):

Color: Orange solid; M.P: 230 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3081, 2958, 1731, 1591, 1482, 1377, 1269, 1118; ^{1}H NMR (400 MHz, DMSO): δ (ppm): 11.23 (s, 1H, OH), 8.05 (t, *J*=8.4Hz, 2H, ArH), 7.77 (m, 2H, ArH), 7.65 (m, 2H, ArH), 7.60 (dd, *J*=8.8Hz, 2Hz, 1H, ArH), 7.51 (d, *J*=8Hz, 1H, ArH), 7.34 (t, *J*=7.6Hz, 1H, ArH), 7.21 (t, *J*=7.6Hz, 1H, ArH), 6.93 (d, *J*=8.8Hz, 1H, ArH), 6.74 (s, 1H, CH), 2.43-2.34 (m, 2H, CH_2); 2.27-2.04 (m, 2H, CH_2), 1.04 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.55, 165.20, 159.37, 147.33, 145.60, 144.83, 138.72, 133.99, 131.20, 124.55, 124.49, 123.59, 123.28, 119.01, 117.19, 112.50, 108.94, 56.52, 50.87, 45.16, 32.75, 29.55, 27.83, 27.08, 26.17, 19.03; ESI-MS: m/z Calcd for $C_{28}H_{23}N_5O_4S$: 525.1471; Found: 526.2342 (M+).

(E)-12-(2-hydroxy-5-((3-nitrophenyl)diazenyl)phenyl)-3,3-dimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4q):

Color: Orange solid; M.P: 242 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3097, 2956, 1628, 1556, 1482, 1366, 1272, 1118; ^{1}H NMR (400 MHz, DMSO): δ (ppm): 11.22 (s, 1H, OH), 8.45(t, *J*=2.4Hz, 1H, ArH), 8.32 (m, 1H, ArH), 8.25 (m, 1H, ArH), 8.20 (s, 1H, ArH), 7.84 (m, 2H, ArH), 7.72 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.56 (d, *J*=8Hz, 1H, ArH), 7.35 (m, 1H, ArH), 7.24 (m, 1H, ArH), 6.94 (s, 1H, ArH), 6.77 (s, 1H, CH), 2.26 (d, 2H, CH_2); 2.08 (d, 2H, CH_2); 1.05 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm):

194.48, 164.87, 159.96, 152.84, 149.08, 145.04, 138.46, 131.43, 129.89, 128.22, 124.98, 123.99, 123.48, 123.32, 117.19, 115.65, 113.02, 108.58, 56.51, 50.81, 32.80, 29.38, 27.01, 19.03; ESI-MS: m/z Calcd for $C_{28}H_{23}N_5O_4S$: 525.1471; Found: 526.2342 (M+).

(E)-12-(2-hydroxy-5-(3-tolyldiazenyl)phenyl)-3,3-dimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4r):

Color: Brown Solid; M.P: 242 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3053, 2954, 1630, 1590, 1484, 1364, 1277, 1087; ^{1}H NMR (400 MHz, DMSO): δ (ppm): 10.90 (s, 1H, OH), 7.98 (d, *J*=2Hz, 1H, ArH), 7.3-7.58 (m, 3H, ArH), 7.53 (s, 1H, ArH), 7.44-7.31 (m, 4H, ArH), 7.12 (d, *J*=8.4Hz, 1H, ArH), 6.89 (d, *J*=8.8Hz, 1H, ArH), 6.69 (s, 1H, CH), 2.40 (s, 3H, -CH_3), 2.30-2.19 (m, 4H, 2×CH_2), 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.48, 165.14, 159.45, 152.55, 145.54, 139.27, 136.64, 131.74, 128.14, 126.88, 123.15, 122.62, 120.31, 117.88, 116.92, 112.32, 108.83, 50.89, 45.19, 32.76, 29.49, 27.10, 21.37, 21.05. ESI-MS: m/z Calcd for $C_{29}H_{26}N_4O_2S$: 494.1776; Found: 495.4514 (M+).

(E)-12-(2-hydroxy-5-(p-tolyldiazenyl)phenyl)-3,3-dimethyl-2,3,4,12-tetrahydro-1*H*-benzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4s):

Color: Brown Solid; M.P: 242 ˚C; FT-IR (KBr) (ϑmax/cm^{-1}): 3053, 2954, 1630, 1590, 1484, 1364, 1277, 1087; ^{1}H NMR (400 MHz, DMSO): δ (ppm): 10.87 (s, 1H, OH), 7.98 (d, *J*=2Hz, 1H, ArH), 7.71 (m, 3H, ArH), 7.60 (dd, *J*=8.8Hz, 2.4Hz, 1H, ArH), 7.50 (d, *J*=8.4Hz, 1H, ArH), 7.35 (m, 2H, ArH), 7.20 (t, *J*=7.6Hz, 1H, ArH), 7.00 (t, *J*=7.6Hz, 1H, ArH), 6.87 (d, *J*=8.4Hz, 1H, ArH), 6.72 (s, 1H, CH), 2.38 (s, 3H, -CH_3), 2.21 (m, 2H, CH_2), 2.05 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO): δ (ppm): 194.55, 165.22, 159.31, 158.33, 150.55, 145.45, 141.20, 138.78, 130.40, 127.36, 125.87, 124.51, 123.27, 121.25, 118.19, 116.91, 112.59, 108.96, 52.45, 50.89, 45.16, 32.78, 29.64, 27.10, 26.60, 26.17, 21.43; ESI-MS: m/z Calcd for $C_{29}H_{26}N_4O_2S$: 494.1776; Found: 495.4514 (M+).

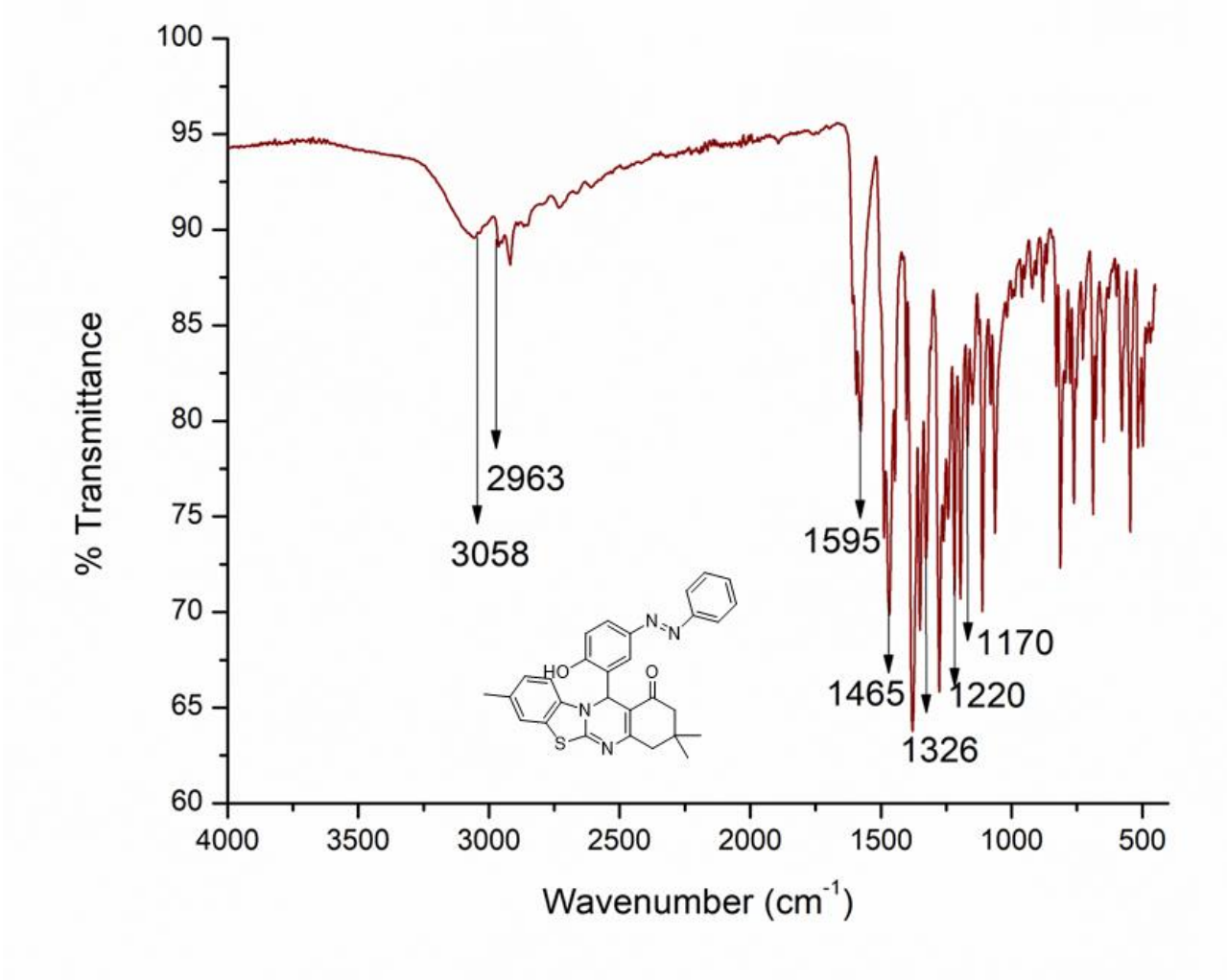


Figure. 1. IR Spectrum of compound **4a**

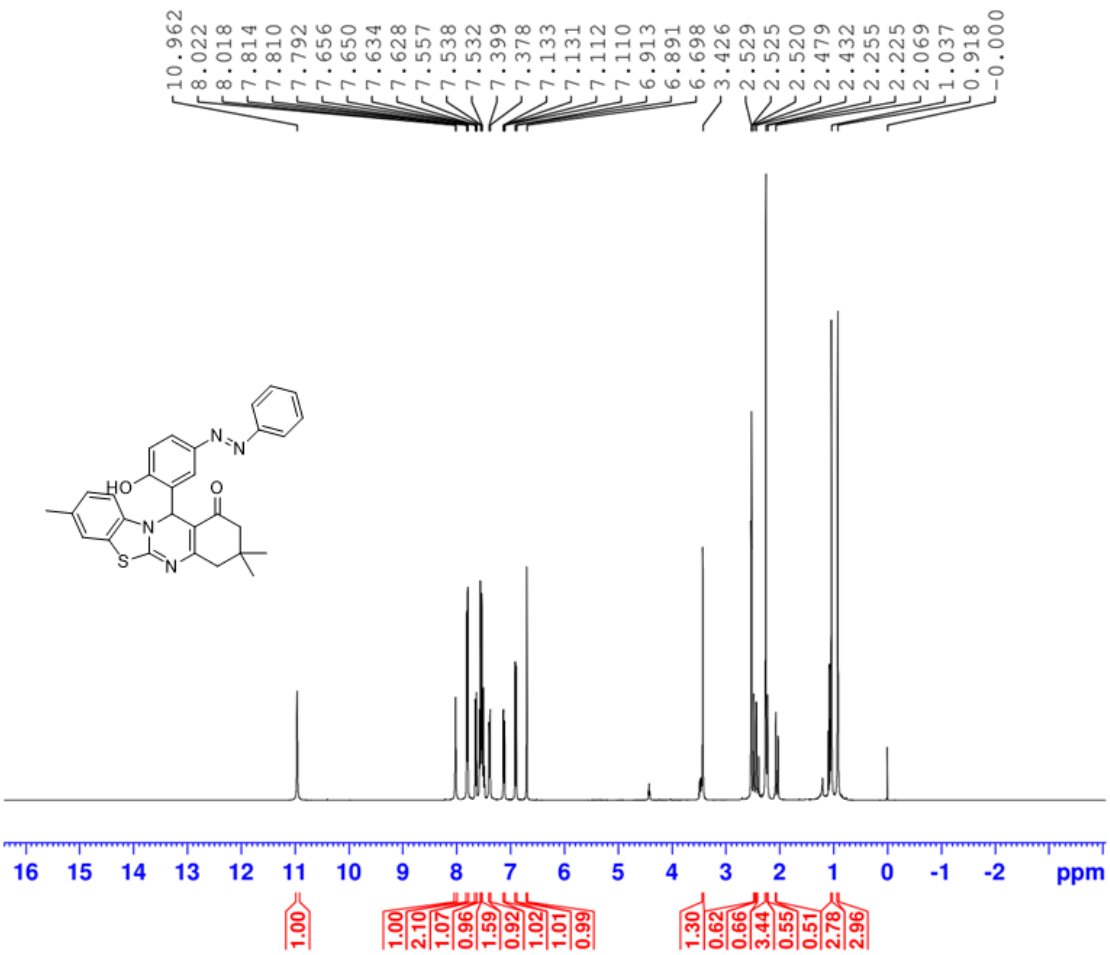


Figure. 2. ^{1}H NMR Spectrum of compound **4a**

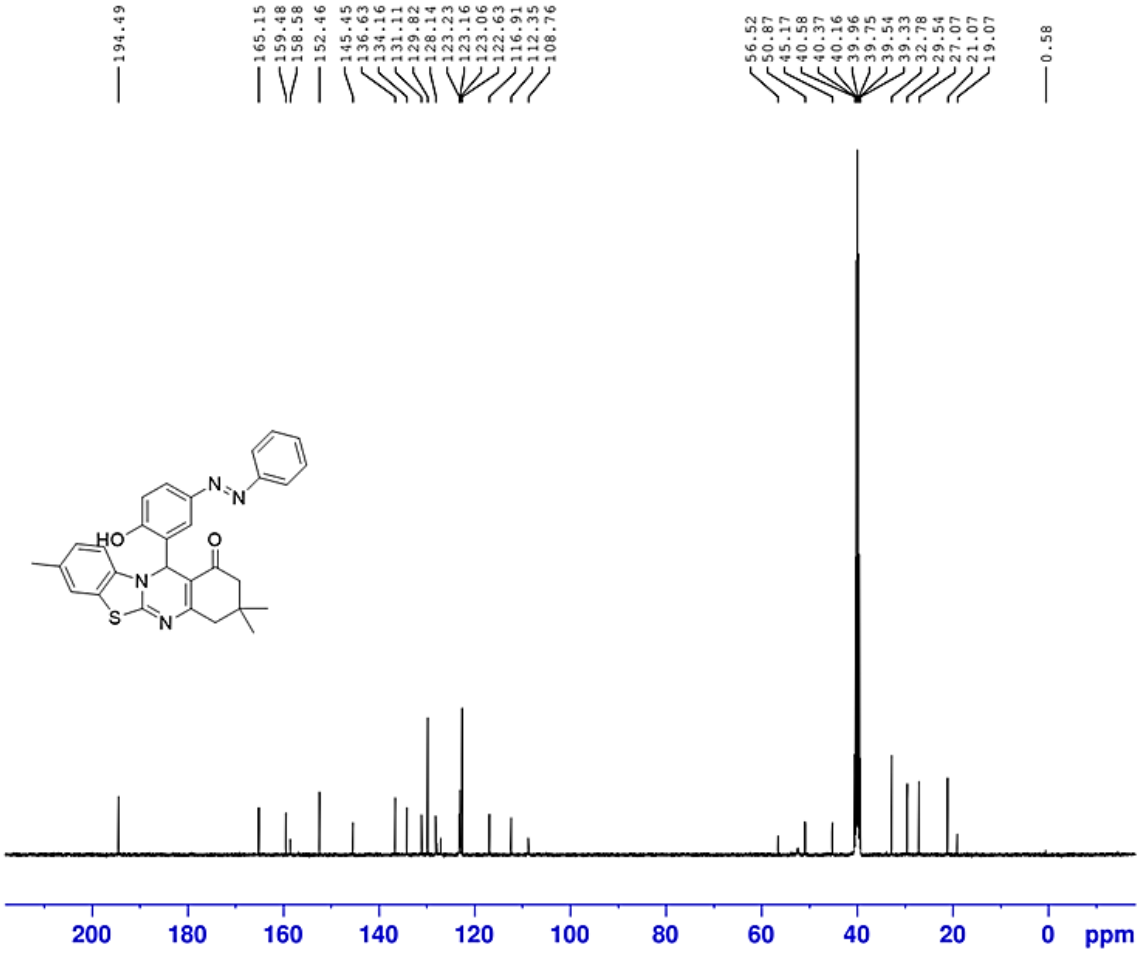


Figure. 3. ^{13}C NMR Spectrum of compound **4a**

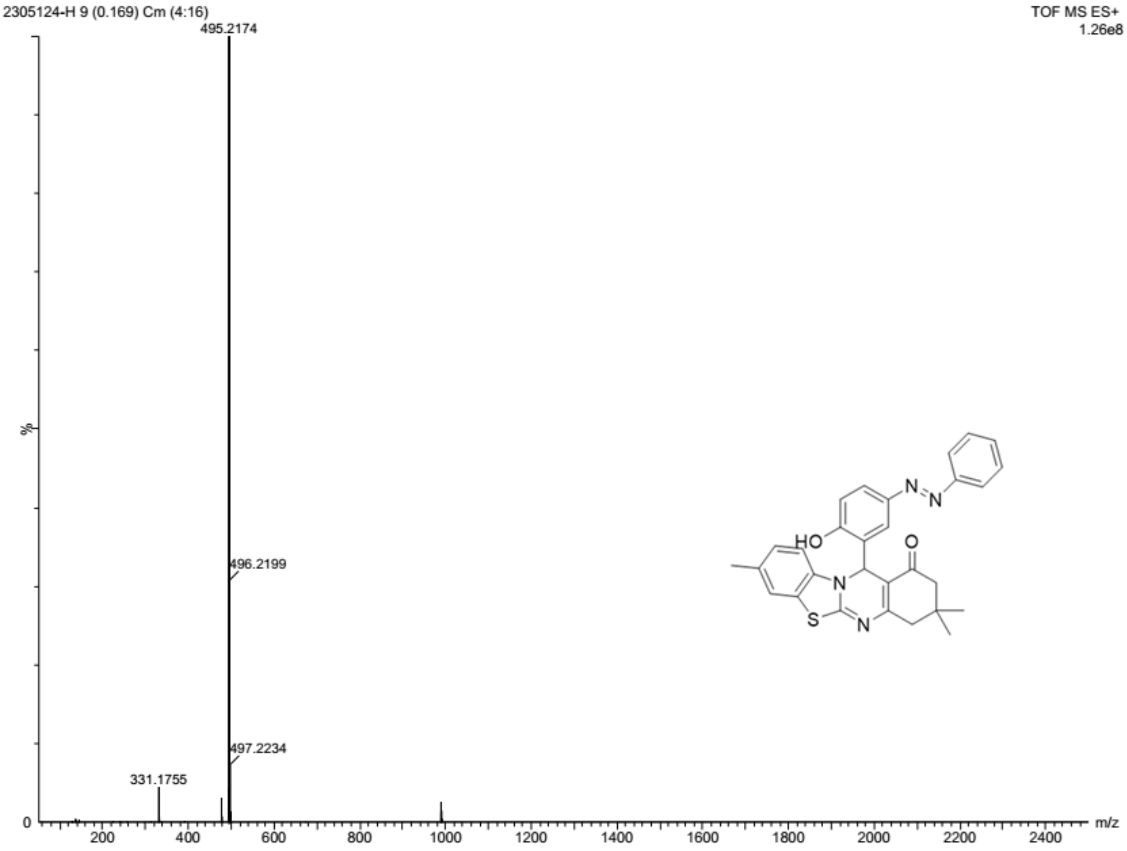


Figure. 4. Mass spectrum of compound **4a**

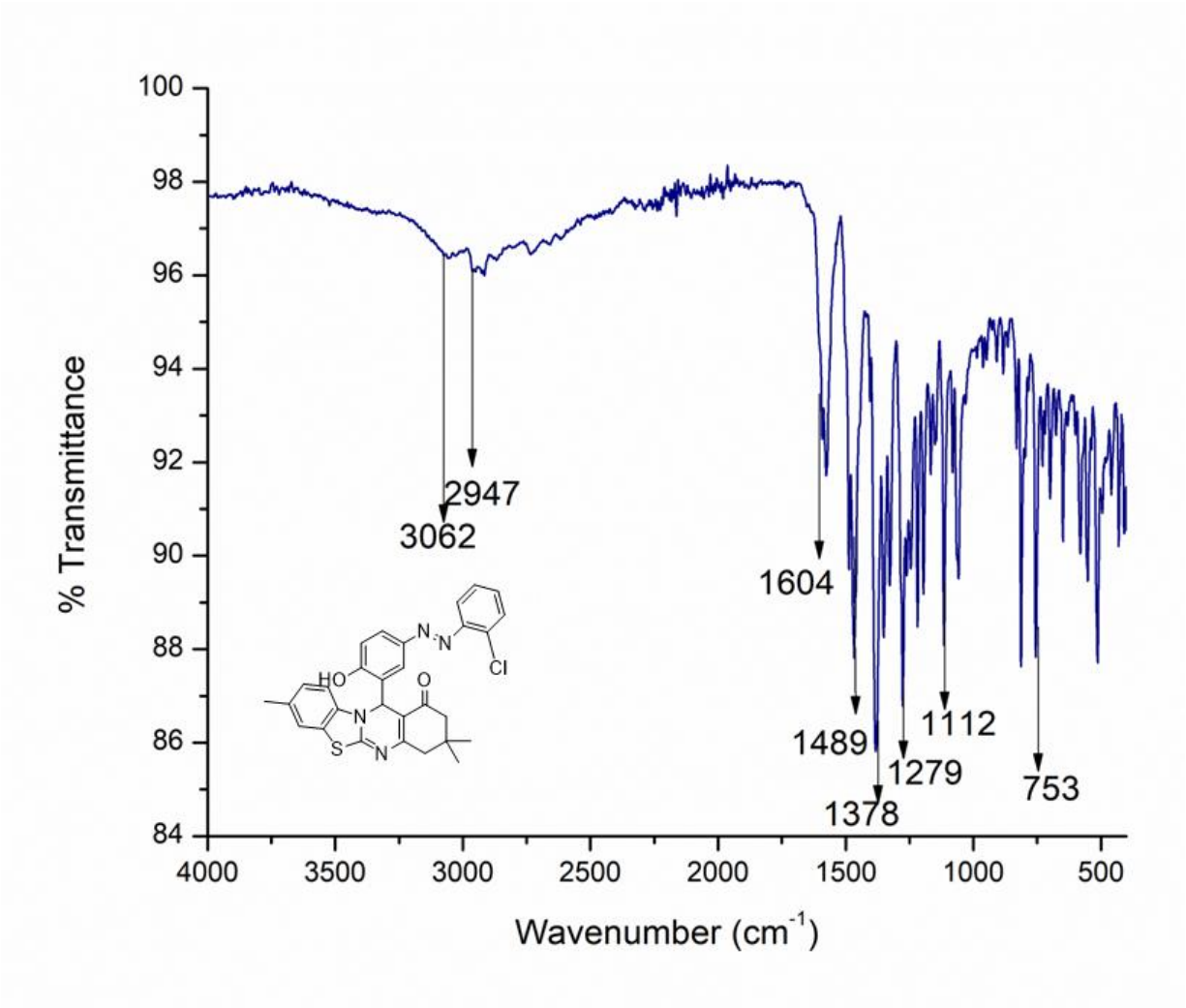


Figure. 5. IR Spectrum of compound **4b**

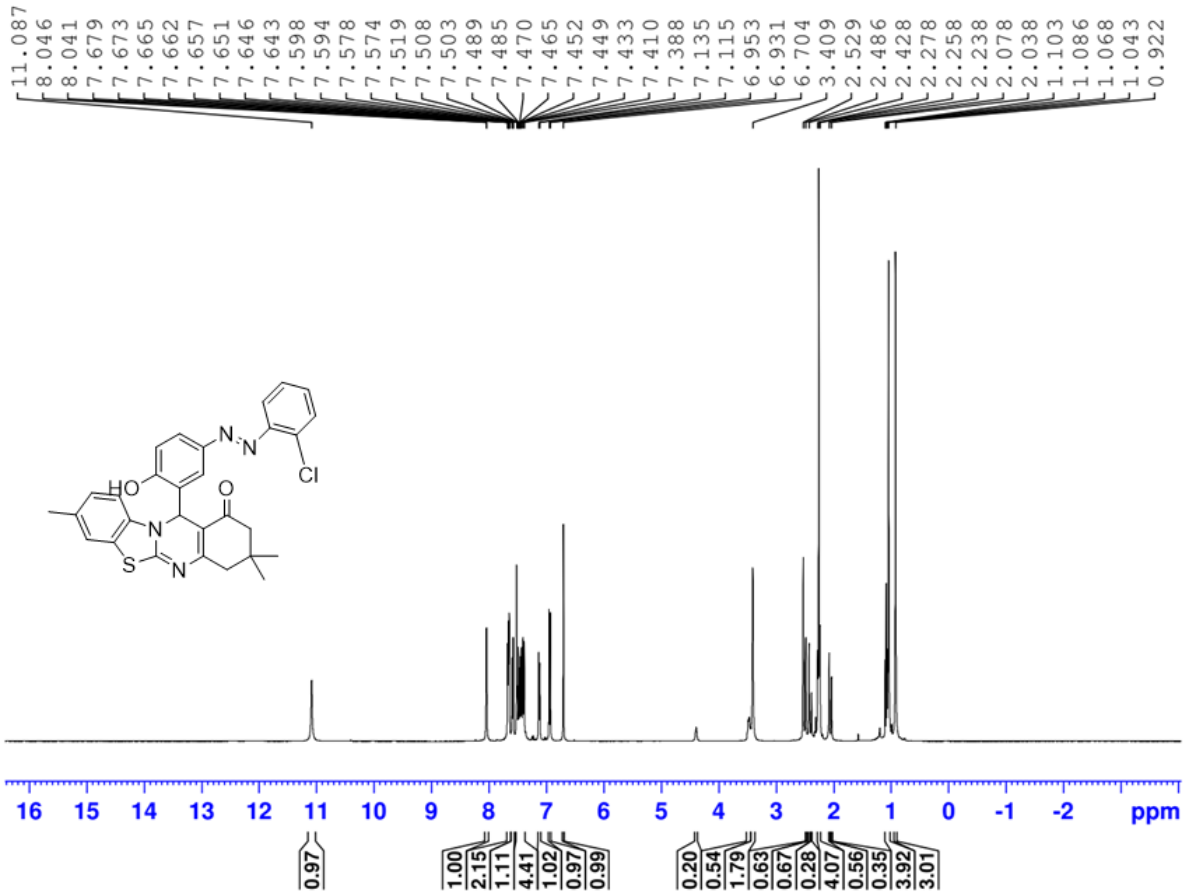


Figure. 6. ^{1}H NMR Spectrum of compound **4b**

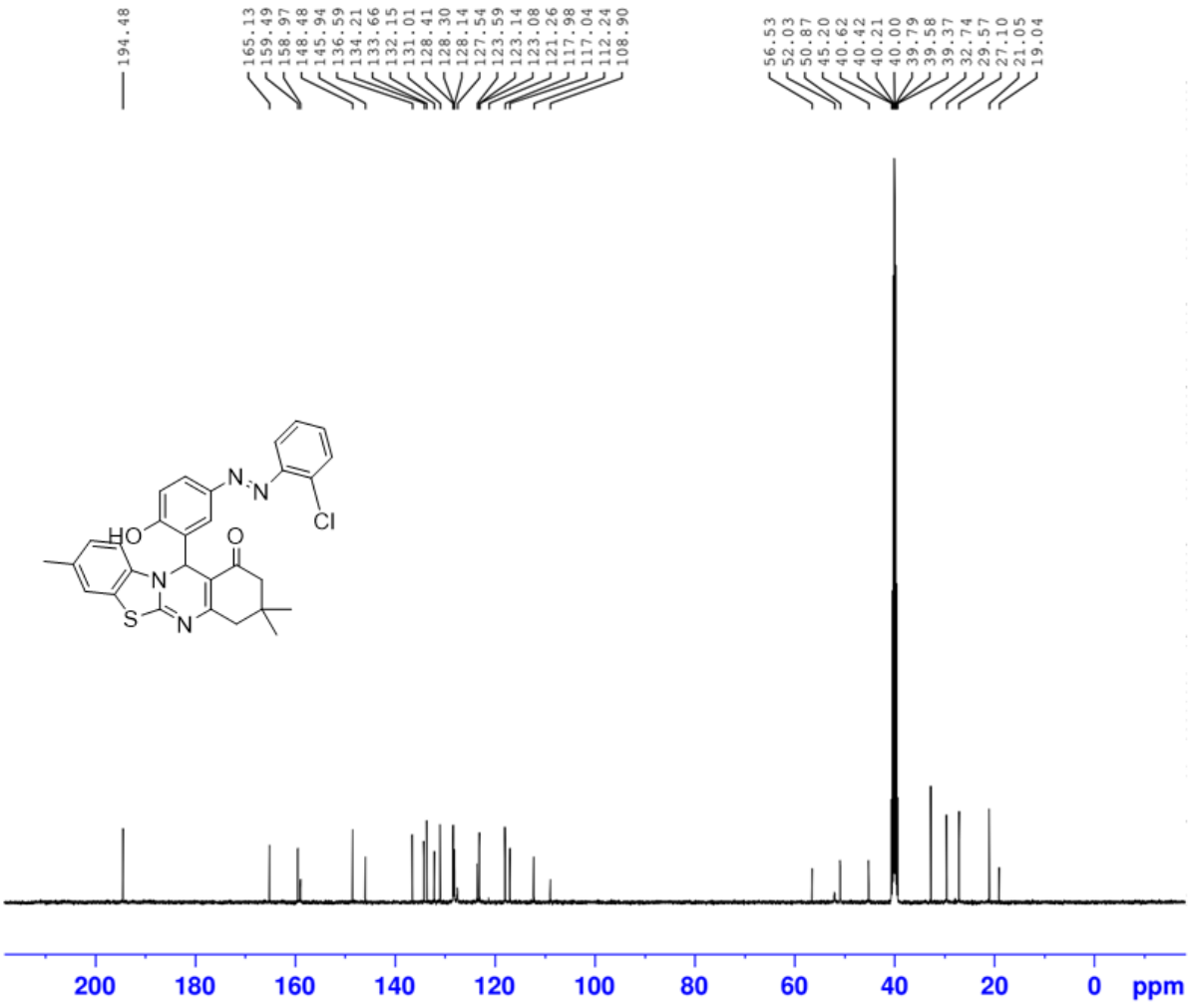


Figure. 7. ^{13}C NMR Spectrum of compound **4b**

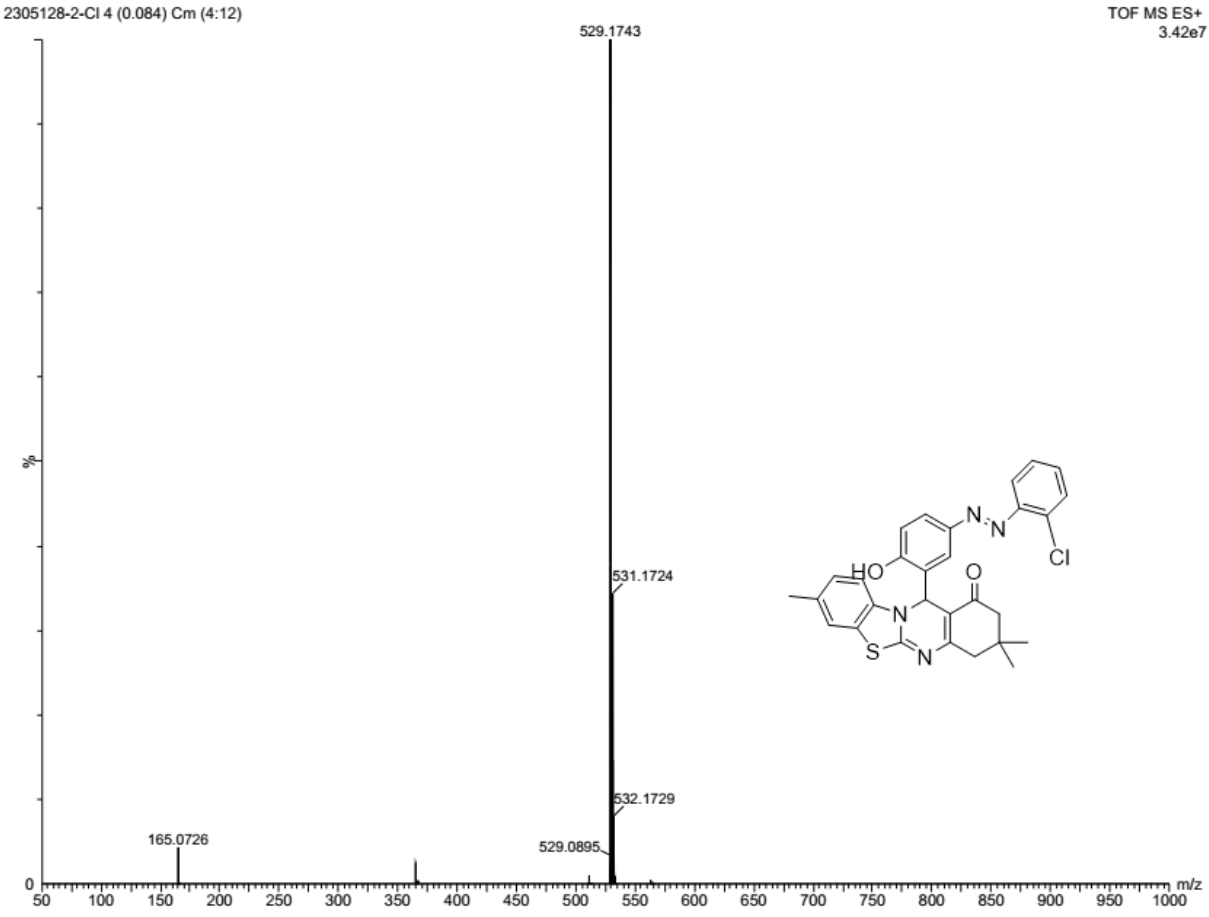


Figure. 8. Mass spectrum of compound **4b**

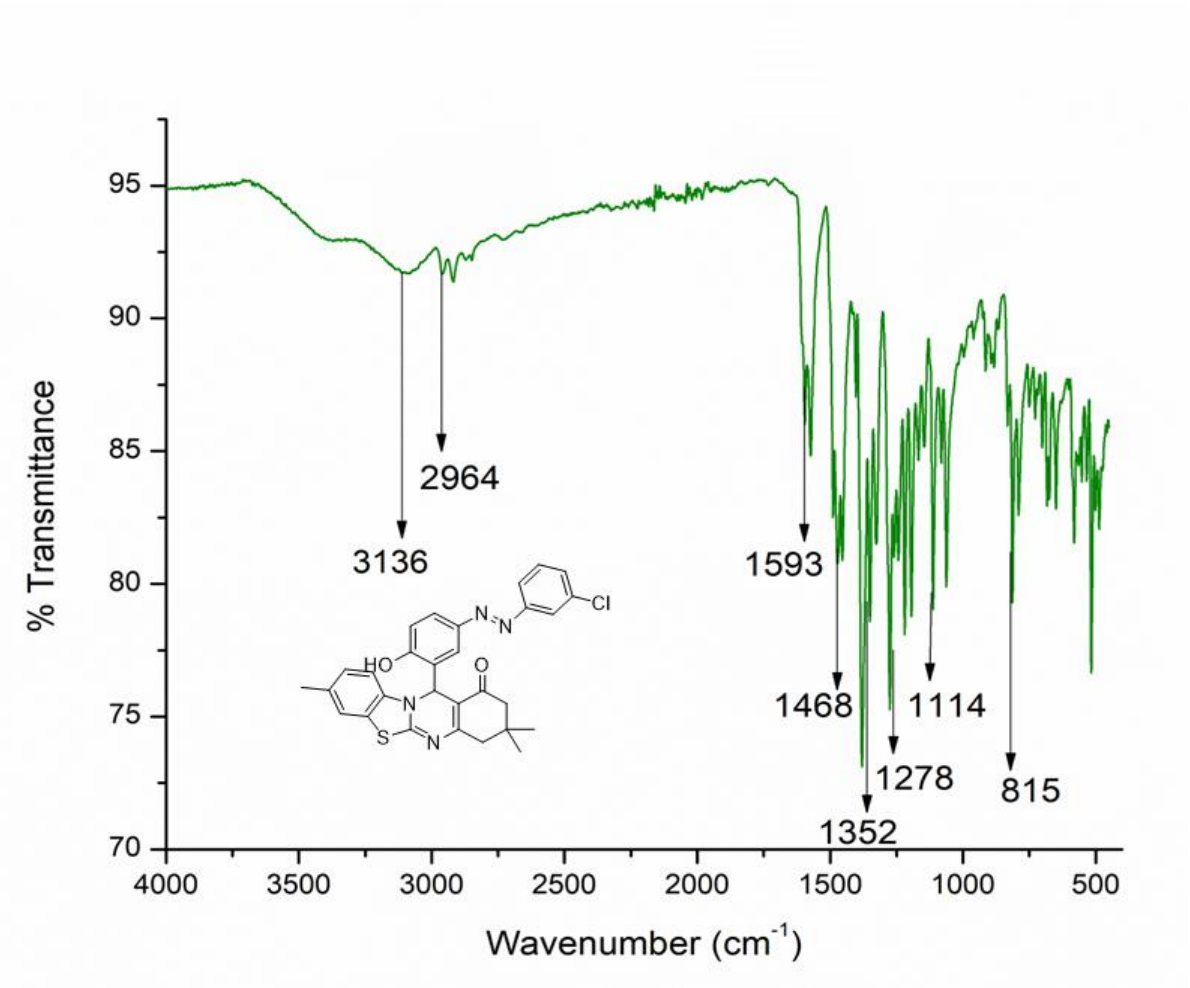


Figure. 9. IR Spectrum of compound **4c**

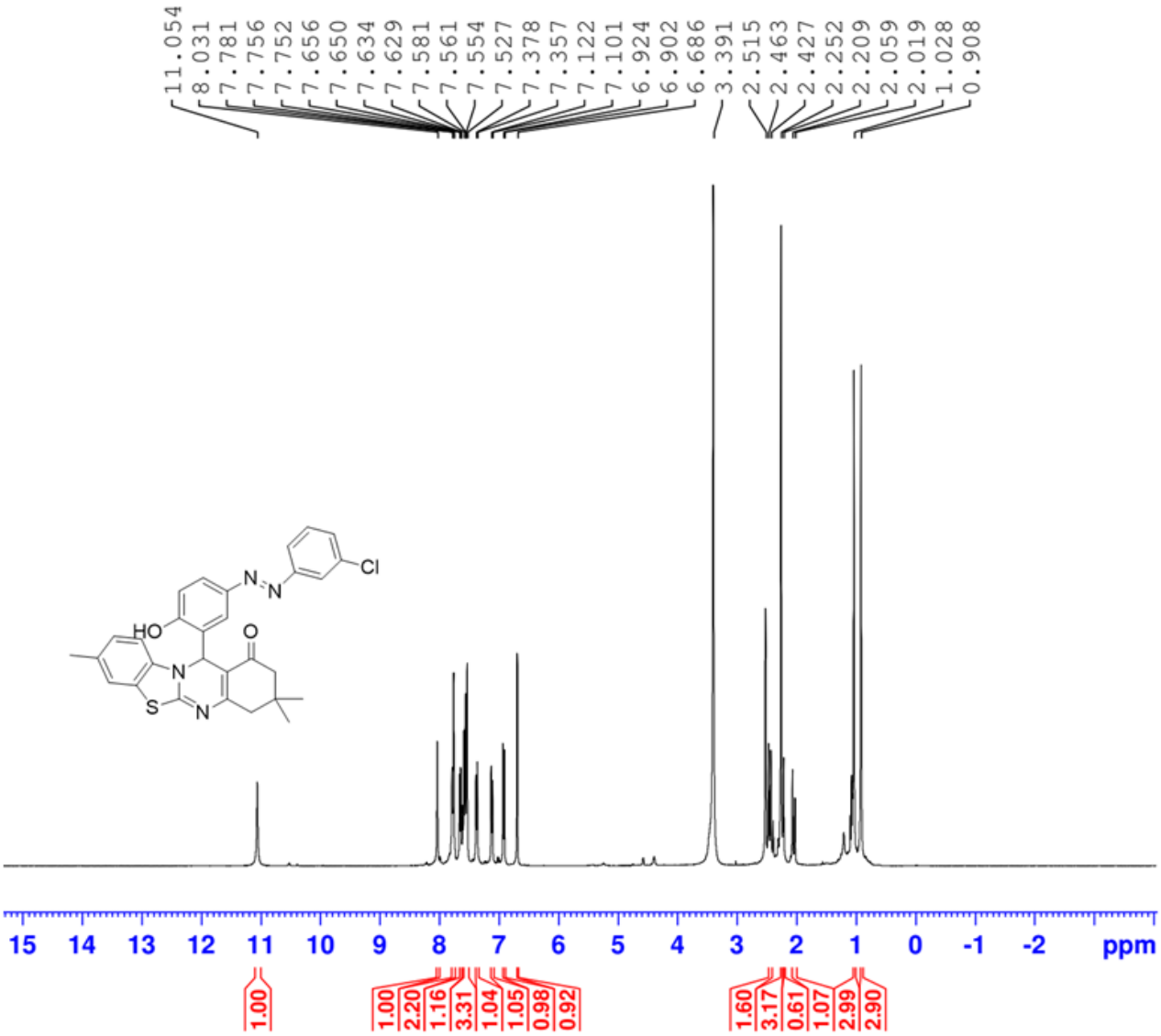


Figure. 10. ^{1}H NMR Spectrum of compound **4c**

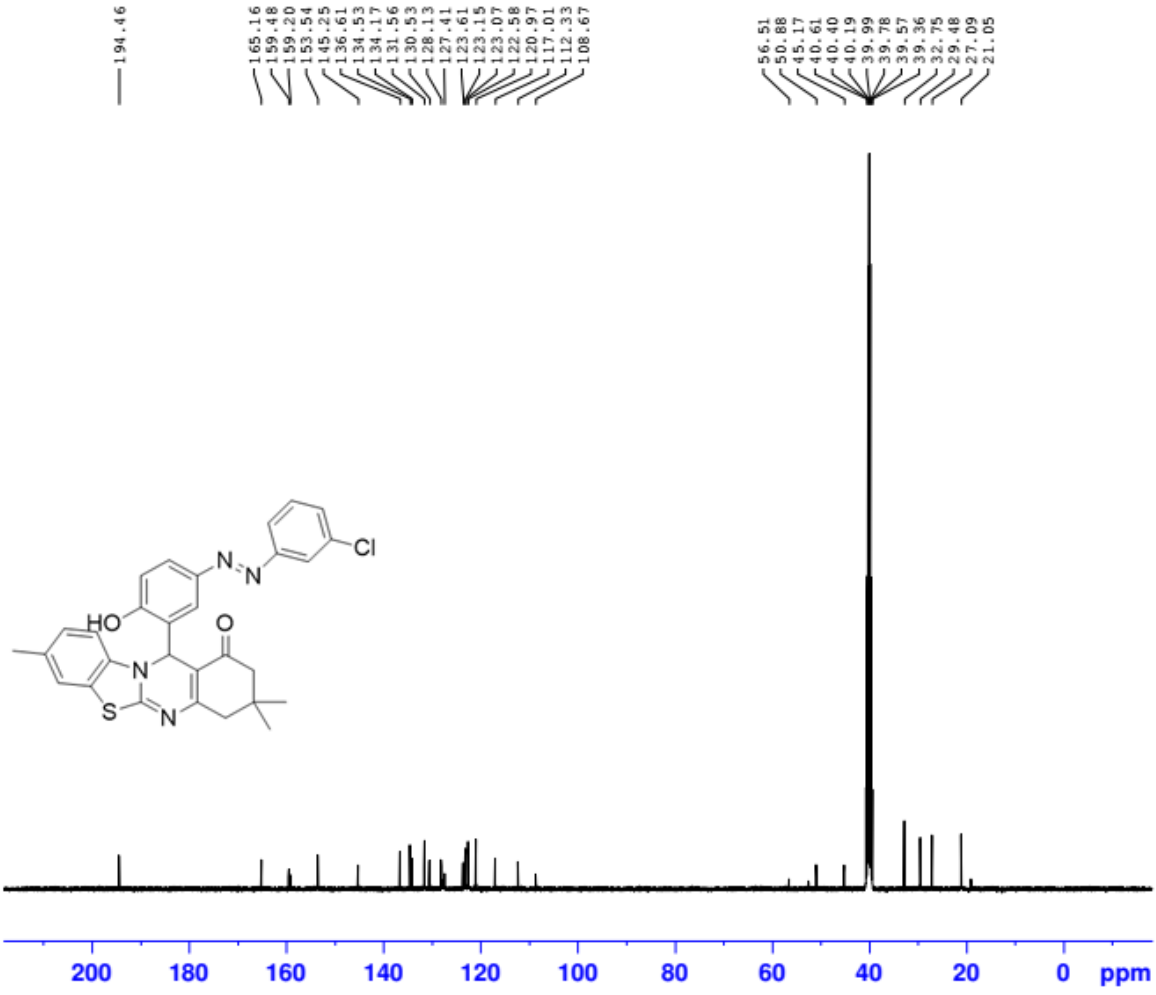


Figure. 11. ^{13}C NMR Spectrum of compound **4c**

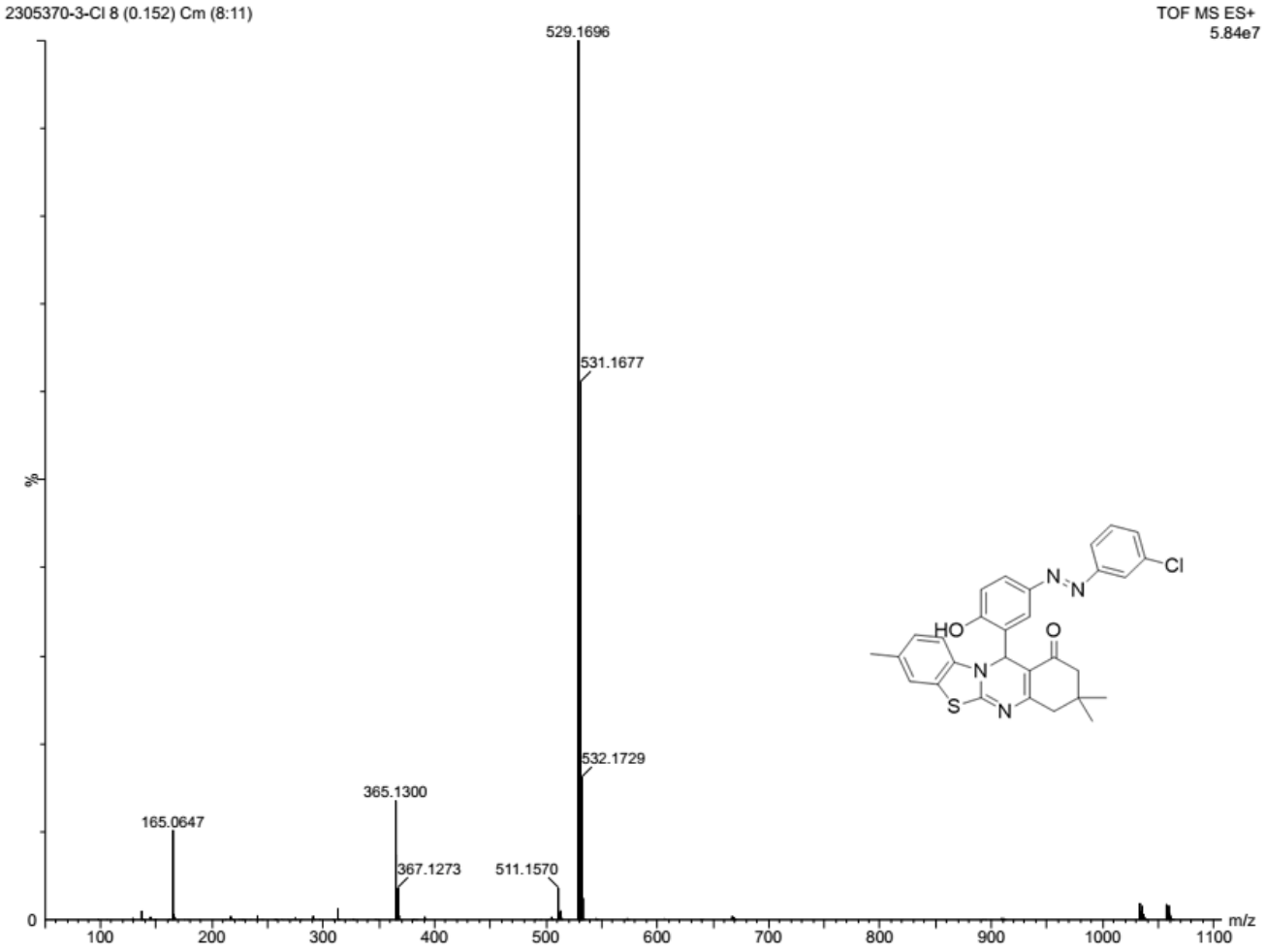


Figure. 12. Mass spectrum of compound **4c**

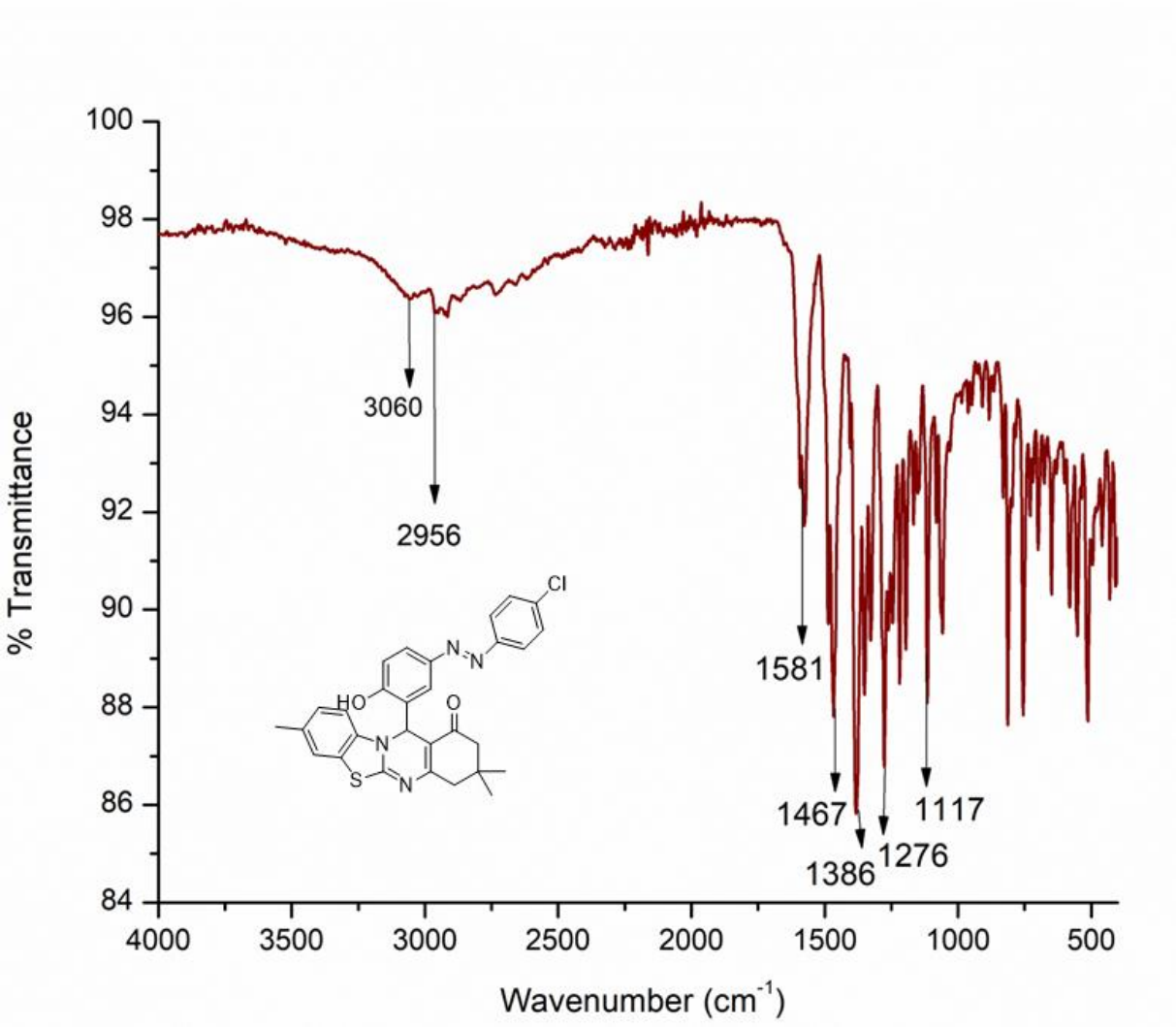


Figure. 13. IR Spectrum of compound **4d**

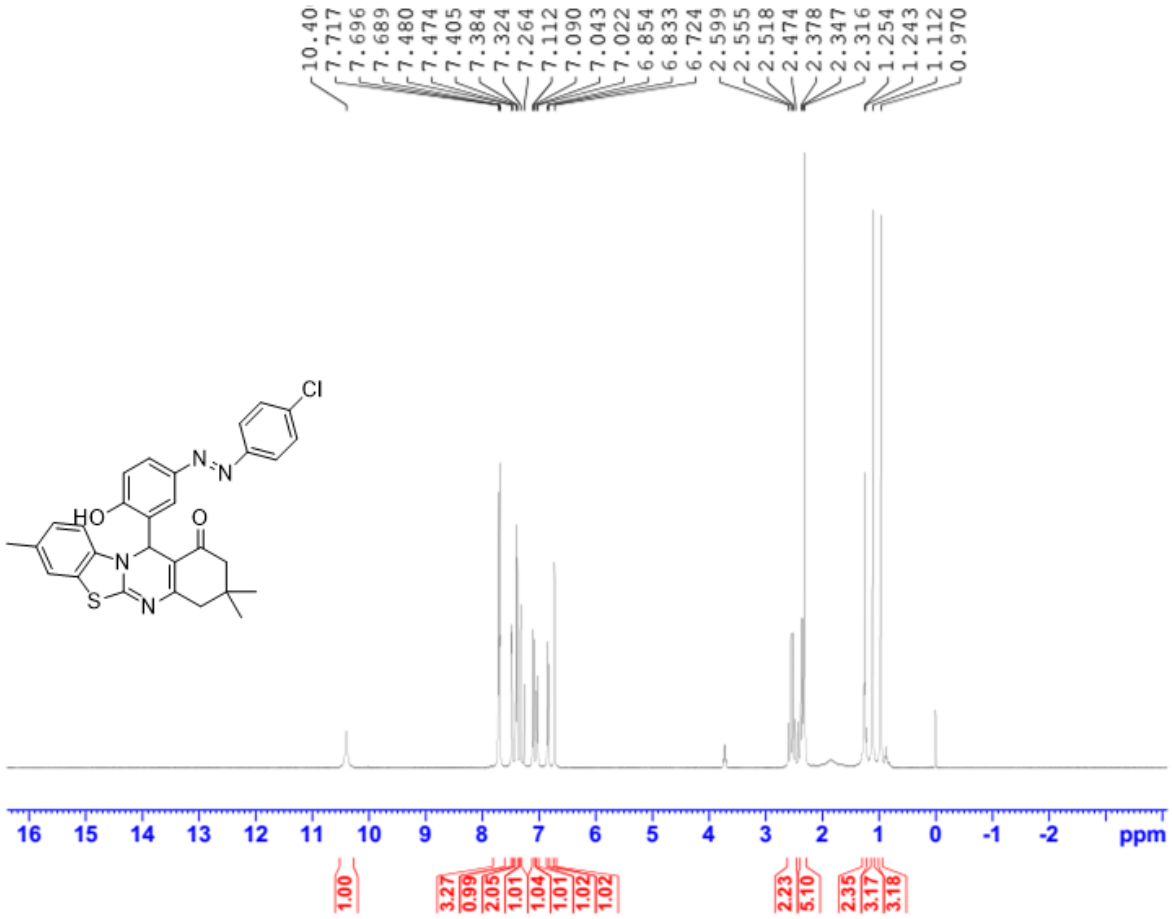


Figure. 14. ^{1}H NMR Spectrum of compound **4d**

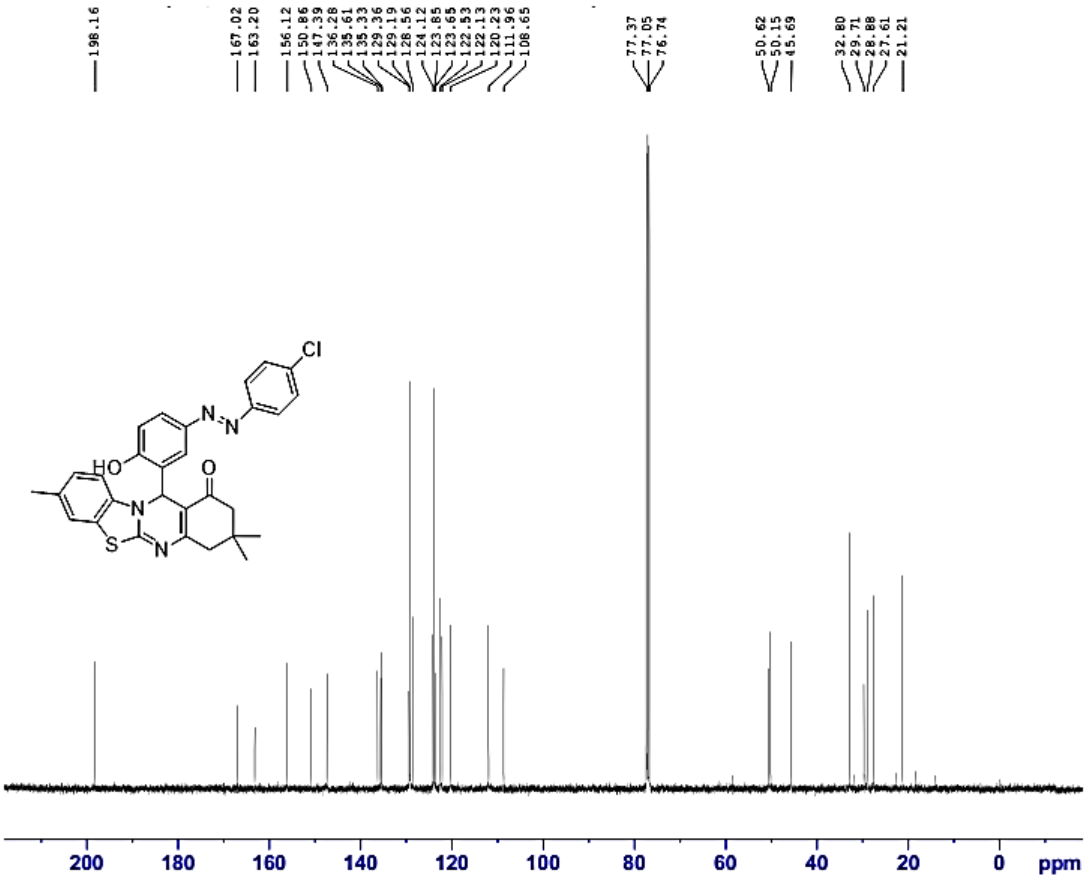


Figure. 15. ^{13}C NMR Spectrum of compound **4d**

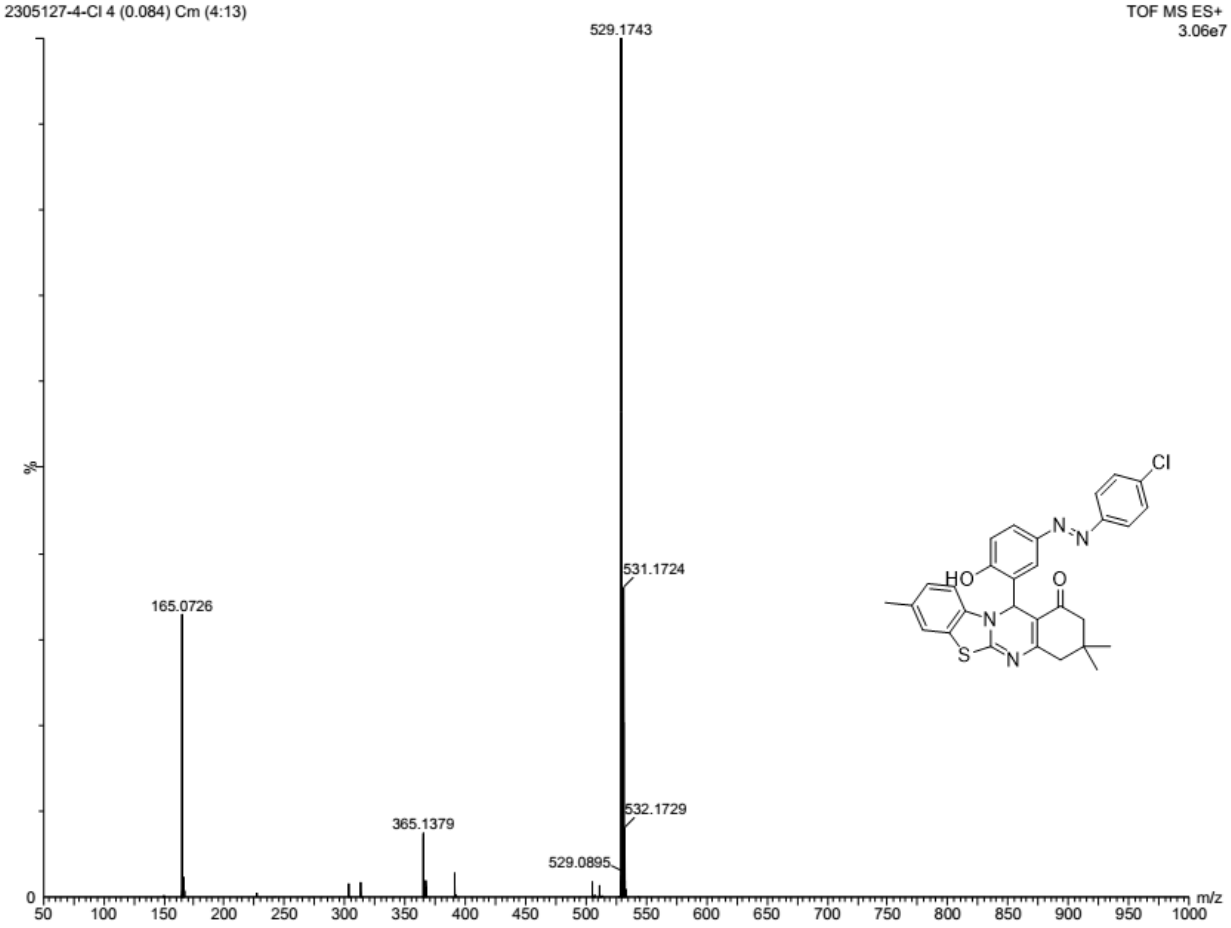


Figure. 16. Mass spectrum of compound **4d**

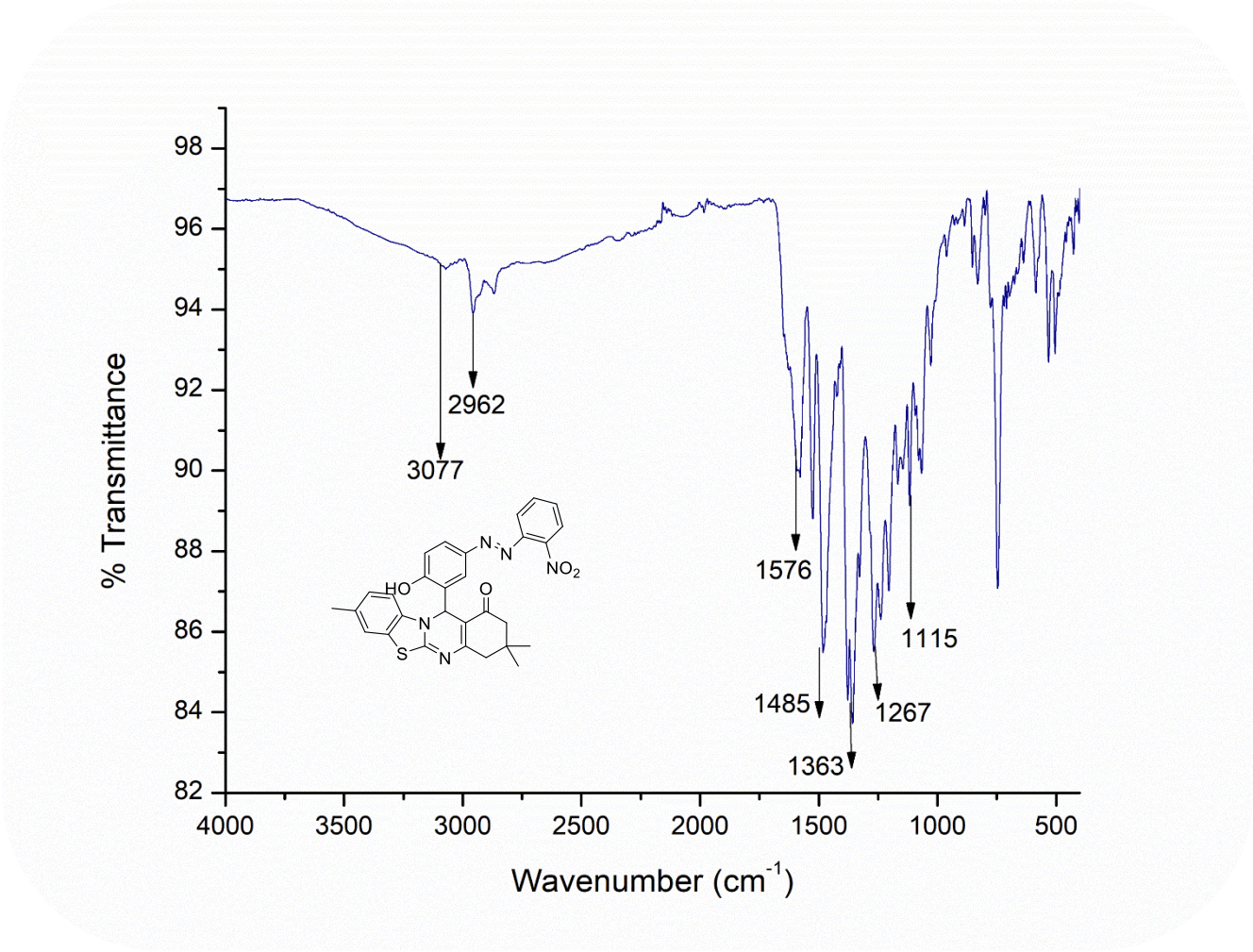


Figure. 17. IR Spectrum of compound **4e**

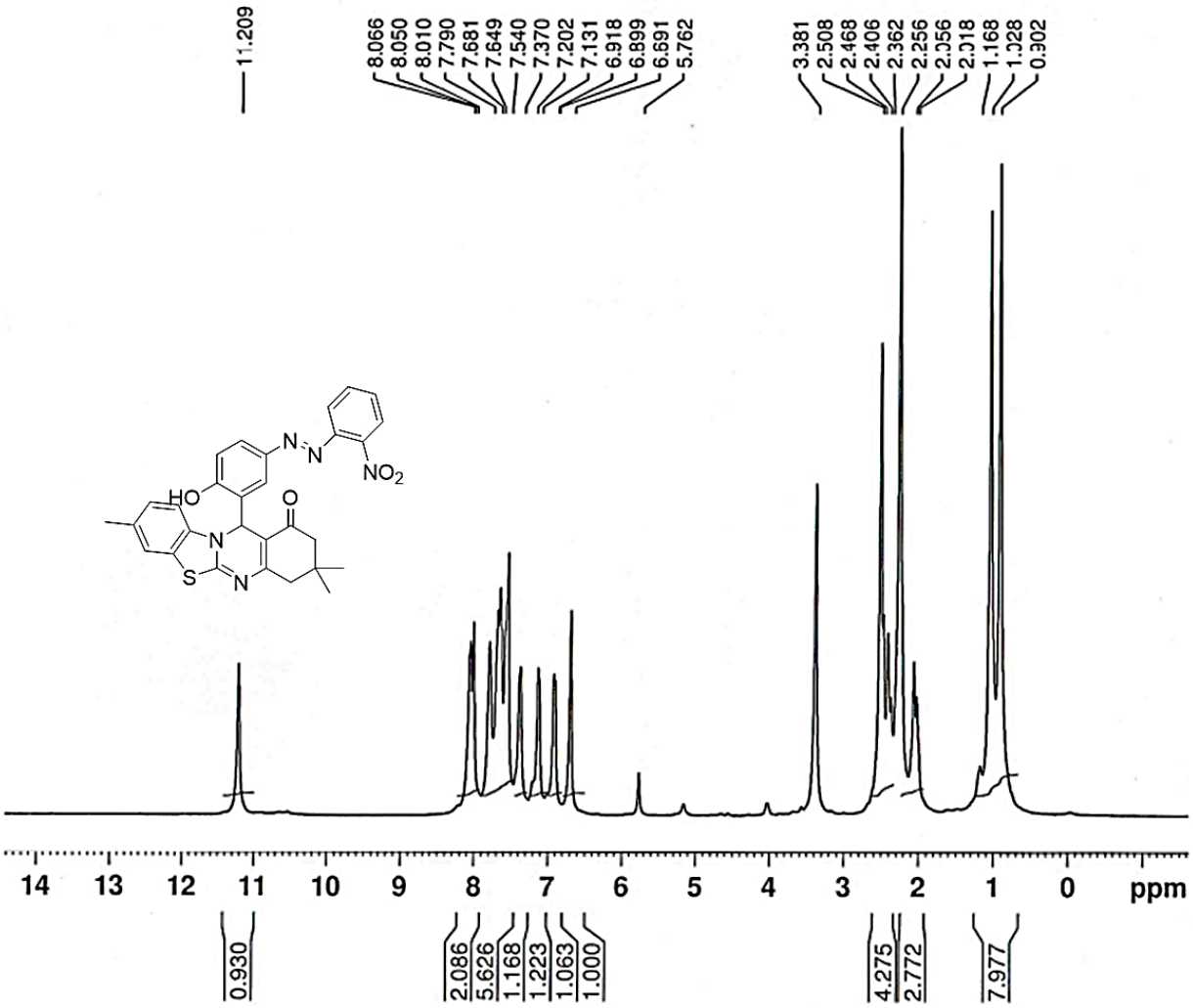


Figure. 18. ^{1}H NMR Spectrum of compound **4e**

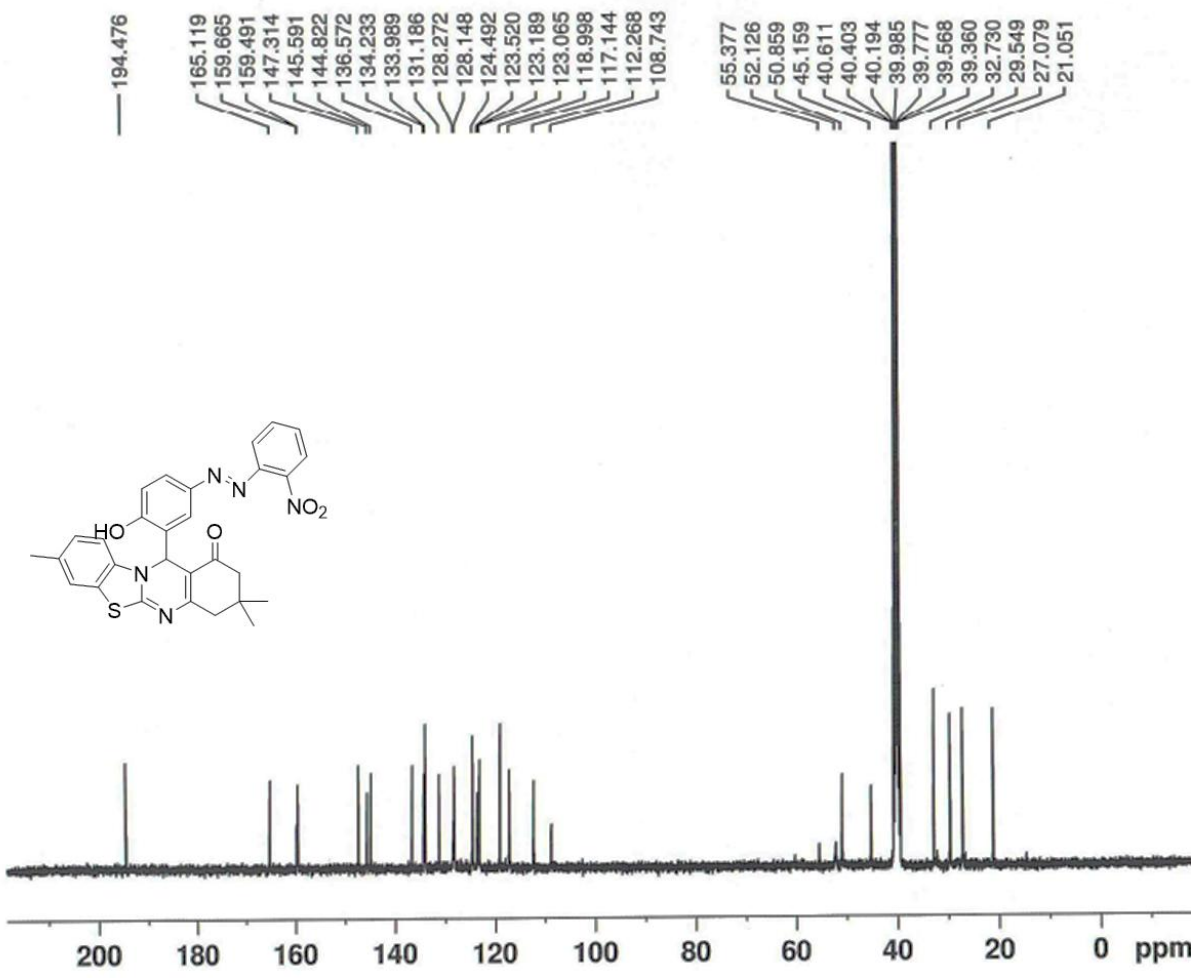


Figure. 19. ^{13}C NMR Spectrum of compound **4e**

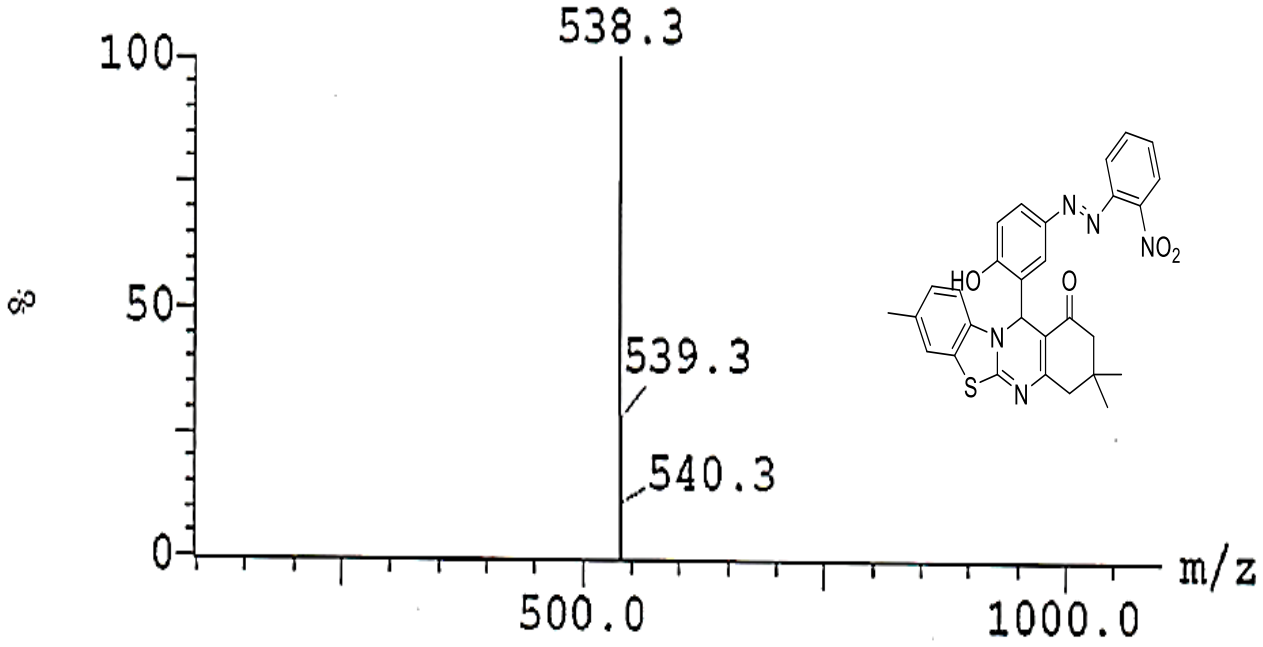


Figure. 20. Mass spectrum of compound **4e**

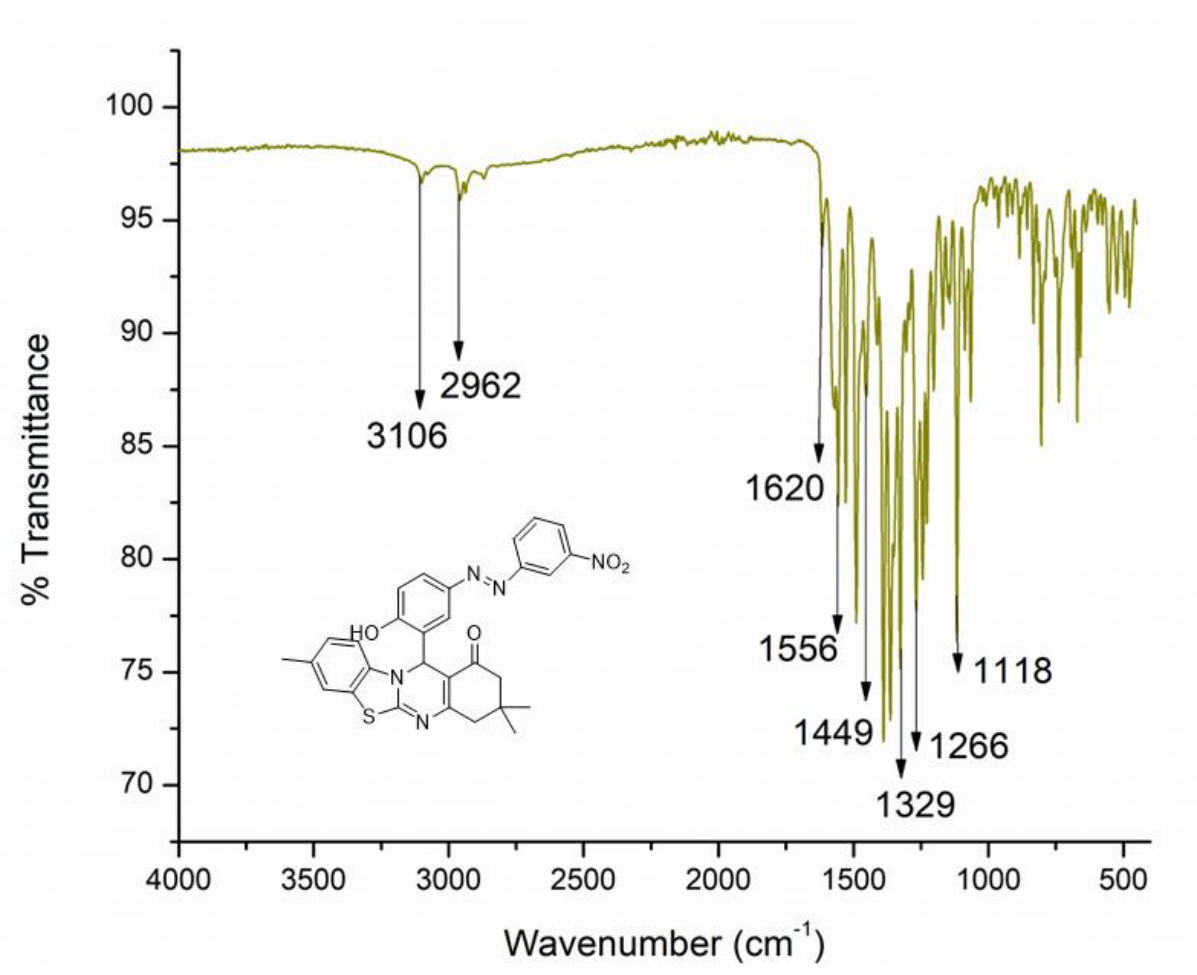


Figure. 21. IR Spectrum of compound **4f**

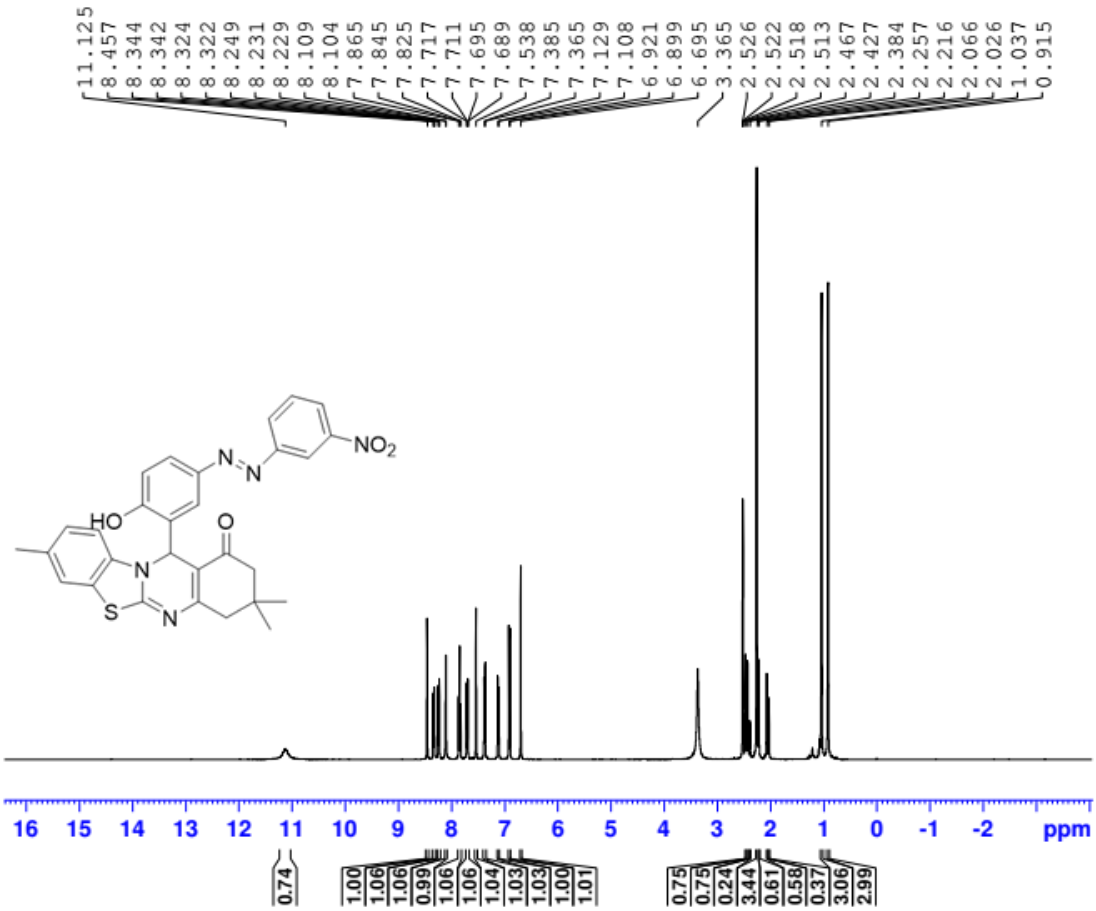


Figure. 22. ^{1}H NMR Spectrum of compound **4f**

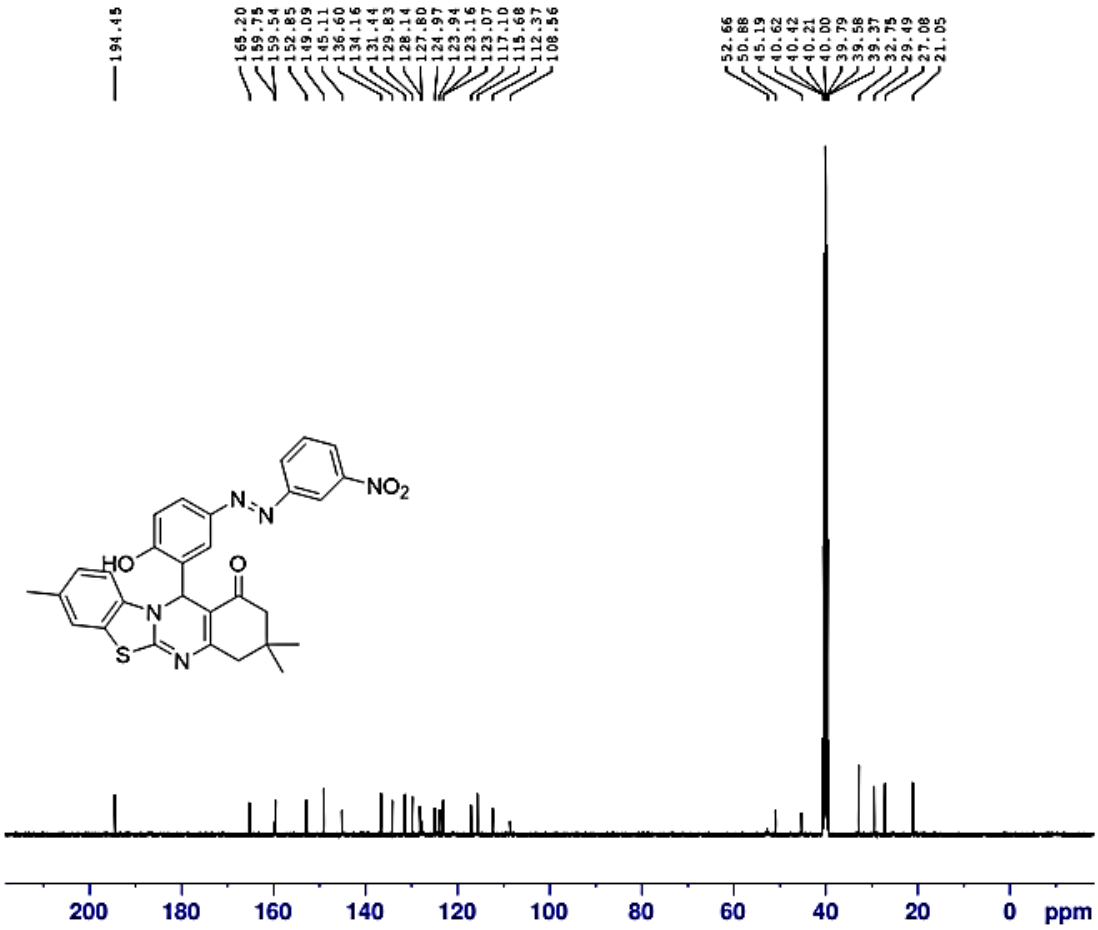


Figure. 23. ^{13}C NMR Spectrum of compound **4f**

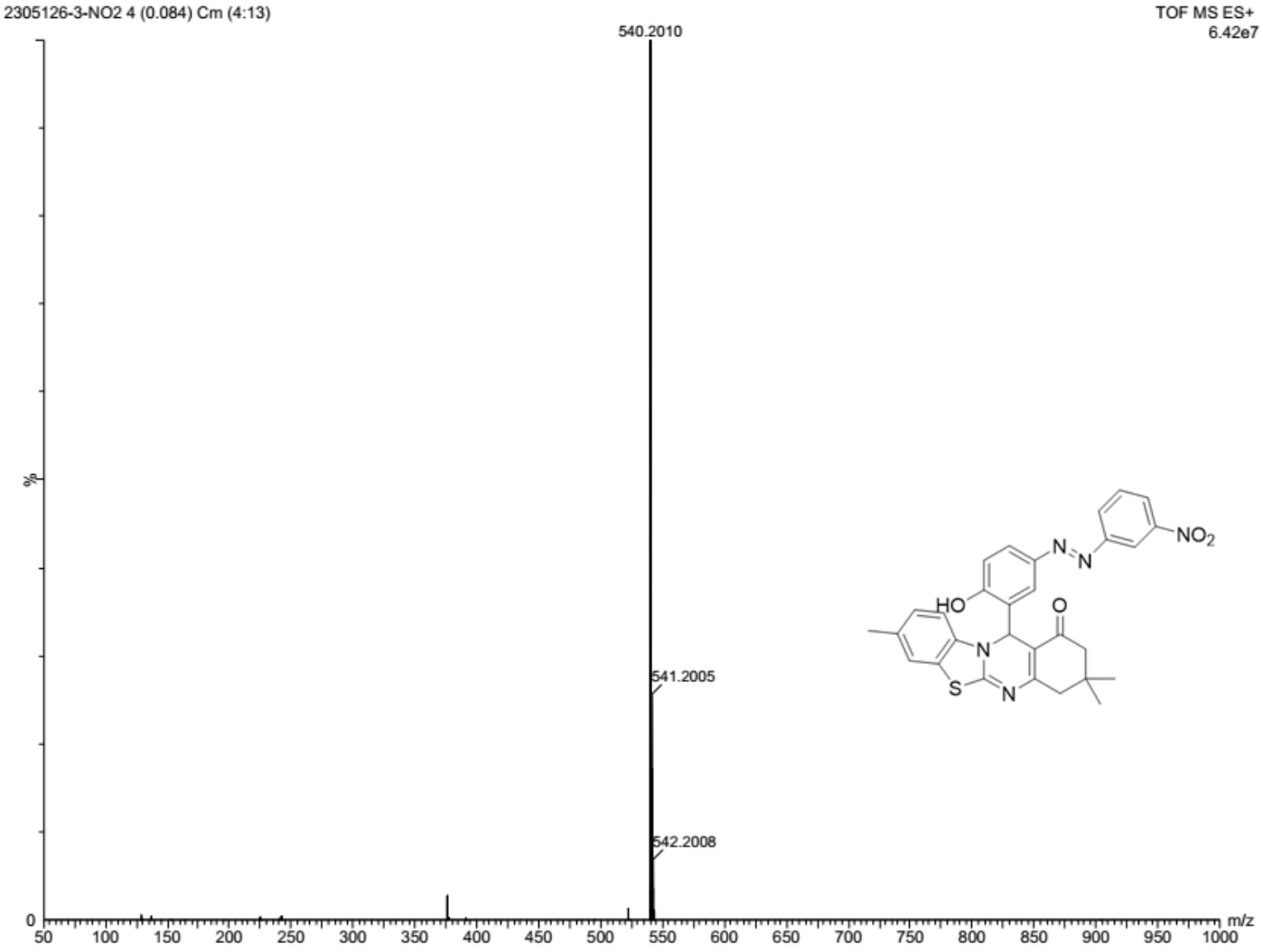


Figure. 24. Mass spectrum of compound **4f**

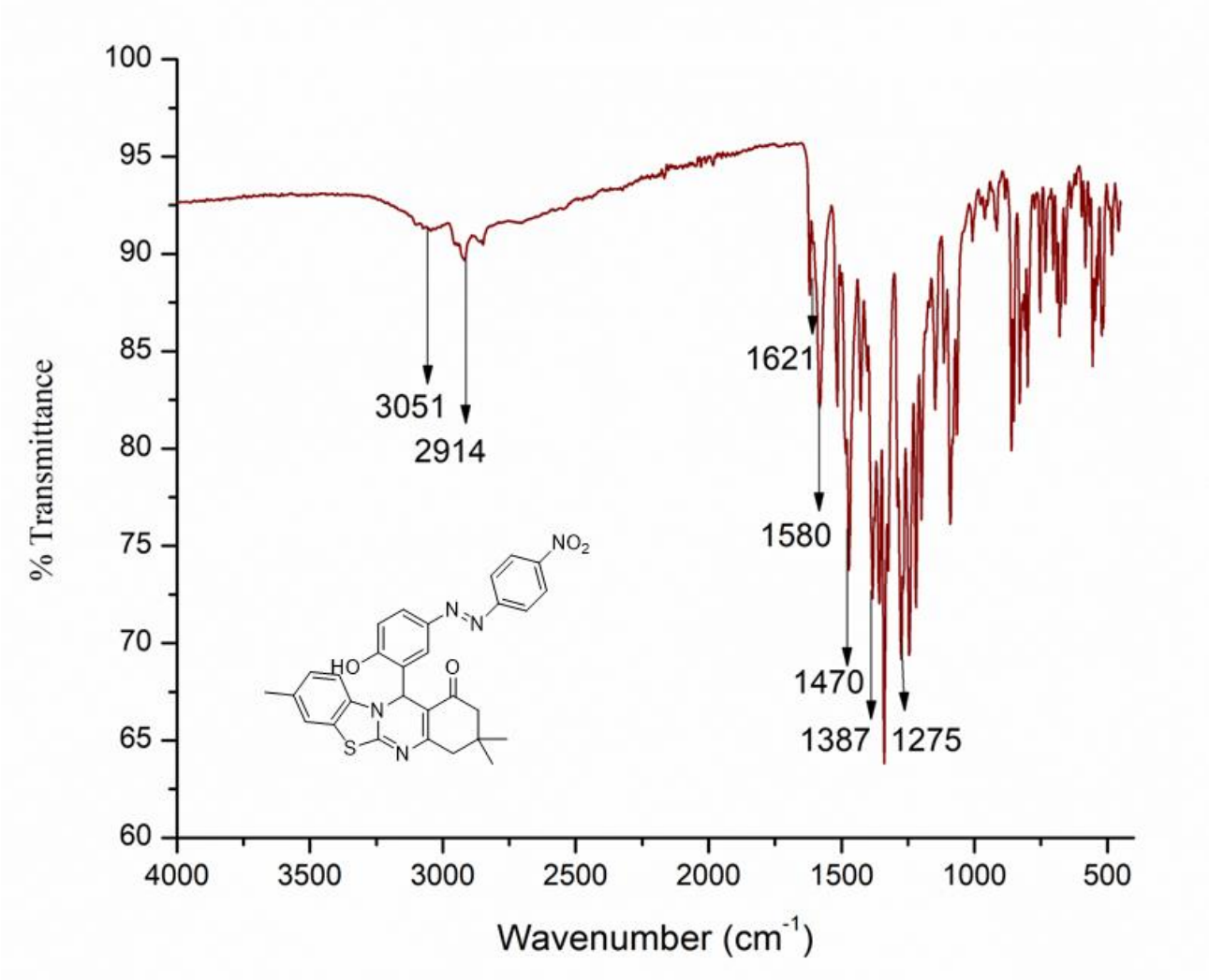


Figure. 25. IR Spectrum of compound **4g**

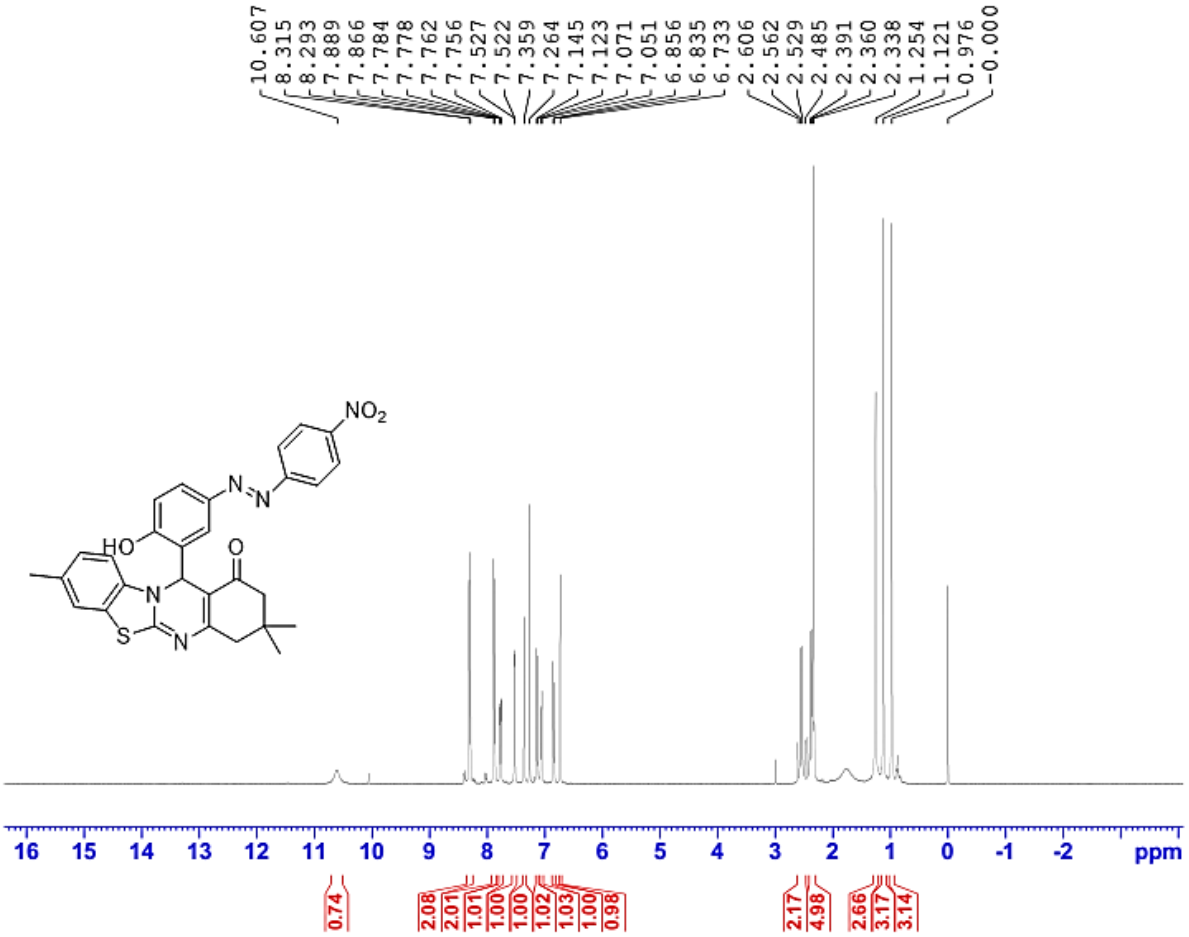


Figure. 26. ^{1}H Spectrum of compound **4g**

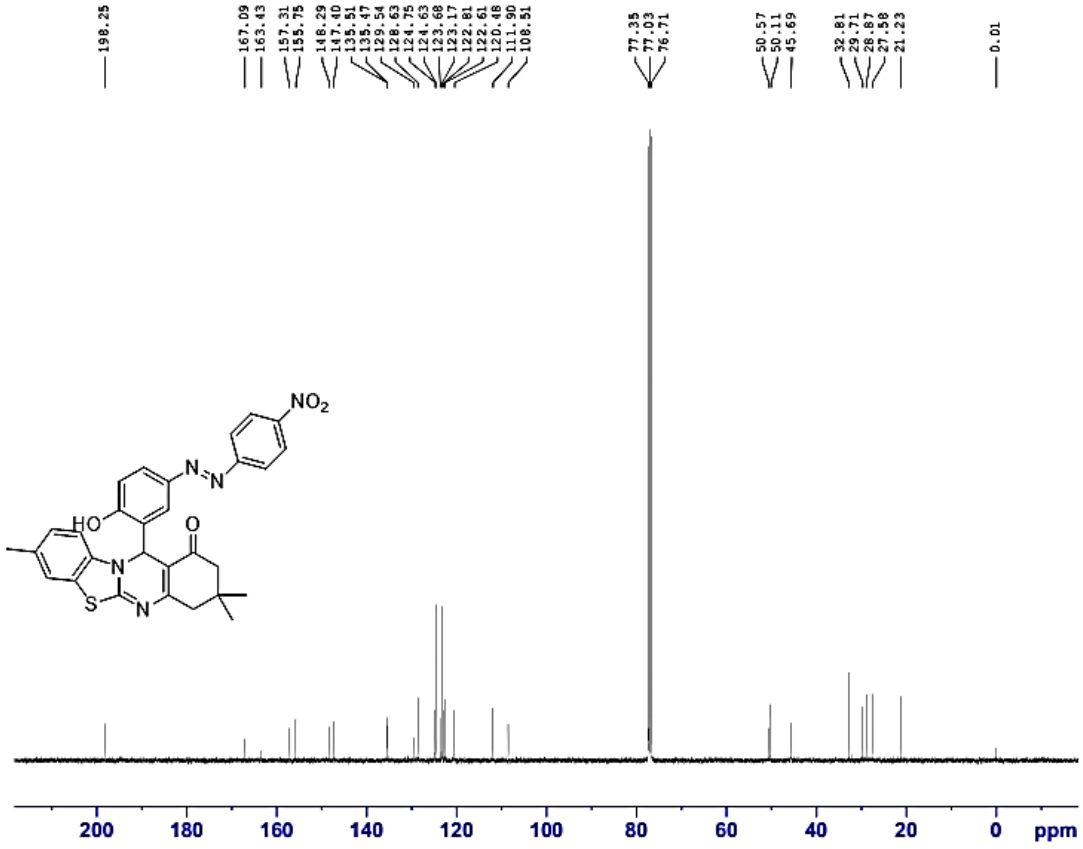


Figure. 27. ^{13}C NMR Spectrum of compound **4g**

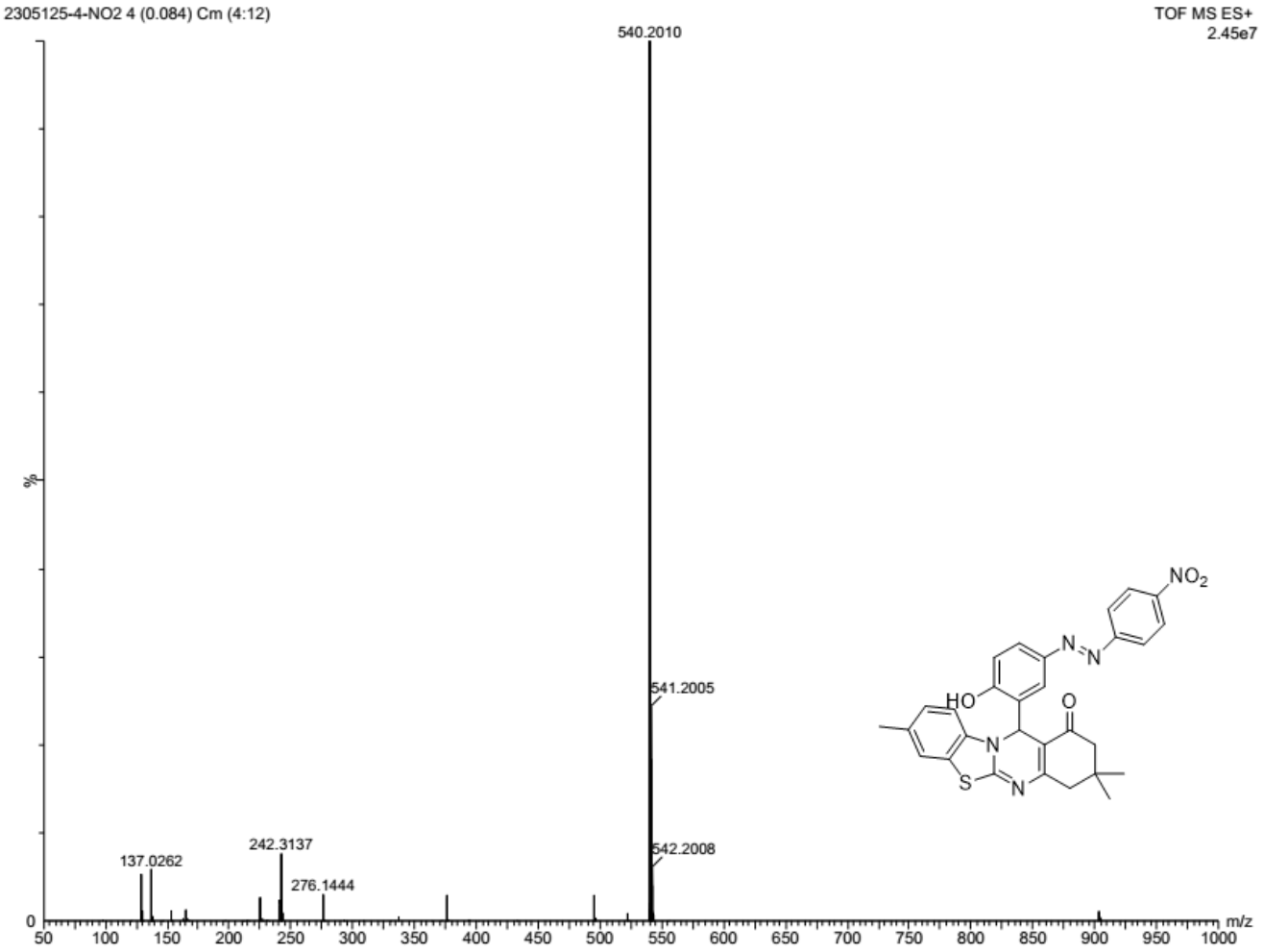


Figure. 28. Mass spectrum of compound **4g**

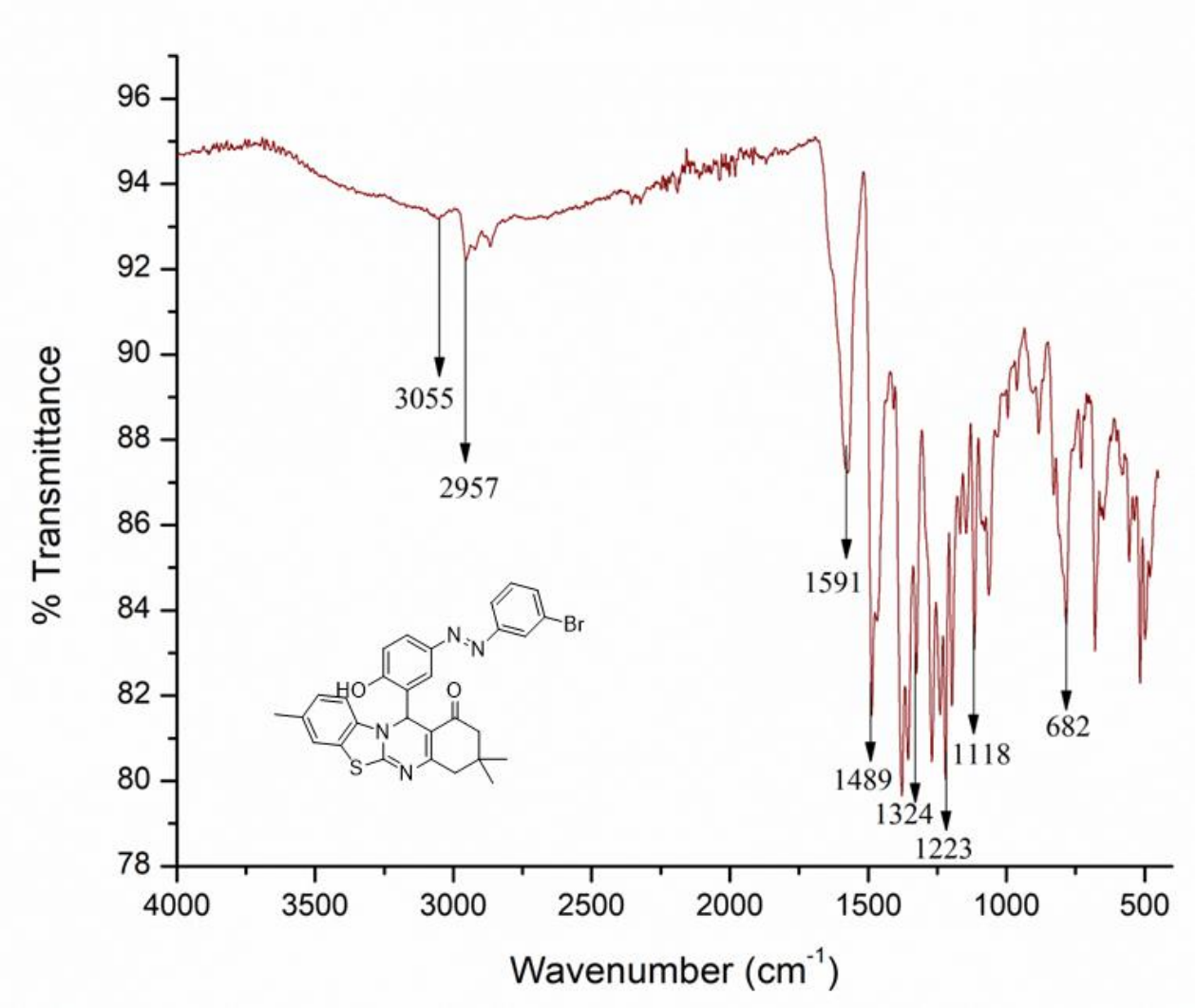


Figure. 29. IR Spectrum of compound 4h

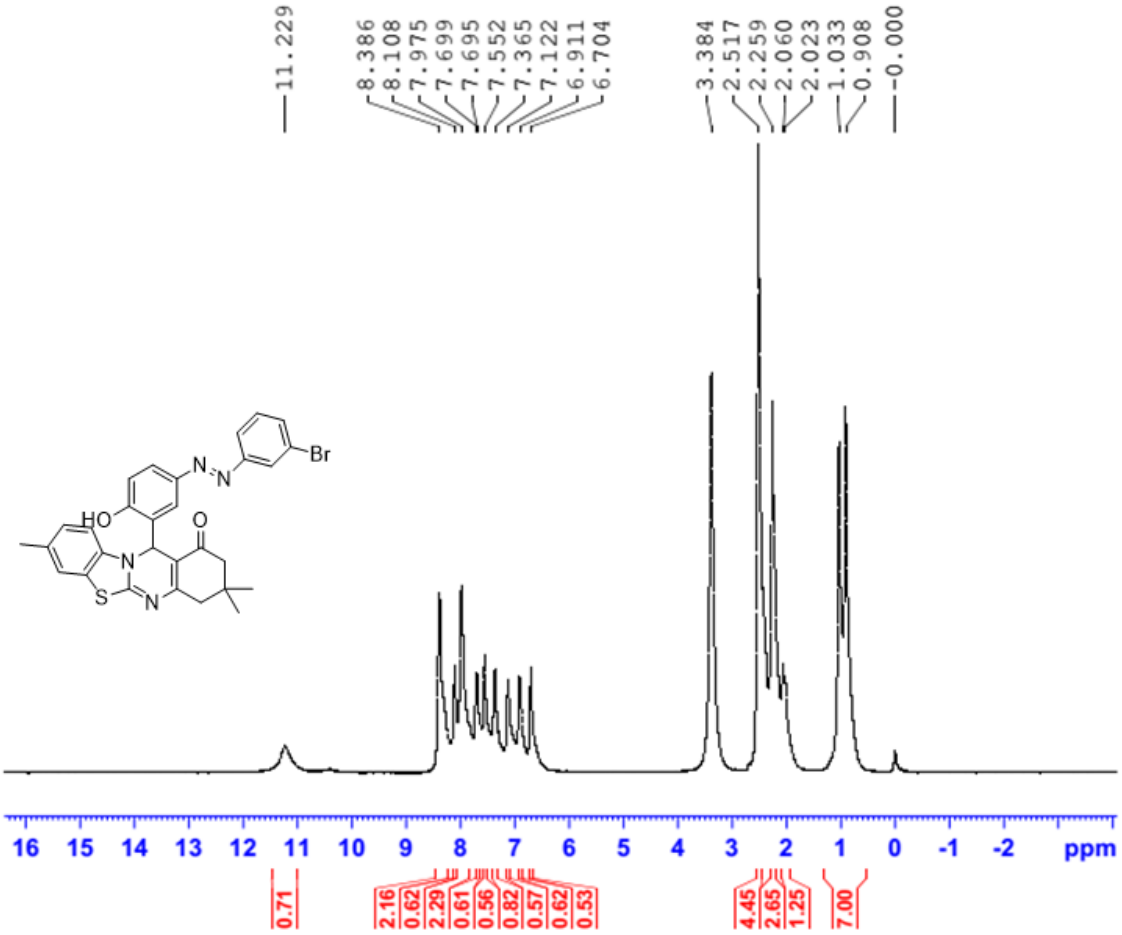


Figure. 30. ^{1}H Spectrum of compound **4h**

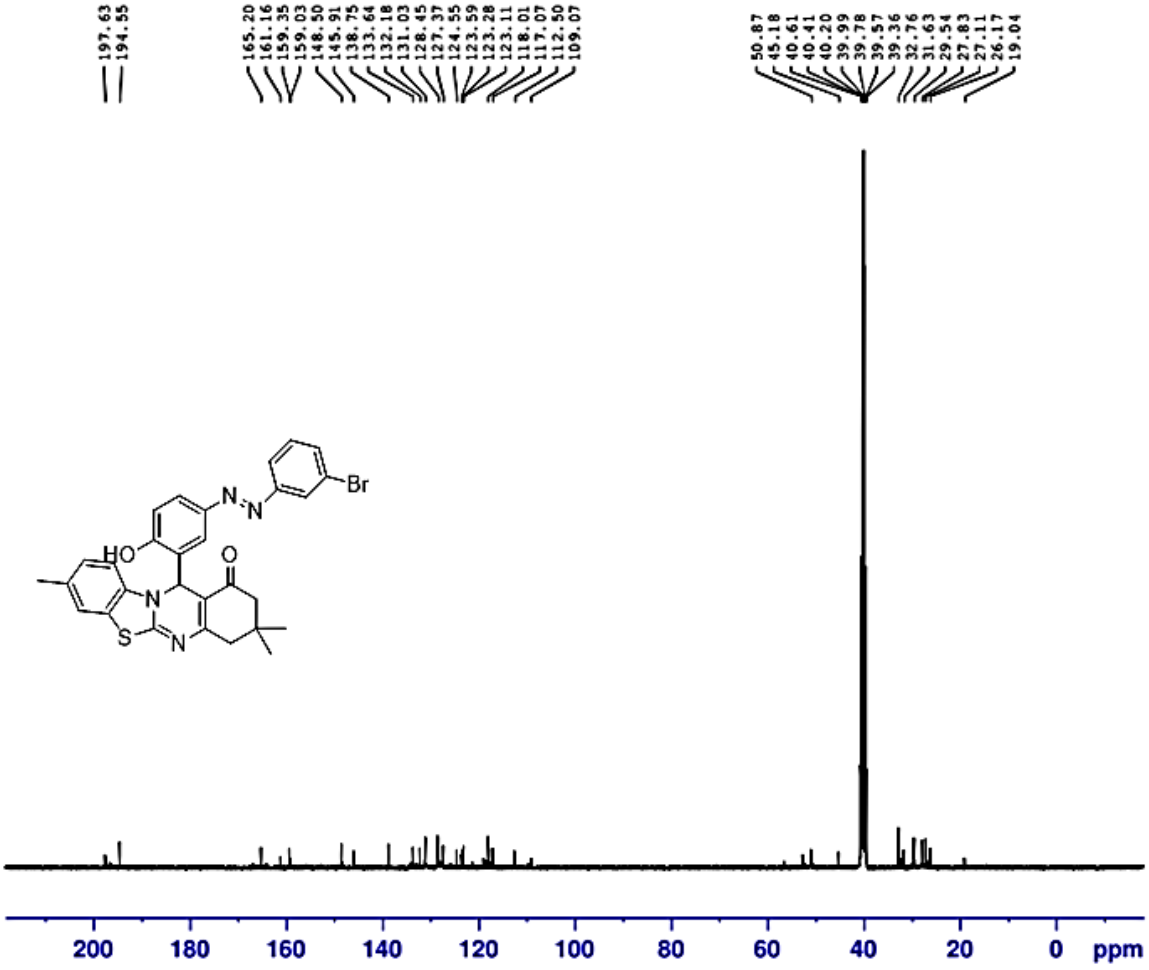


Figure. 31. ^{13}C NMR Spectrum of compound **4h**

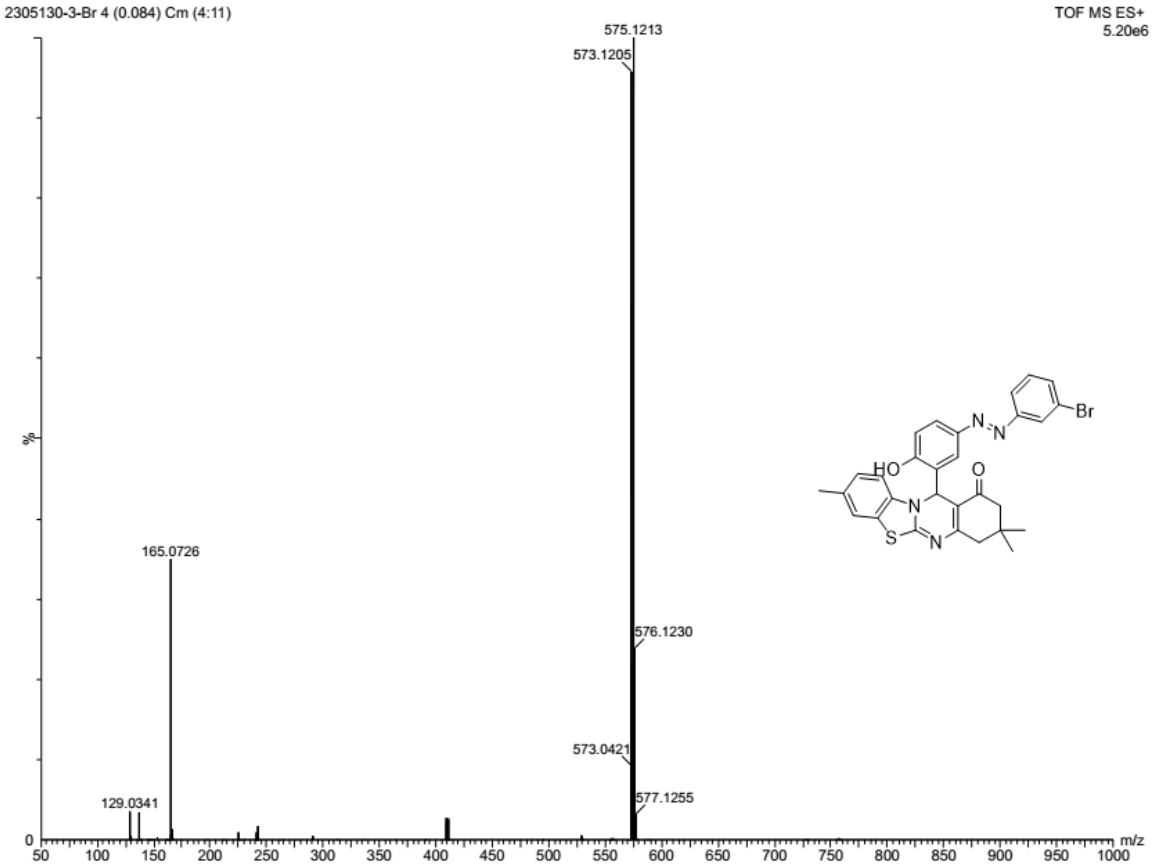


Figure. 32. Mass spectrum of compound **4h**

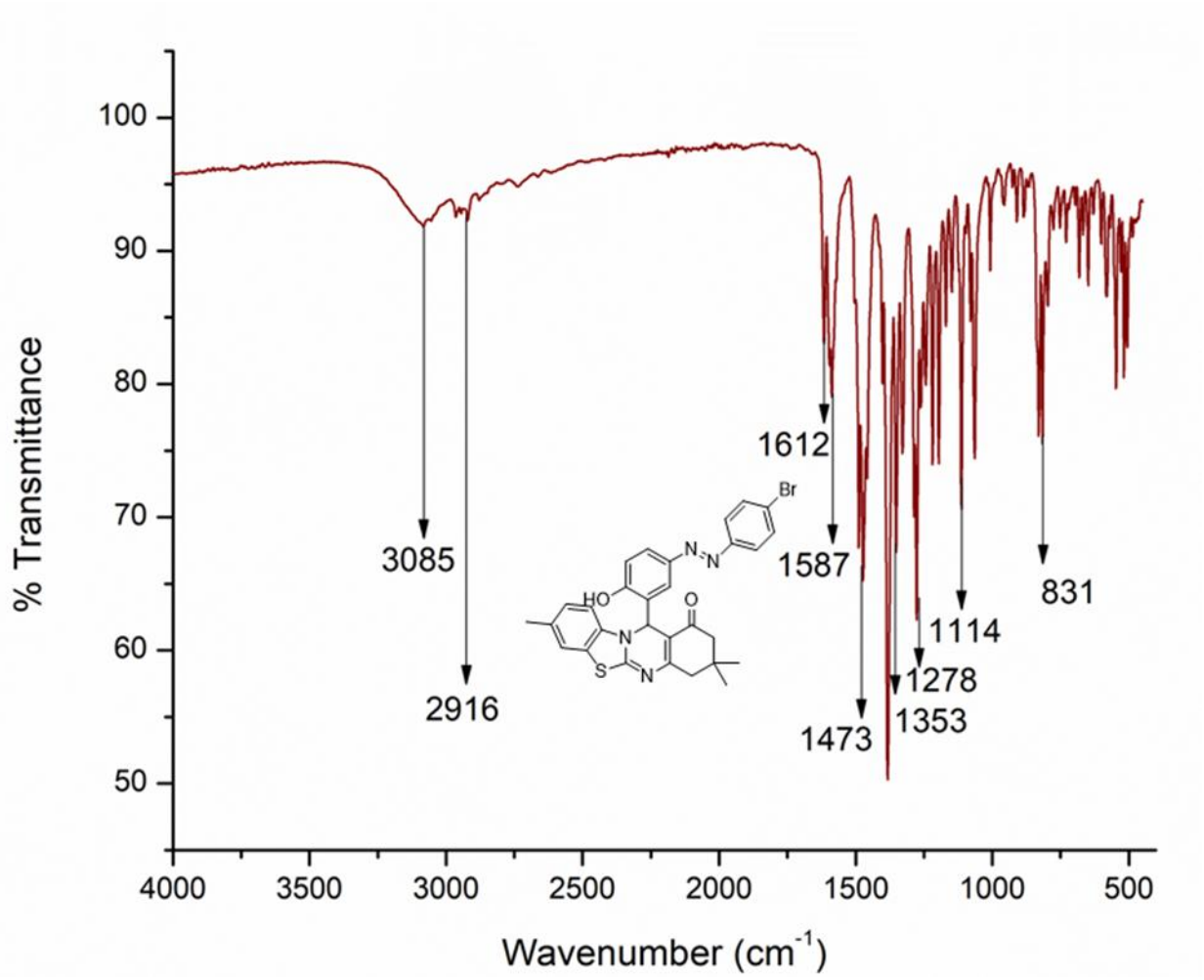


Figure. 33. IR Spectrum of compound **4i**

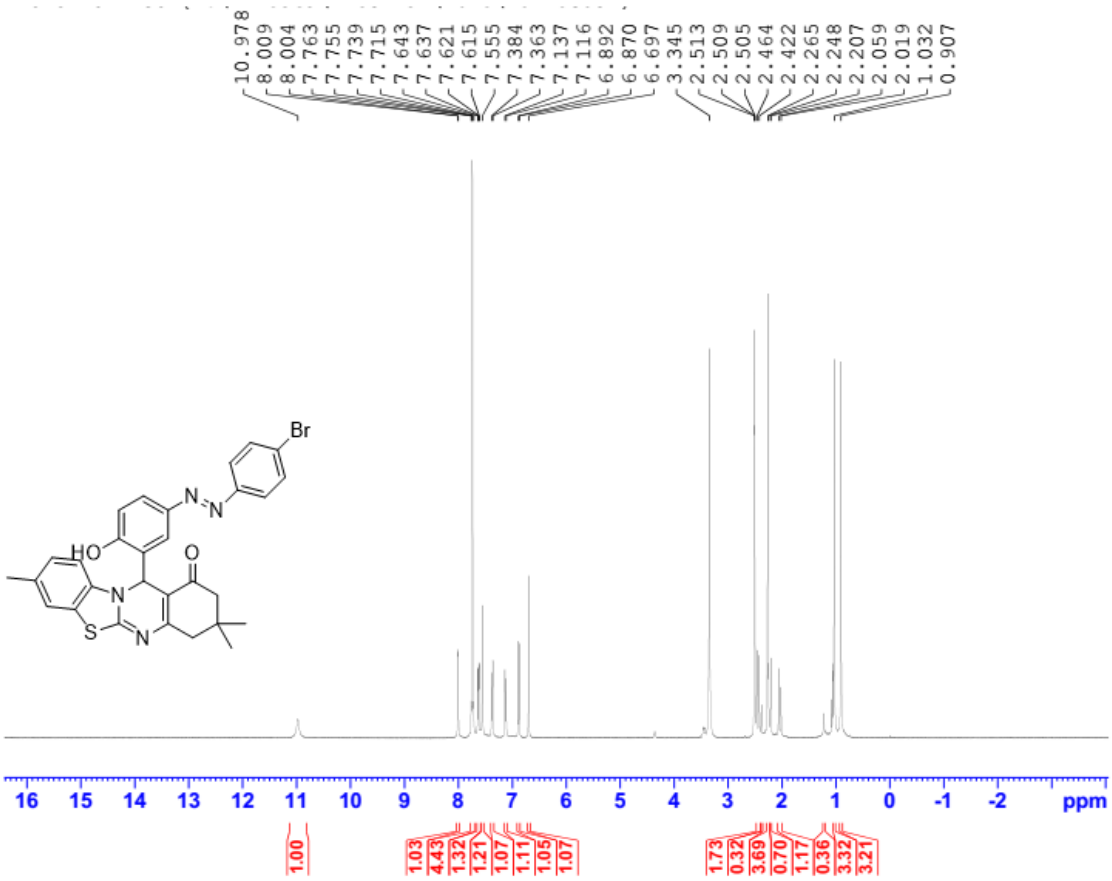


Figure. 34. ^{1}H Spectrum of compound **4i**

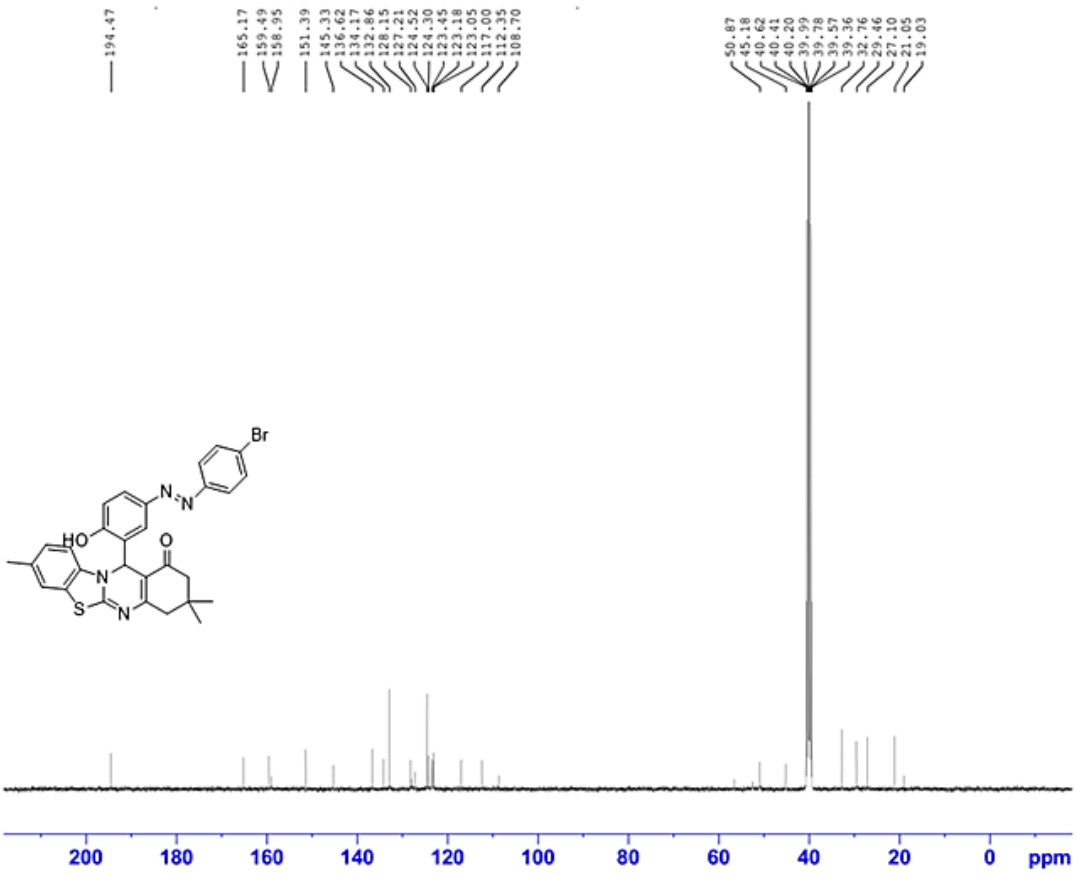


Figure. 35. ^{13}C NMR Spectrum of compound **4i**

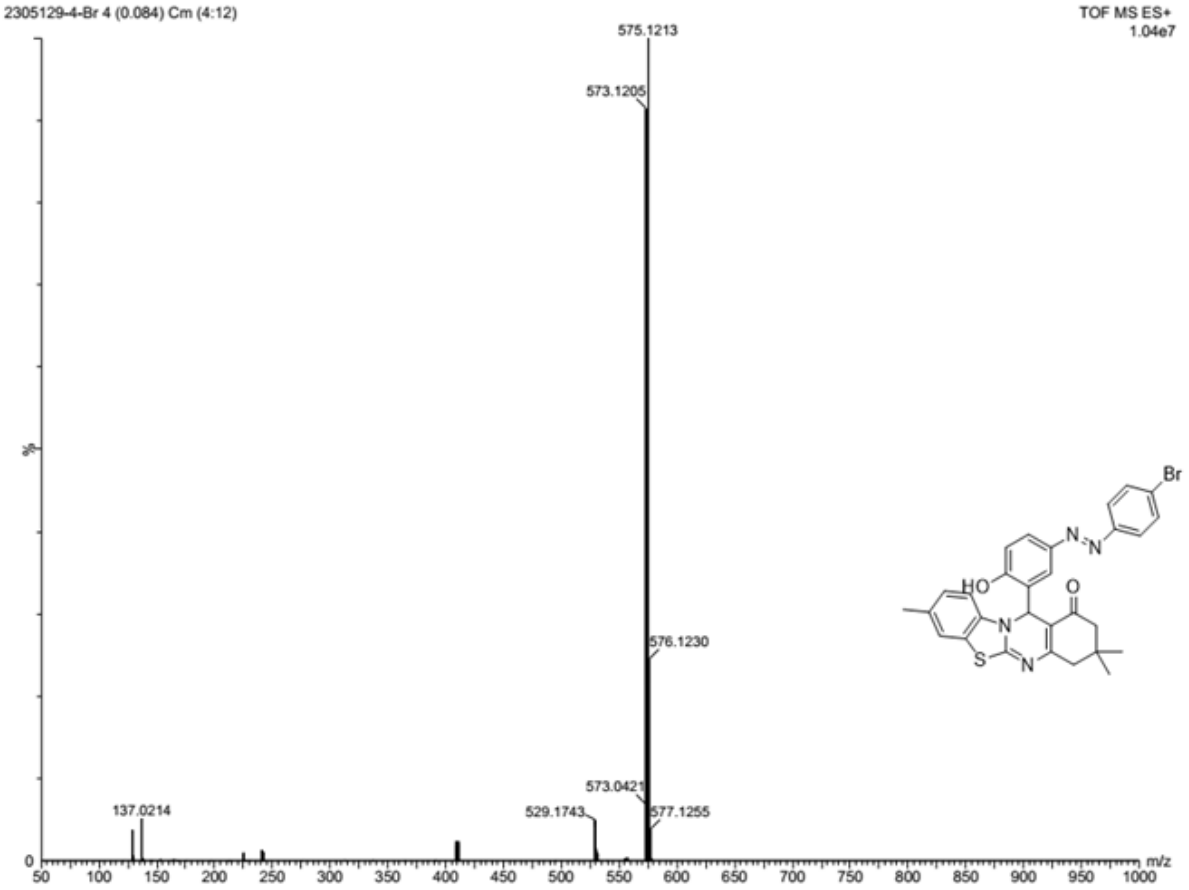


Figure. 36. Mass spectrum of compound **4i**

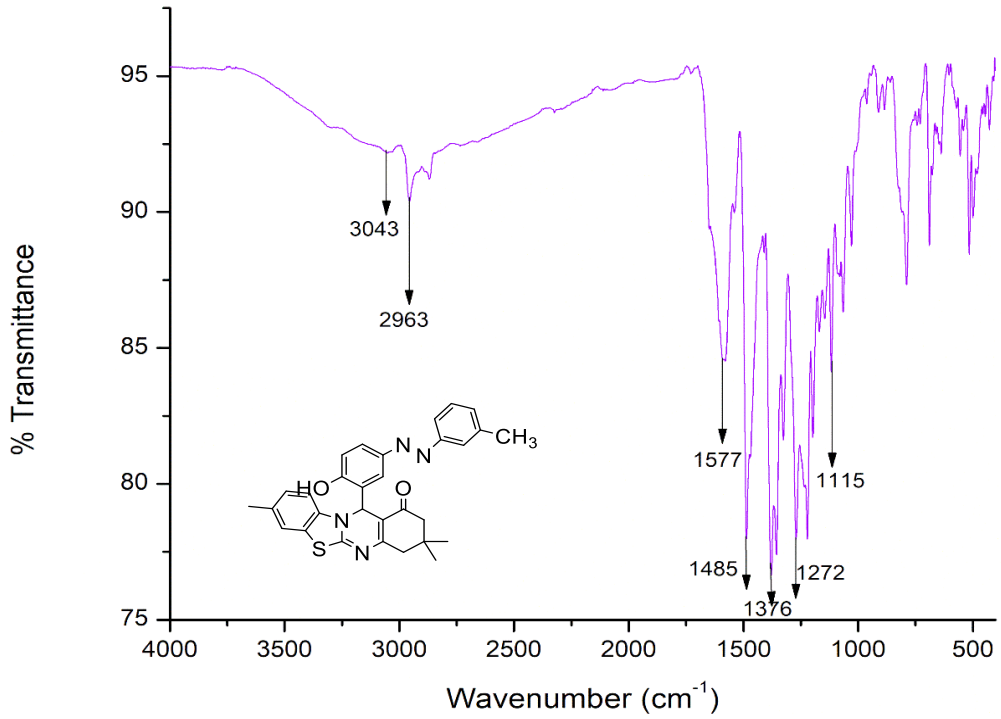


Figure. 37. IR Spectrum of compound **4j**

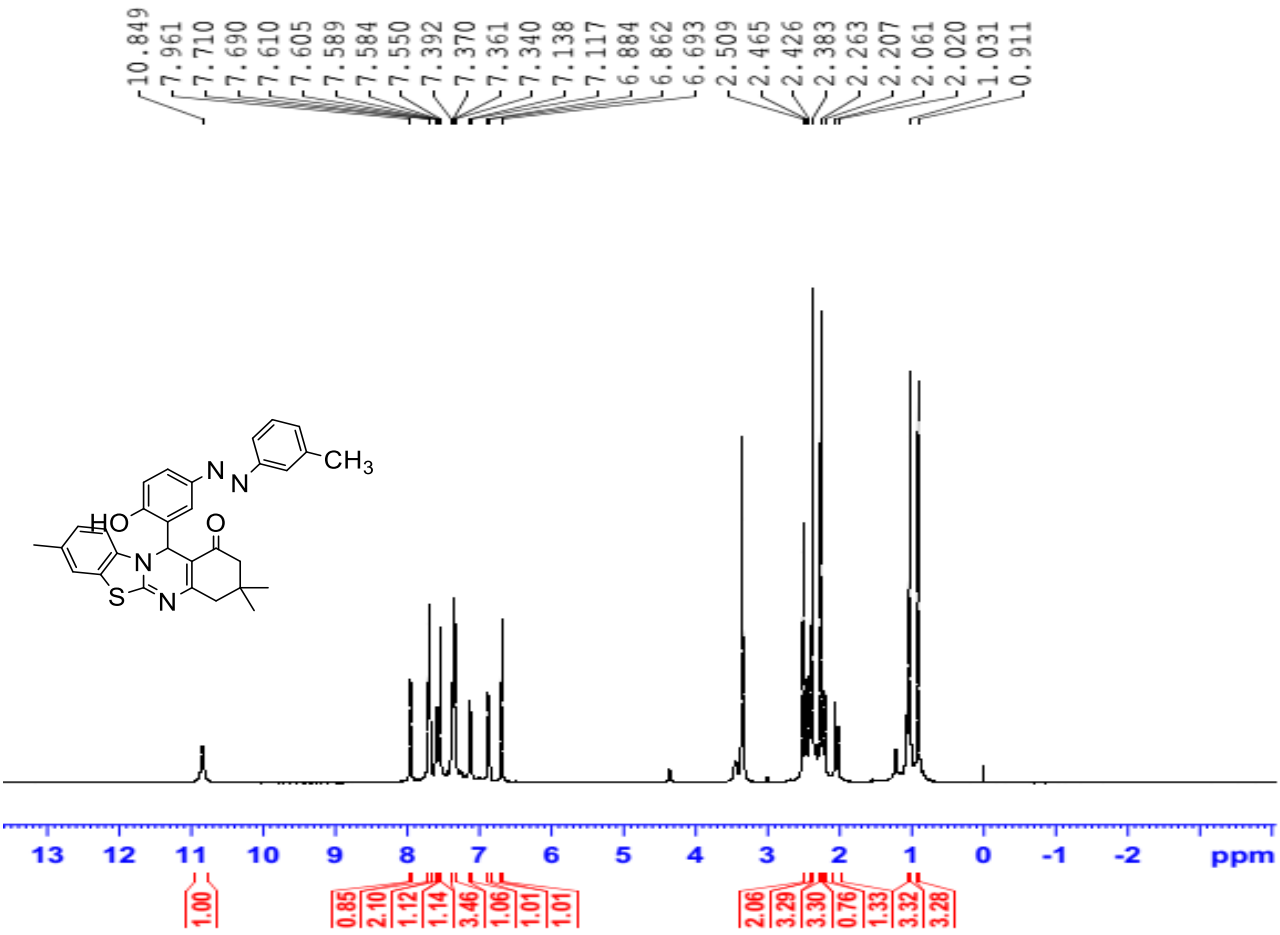


Figure. 38. ^{1}H NMR spectrum of compound **4j**

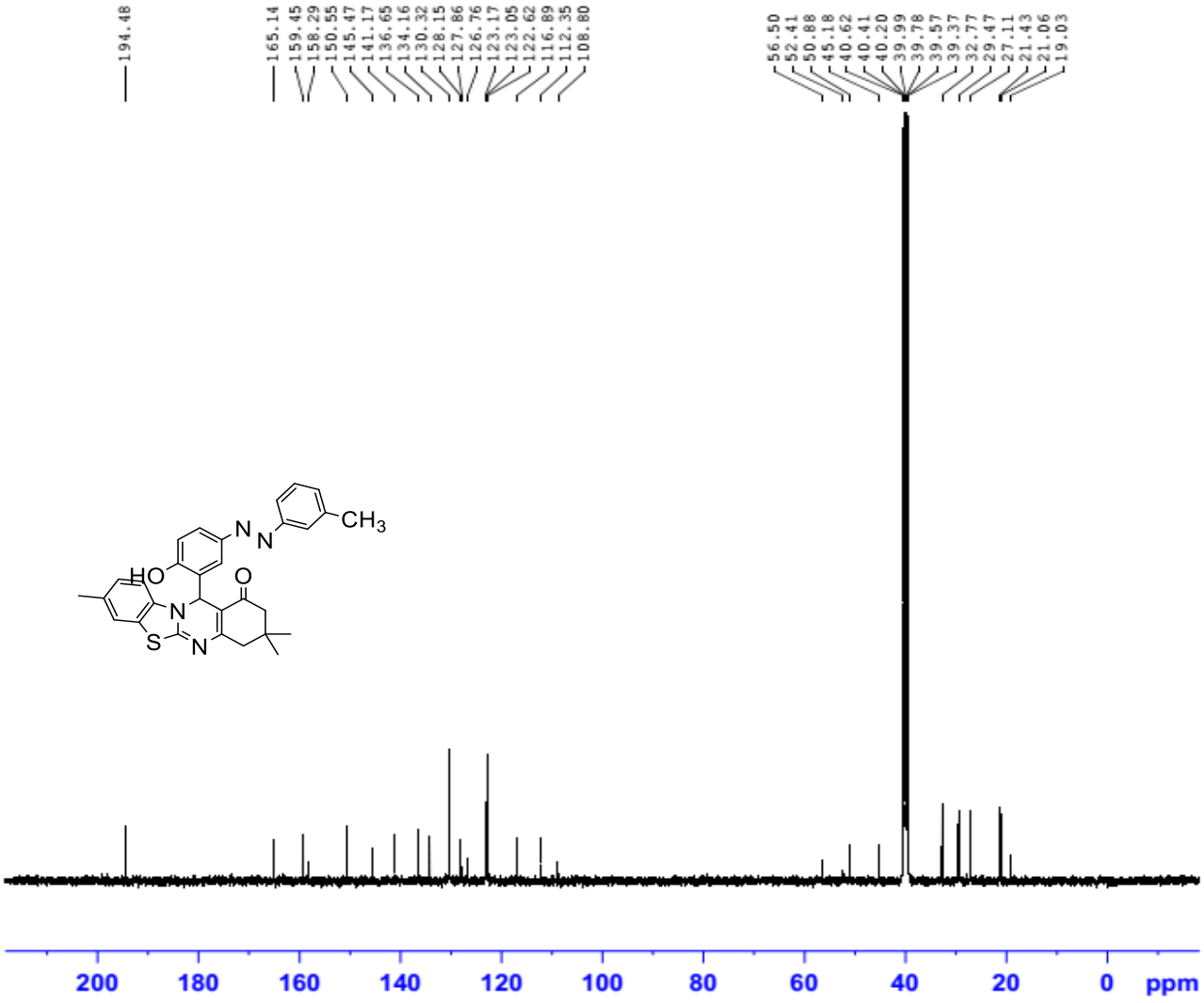


Figure. 39. ^{13}C NMR Spectrum of compound **4j**

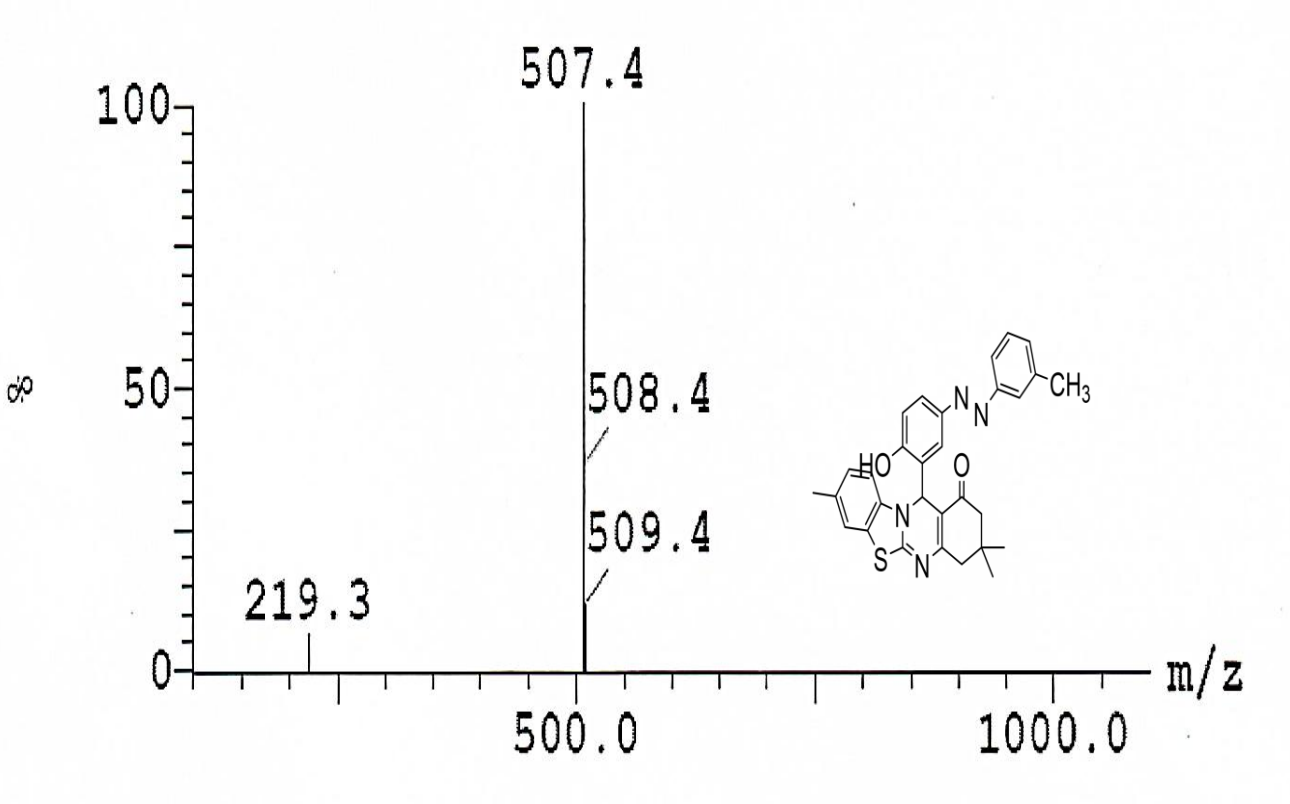


Figure. 40. Mass spectrum of compound **4j**

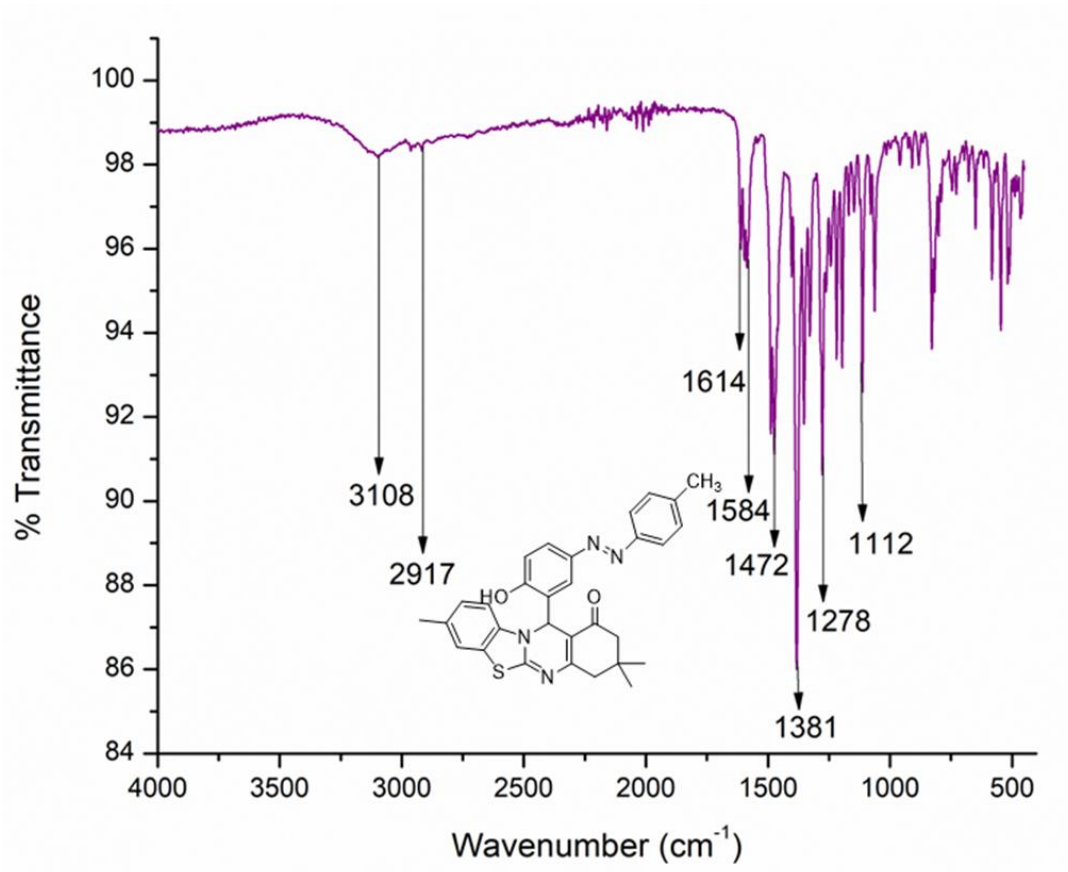


Figure. 41. IR Spectrum of compound **4k**

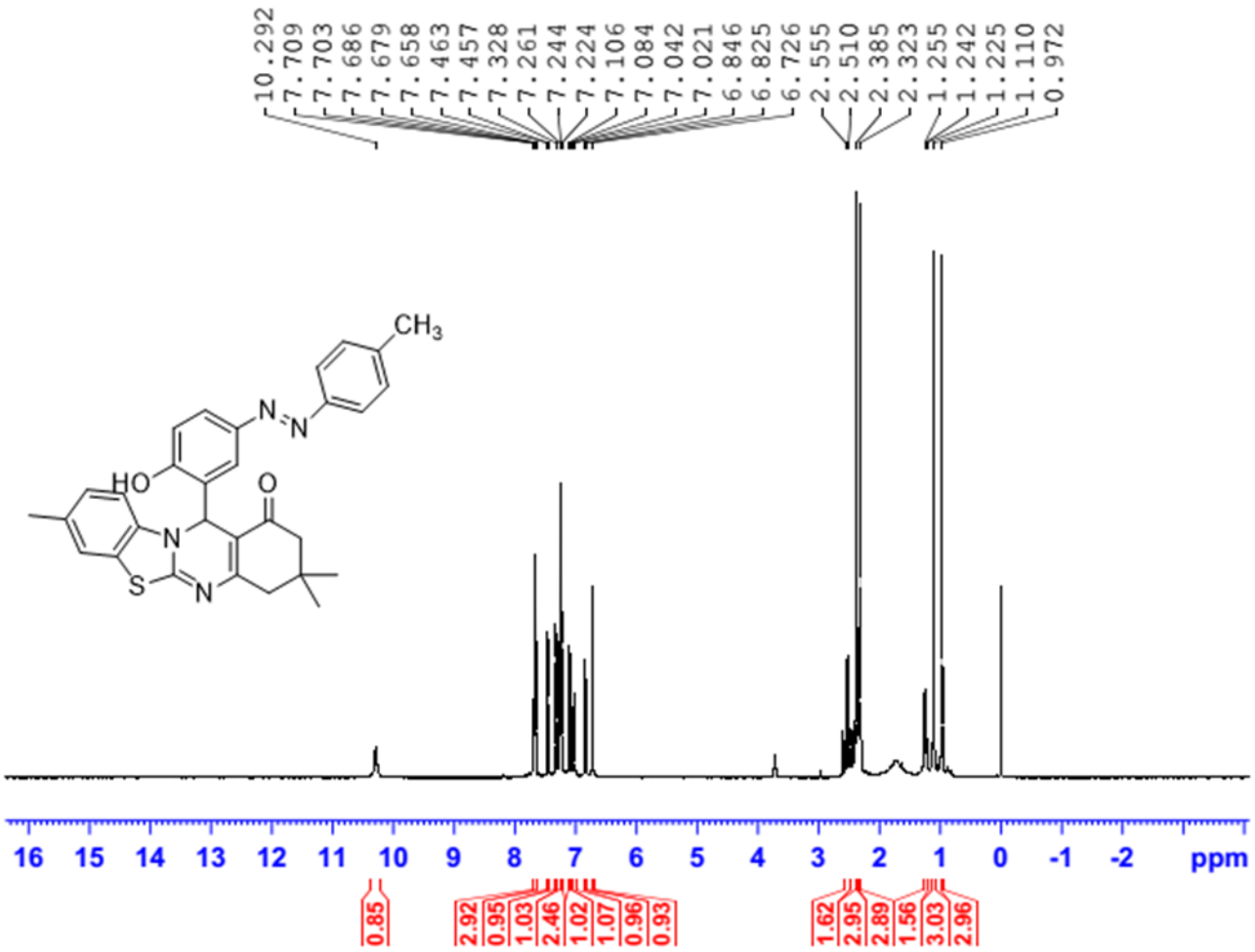


Figure. 42. ^{1}H Spectrum of compound **4k**

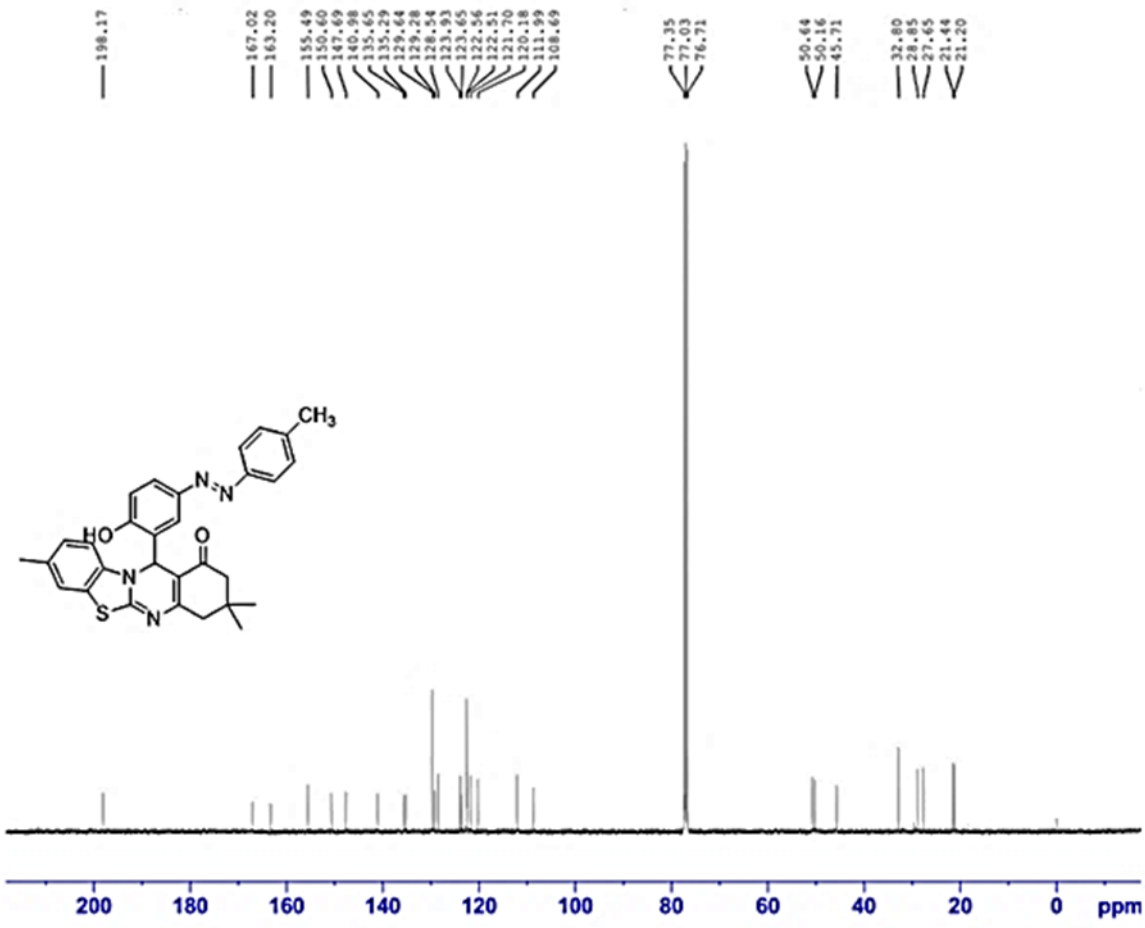


Figure. 43. ^{13}C NMR Spectrum of compound **4k**

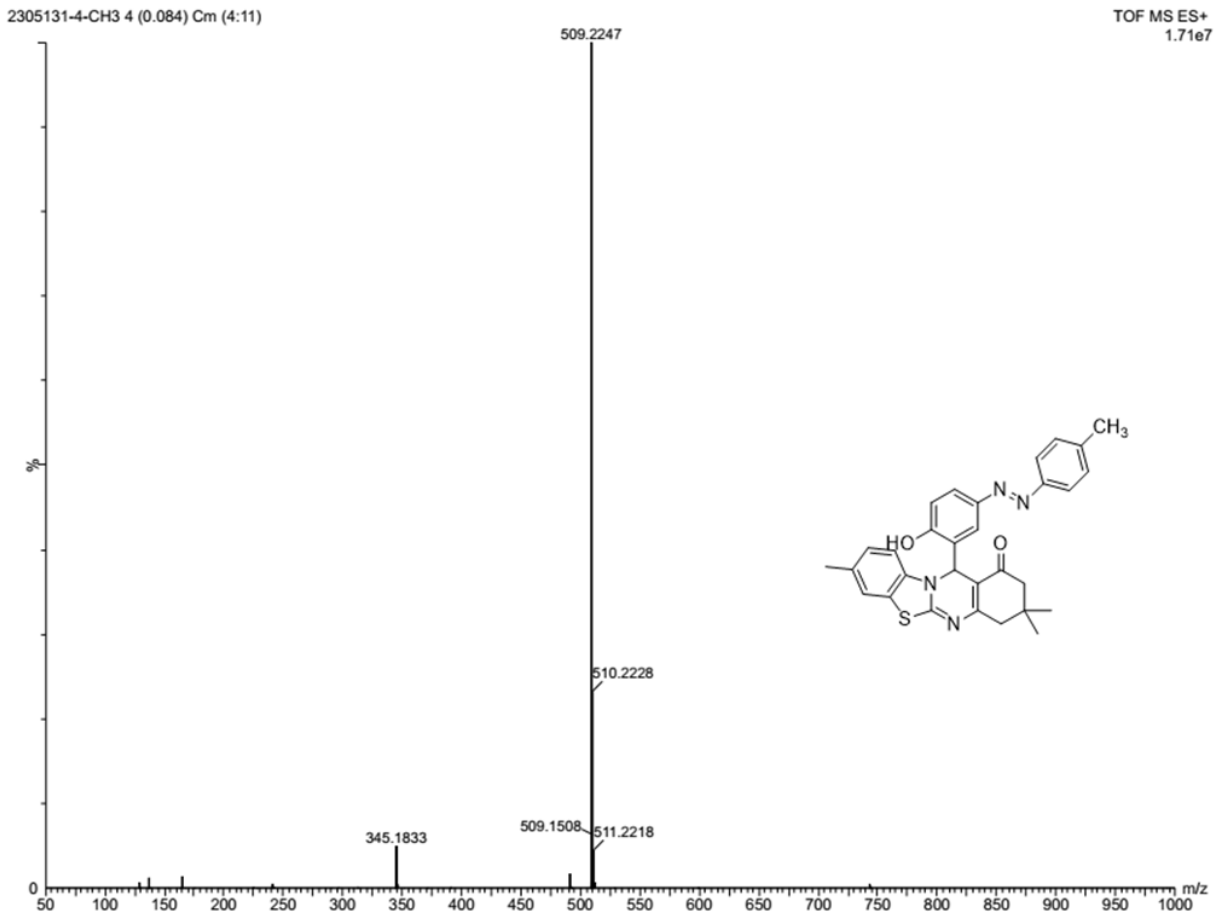


Figure. 44. Mass spectrum of compound **4k**

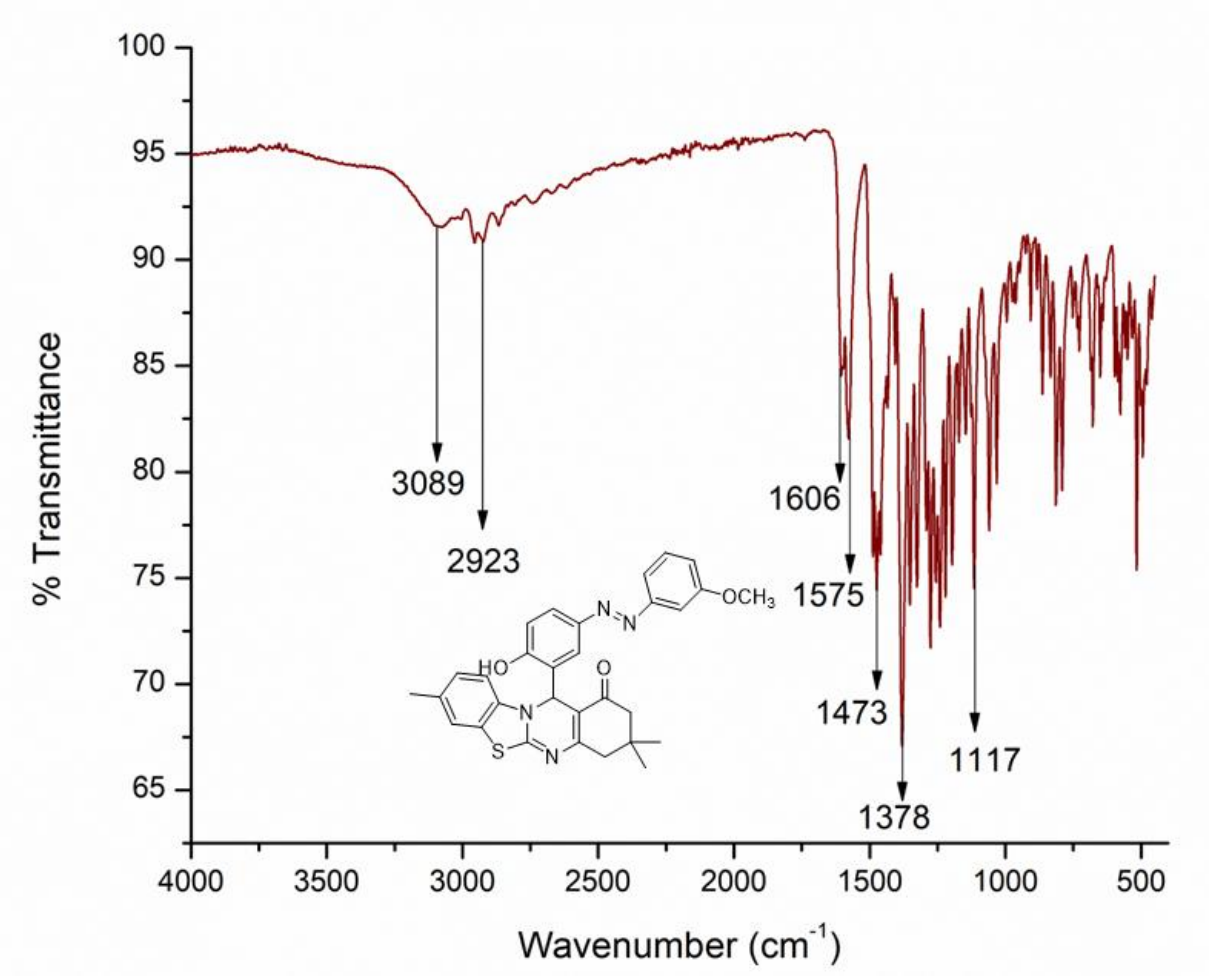


Figure. 45. IR Spectrum of compound **4l**

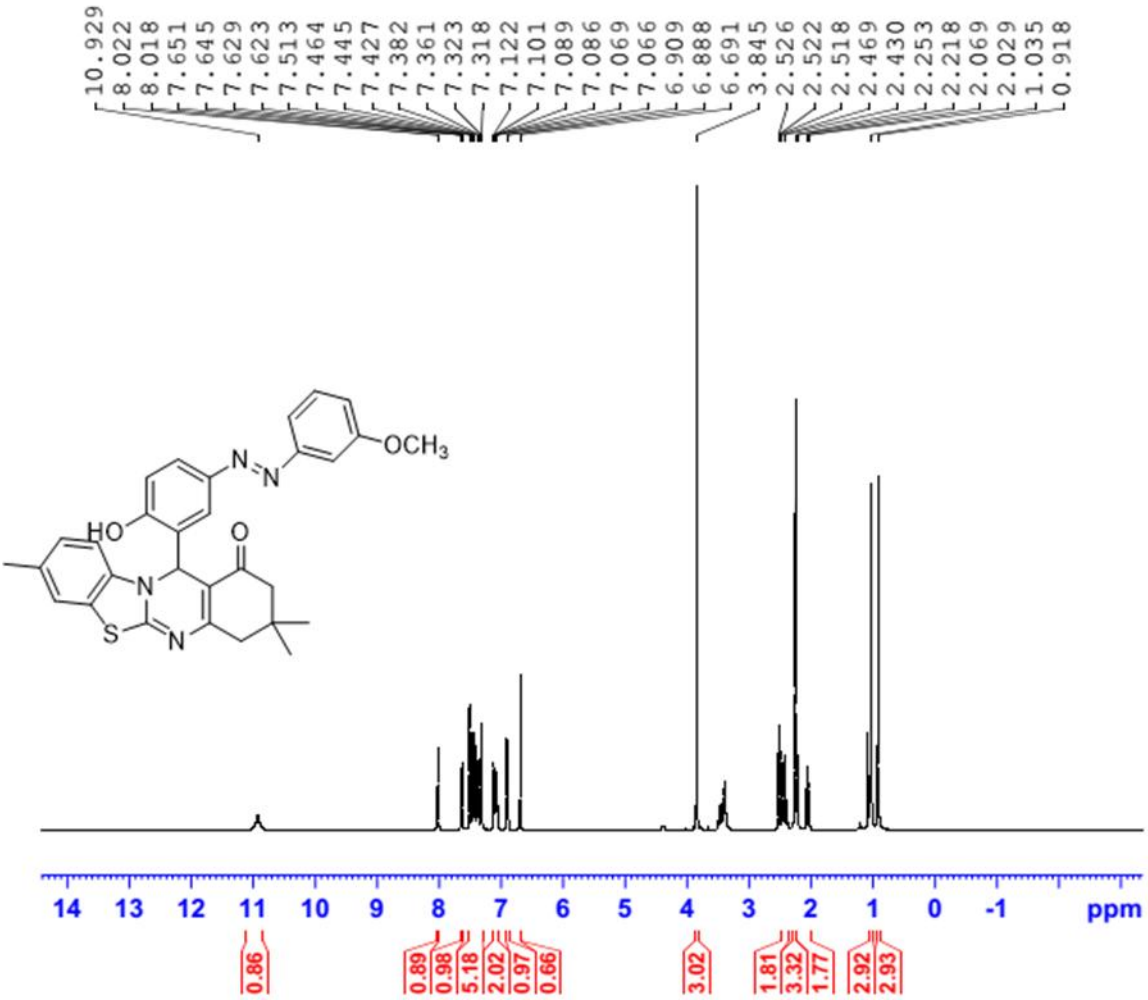


Figure. 46. ^{1}H Spectrum of compound **4l**

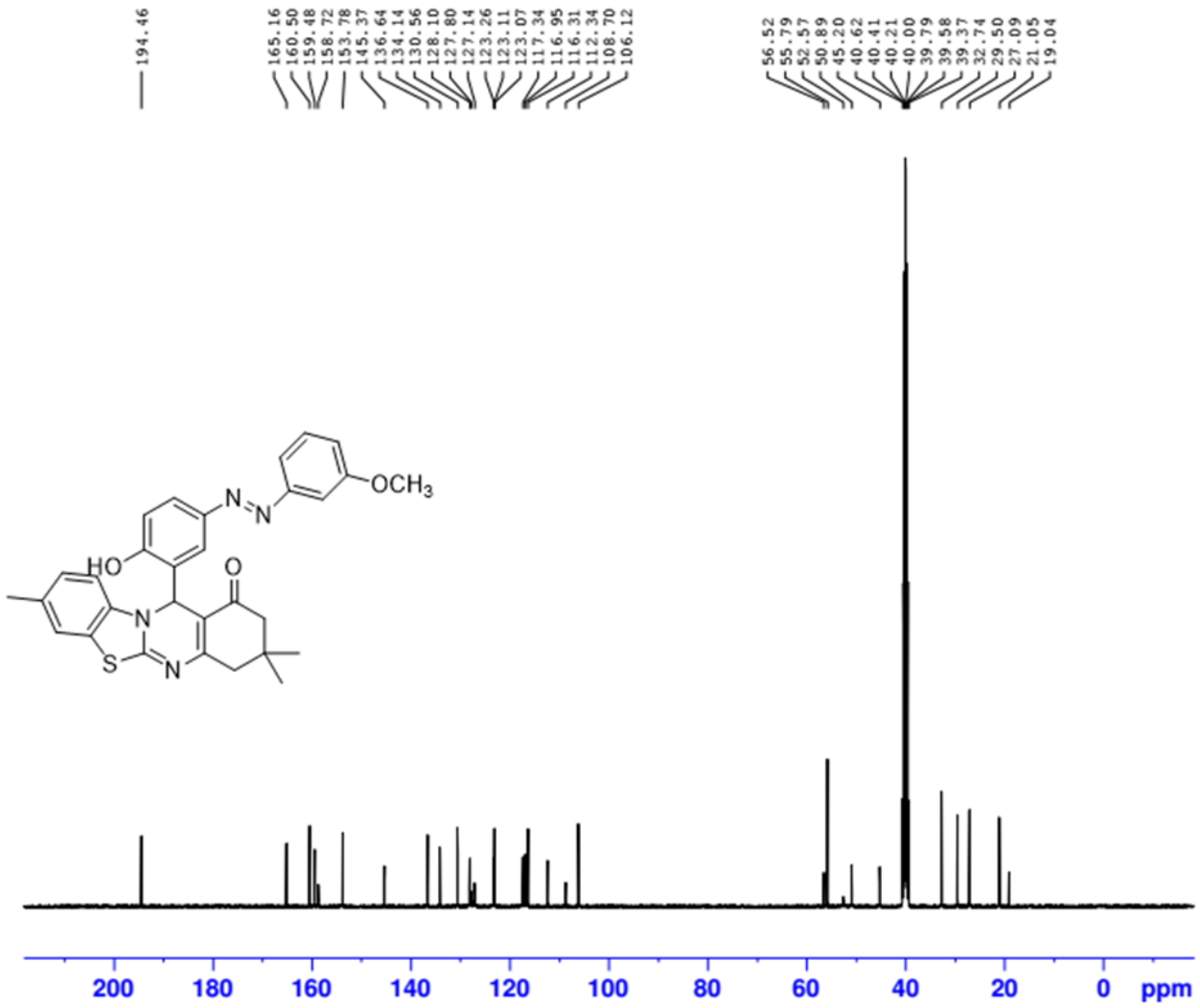


Figure. 47. ^{13}C NMR Spectrum of compound **4l**

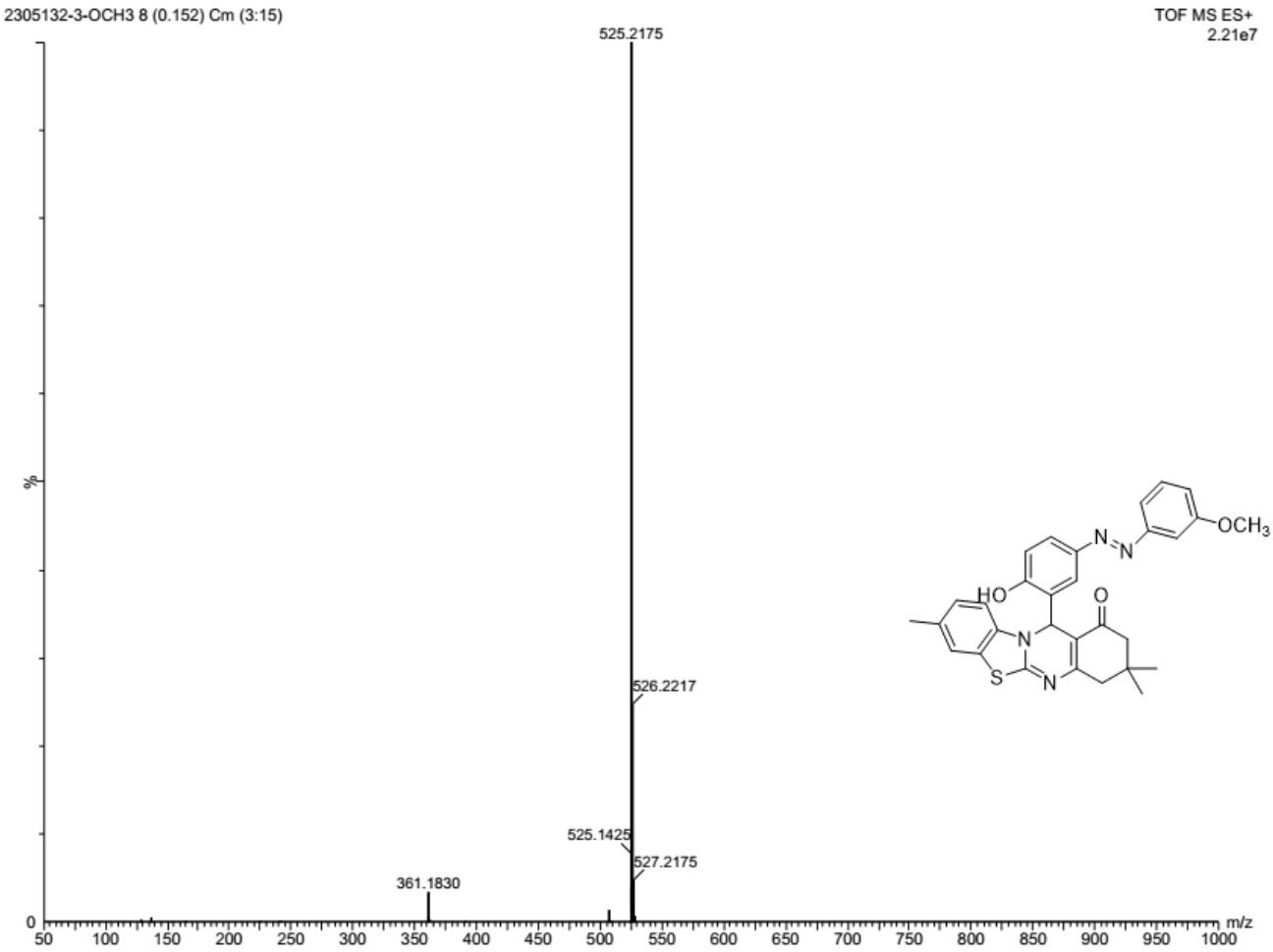


Figure. 48. Mass spectrum of compound **4l**

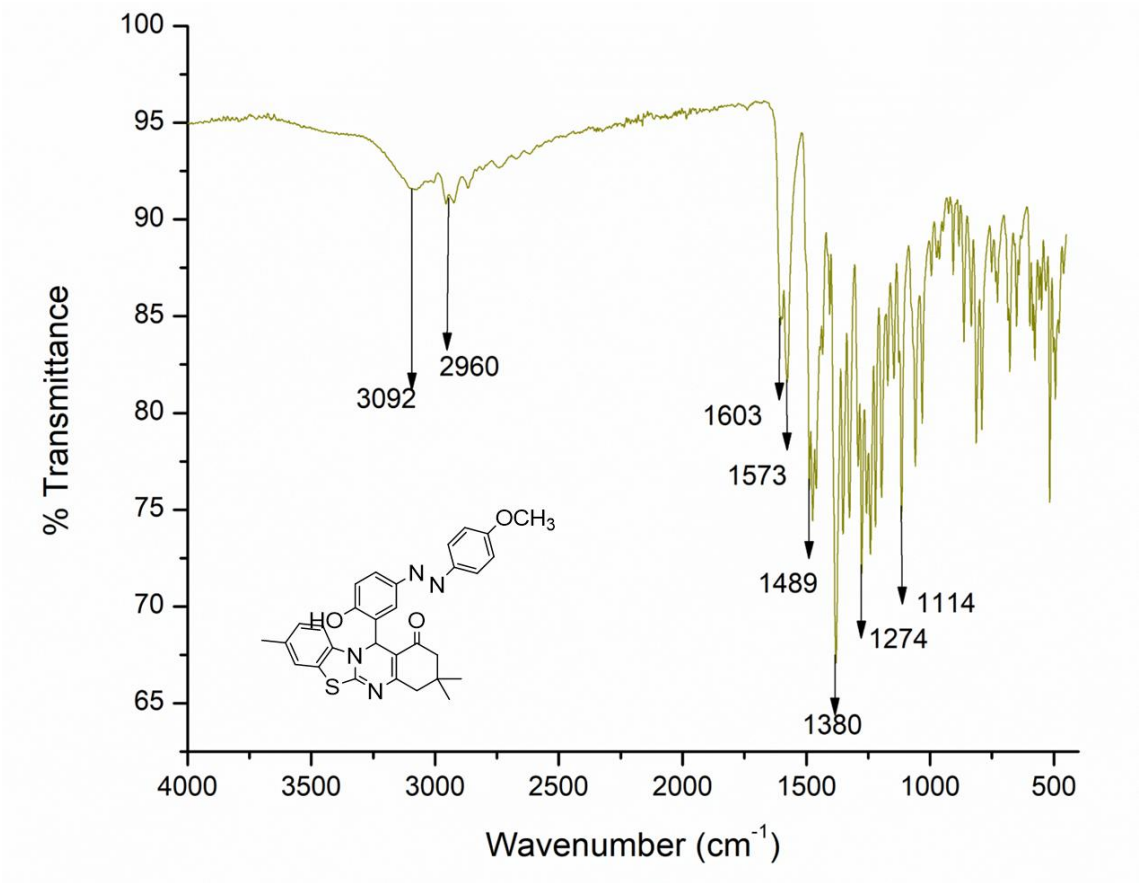


Figure. 49. IR Spectrum of compound **4m**

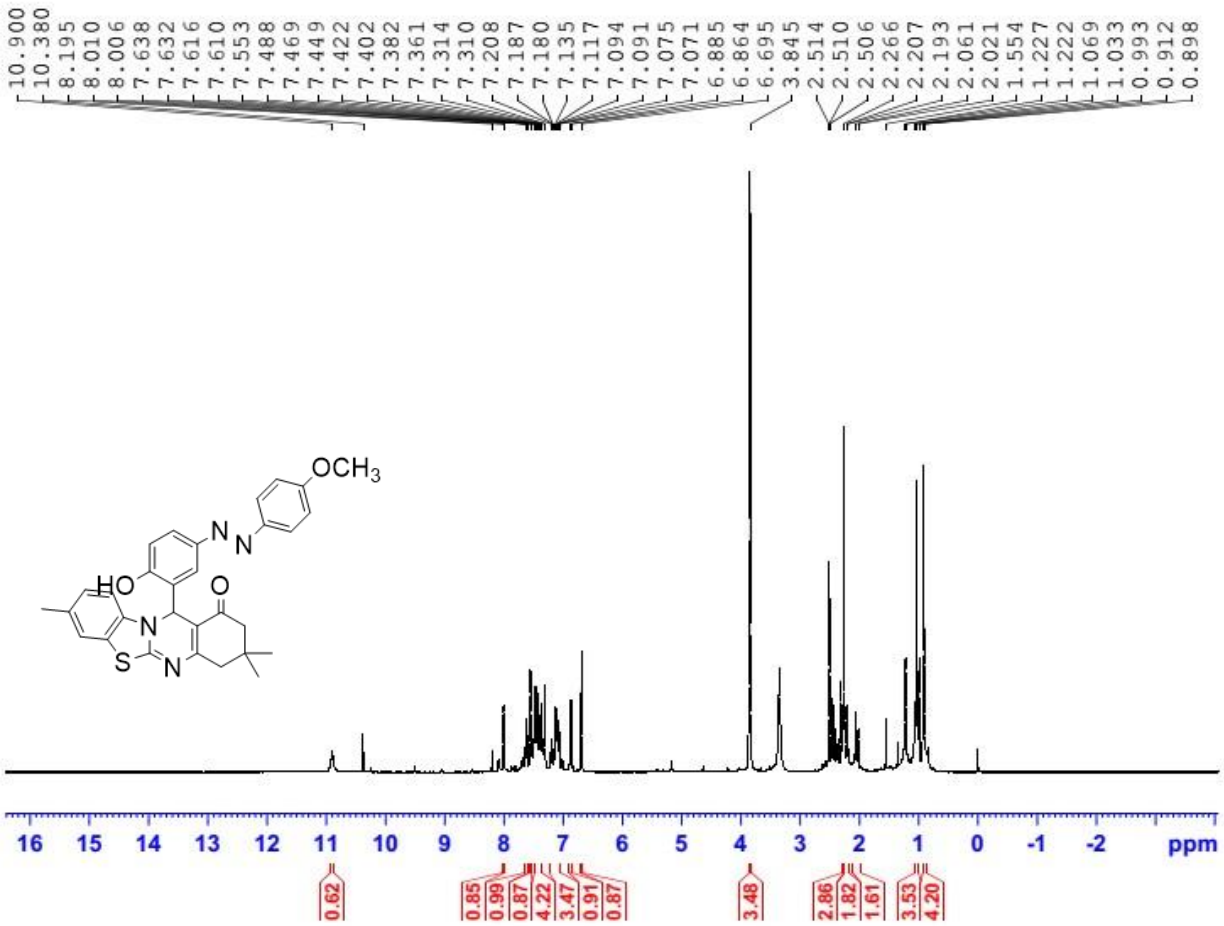


Figure. 50. ^{1}H Spectrum of compound **4m**

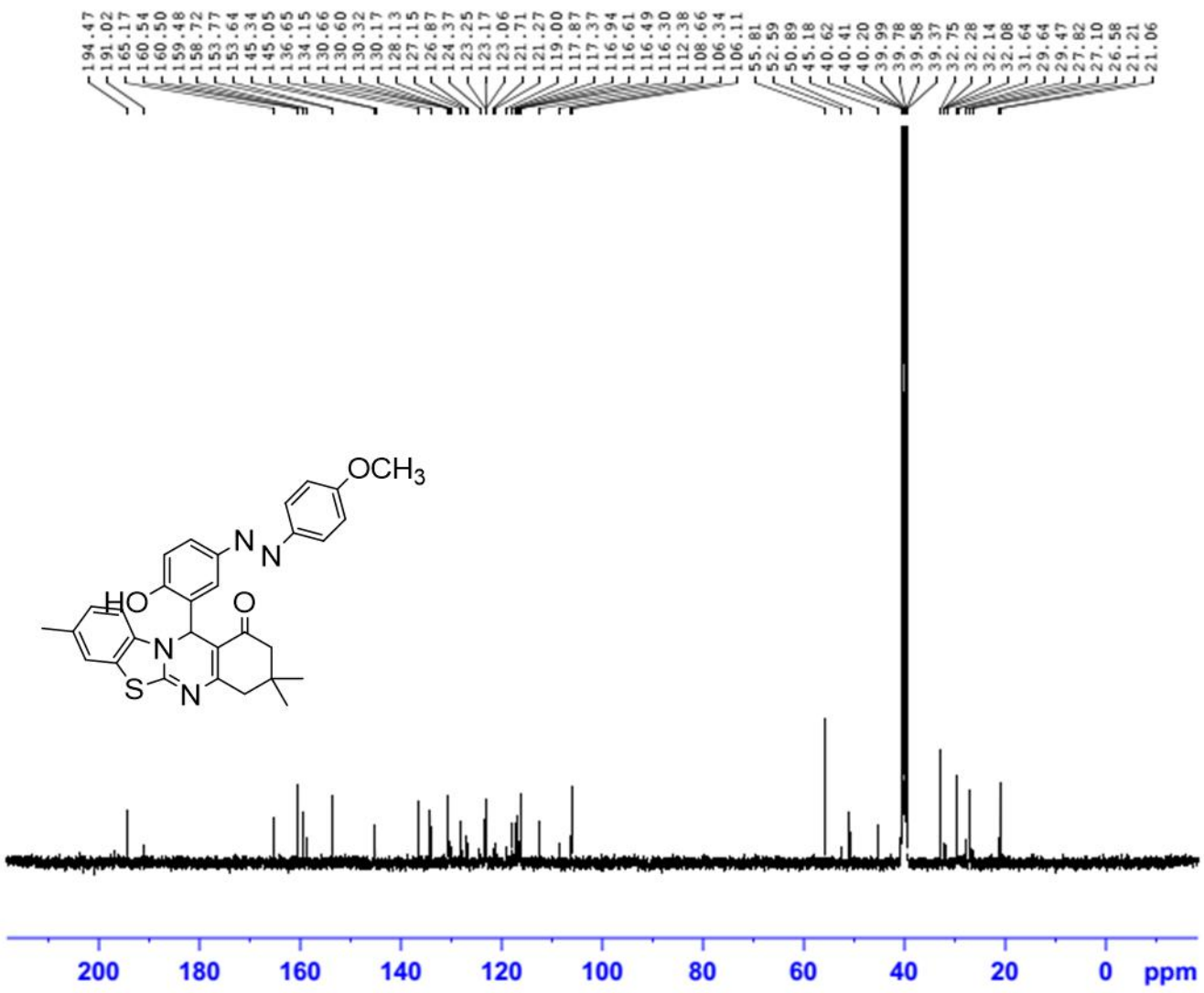


Figure. 51. ^{13}C NMR Spectrum of compound **4m**

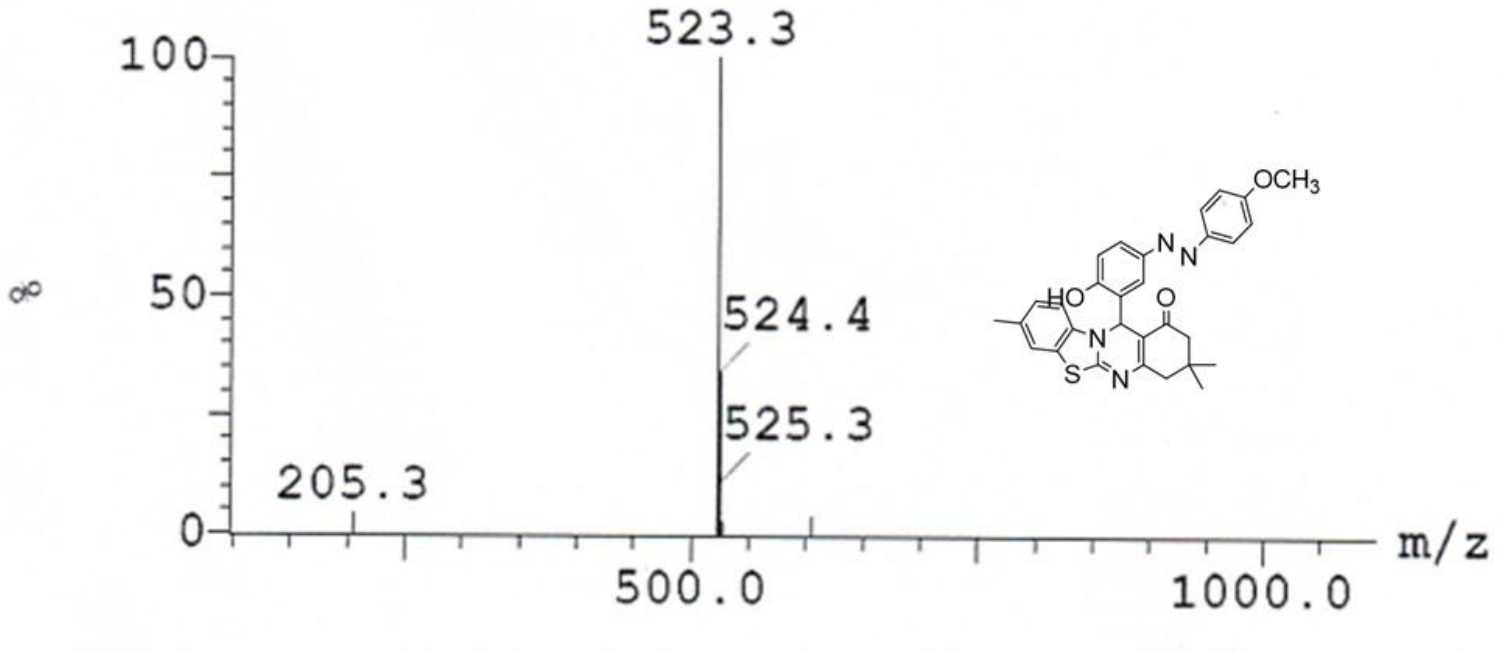


Figure. 52. Mass spectrum of compound **4m**

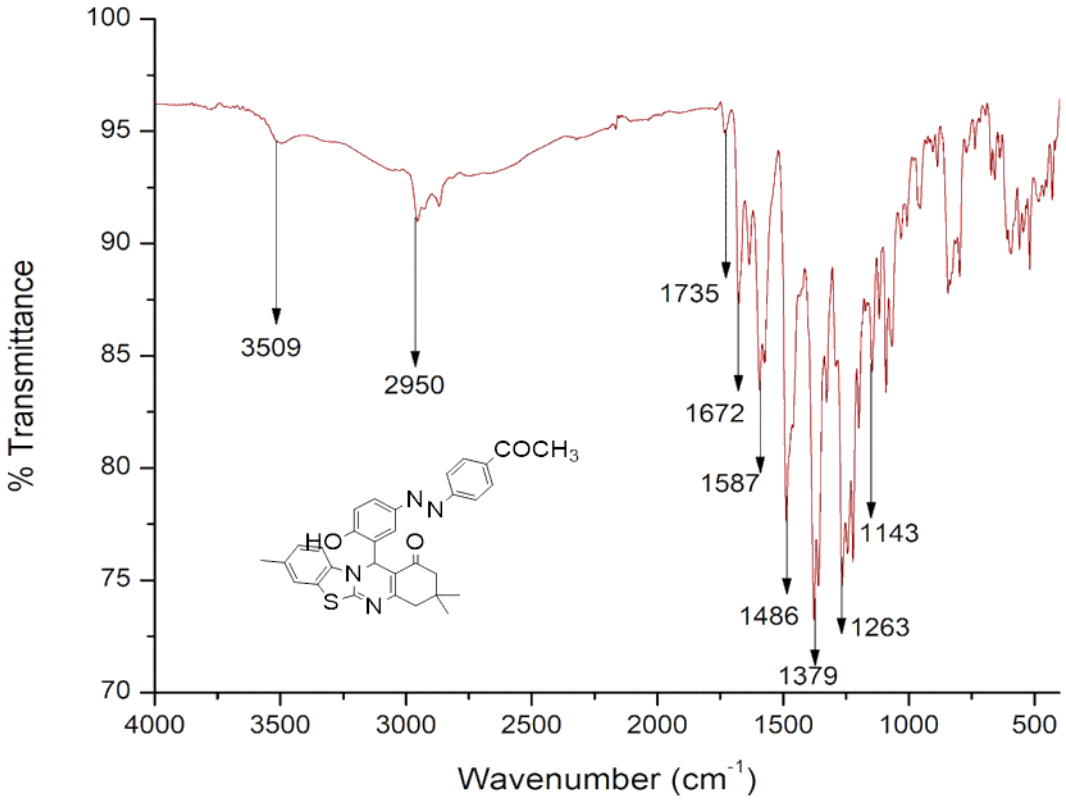


Figure. 53. IR Spectrum of compound **4n**

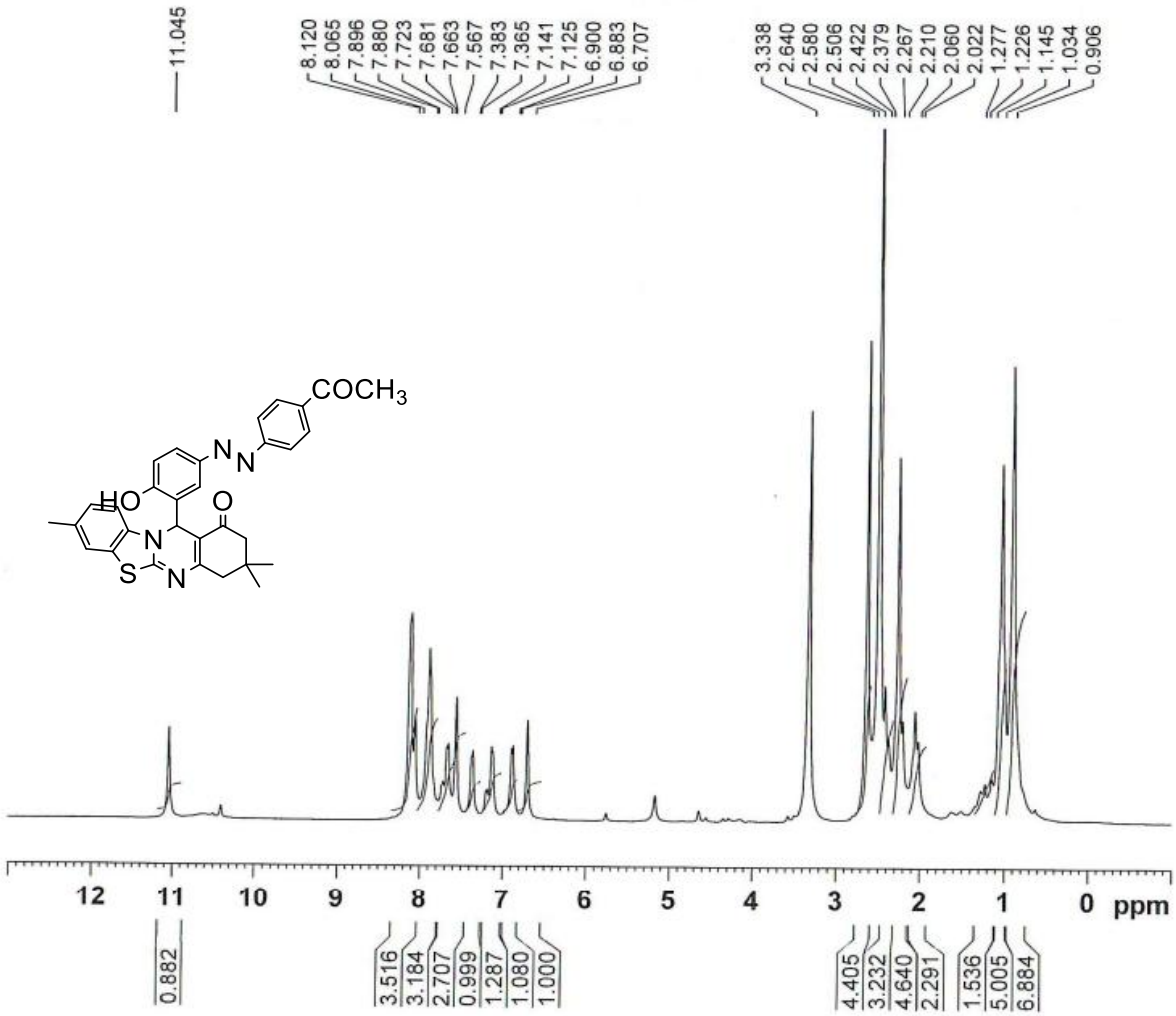


Figure. 54. ^{1}H Spectrum of compound **4n**

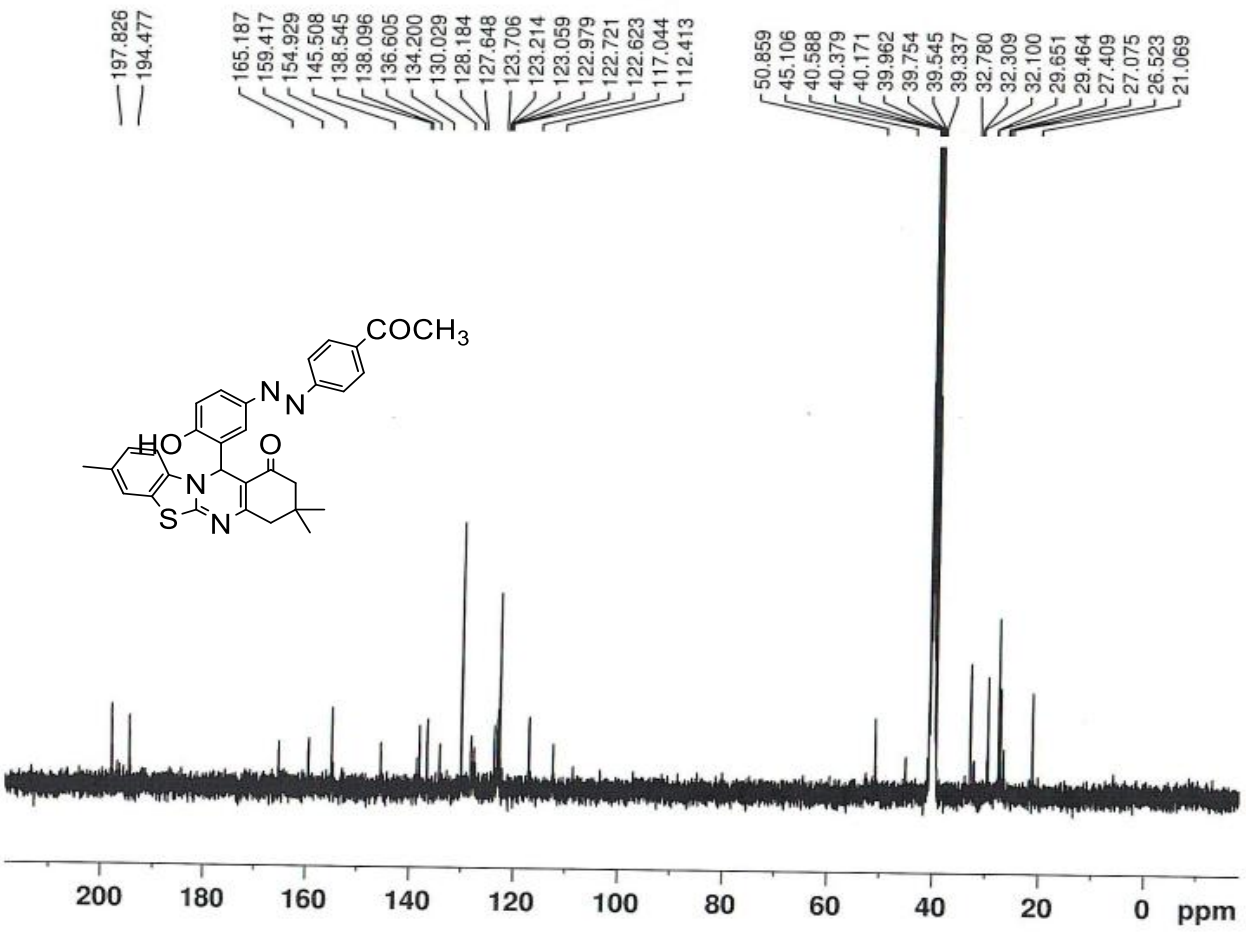


Figure. 55. ^{13}C NMR Spectrum of compound **4n**

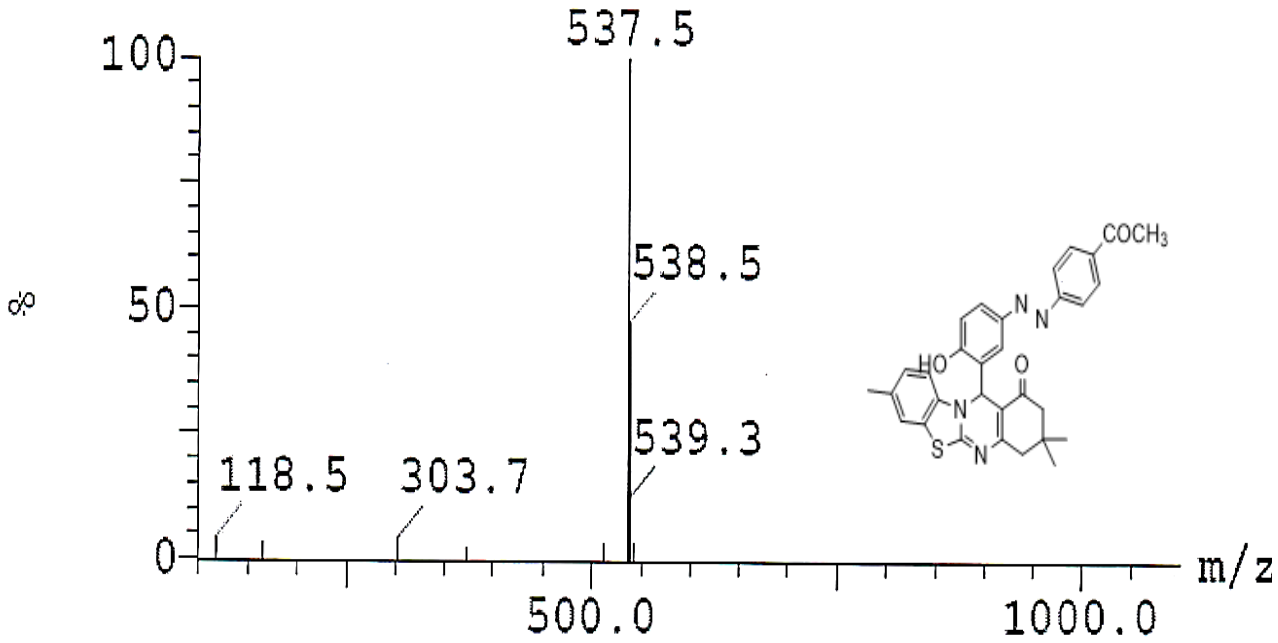


Figure. 56. Mass spectrum of compound **4n**

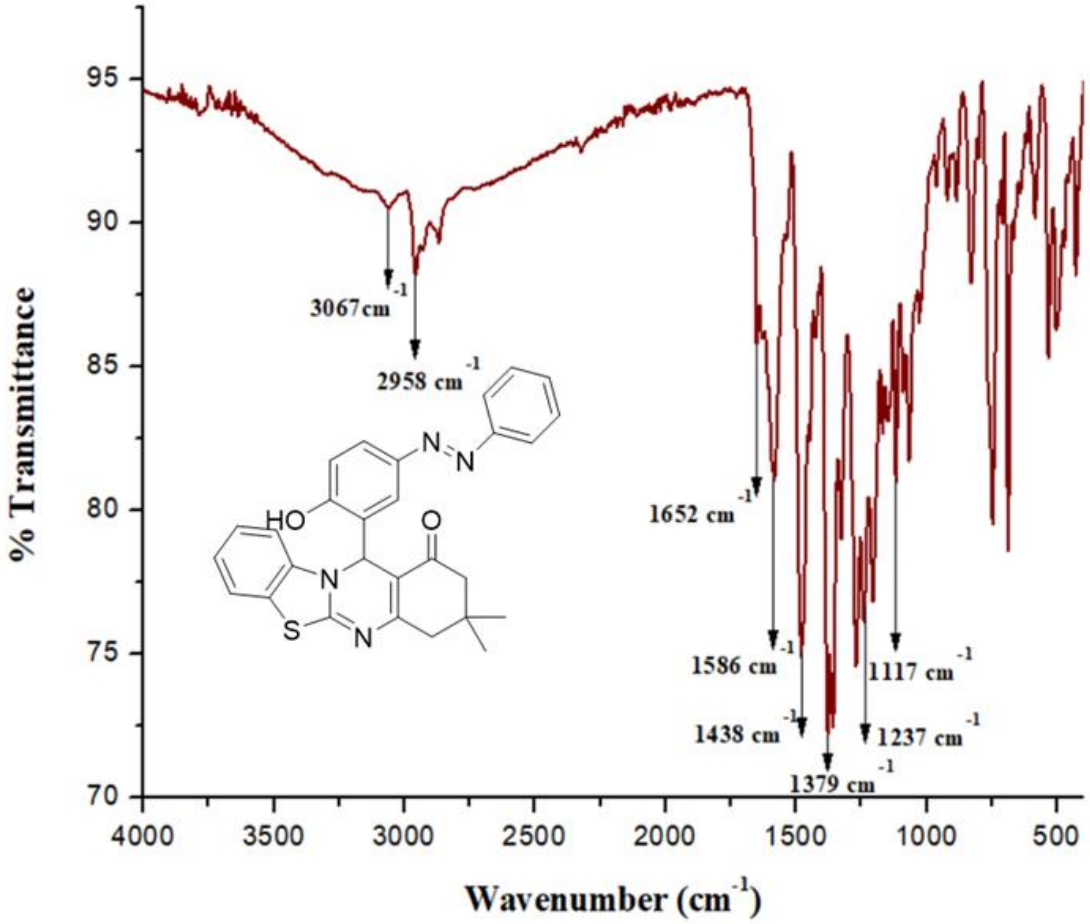


Figure. 57. IR Spectrum of compound **4o**

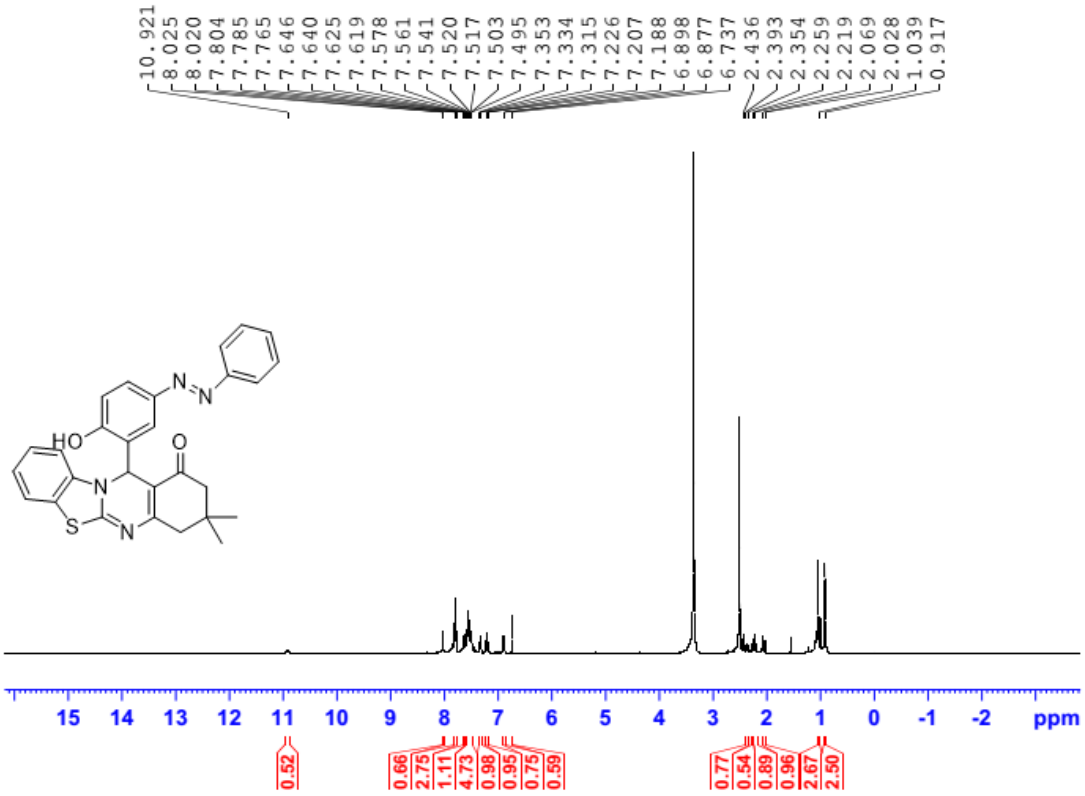


Figure. 58. ^{1}H Spectrum of compound **4o**

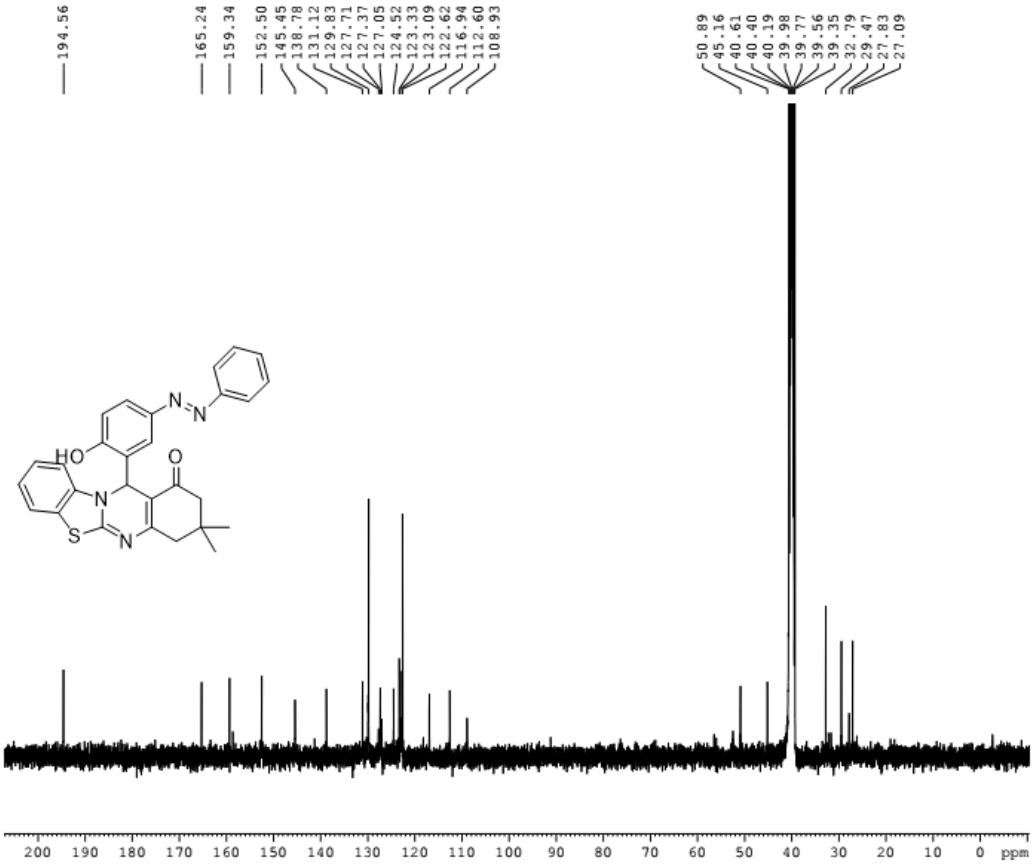


Figure. 59. ^{13}C NMR Spectrum of compound **4o**

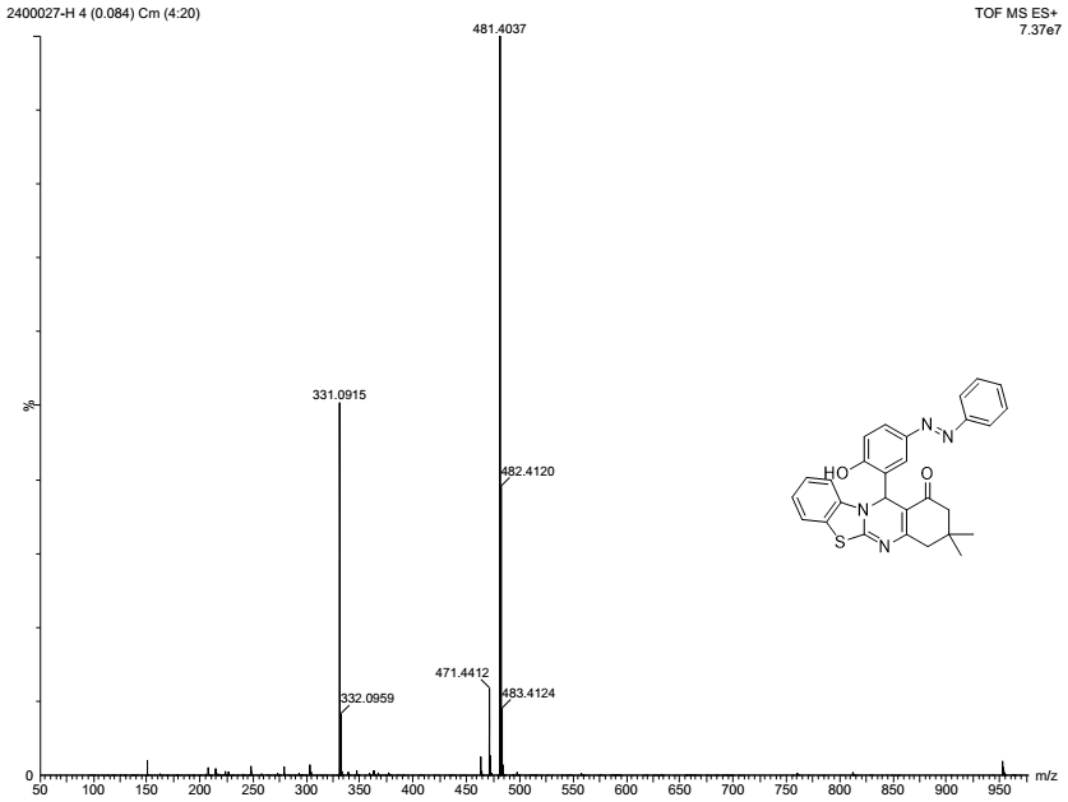


Figure. 60. Mass spectrum of compound **4o**

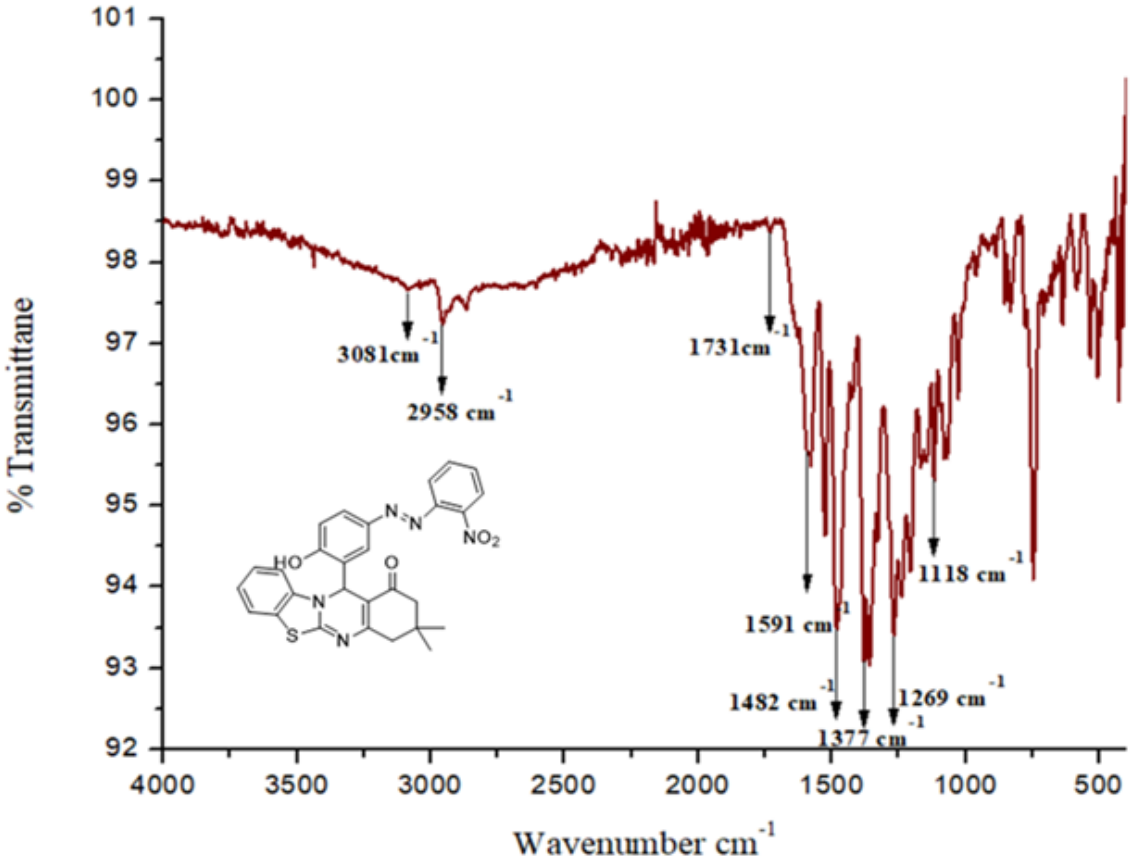


Figure. 61. IR Spectrum of compound **4p**

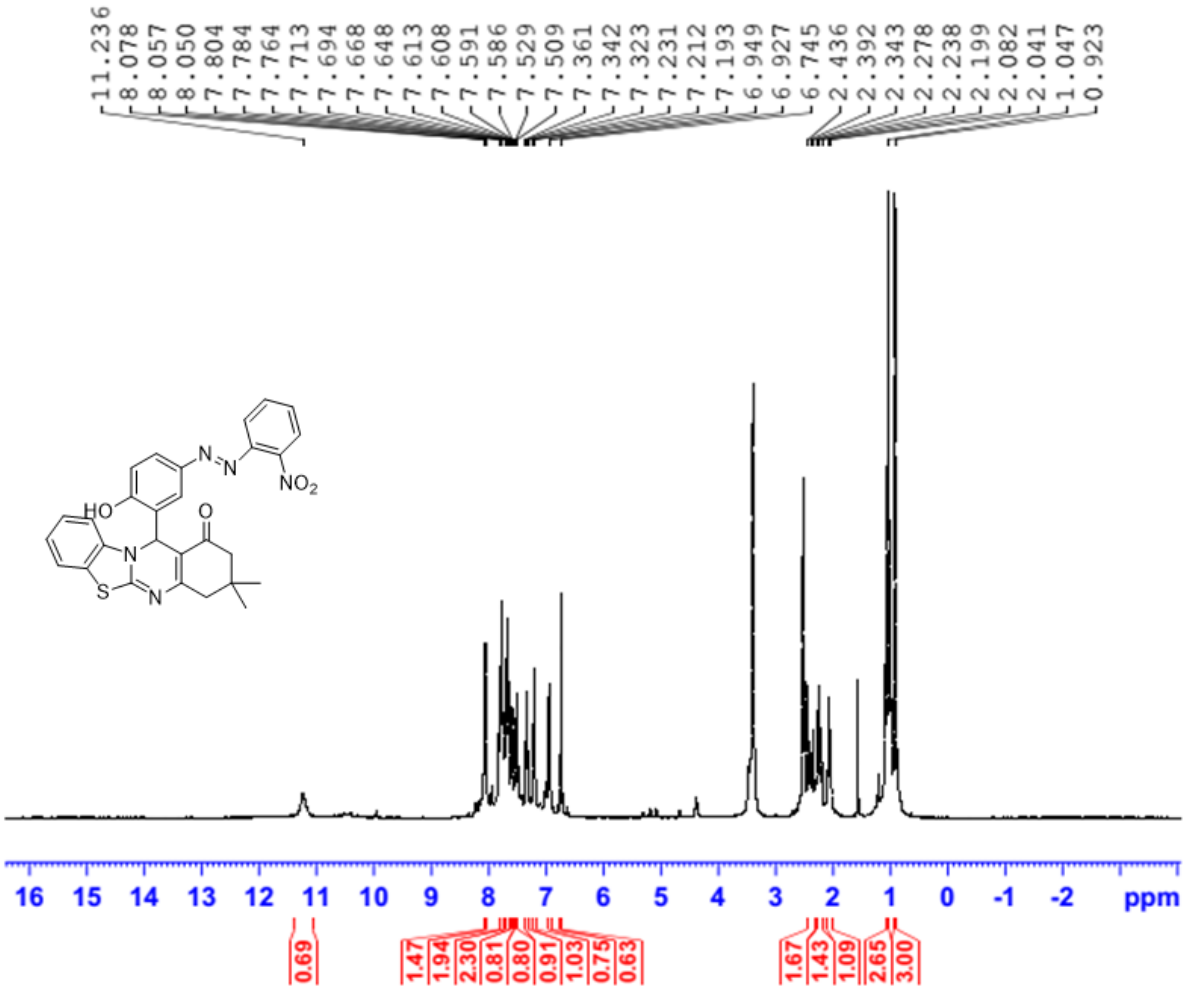


Figure. 62. ^{1}H Spectrum of compound **4p**

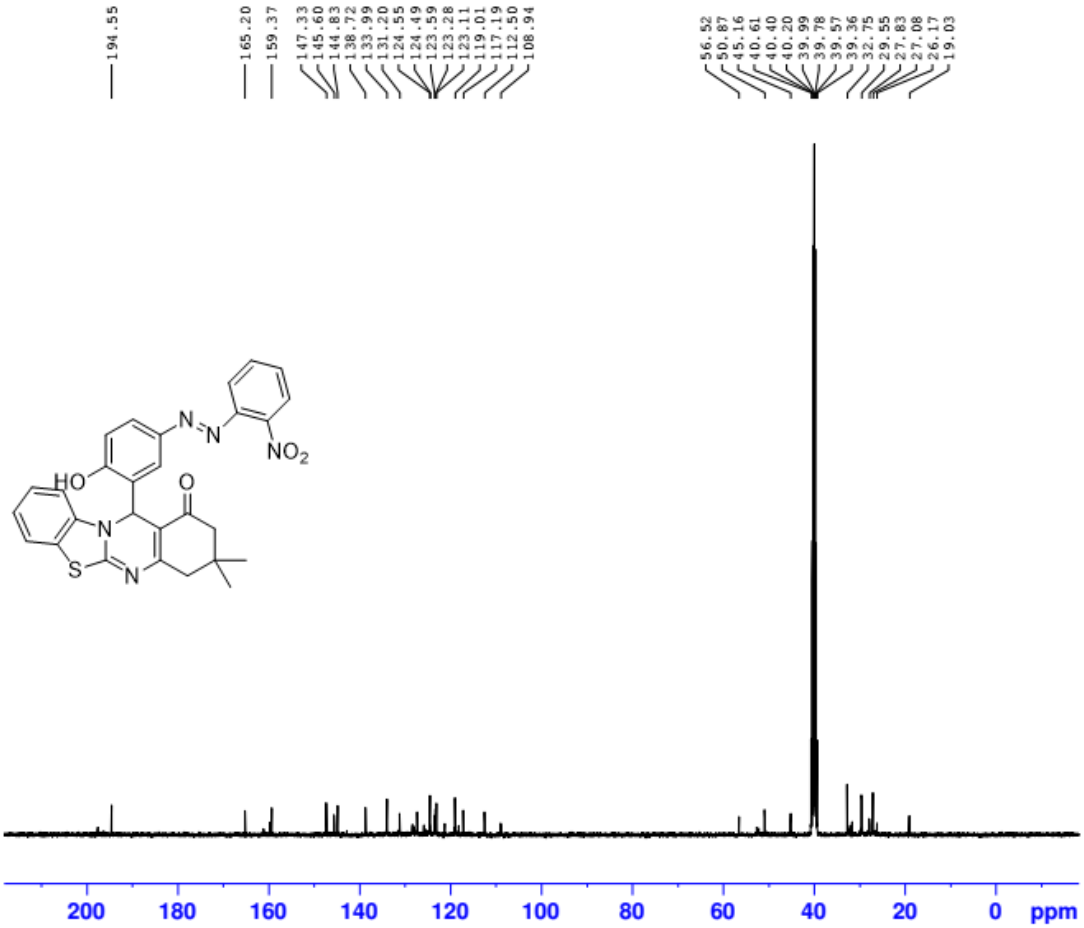


Figure. 63. ^{13}C NMR Spectrum of compound **4p**

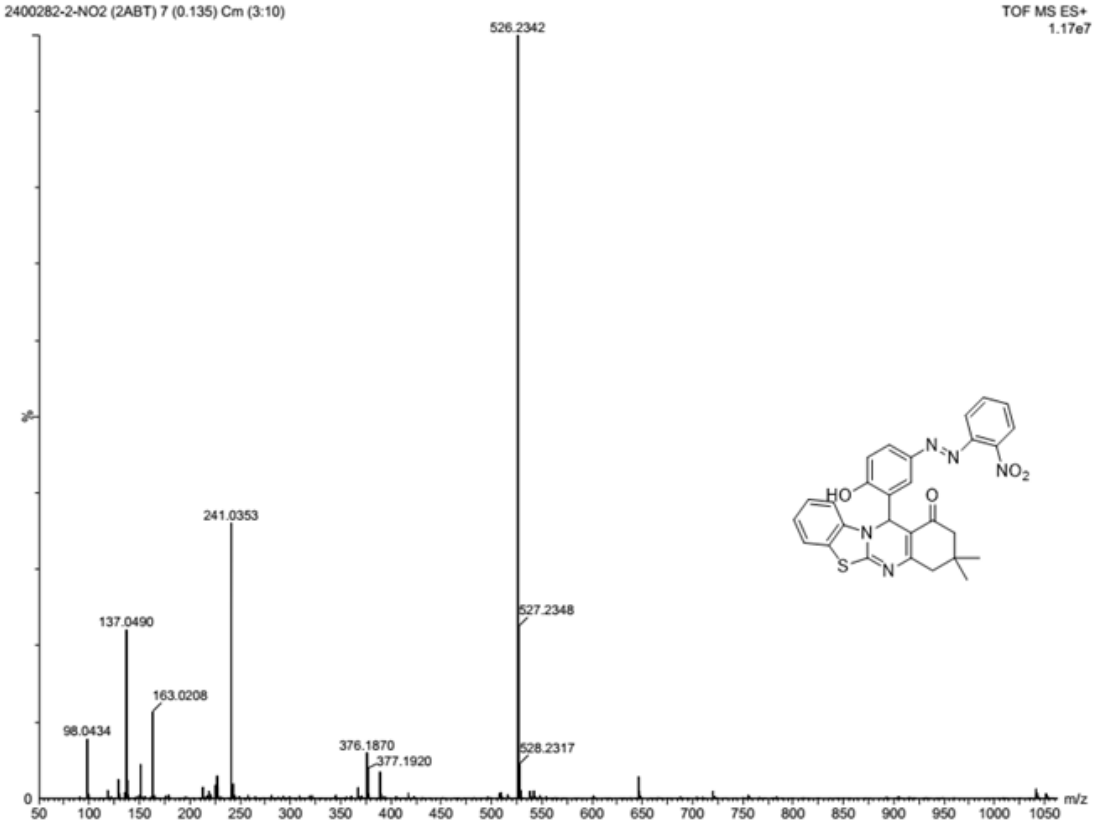


Figure. 64. Mass spectrum of compound **4p**

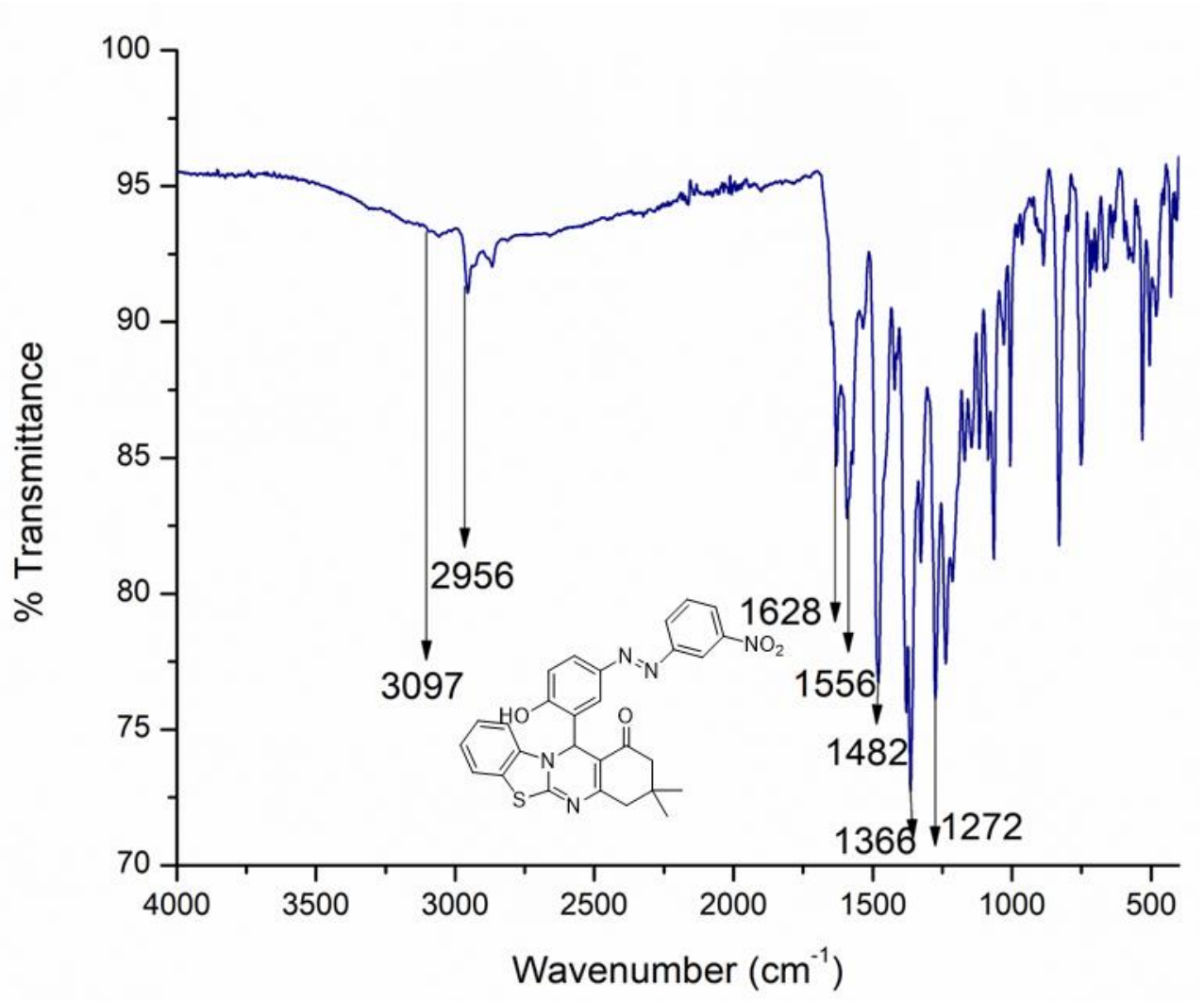


Figure. 65. IR Spectrum of compound **4q**

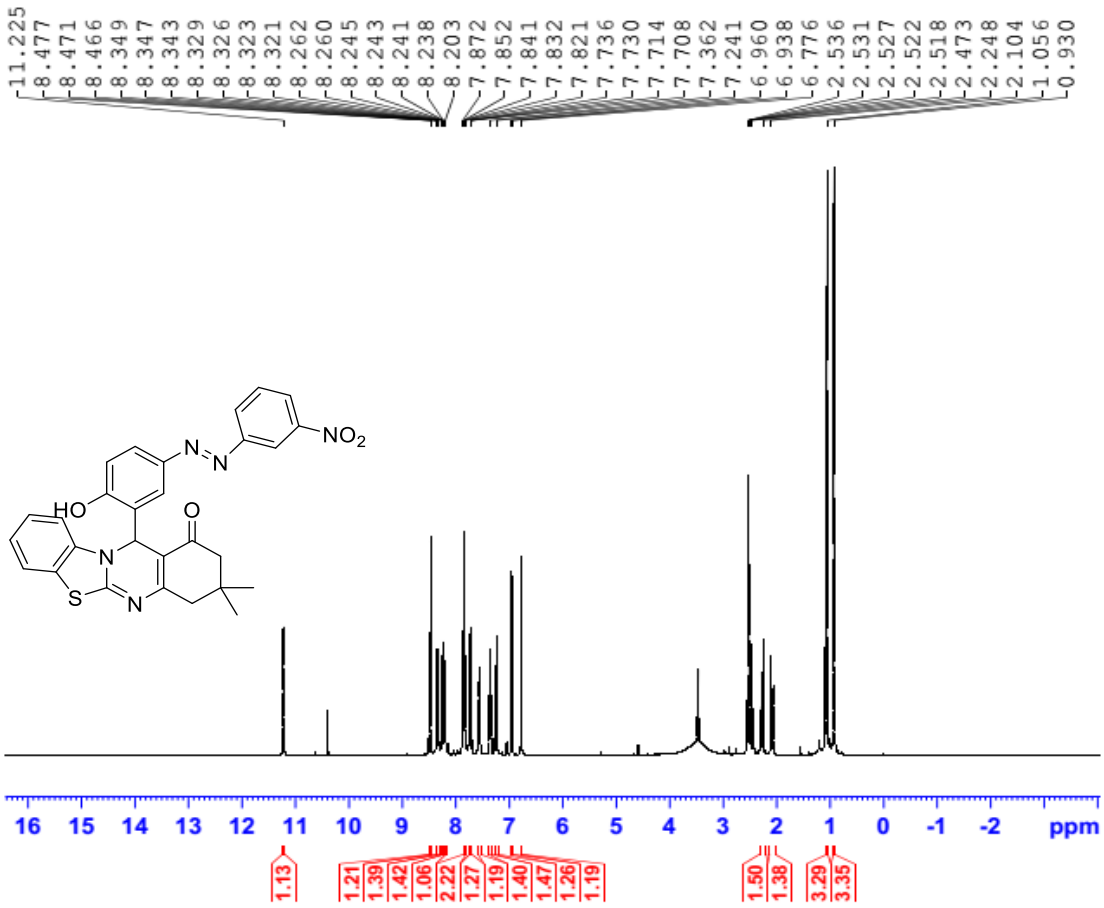


Figure. 66. ^{1}H Spectrum of compound **4q**

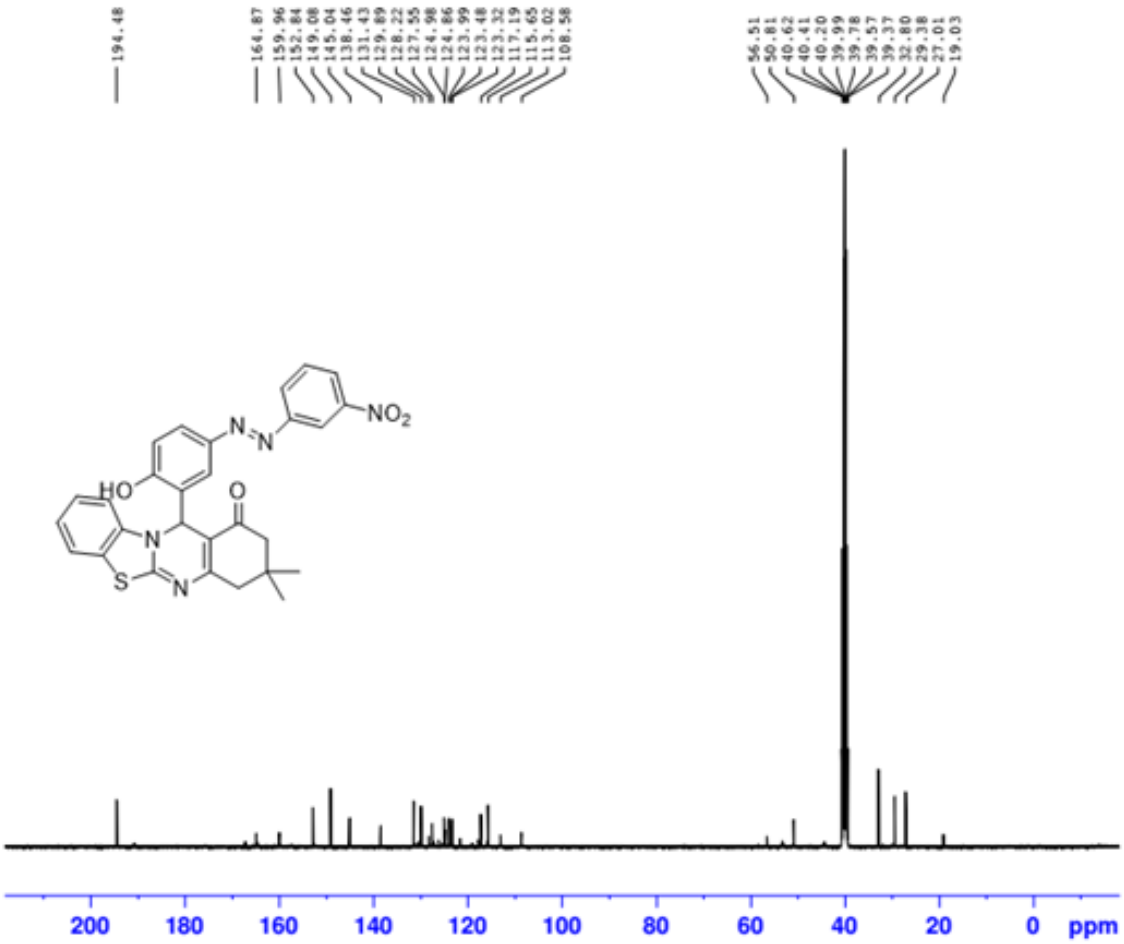


Figure. 67. ^{13}C NMR Spectrum of compound **4q**

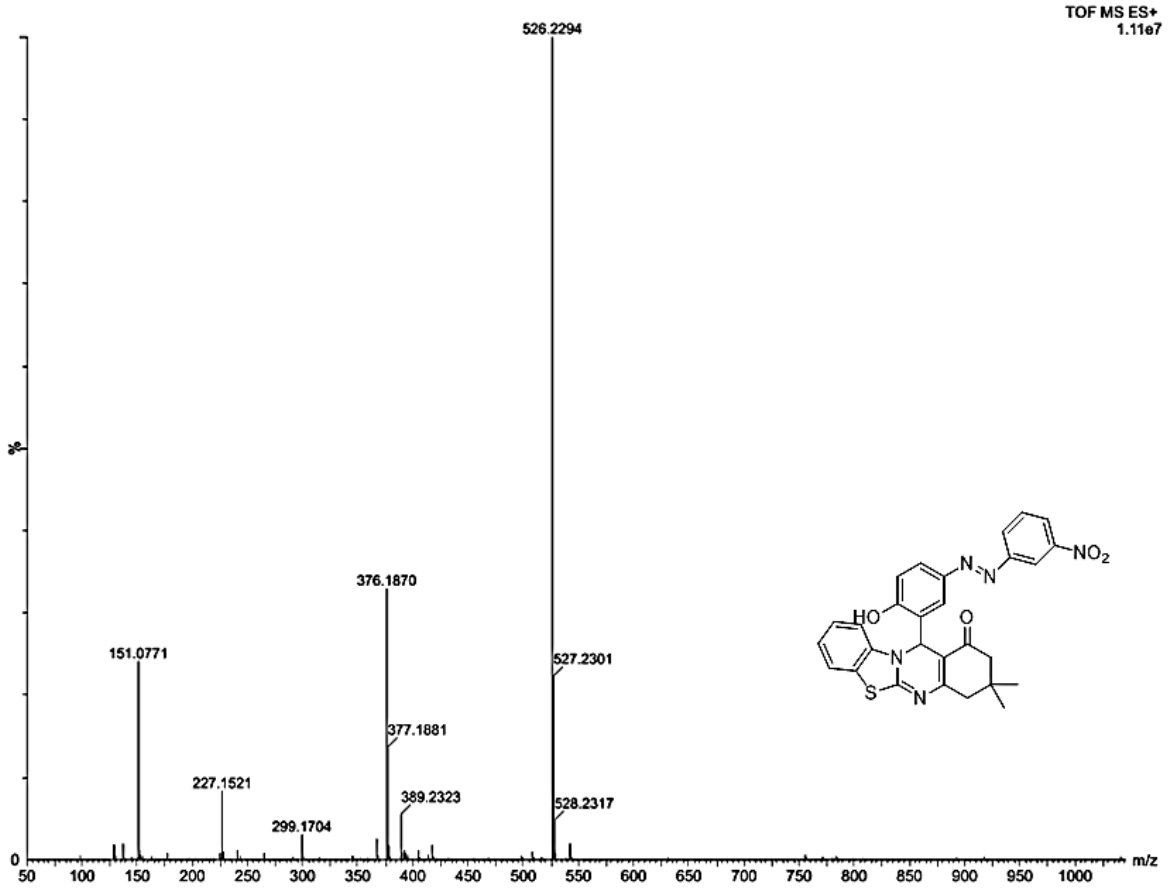


Figure. 68. Mass spectrum of compound **4q**

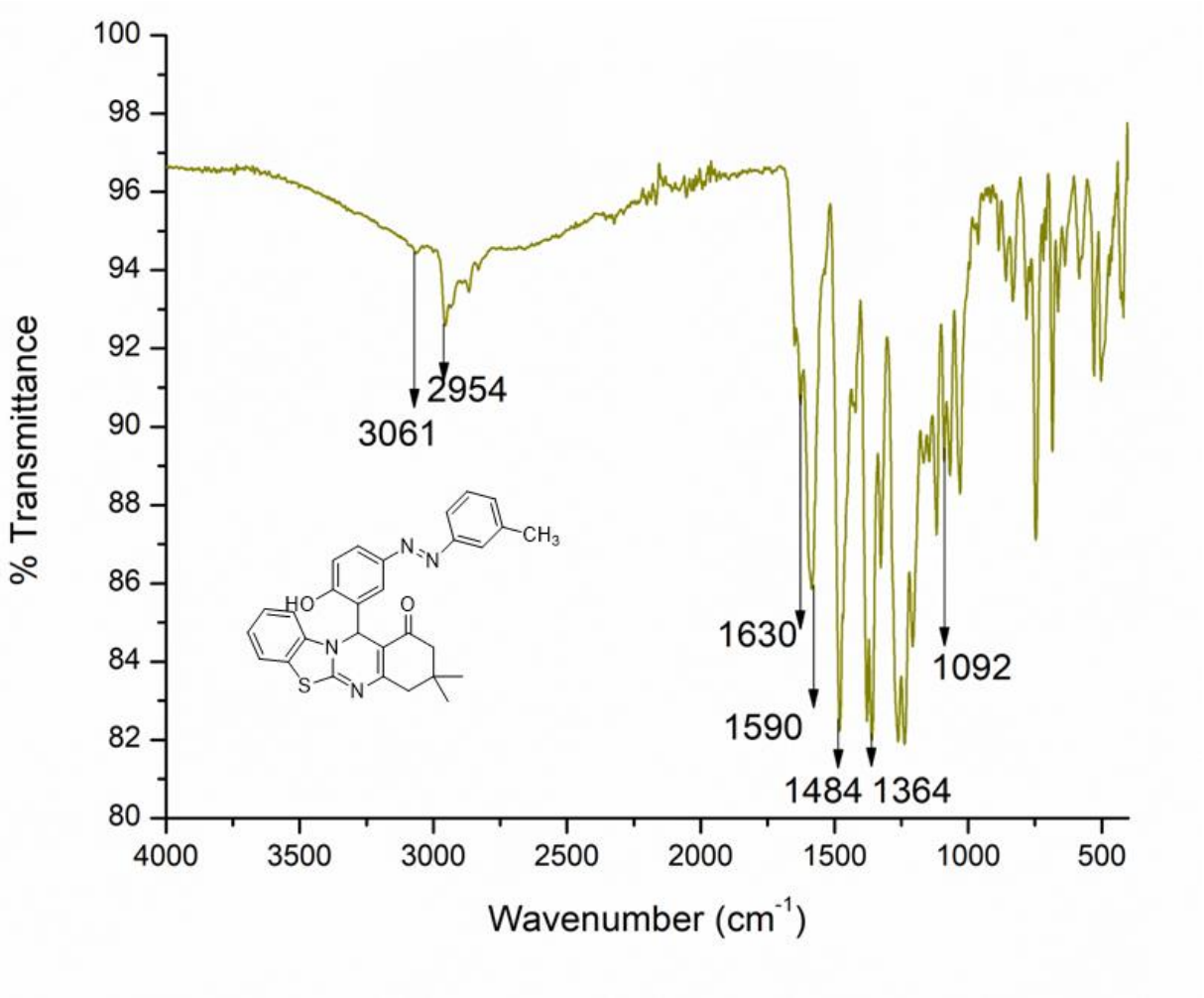


Figure. 69. IR Spectrum of compound **4r**

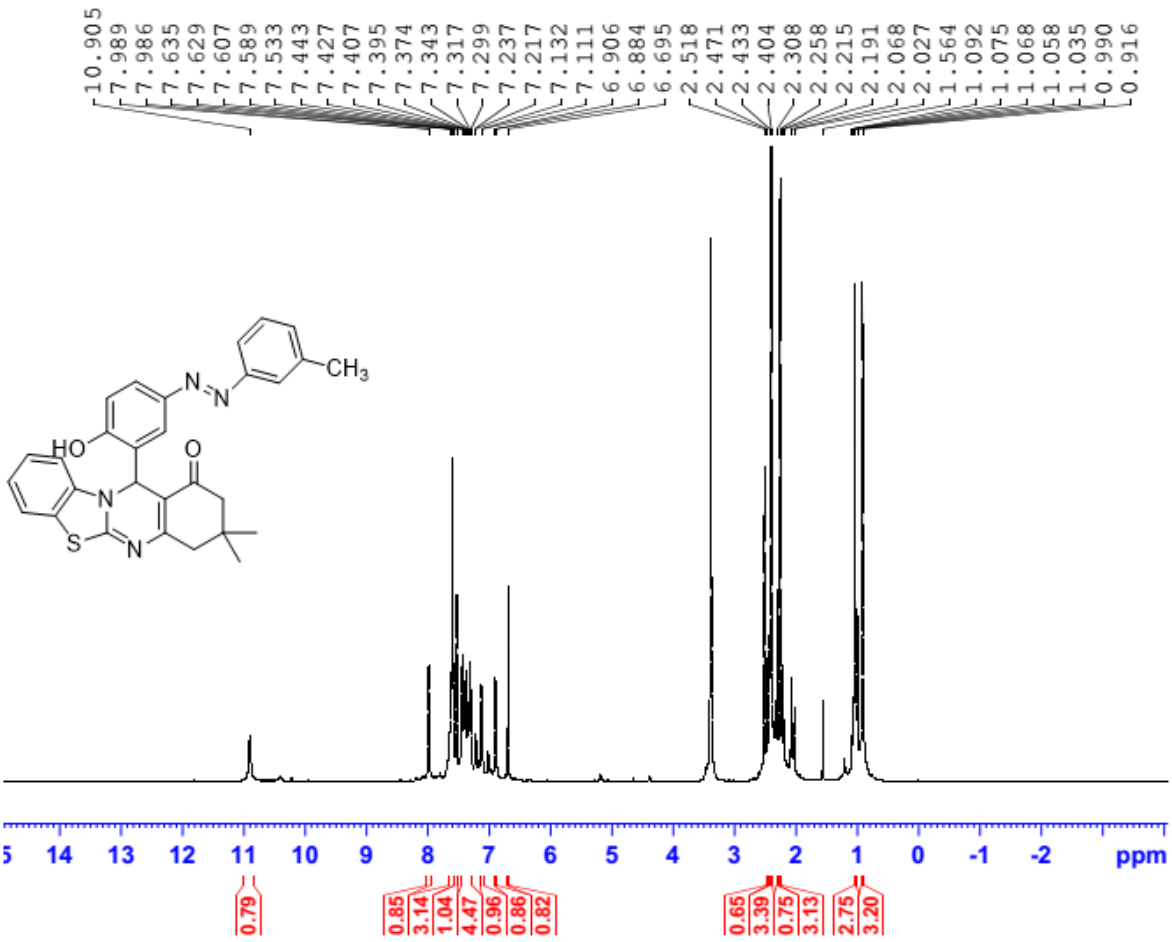


Figure. 70. ^{1}H Spectrum of compound **4r**

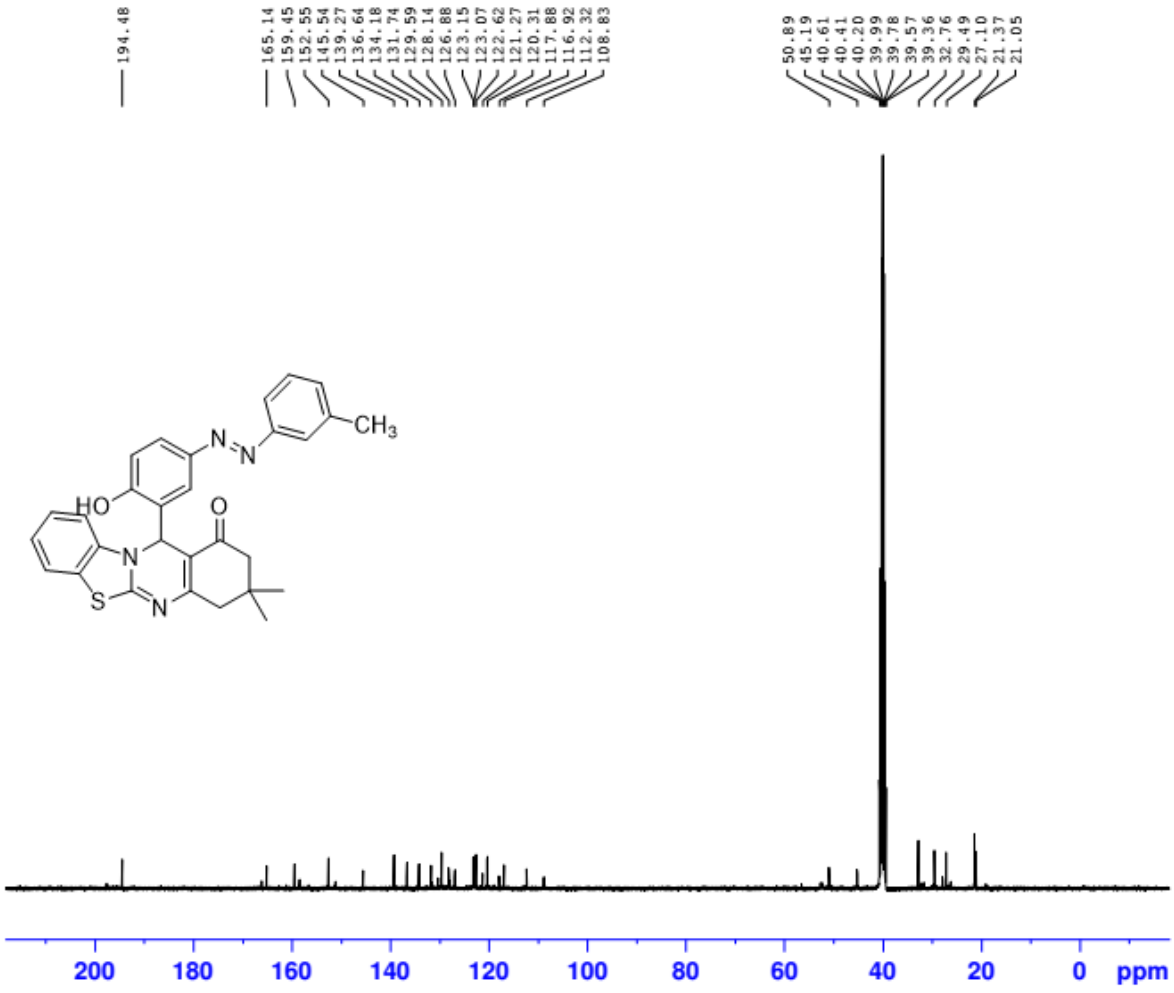


Figure. 71. ^{13}C NMR Spectrum of compound **4r**

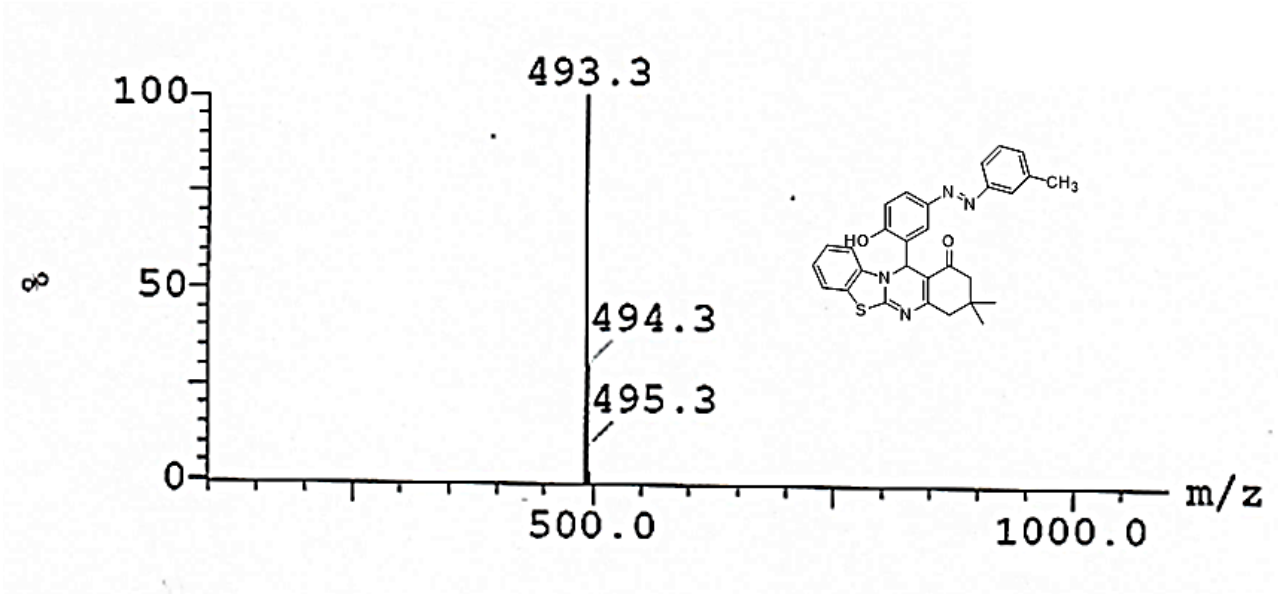


Figure. 72. Mass spectrum of compound **4r**

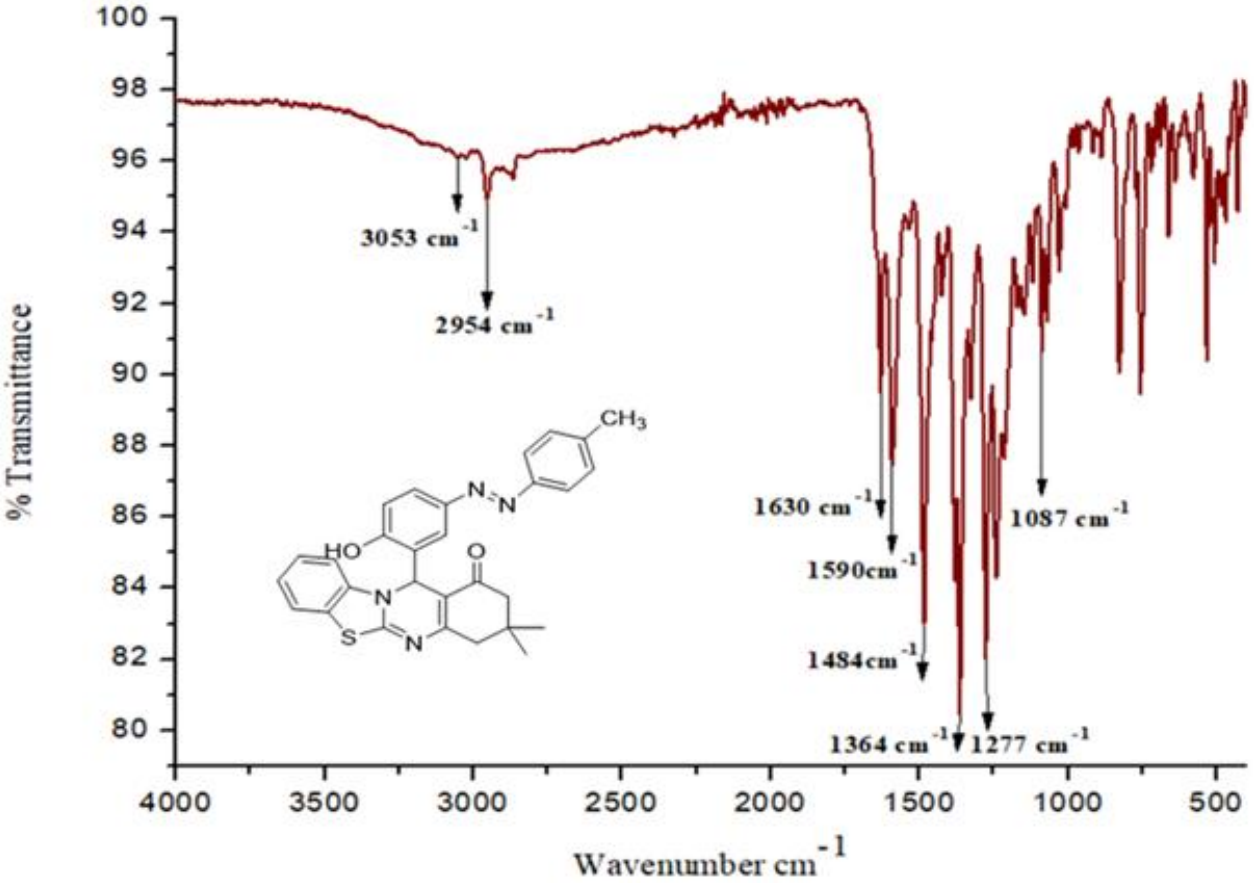


Figure. 73. IR Spectrum of compound **4s**

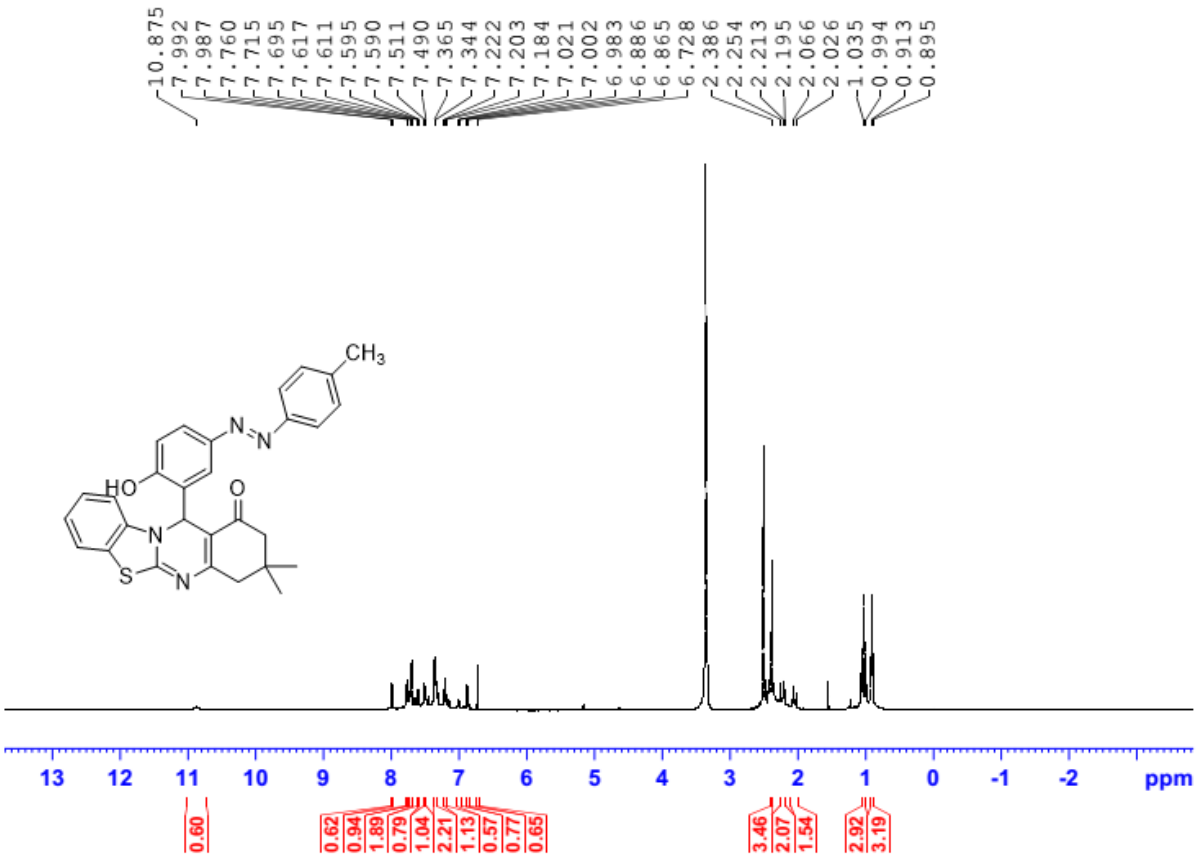


Figure. 74. ^{1}H Spectrum of compound **4s**

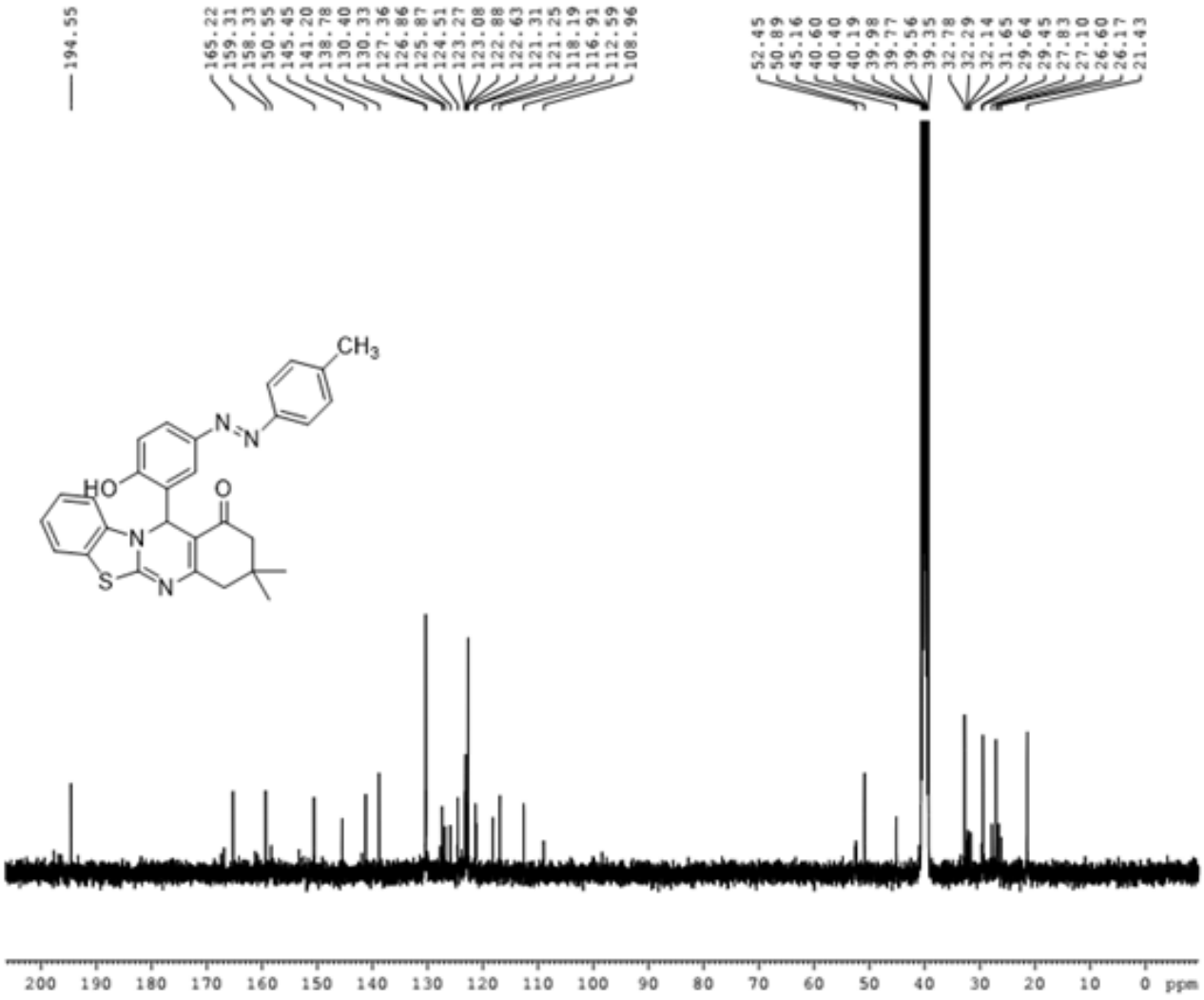


Figure. 75. ^{13}C NMR Spectrum of compound **4s**

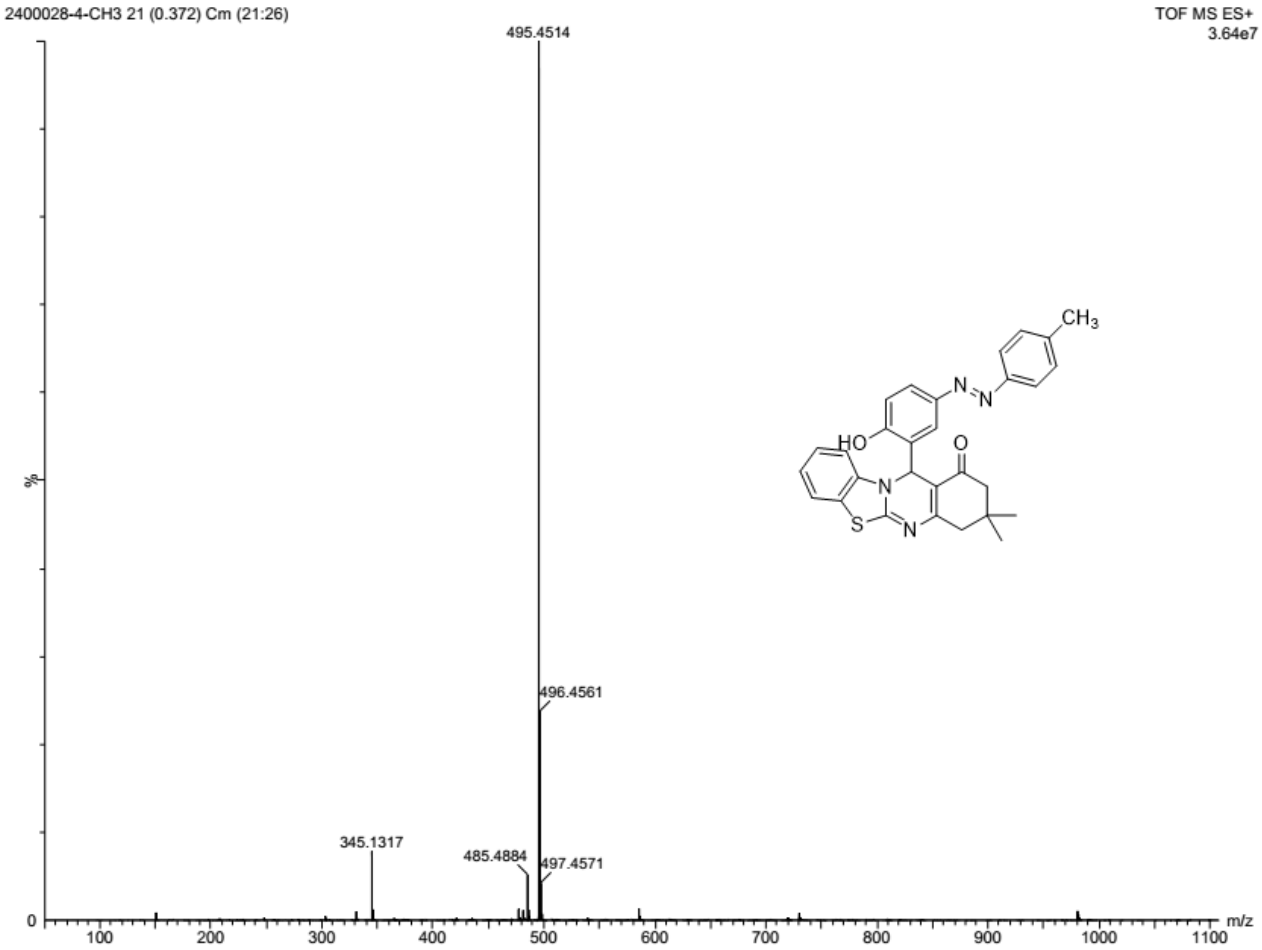
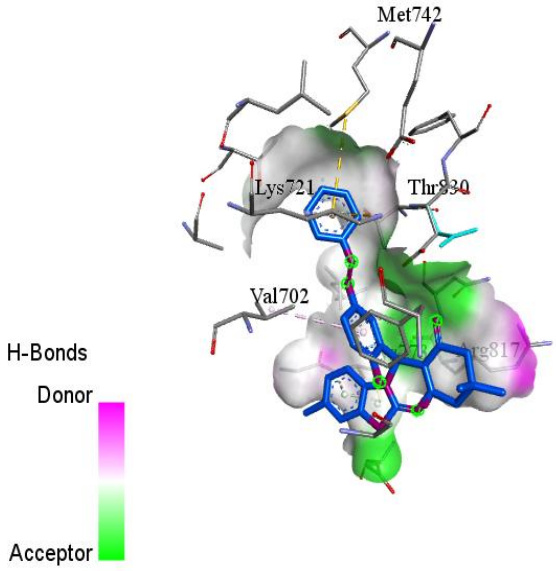


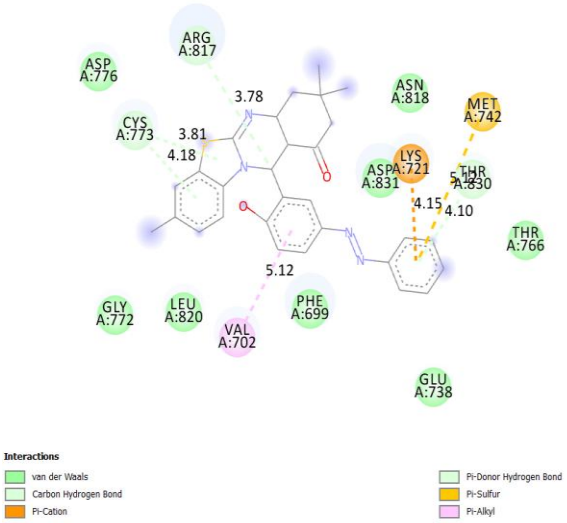
Figure. 76. Mass spectrum of compound **4s**

Molecular docking diagrams of (4a-s).

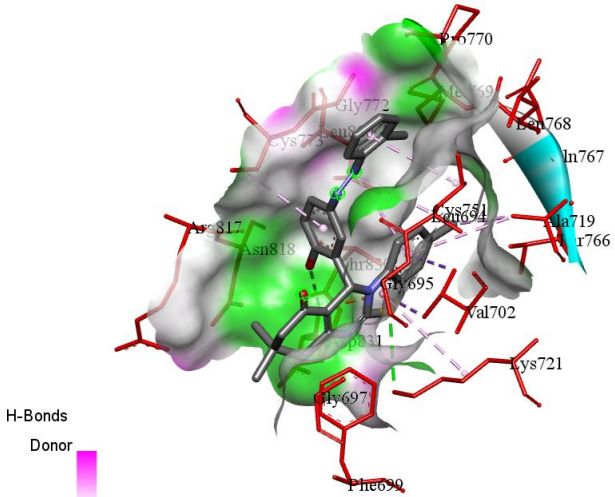
Molecular Docking 3D and 2D diagrams of the synthesized compounds (4a-s) towards the target of *EGFR*

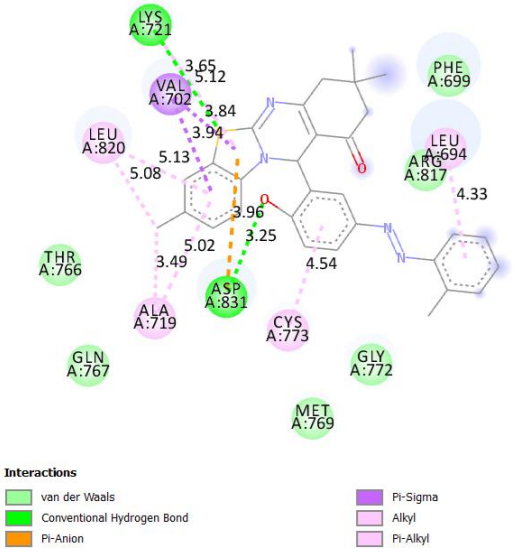
i. 4a



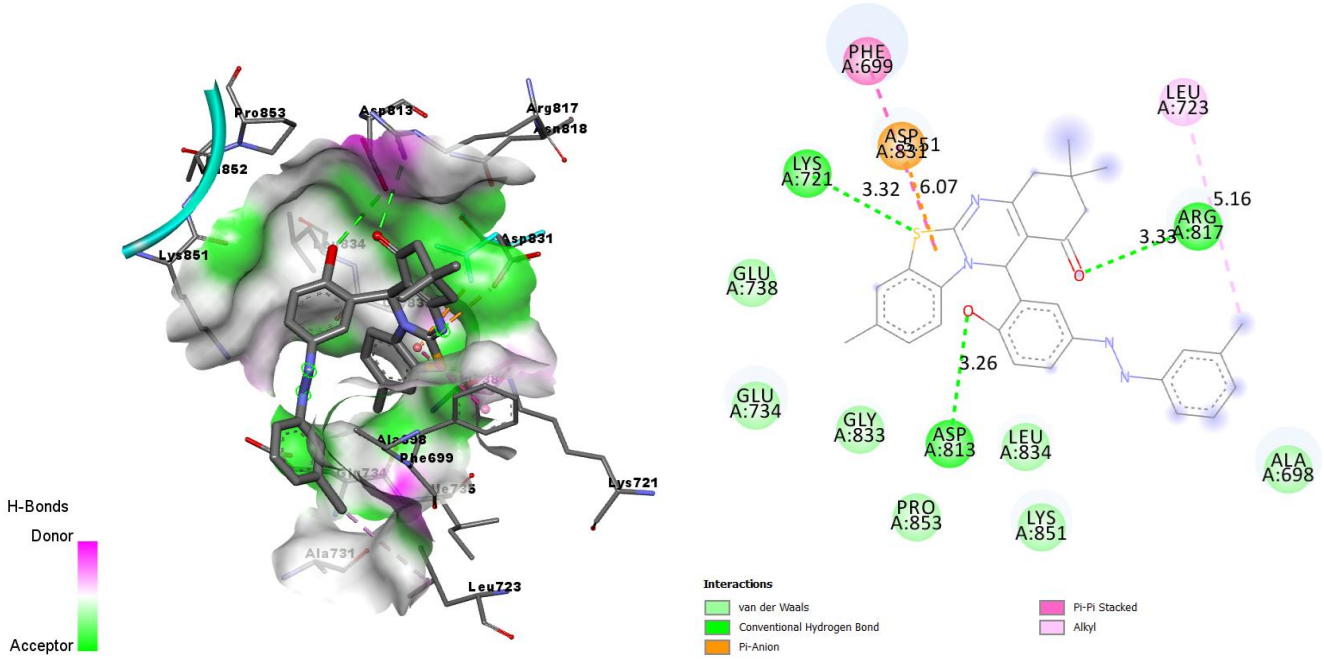


ii. 4b

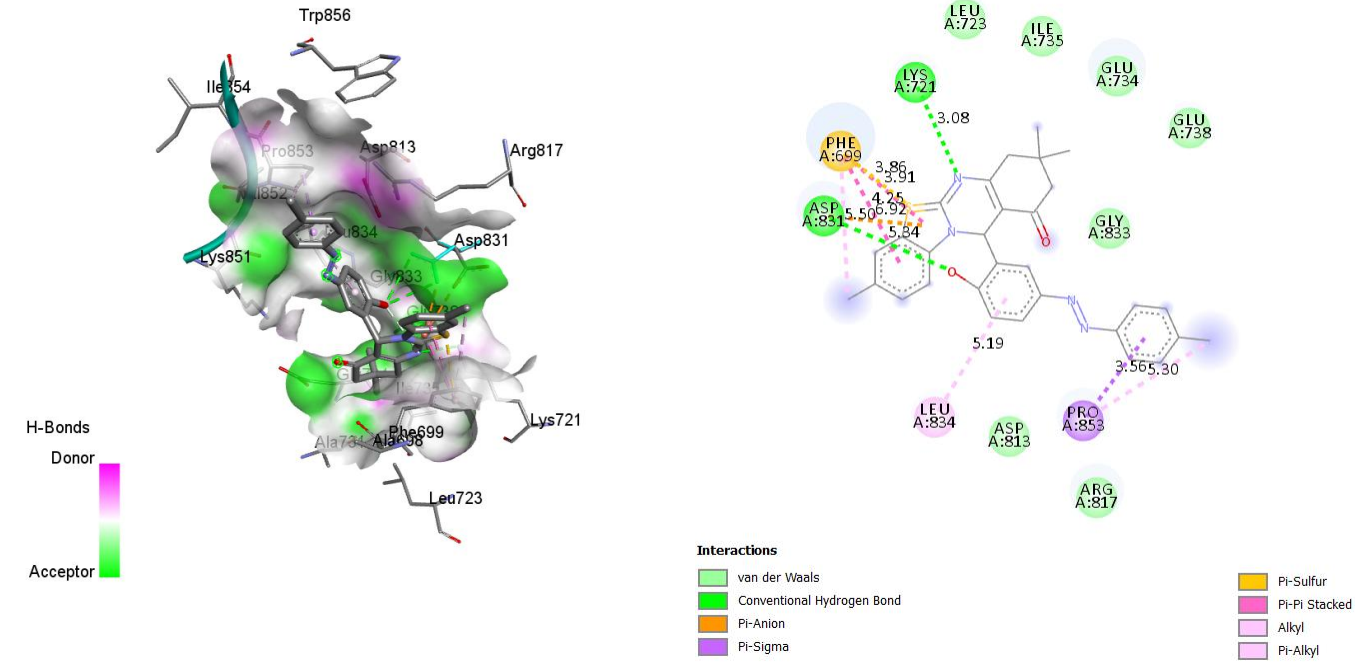




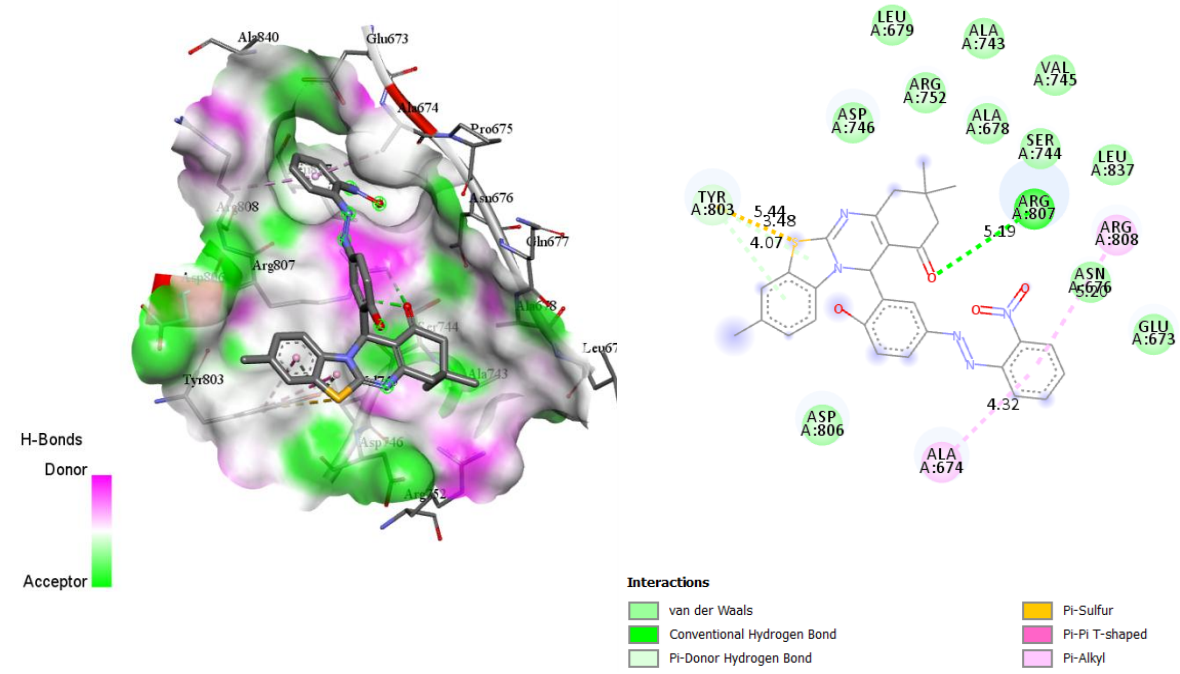
iii. 4c


Pro853
Asp813
Arg817
Asn818
Lys851
Asp831
Phe699
Lys721
Ala731
Leu723
H-Bonds
Donor
Acceptor
PHE A:699
LEU A:723
ASP A:831
LYS A:721
3.32
6.07
5.16
ARG A:817
3.33
GLU A:738
3.26
GLU A:734
GLY A:833
ASP A:813
LEU A:834
ALA A:698
PRO A:853
LYS A:851
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Pi Stacked
Alkyl

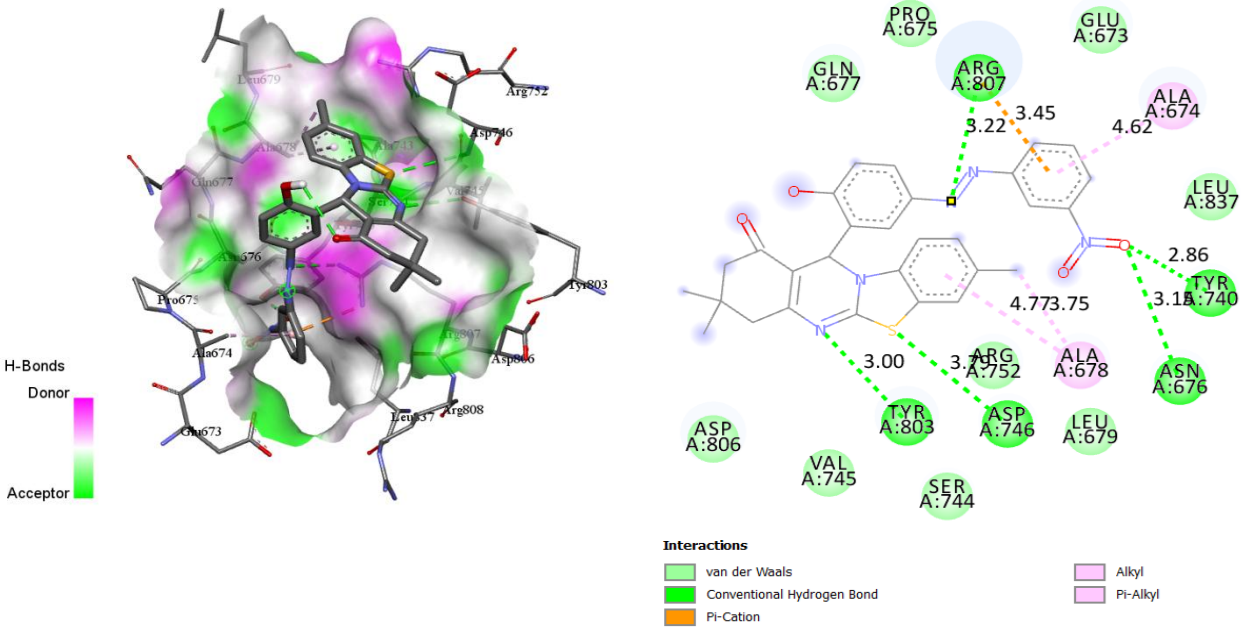
iv. 4d


Trp856
Pro853
Asp813
Arg817
Lys851
Asp831
Gly833
Phe699
Lys721
Leu723
H-Bonds
Donor
Acceptor
LEU A:723
ILE A:735
GLU A:734
LYS A:721
3.08
GLU A:738
PHE A:699
3.86
3.91
4.25
ASP A:831
5.50
6.92
5.84
GLY A:833
5.19
3.56
5.30
LEU A:834
ASP A:813
PRO A:853
ARG A:817
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sigma
Pi-Sulfur
Pi-Pi Stacked
Alkyl
Pi-Alkyl

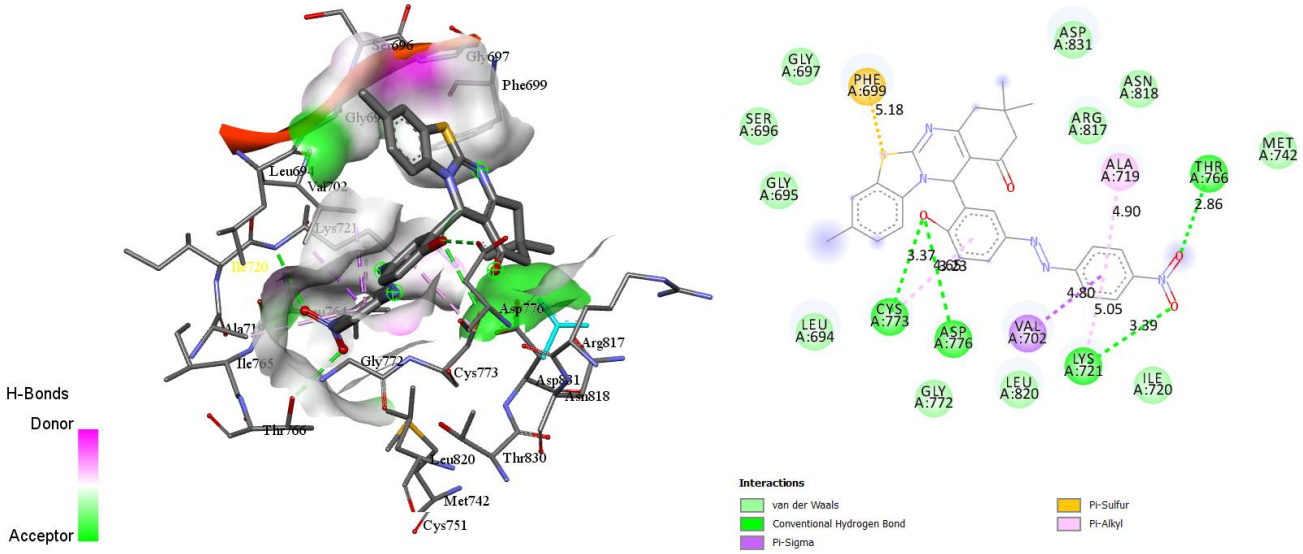
v. 4e


Ala840
Glu673
Ala674
Pro675
Asn676
Gln677
Arg807
Tyr803
Asp746
Arg752
H-Bonds
Donor
Acceptor
LEU A:679
ALA A:743
VAL A:745
ARG A:752
ASP A:746
ALA A:678
SER A:744
LEU A:837
TYR A:803
ARG A:807
ARG A:808
ASN A:676
GLU A:673
ASP A:806
ALA A:674
5.44
5.48
4.07
5.19
4.32
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Donor Hydrogen Bond
Pi-Sulfur
Pi-Pi T-shaped
Pi-Alkyl

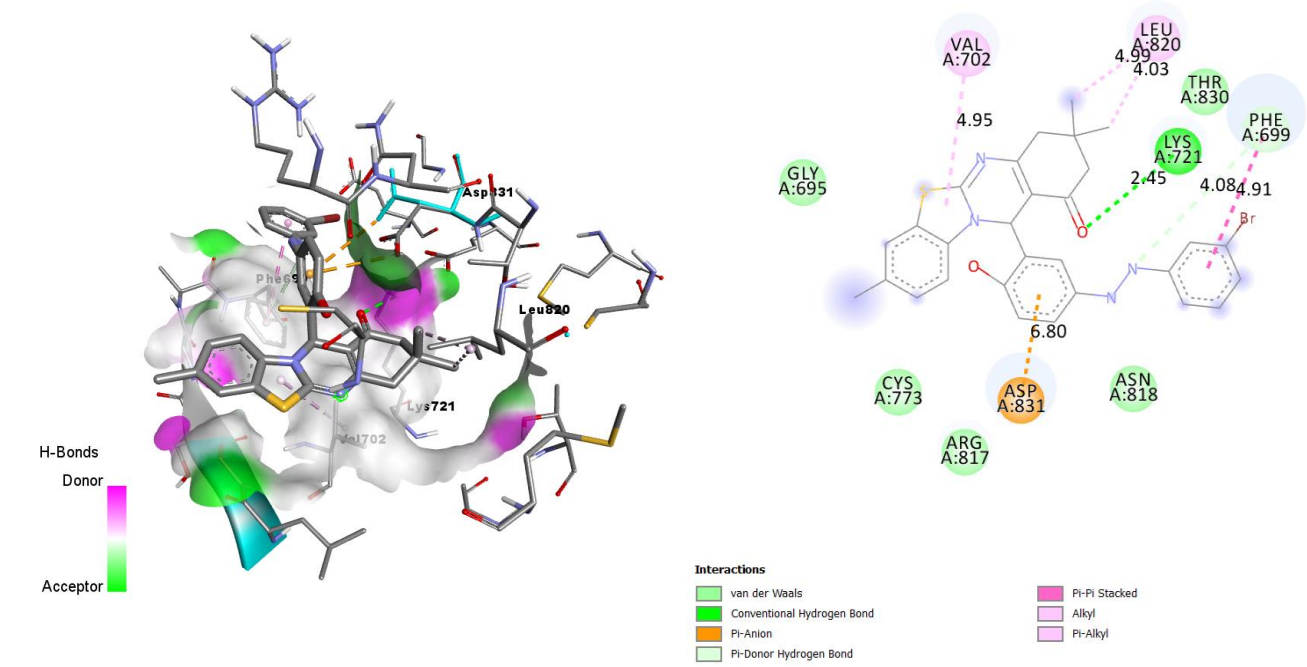
vi. 4f


Leu679
Arg752
Asp746
Gln677
Asn676
Pro675
Ala674
Glu673
Tyr803
Arg807
Asp806
Leu837
Arg808
H-Bonds
Donor
Acceptor
PRO A:675
GLU A:673
GLN A:677
ARG A:807
ALA A:674
3.22
3.45
4.62
LEU A:837
2.86
TYR A:740
4.77
3.75
3.00
3.29
ARG A:752
ALA A:678
ASN A:676
TYR A:803
ASP A:746
LEU A:679
ASP A:806
VAL A:745
SER A:744
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Cation
Alkyl
Pi-Alkyl

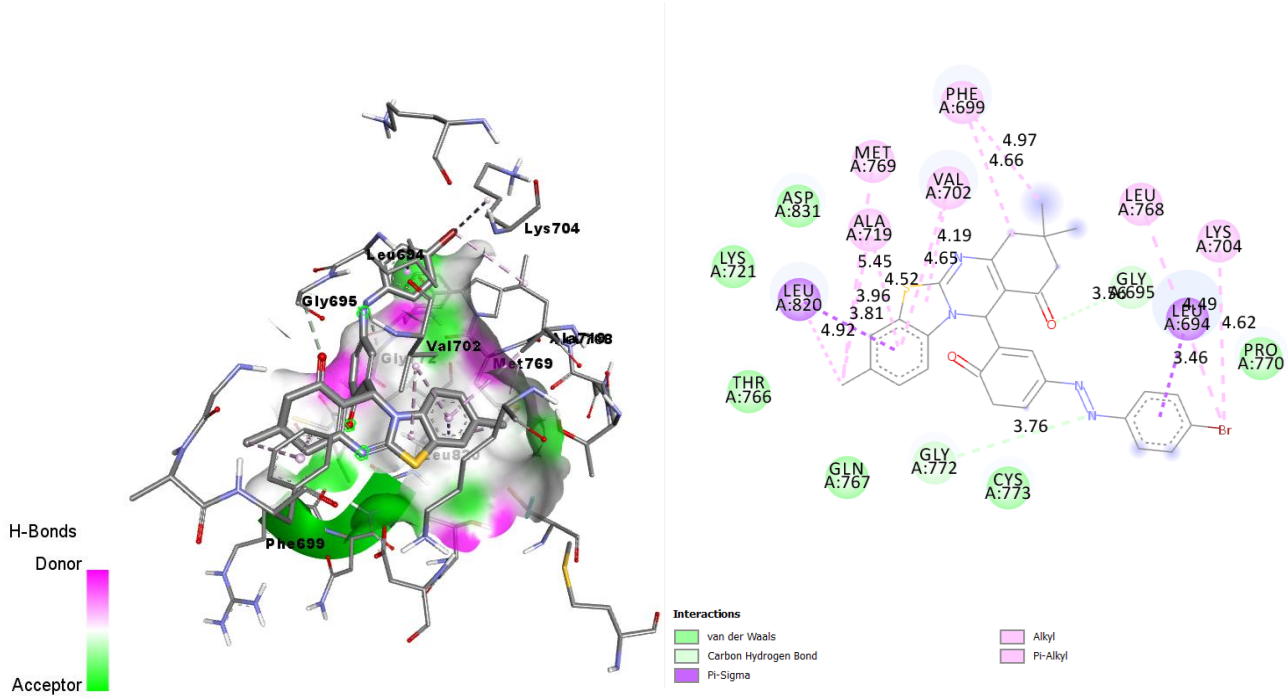
vii. 4g



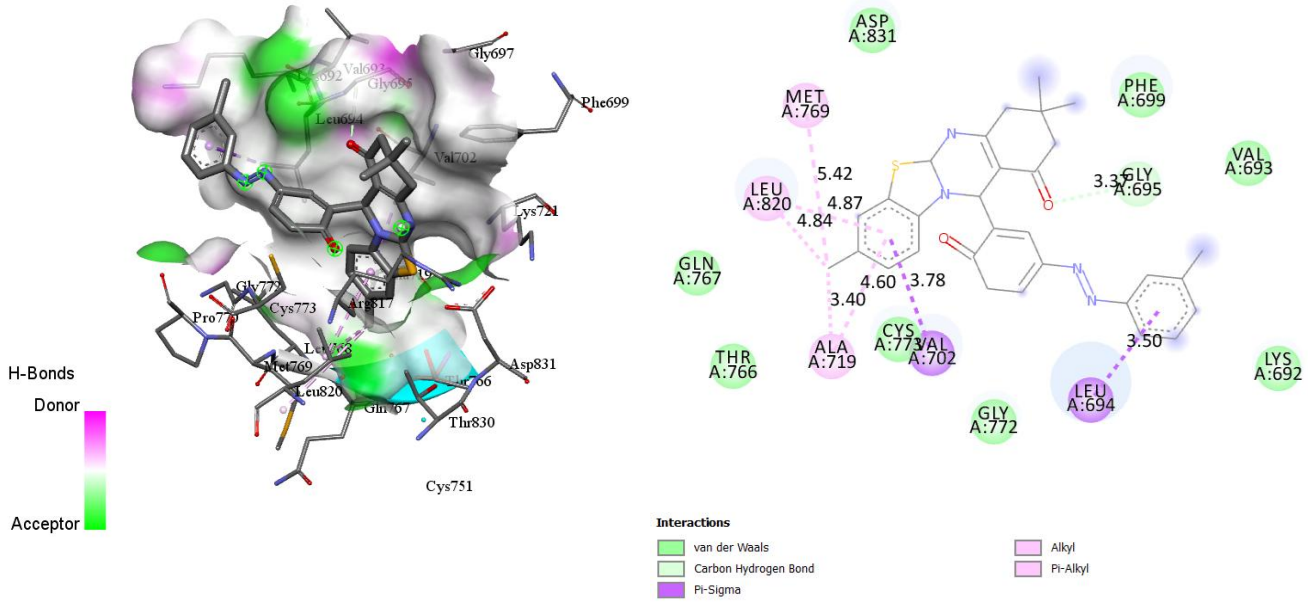
viii. 4h



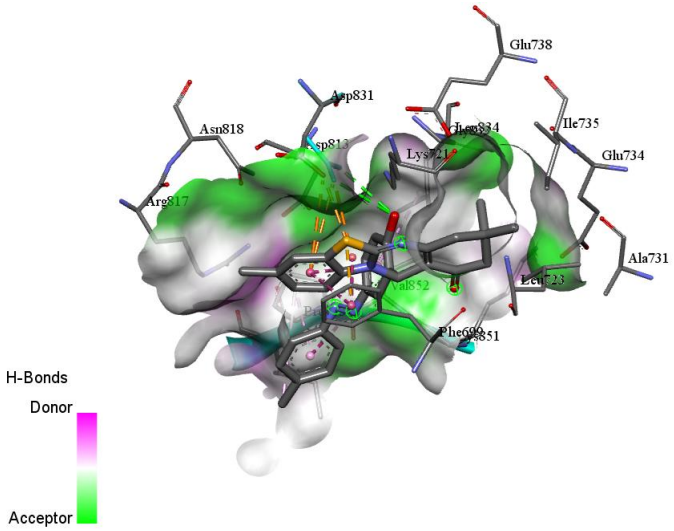
ix. 4i

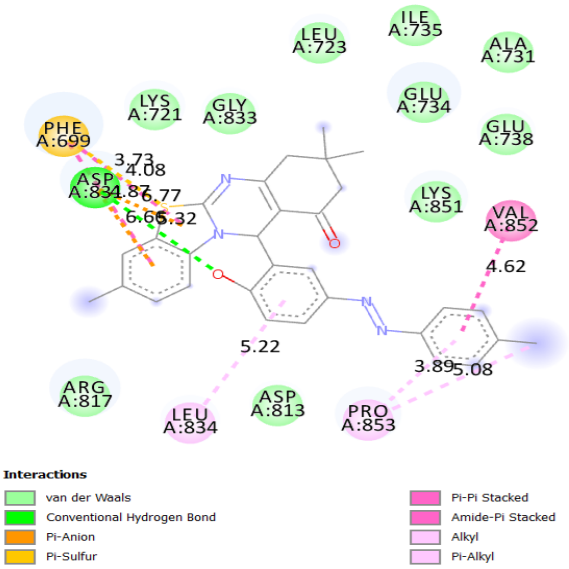

Lys704
Leu694
Gly695
Val702
Met769
Phe699
H-Bonds
Donor
Acceptor
PHE A:699
MET A:769
VAL A:702
ASP A:831
ALA A:719
LEU A:768
LYS A:704
LYS A:721
LEU A:820
GLY A:695
LEU A:694
PRO A:770
THR A:766
GLN A:767
GLY A:772
CYS A:773
4.97
4.66
4.19
4.65
5.45
4.52
3.96
3.81
4.92
4.49
4.62
3.46
3.76
Br
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Sigma
Alkyl
Pi-Alkyl

x. 4j

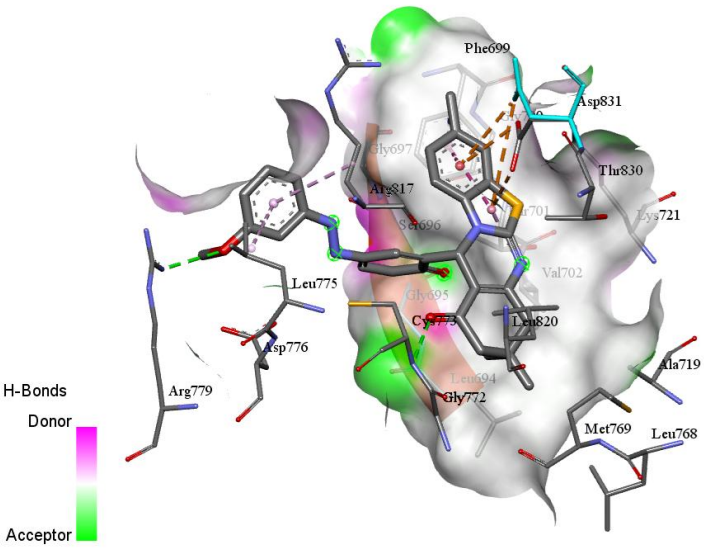

Gly697
Phe699
Leu694
Val702
Cys724
Gly772
Pro770
Cys773
Arg817
Met769
Leu820
Asp831
Thr830
Cys751
H-Bonds
Donor
Acceptor
ASP A:831
MET A:769
PHE A:699
VAL A:693
LEU A:820
GLY A:695
GLN A:767
THR A:766
ALA A:719
CYS A:773
VAL A:702
LEU A:694
LYS A:692
GLY A:772
5.42
4.87
4.84
4.60
3.78
3.40
3.50
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Sigma
Alkyl
Pi-Alkyl

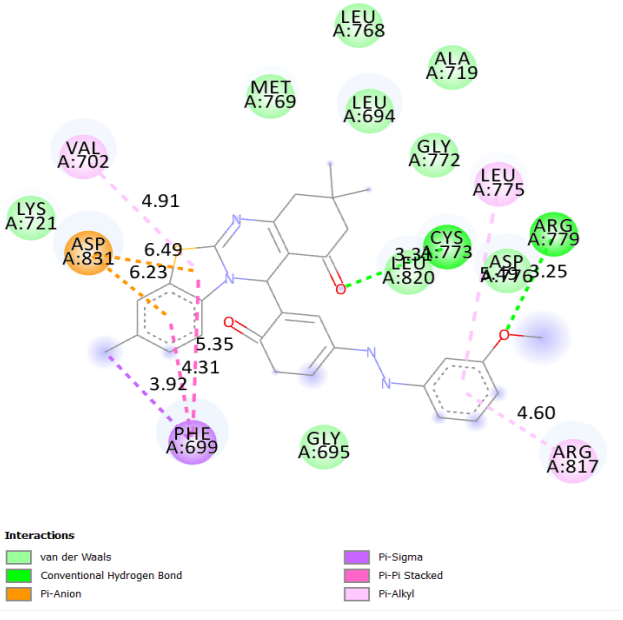
xi. 4k


Glu738
Asp831
Asn818
Ile735
Glu734
Arg817
Ala731
Val852
Phe699
H-Bonds
Donor
Acceptor

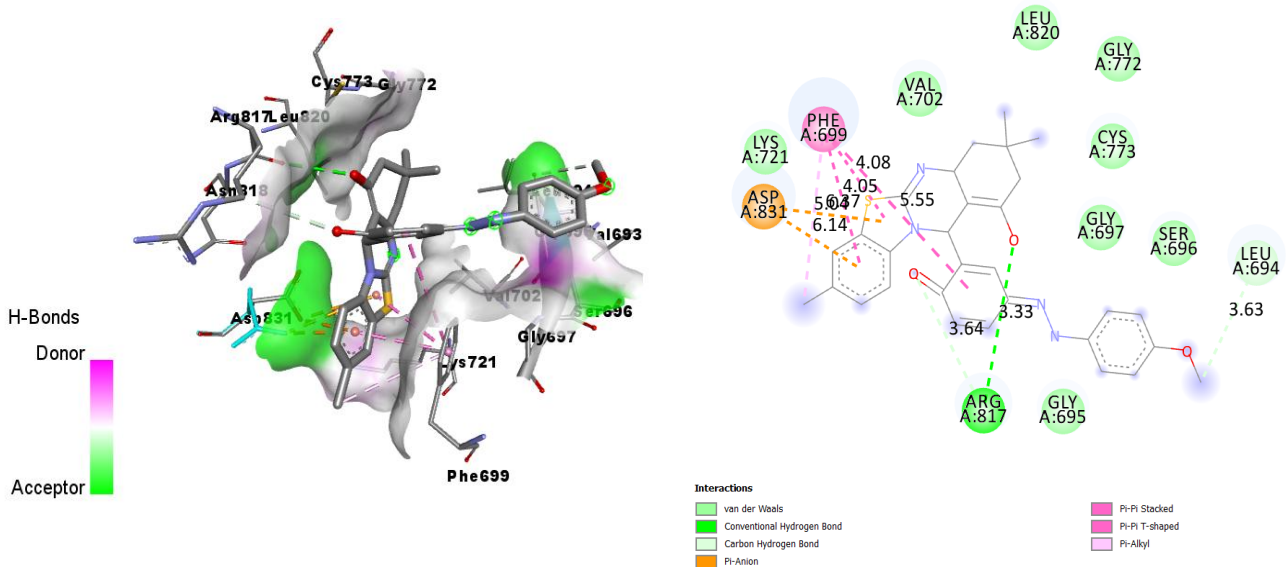

LEU A:723
ILE A:735
ALA A:731
LYS A:721
GLY A:833
GLU A:734
GLU A:738
PHE A:699
3.73
4.08
ASP A:834
6.77
6.65
5.32
LYS A:851
VAL A:852
4.62
5.22
3.89
5.08
ARG A:817
LEU A:834
ASP A:813
PRO A:853
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sulfur
Pi-Pi Stacked
Amide-Pi Stacked
Alkyl
Pi-Alkyl

xii. 4l

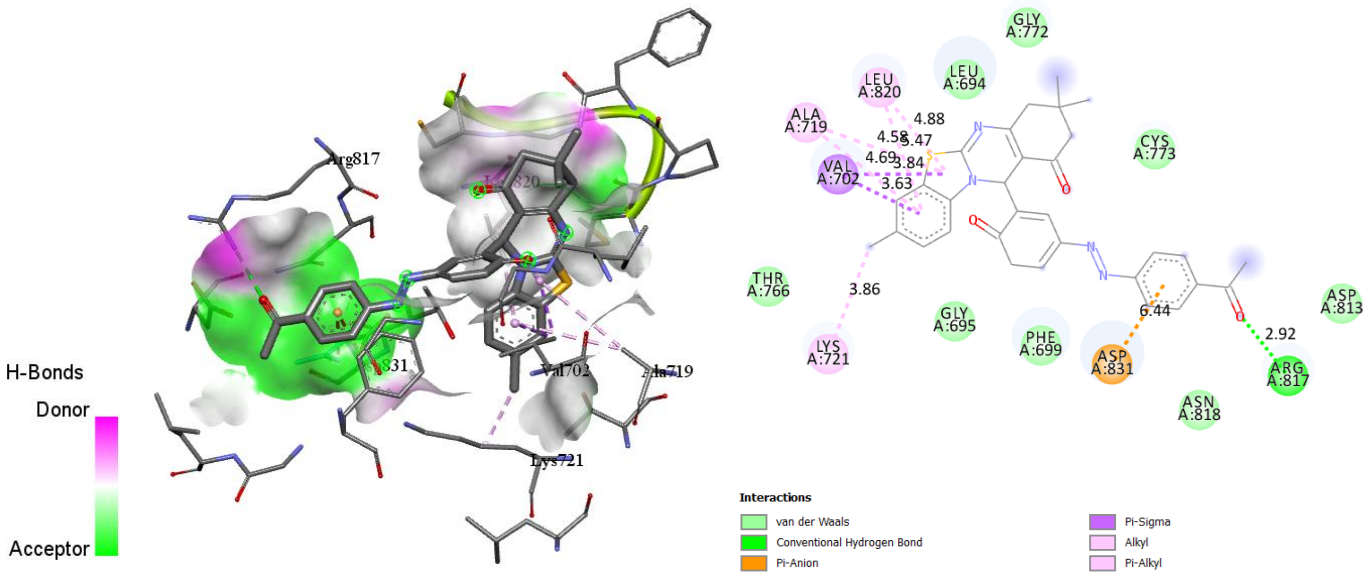

Phe699
Asp831
Thr830
Arg817
Lys721
Leu775
Val702
Cys773
Leu820
Asp776
Ala719
Arg779
Gly772
Met769
Leu768
H-Bonds
Donor
Acceptor


LEU A:768
ALA A:719
MET A:769
LEU A:694
VAL A:702
GLY A:772
LEU A:775
4.91
LYS A:721
ASP A:831
6.49
6.23
CYS A:773
ARG A:779
LEU A:820
3.25
5.35
4.31
3.92
4.60
PHE A:699
GLY A:695
ARG A:817
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sigma
Pi-Pi Stacked
Pi-Alkyl

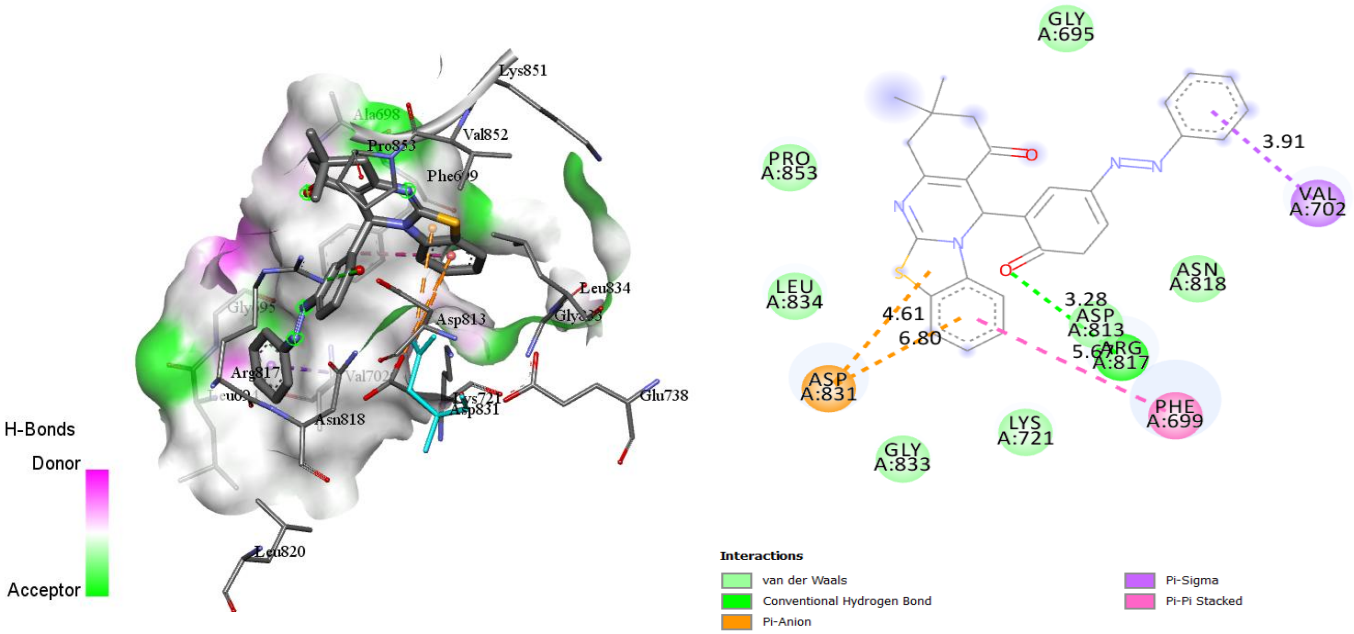
xiii. 4m



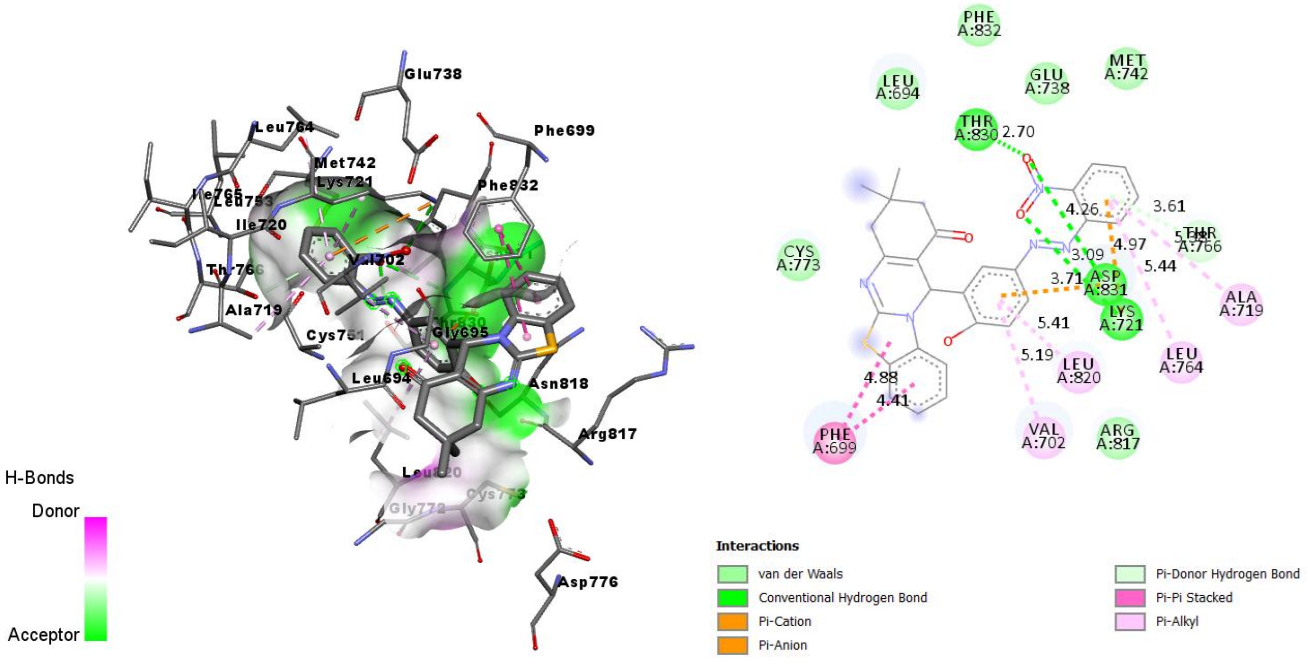
xiv. 4n



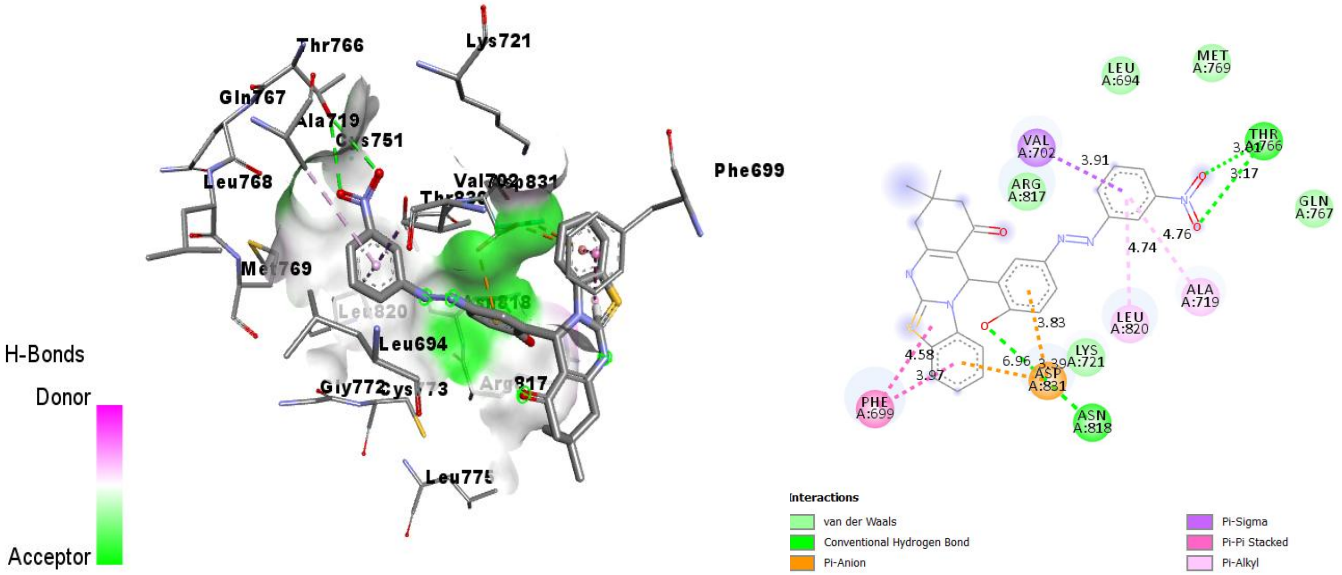
xv. 4o


Lys851
Ala698
Val852
Pro853
Phe699
Leu834
Gly695
Asp813
Arg817
Val702
Lys721
Asp831
Glu738
Asn818
Leu820
H-Bonds
Donor
Acceptor
GLY A:695
PRO A:853
3.91
VAL A:702
LEU A:834
ASN A:818
3.28
4.61
6.80
ASP A:813
ARG A:817
ASP A:831
PHE A:699
LYS A:721
GLY A:833
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Anion
Pi-Sigma
Pi-Pi Stacked

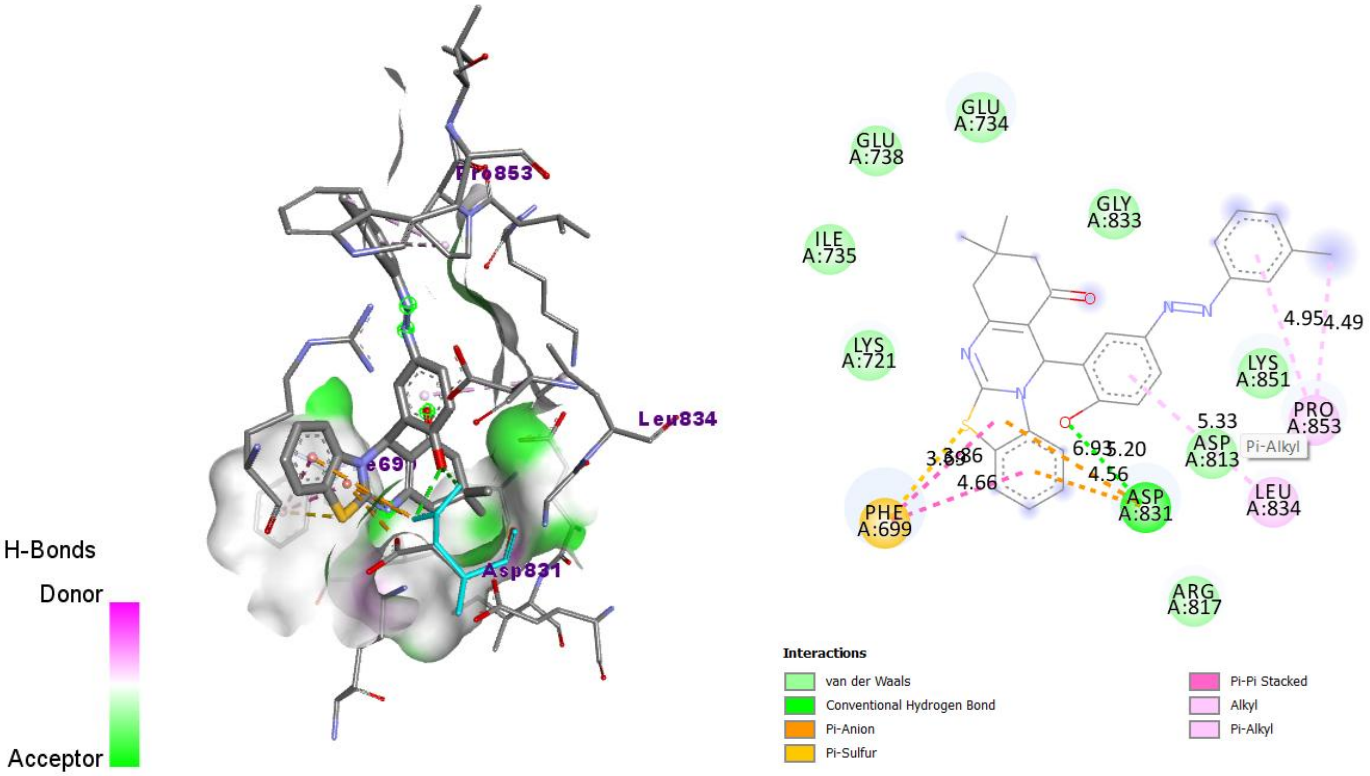
xvi. 4p


Glu738
Leu764
Phe699
Met742
Lys721
Phe832
Ile766
Leu753
Ile720
Val702
Thr766
Ala719
Cys761
Gly695
Leu694
Asn818
Arg817
Leu820
Gly772
Cys773
Asp776
H-Bonds
Donor
Acceptor
PHE A:832
LEU A:694
GLU A:738
MET A:742
THR A:830
2.70
4.26
3.61
CYS A:773
4.97
THR A:766
3.09
5.44
3.71
ASP A:831
ALA A:719
LYS A:721
5.41
5.19
LEU A:820
LEU A:764
4.88
4.41
PHE A:699
VAL A:702
ARG A:817
Interactions
van der Waals
Conventional Hydrogen Bond
Pi-Cation
Pi-Anion
Pi-Donor Hydrogen Bond
Pi-Pi Stacked
Pi-Alkyl

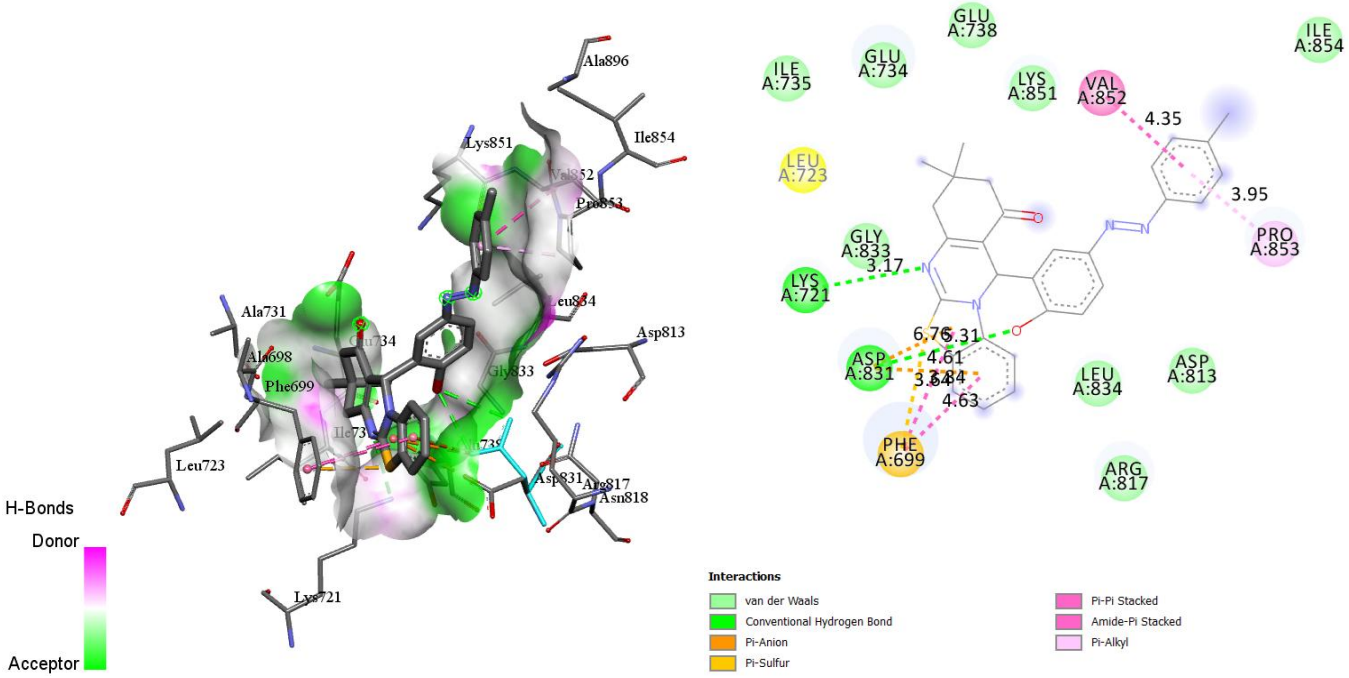
xvii. 4q



xviii. 4r



xix. 4s



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