

Five and six membered heterocyclic rings endowed with azobenzene as dual EGFR^{T790M} and VEGFR-2 inhibitors:

Design, synthesis, *in silico* ADMET profile, molecular docking, dynamic simulation and anticancer evaluations

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Docking studies

In the present work, all the target compounds were subjected to docking study to explore their binding mode towards VEGFR-2 and EGFR^{T790M} receptors. All modeling experiments were performed using molsoft program, which provides a unique set of tools for the modeling of protein/ligand interactions. It predicts how small flexible molecule such as substrates or drug candidates bind to a protein of known 3D structure represented by grid interaction potentials (http://www.molsoft.com/icm_pro.html). The experimental work used the biological target VEGFR-2 downloaded from the Brookhaven Protein Databank (<https://www.rcsb.org/structure/4ASD>). Also experiments used EGFR downloaded from the Brookhaven Protein Databank (<https://www.rcsb.org/structure/3W2O>). In order to qualify the docking results in terms of accuracy of the predicted binding conformations in comparison with the experimental procedure, the reported VEGFR-2 and EGFR inhibitors sorafenib and erlotinib were used as reference ligands respectively.

Molecular dynamics simulation

The highly active derivatives **5**, **6**, **10** and **14** in the proteins VEGFR-2 and EGFR^{T790M} were processed to a molecular dynamics study to address their binding affinity to the specific enzyme. Ligand force fields were generated using GAFF2 [50,51] and the force field AMBERff14SB for the protein [52]. The complex was solvated expanding 15.0 Å in each direction with TIP3P water box of octahedral truncated box neutralized to a salt concentration of 150 mM of NaCl. The system was prepared *via* multiple energy minimization and equilibration steps under gradual decline position restraints on the ligand and protein achieving 310 K of temperature and 1.0 bar of pressure followed by a restraint-free production run of 100 ns. The coordinates saved every 2 ns. The binding energy between the ligand and the receptor was determined by applying MM/GBSA approach on the trajectory using MM/PBSA.py script of Amber, the calculations were for the last 50 ns using snapshots of 1 ns intervals from the simulation trajectory.

Biological testing

In vitro anti-cancer activity

Cancer cells from different cancer cell lines hepatocellular carcinoma (HepG2), breast cancer (MCF-7), colorectal carcinoma (HCT-116) and lung cancer (A549) were purchased from American type Cell Culture collection (ATCC, Manassas, USA) and grown on the appropriate growth medium Roswell Park Memorial Institute medium (RPMI 1640) supplemented with 100 mg/ mL of streptomycin, 100 units/ mL of penicillin and 10% of heat-inactivated fetal bovine serum in a humidified, 5% (v/v) CO₂ atmosphere at 37 °C Cytotoxicity assay by 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide (MTT).

Exponentially growing cells from different cancer cell lines were trypsinized, counted and seeded at the appropriate densities (2000-1000 cells/0.33 cm² well) into 96-well microtiter plates. Cells then were incubated in a humidified atmosphere at 37°C for 24 hours. Then, cells were exposed to different concentrations of compounds (0.1, 10, 100 and 1000 µM) for 72 hours. Then the viability of treated cells was determined using MTT technique as follow. Cells were incubated with 200 µl of 5% MTT solution/well (Sigma Aldrich, MO) and were allowed to metabolize the dye into colored-insoluble formazan crystals for 2 hours. The remaining MTT solution were discarded from the wells and the formazan crystals were dissolved in 200 µl/well acidified isopropanol for 30 min, covered with aluminum foil and with continuous shaking using a MaxQ 2000 plate shaker (Thermo Fisher Scientific Inc, MI) at room temperature. The colorimetric assay was measured and recorded at absorbance of 570 nm using a Stat FaxR 4200 plate reader (Awareness Technology, Inc., FL). The cell viability were expressed as percentage of control and the concentration that induces 50% of maximum inhibition of cell proliferation (IC₅₀) were determined using Graph Pad Prism version 5 software (Graph Pad software Inc, CA) [[53-55](#)].

VEGFR-2 kinase inhibitory assay

The kinase activity of VEGFR-2 was measured by use of an anti-phosphotyrosine antibody with the Alpha Screen system (PerkinElmer, USA) according to manufacturer's instructions [56]. Enzyme reactions were performed in 50 mM Tris-HCl pH 7.5, 5 mM MnCl₂, 5 mM MgCl₂, 0.01% Tween-20 and 2 mM DTT, containing 10 μM ATP, 0.1 μg/mL biotinylated poly-GluTyr (4:1) and 0.1 nM of VEGFR-2 (Millipore, UK). Prior to catalytic initiation with ATP, the tested compounds at final concentrations ranging from 0-300 μg/mL and enzyme were incubated for 5 min at room temperature. The reactions were quenched by the addition of 25 μL of 100 mM EDTA, 10 μg/mL Alpha Screen streptavidine donor beads and 10 μg/mL acceptor beads in 62.5 mM HEPES pH 7.4, 250 mM NaCl, and 0.1% BSA. Plate was incubated in the dark overnight and then read by ELISA Reader (PerkinElmer, USA). Wells containing the substrate and the enzyme without compounds were used as reaction control. Wells containing biotinylated poly-GluTyr (4:1) and enzyme without ATP were used as basal control. Percent inhibition was calculated by the comparison of compounds treated to control incubations. The concentration of the test compound causing 50% inhibition (IC₅₀) was calculated from the concentration-inhibition response curve (triplicate determinations) and the data were compared with Sorafenib (Sigma-Aldrich, USA) as standard VEGFR-2 inhibitor.

EGFR^{T790M} kinase inhibitory assay

Homogeneous time resolved fluorescence (HTRF) assay was applied in this test [57]. EGFR^{T790M} and ATP were purchased from Sigma. Firstly EGFR^{T790M} and its substrates were incubated with the tested compounds in enzymatic buffer for 5 min. ATP (1.65 μM) was added into the reaction mixture to allow starting the enzymatic reaction. The assay was conducted for 30 min at room temperature. The reaction was stopped by addition of detection reagents which contain EDTA. The detection step continued for 1 h, and then the IC₅₀ values were determined by GraphPad Prism 5.0. Three independent experiments were performed for each concentration.

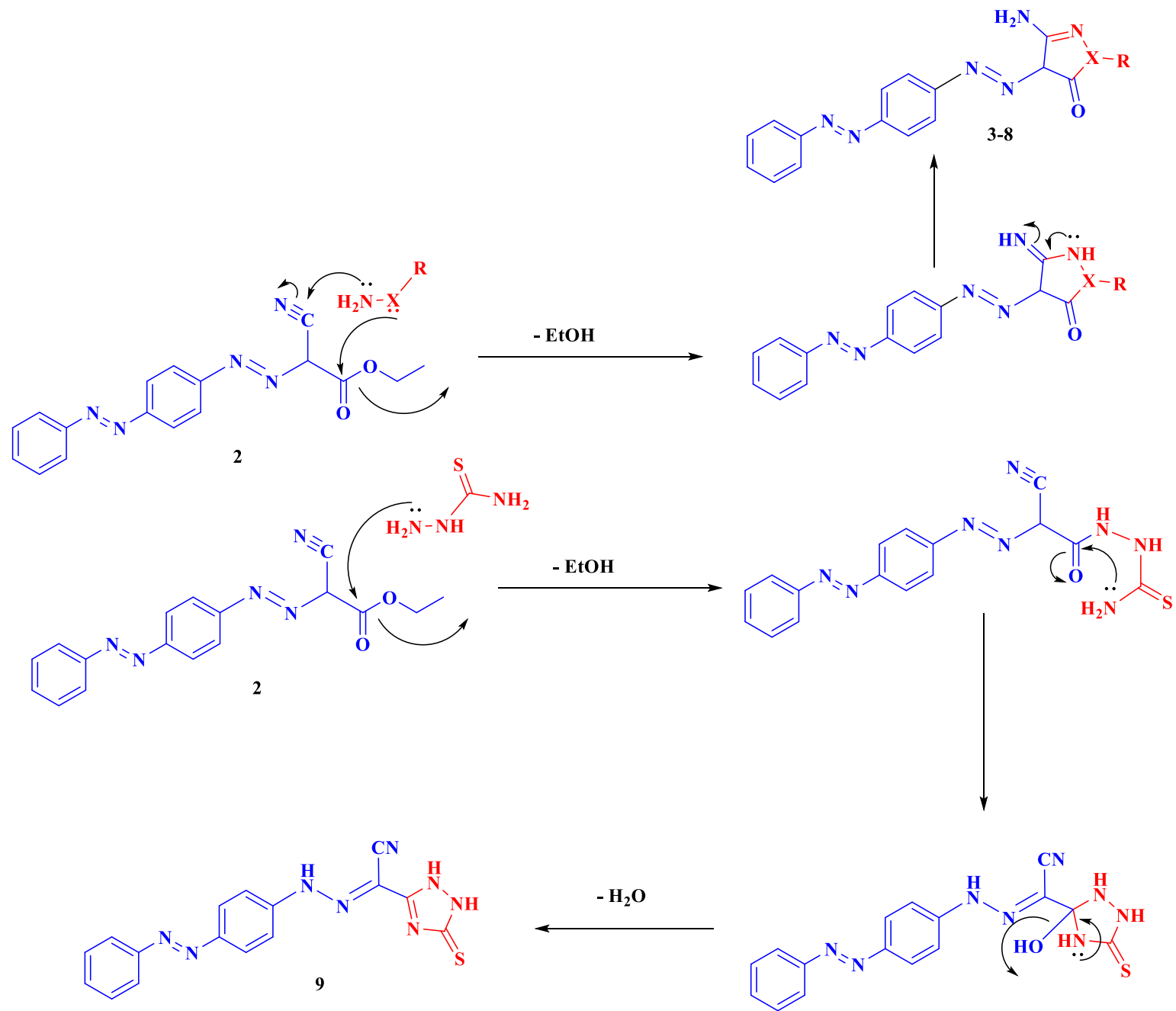


Fig. 1: The suggested pathway for formation of (6-9) derivatives.

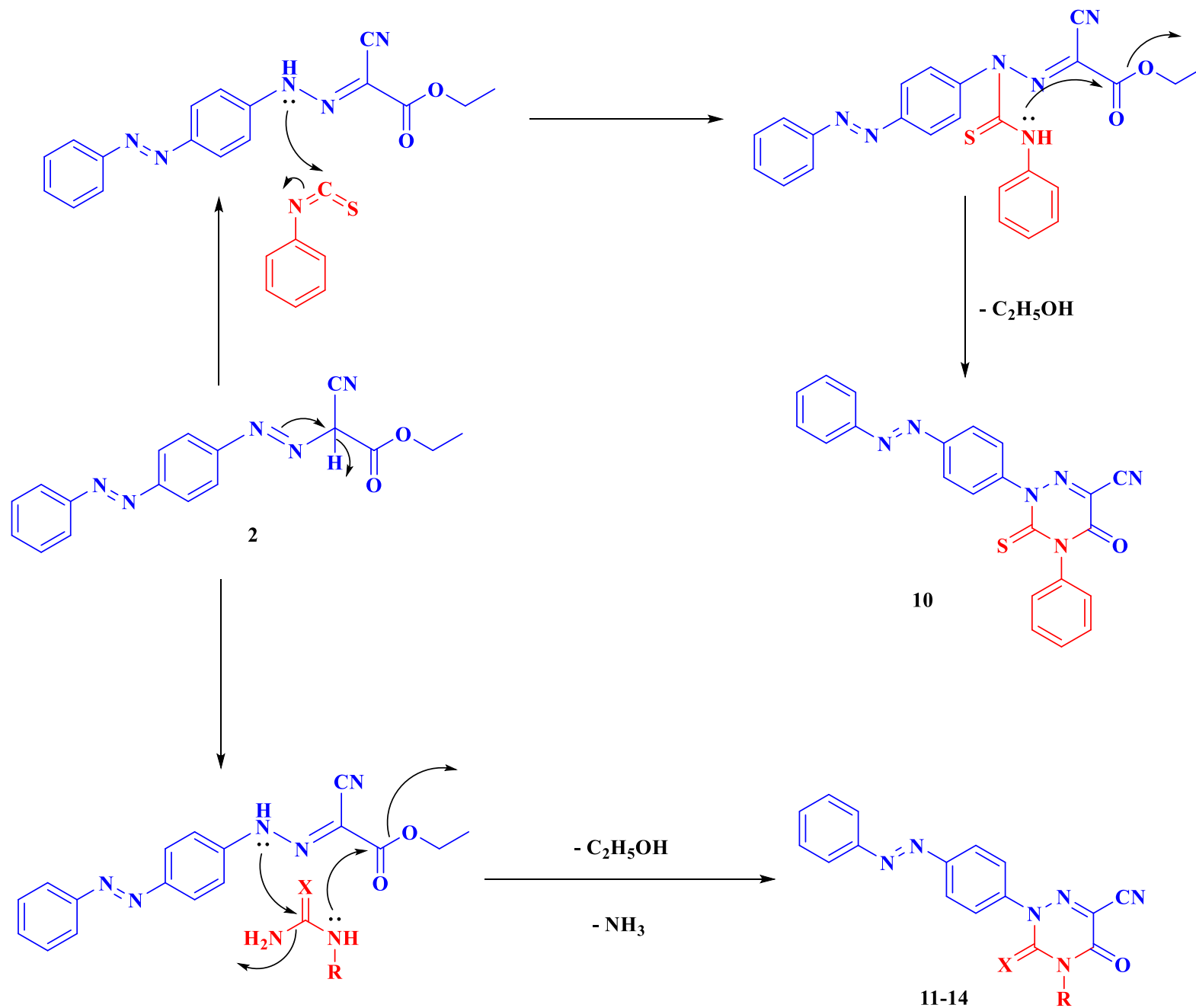


Fig. 2: The suggested pathway for syntheses of (10-14) derivatives.

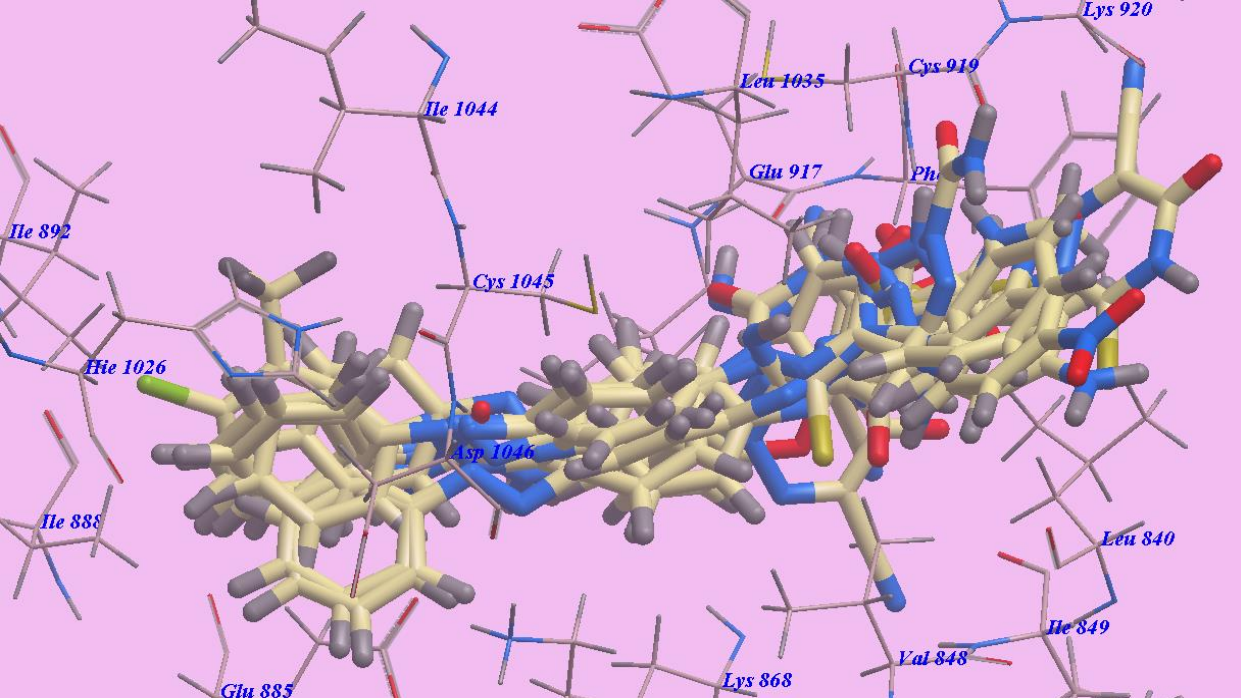


Fig. 3: A few docked compounds superimposed inside the 4ASD's binding space.

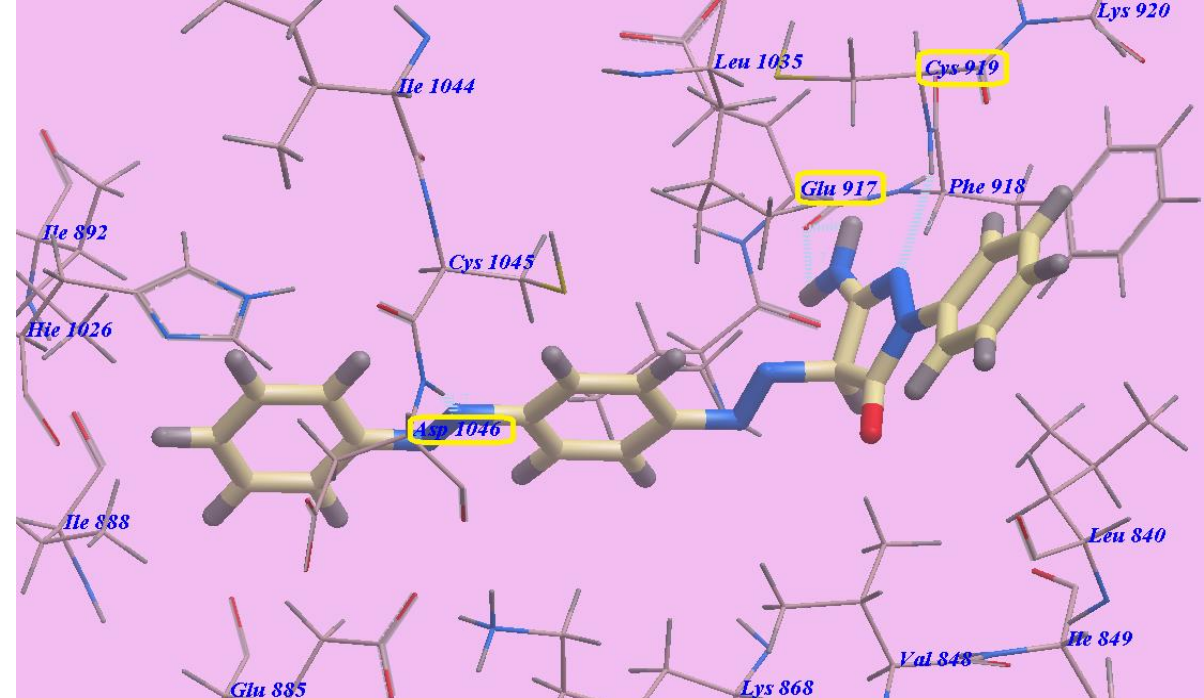


Fig. 4: Anticipated mode of binding for 5 with 4ASD.

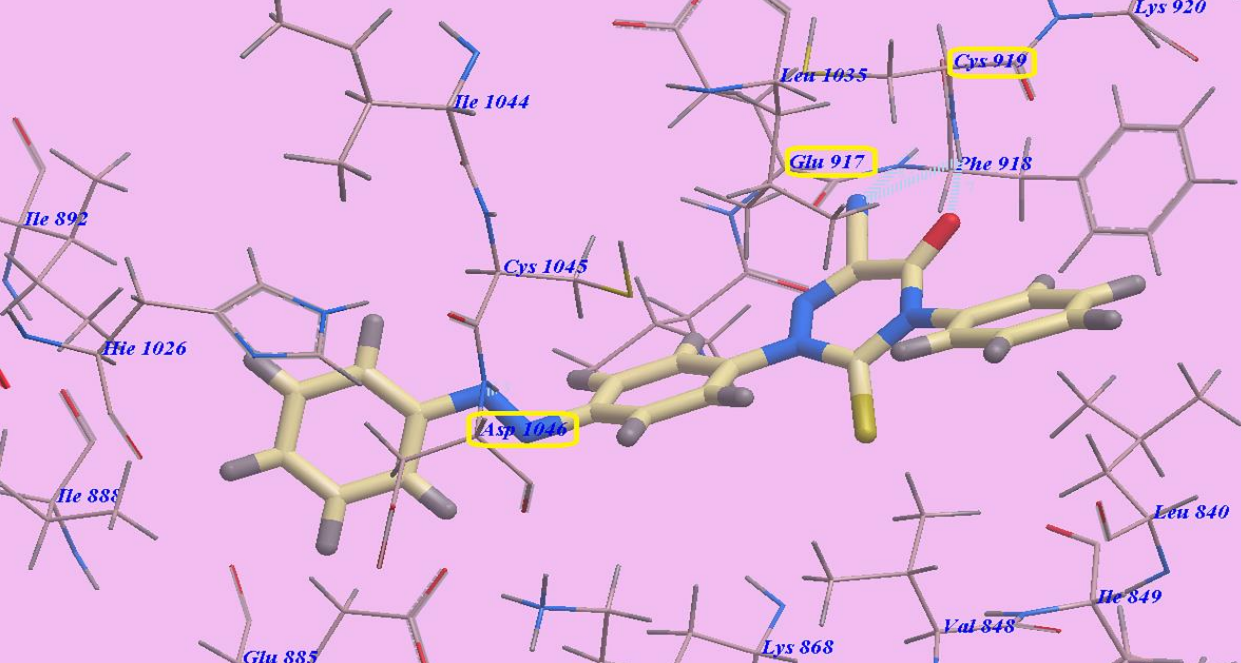


Fig. 5: Anticipated mode of binding for 10 with 4ASD.

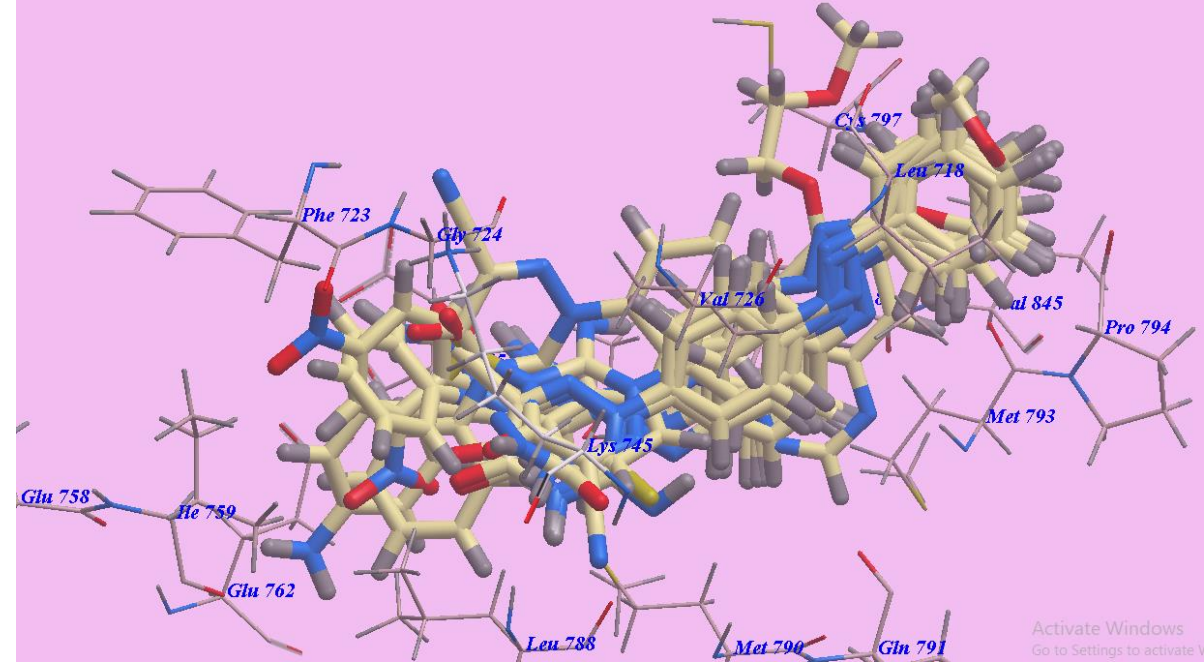


Fig. 6: A few docked compounds superimposed inside the 3W2O's binding space.

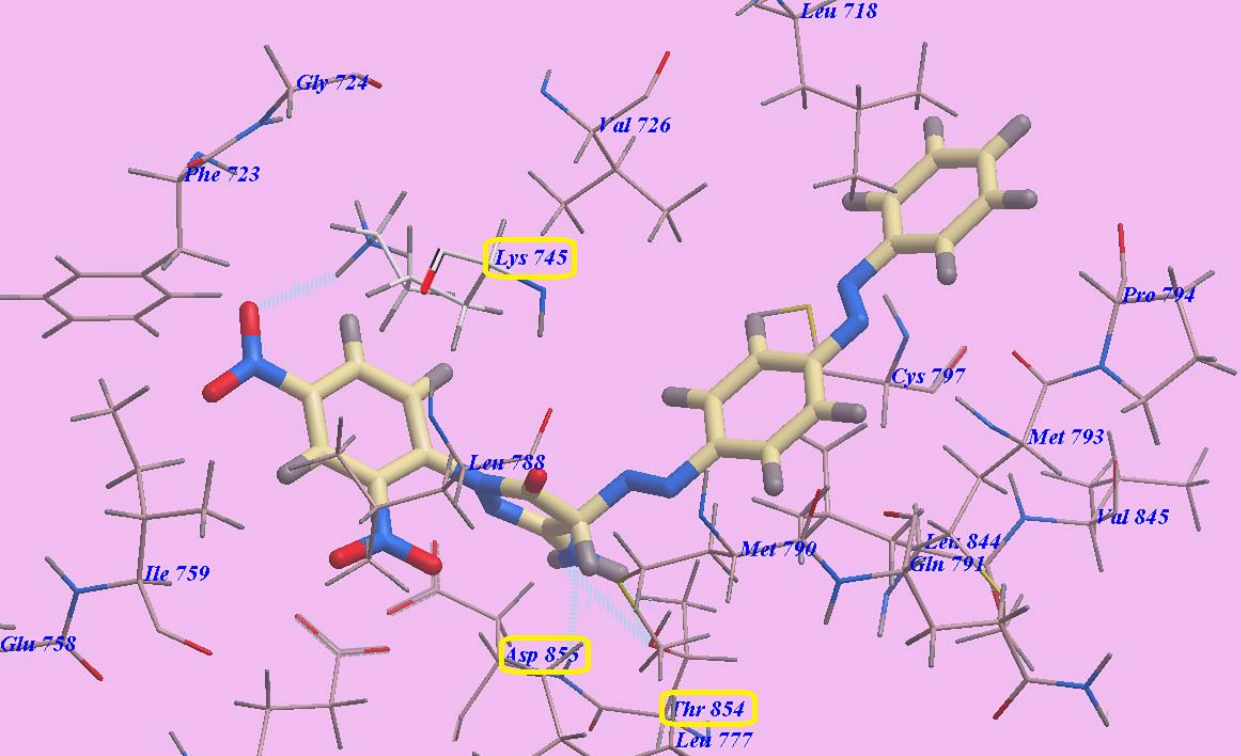


Fig. 7: Anticipated binding style for **6** with 3W2O.

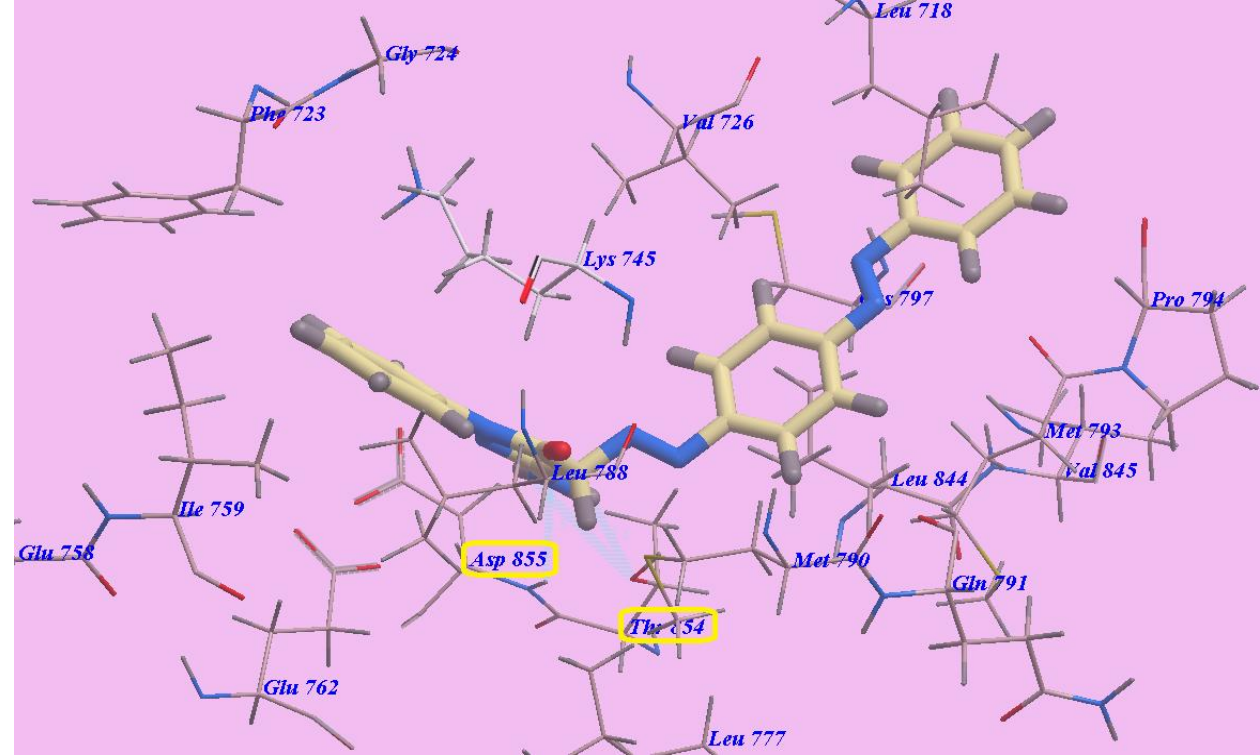


Fig. 8: Anticipated binding style for **5** with 3W2O.

1. Conventional and microwave methods comparison.

On the other hand, comparison between conventional and microwave methods by using different physical tools as YE (yield economy), AE (atomic economy), RME (reaction mass efficiency) and OE (optimum efficiency). The yields and times of compounds produced utilising microwave technology and conventional methods were compared and published [46-50]. However, in order to compare the differing efficiency of the same reaction in the microwave and traditional synthetic processes, we utilised the yield economy (YE) as an expression.

Calculation of YE was occurred through: $YE = \frac{yield\%}{Reaction\ time\ "min"}$. In this report, the YE was used to provide the obtained yields conclusively improved using the microwave and conventional conditions.

RME equation is: $RME = \frac{Wt\ of\ isolated\ product}{Wt\ of\ reactants}$. OE was utilised to compare the three reaction types directly, and it may be calculated through. Therefore, we may use the yield economy (YE) as a metric to improve the conversion efficiencies of these three various synthetic processes for the same reaction. While RME provides the actual mass efficiency, atomic economy (AE) indicated the reaction's theoretical maximum efficiency. Due to applying two distinct reaction conditions to produce the same target molecules, as presented in (Table 1), the AE of conventional and microwave processes have the same values.

Table 1: Comparing microwave and conventional techniques used in syntheses of our compounds 3-14

| Cpd. n | Time "min" | | Yield % | | YE | | OE | | RME | | AE |
|--------|------------|------|---------|------|-------|--------|-------|-------|-------|-------|-------|
| | M.W. | Con. | M.W. | Con. | M.W. | Con. | M.W. | Con. | M.W. | Con. | |
| 3 | 1 | 180 | 90 | 56 | 90 | 0.3111 | 82.79 | 51.52 | 48.29 | 30.05 | 58.33 |
| 4 | 0.5 | 120 | 95 | 52 | 190 | 0.4333 | 87.13 | 47.69 | 52.55 | 28.76 | 60.31 |
| 5 | 1.5 | 240 | 92 | 55 | 61.33 | 0.2292 | 85.09 | 50.87 | 57.48 | 34.36 | 67.55 |
| 6 | 3 | 360 | 91 | 54 | 30.33 | 0.1500 | 83.39 | 49.48 | 60.03 | 35.62 | 71.99 |
| 7 | 2 | 360 | 94 | 57 | 47 | 0.1583 | 86.99 | 52.75 | 53.41 | 32.39 | 61.40 |
| 9 | 4 | 360 | 94 | 53 | 23.50 | 0.1472 | 86.76 | 48.92 | 54.89 | 30.95 | 63.27 |
| 10 | 3 | 300 | 91 | 51 | 30.33 | 0.1700 | 76.28 | 42.75 | 68.58 | 38.44 | 89.91 |
| 11 | 3.5 | 480 | 90 | 50 | 25.71 | 0.1042 | 73.67 | 40.92 | 61.98 | 34.43 | 84.13 |
| 12 | 3.5 | 540 | 93 | 52 | 26.57 | 0.0963 | 75.56 | 42.25 | 63.06 | 35.26 | 83.46 |
| 13 | 4 | 540 | 93 | 54 | 23.25 | 0.1000 | 76.76 | 44.57 | 58.49 | 33.96 | 76.20 |
| 14 | 5 | 720 | 90 | 51 | 18 | 0.0708 | 77.30 | 43.80 | 68.19 | 38.64 | 88.22 |



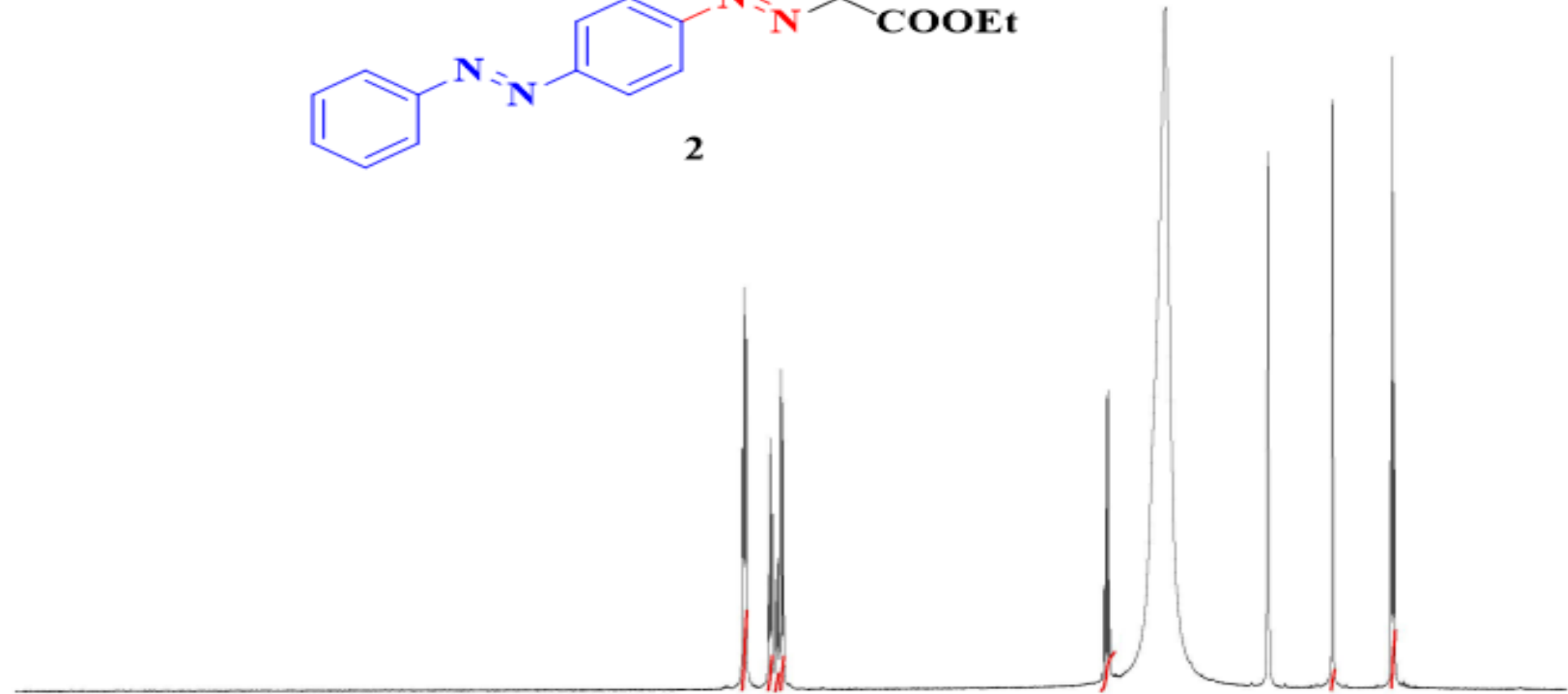
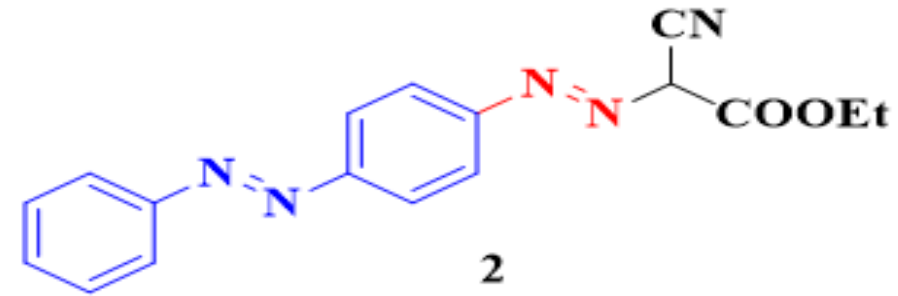
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7.452
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4.134
4.117
3.553
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2.507
2.503
1.852
1.259
1.242
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1.00
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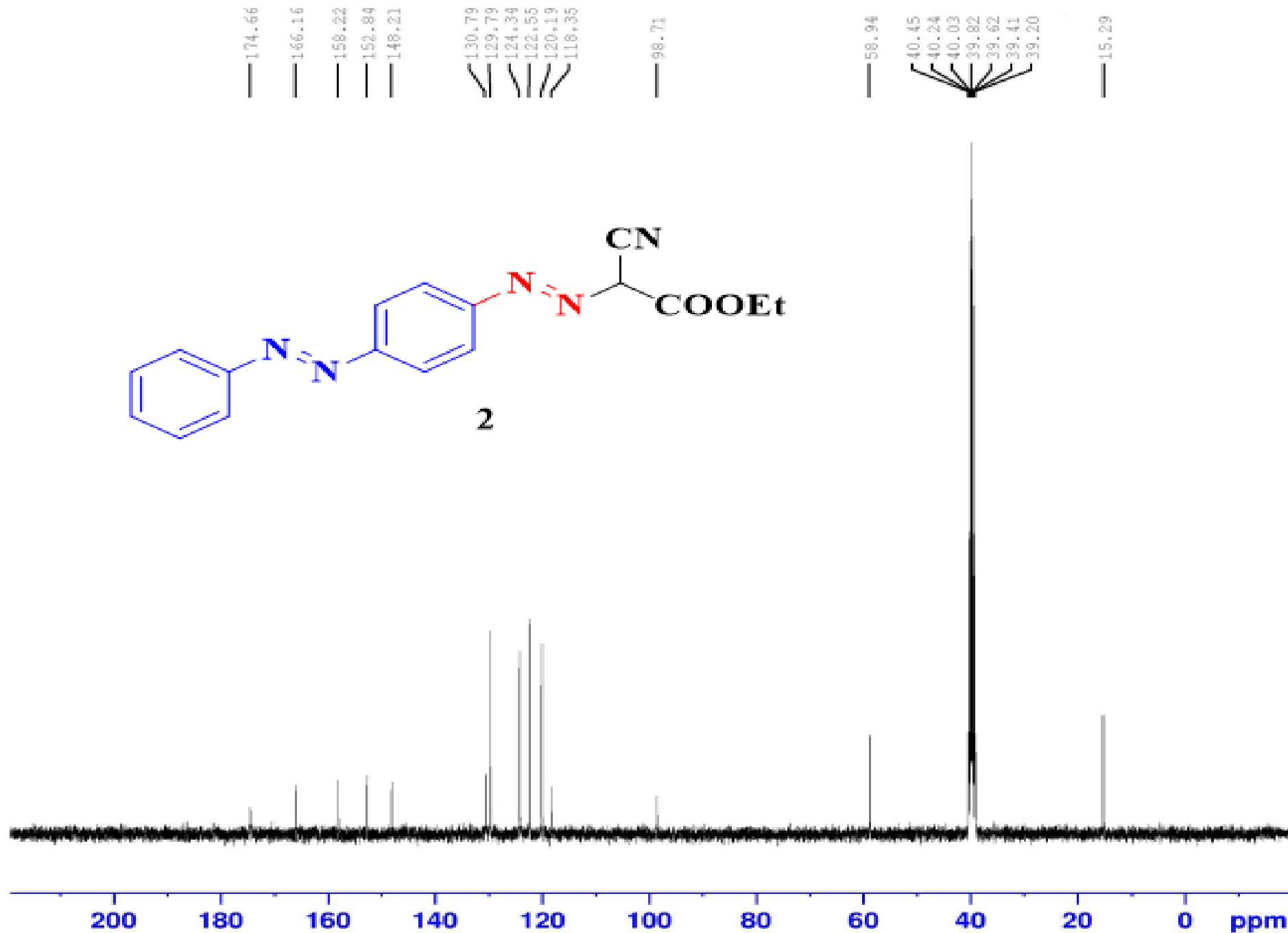
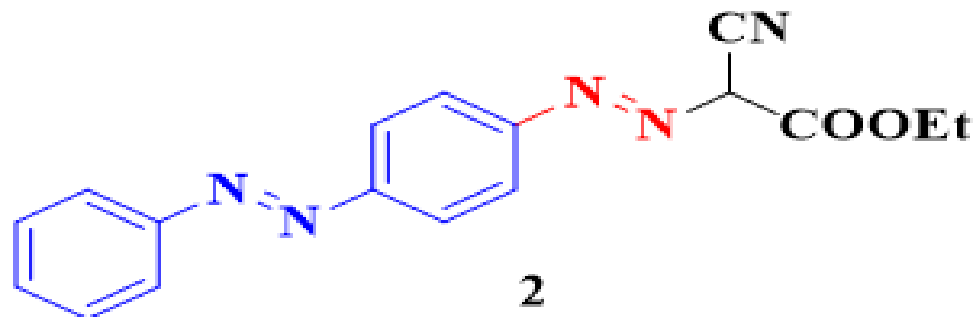
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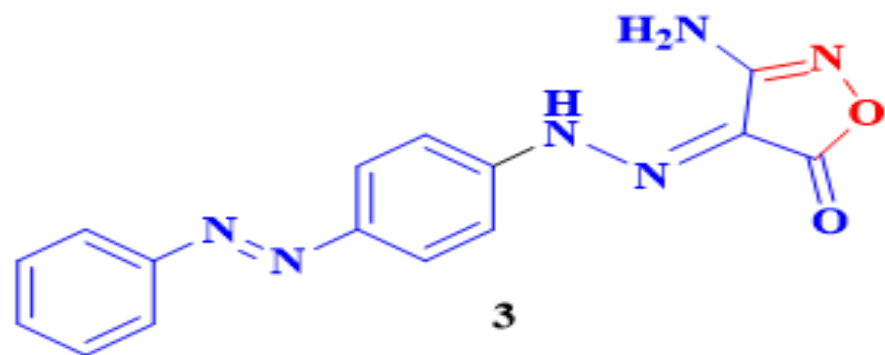


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7.514

—3.359

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4.09
1.54
4.04



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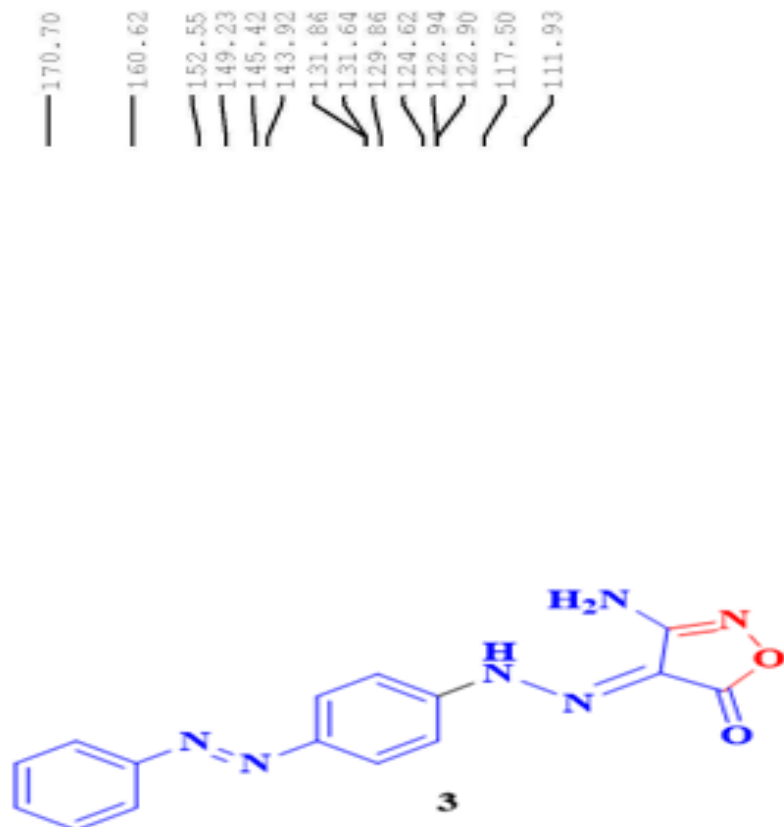
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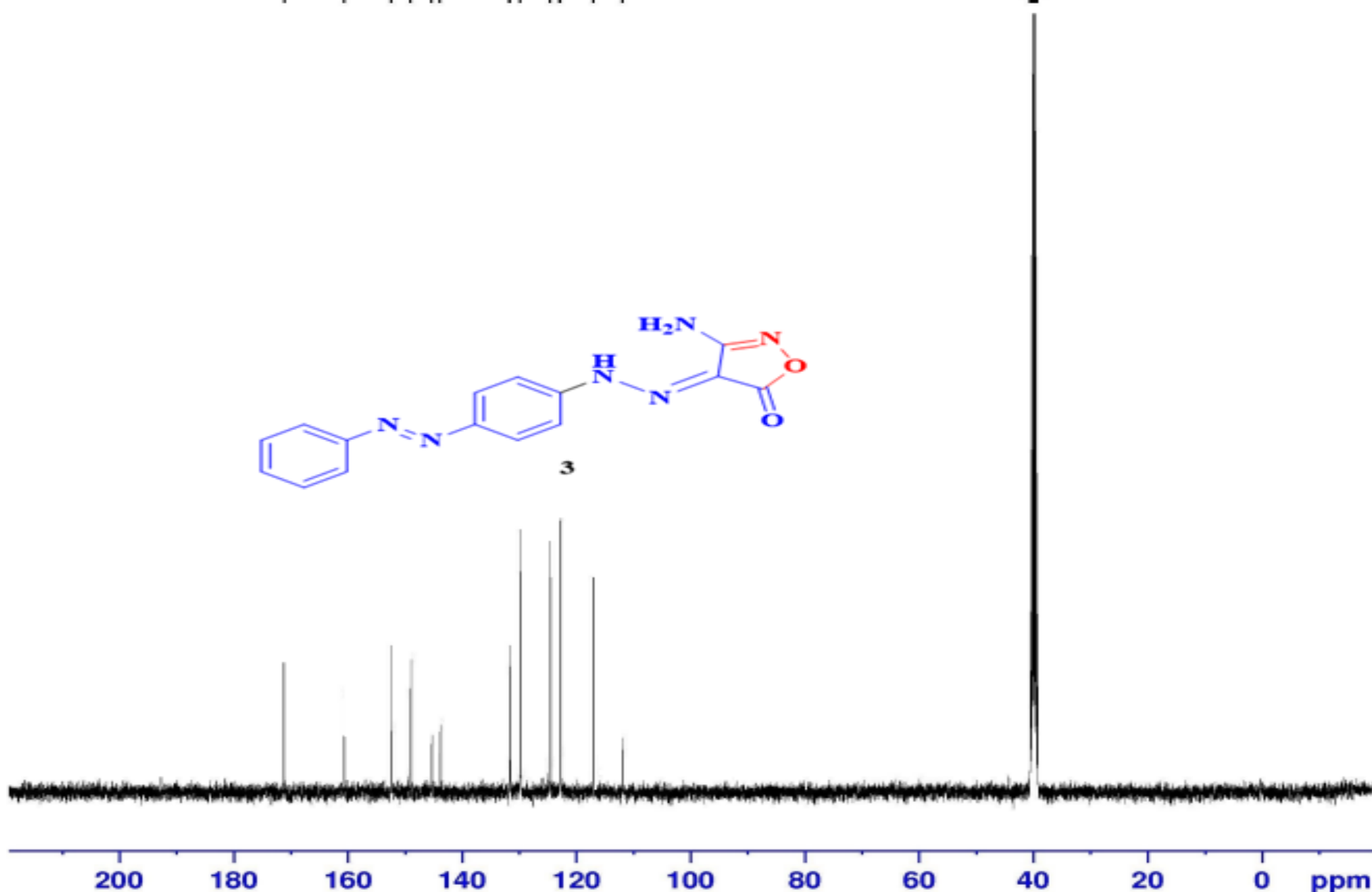
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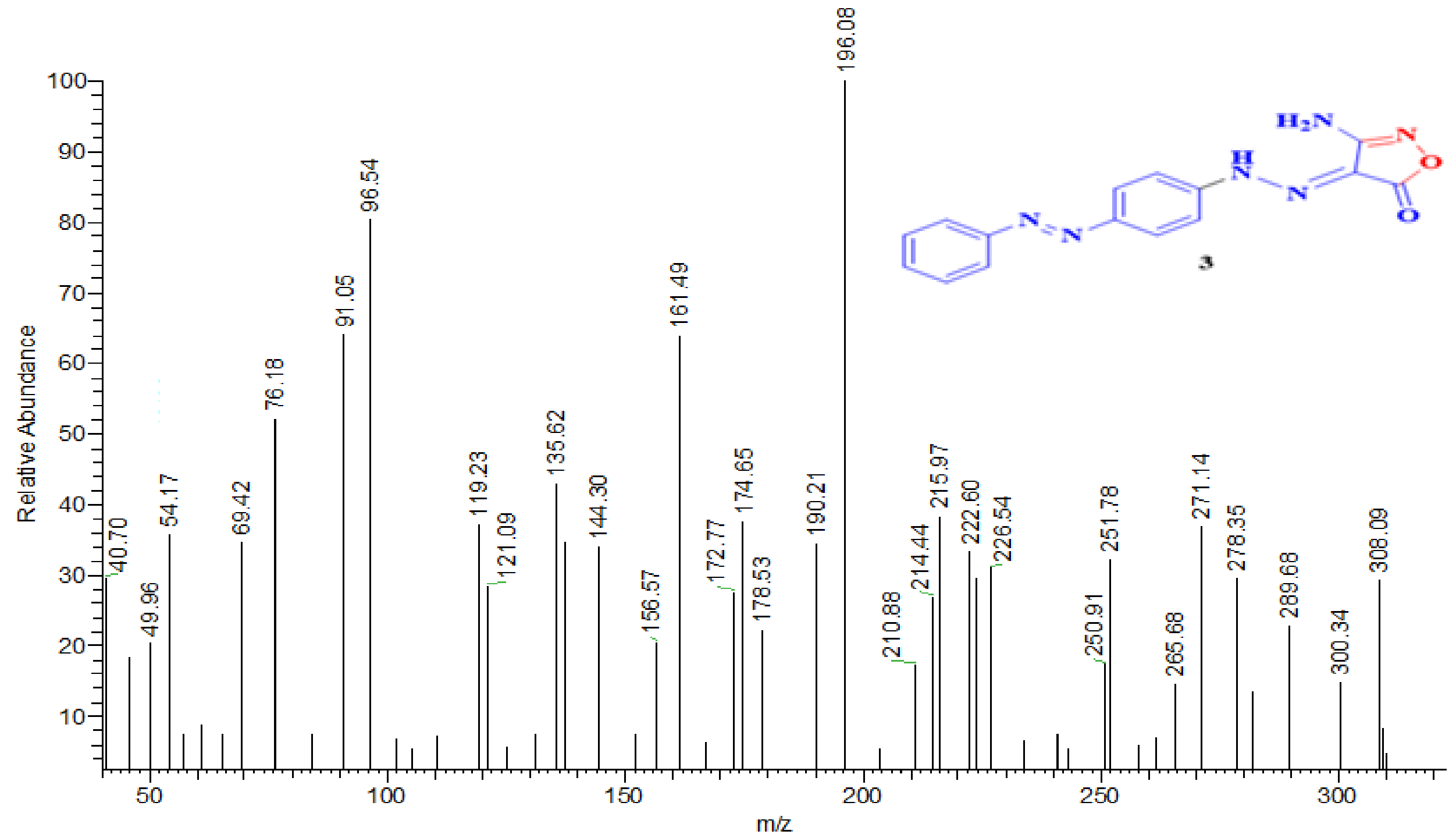


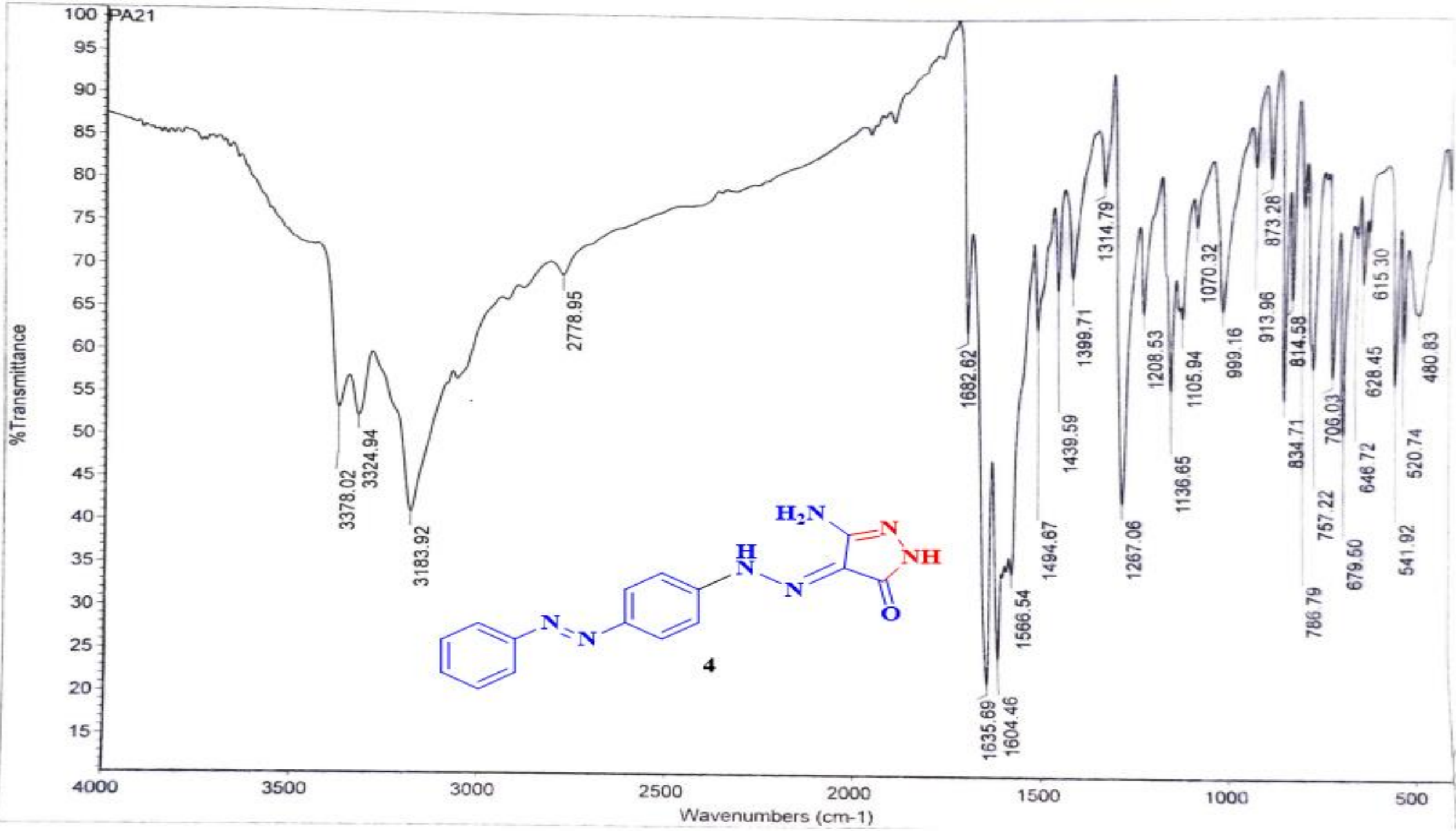
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39.56
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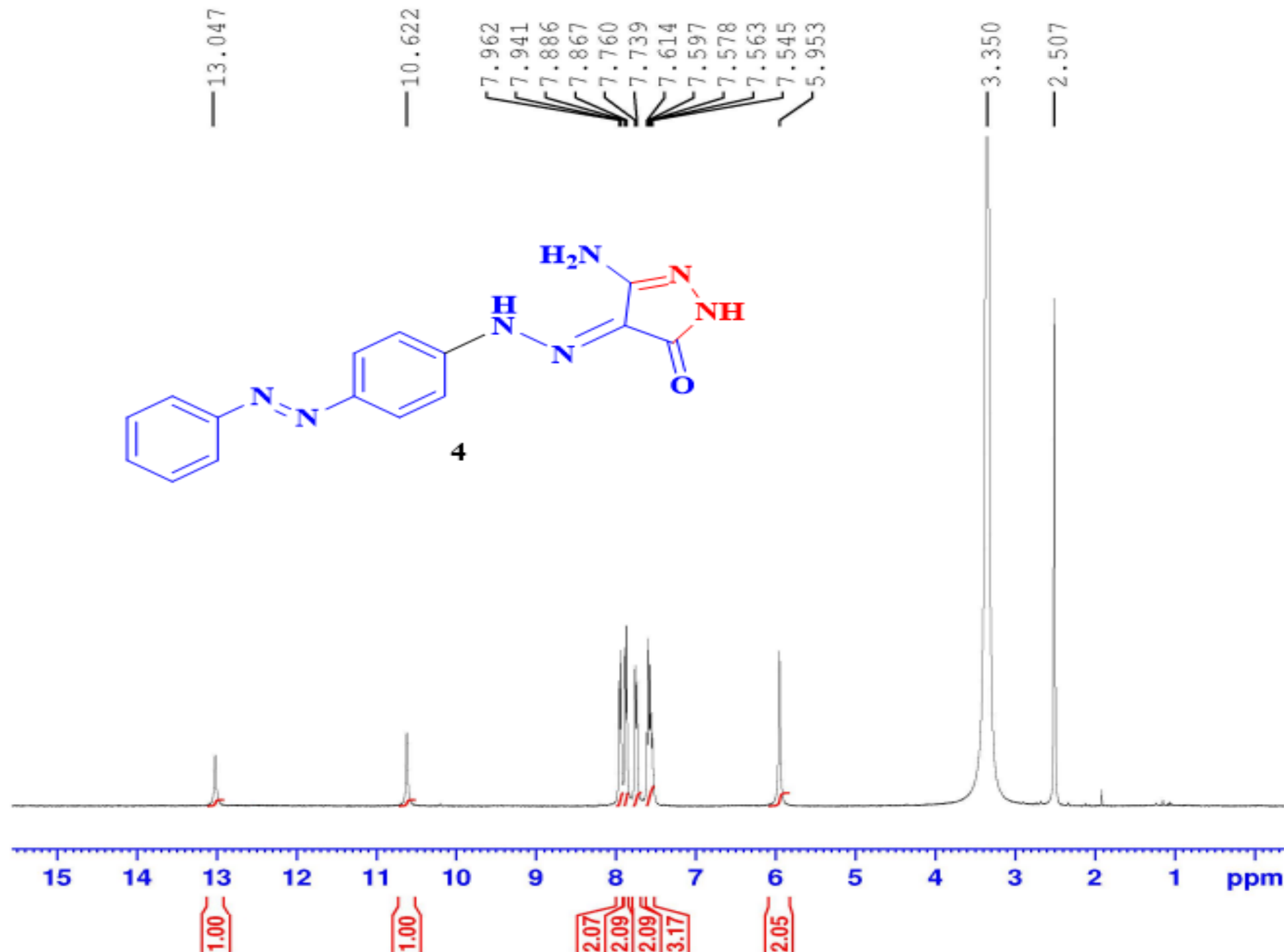
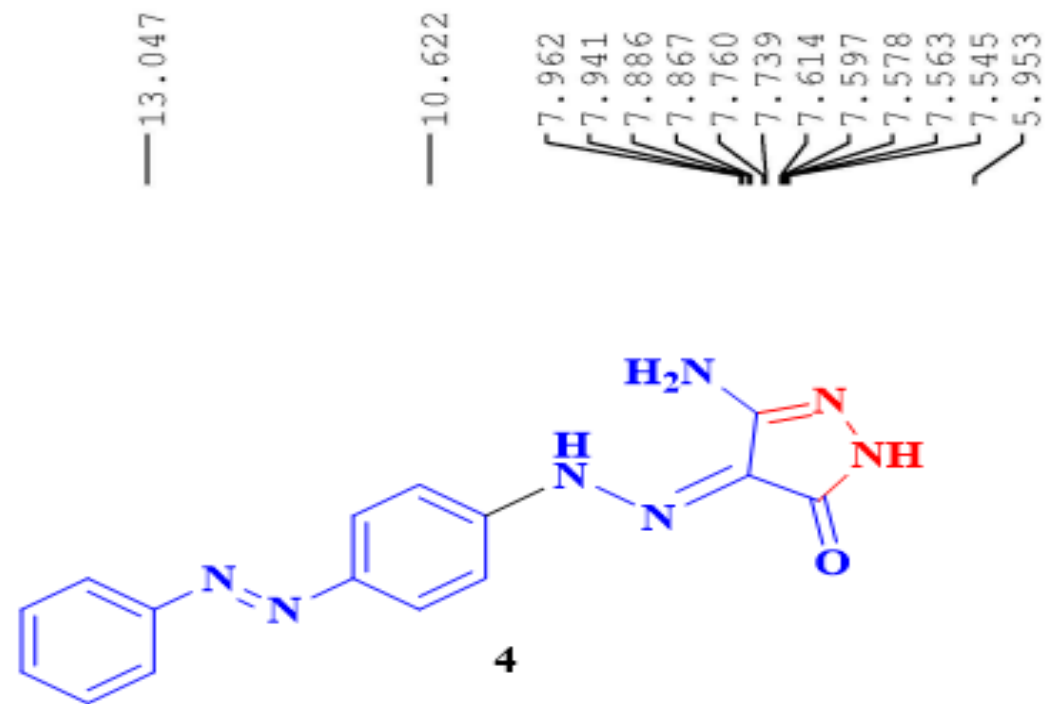


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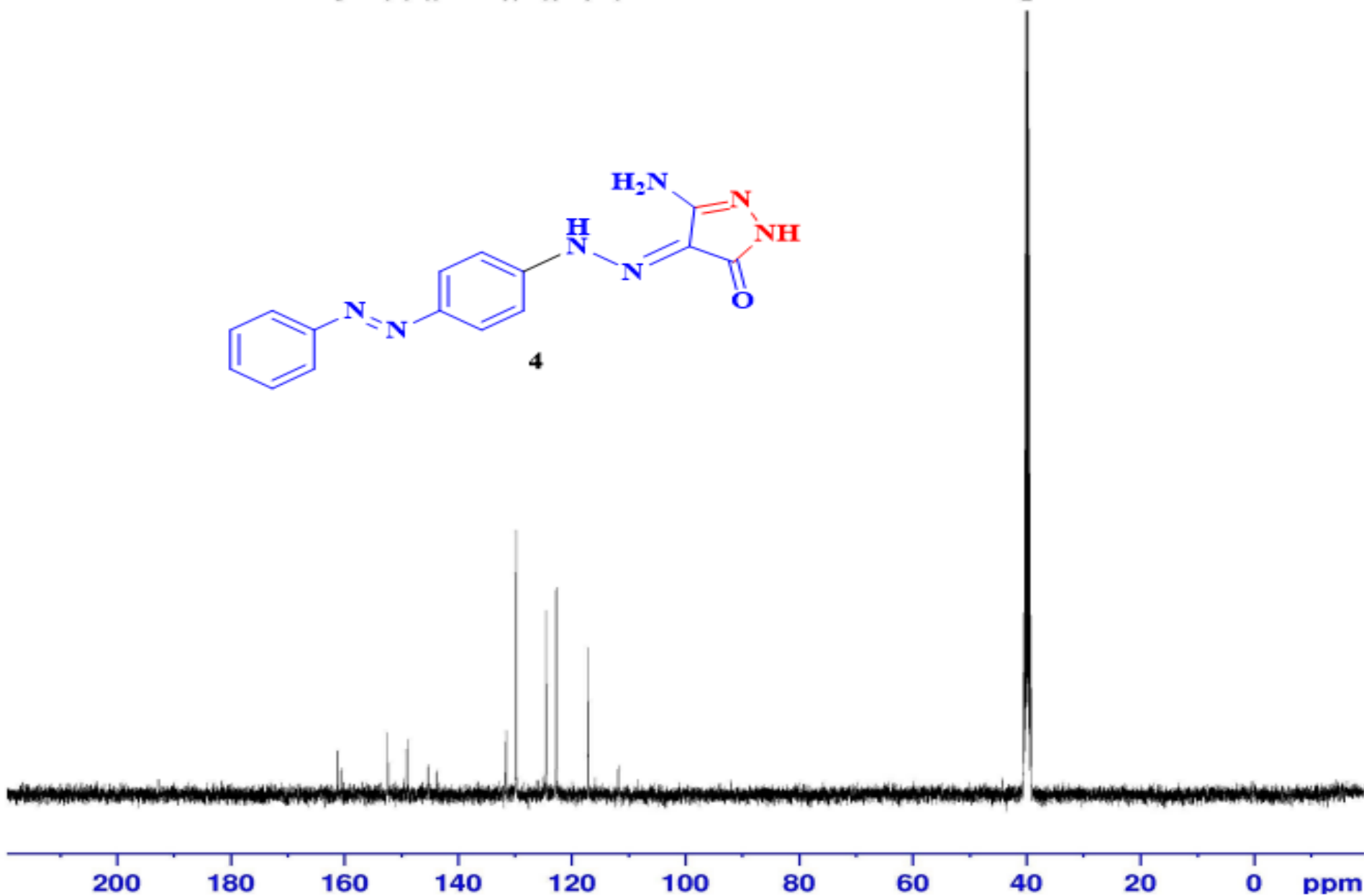
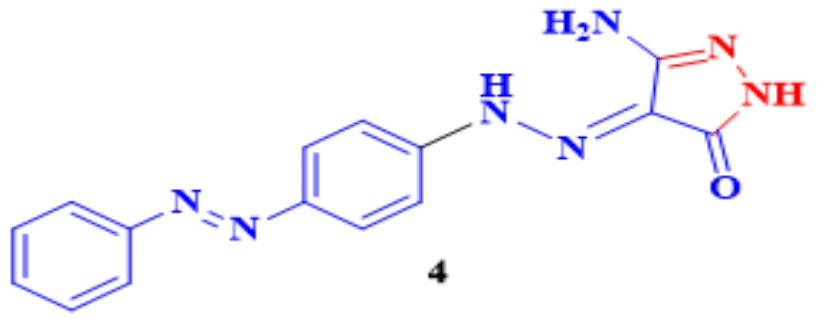
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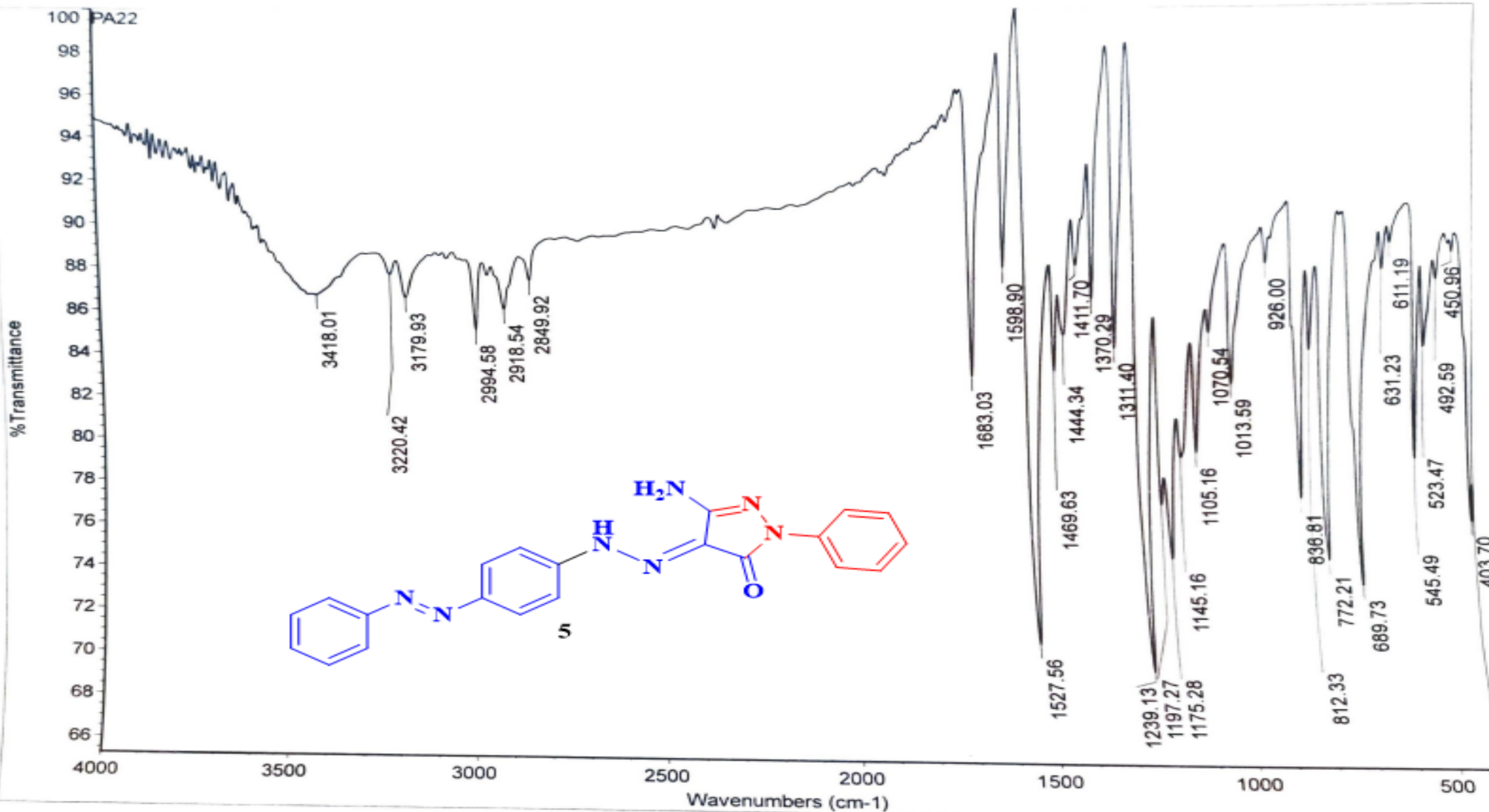
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PLW13 0.28125000 W

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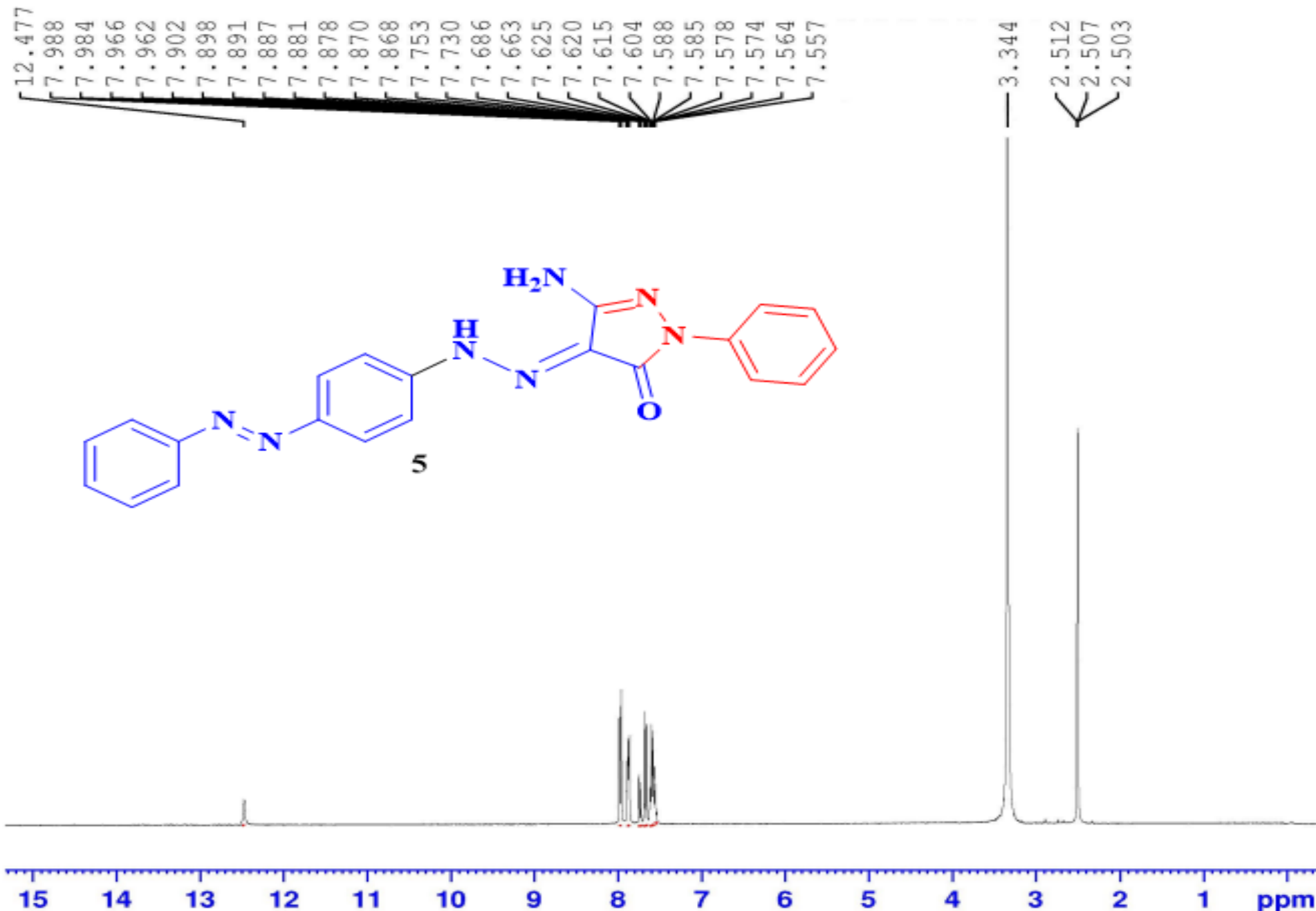


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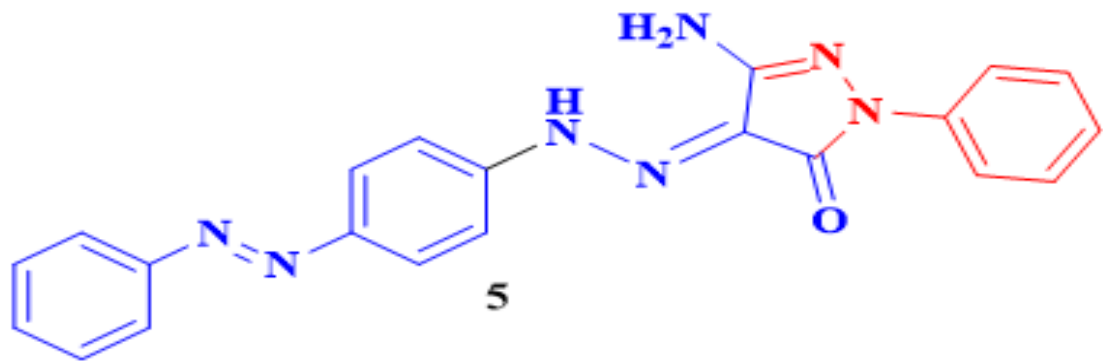
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7.585
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7.564
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3.344
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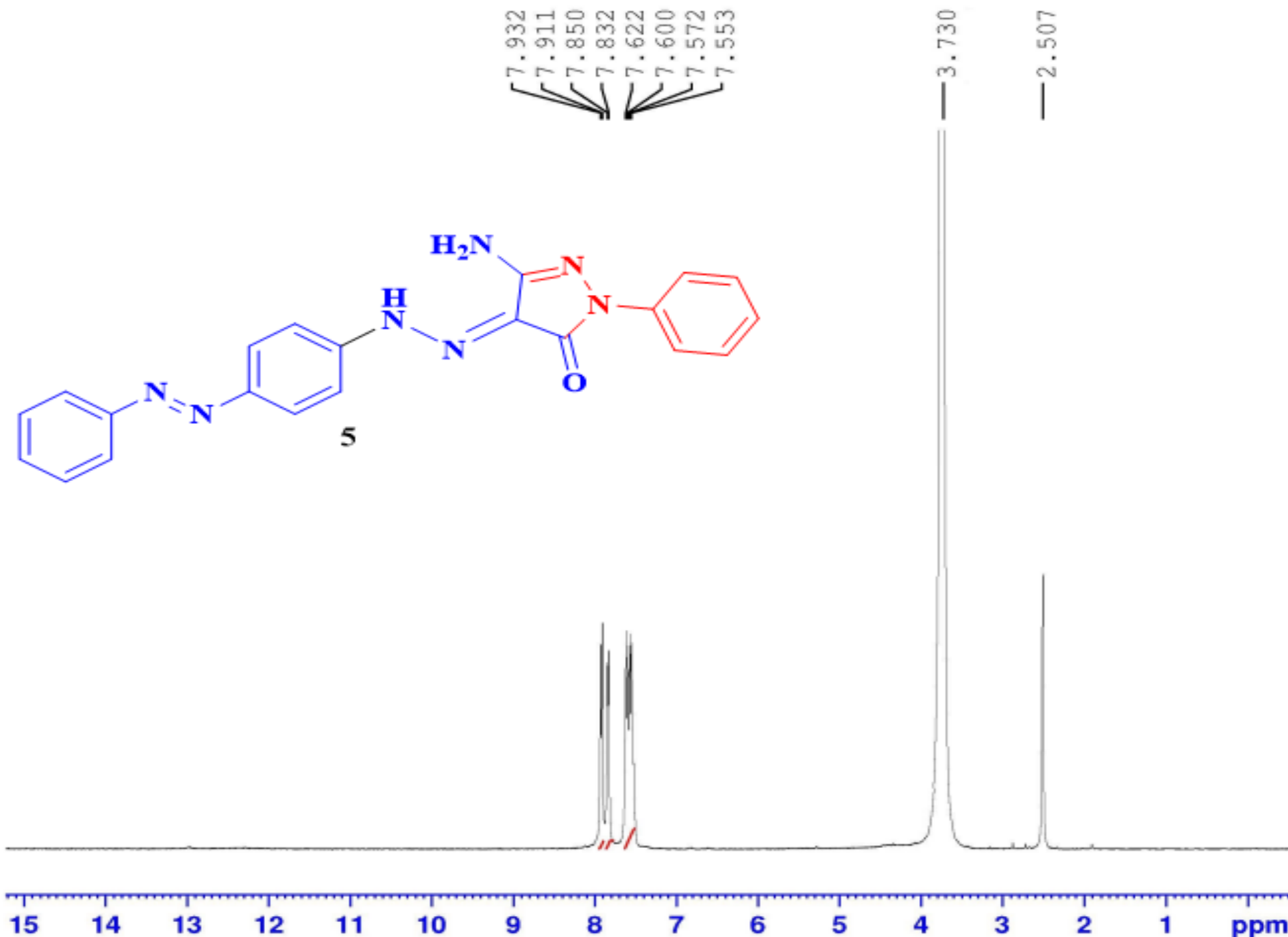


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Time 12.50
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 900
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

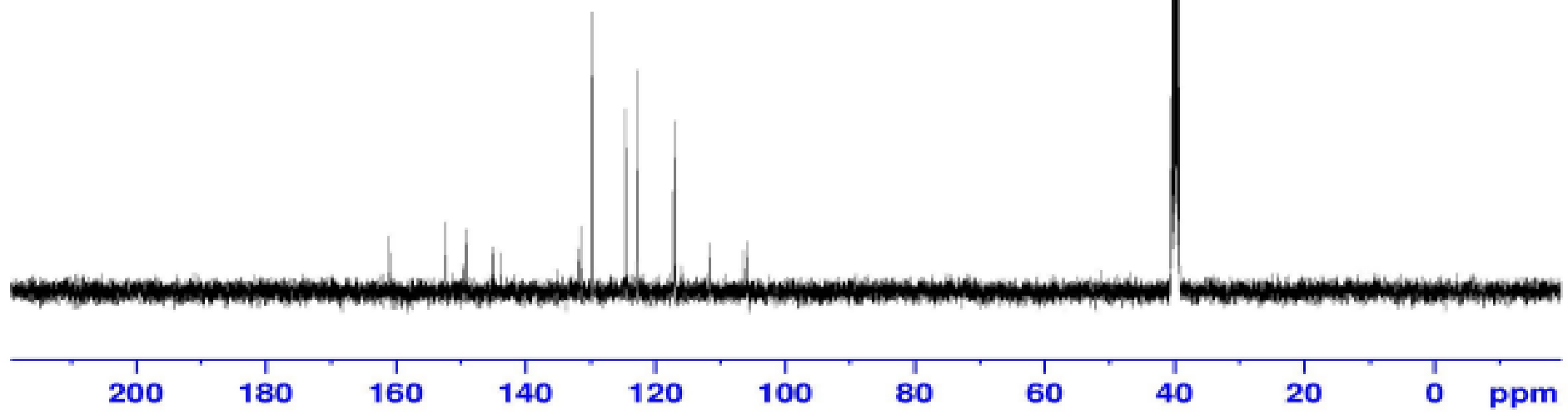
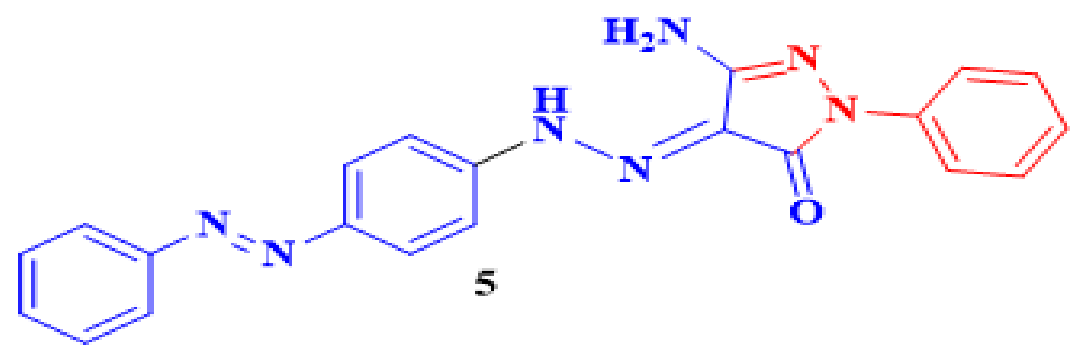
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

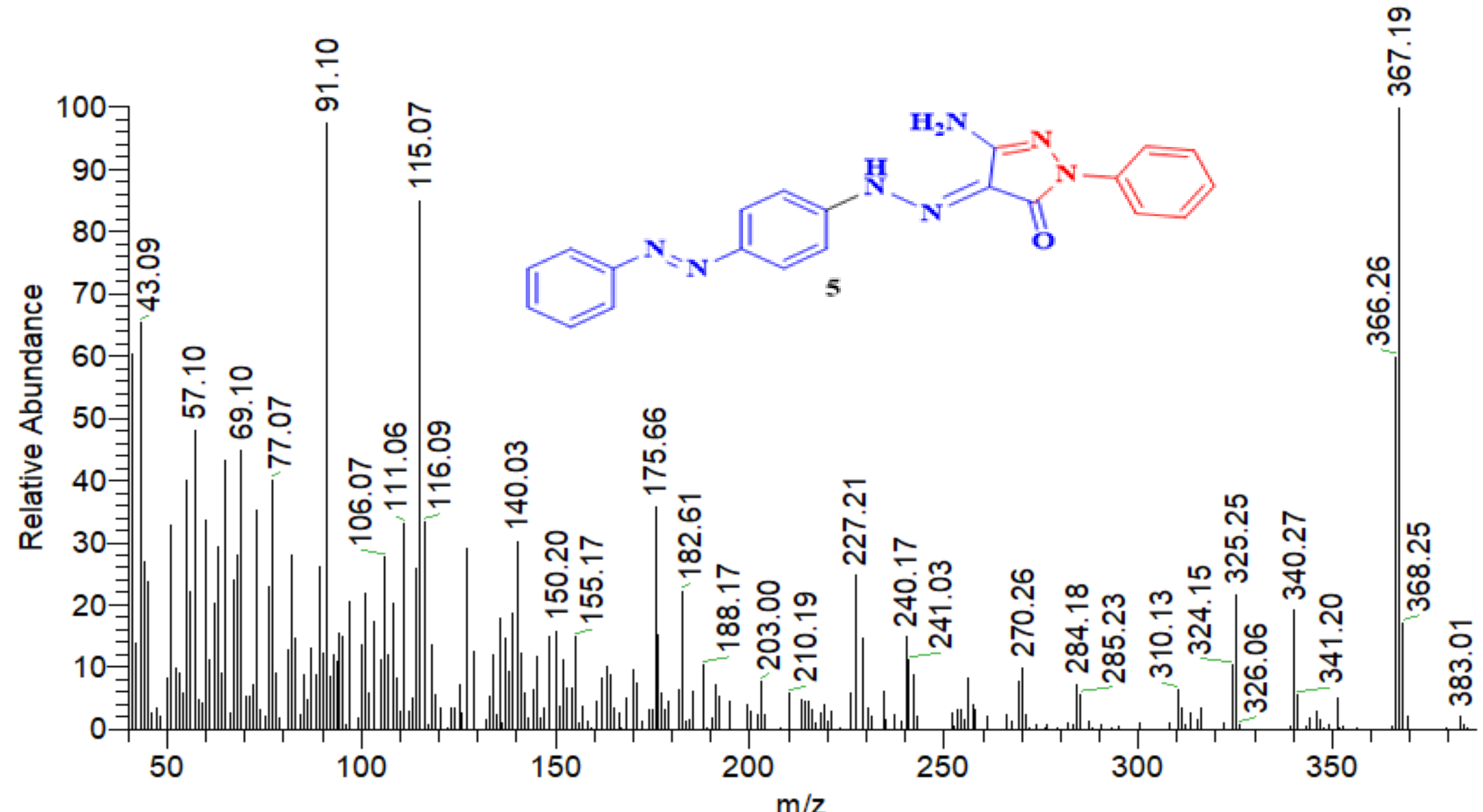
161.16
160.72
152.49
149.11
145.04
143.96
131.82
131.69
129.90
124.70
124.66
122.94
122.89
117.30
117.14
111.75
106.54
105.94

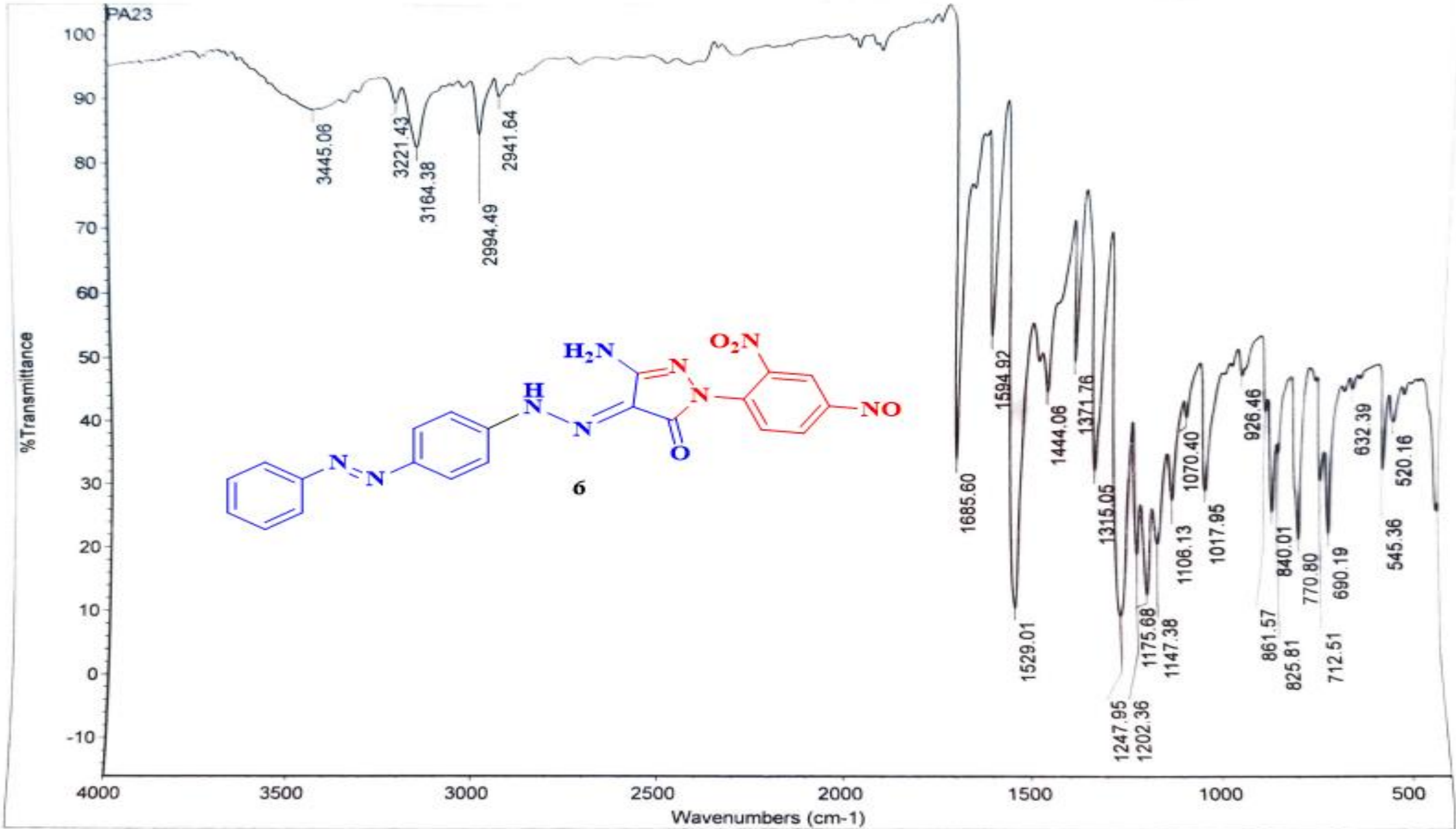
40.59
40.38
40.17
39.96
39.75
39.55
39.34



kerles-PA22 #101 RT: 1.71 AV: 1 SB: 26 1.21-1.34 , 0.87-1.14 NL: 2.55E4

T: {0,0} + c EI Full ms [40.00-1000.00]





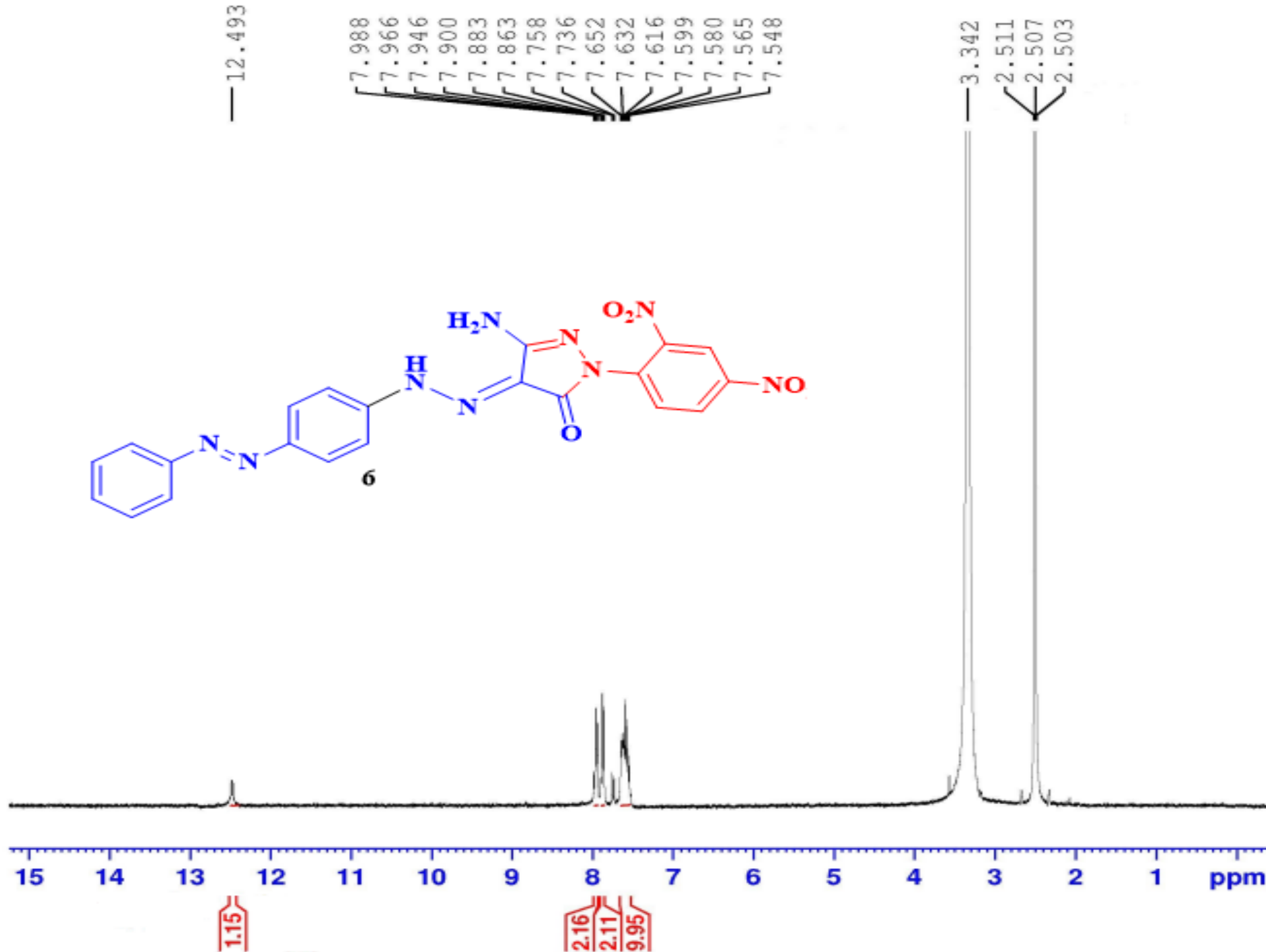


Current Data Parameters
NAME nour eldin-PA23
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 15.53
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 128
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 205.37
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TDO 1

----- CHANNEL f1 -----
SF01 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00





Current Data Parameters
NAME nour eldin-PA23
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230316
Time 10.53
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
ID 65536
SOLVENT DMSO
NS 1534
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
ID0 1

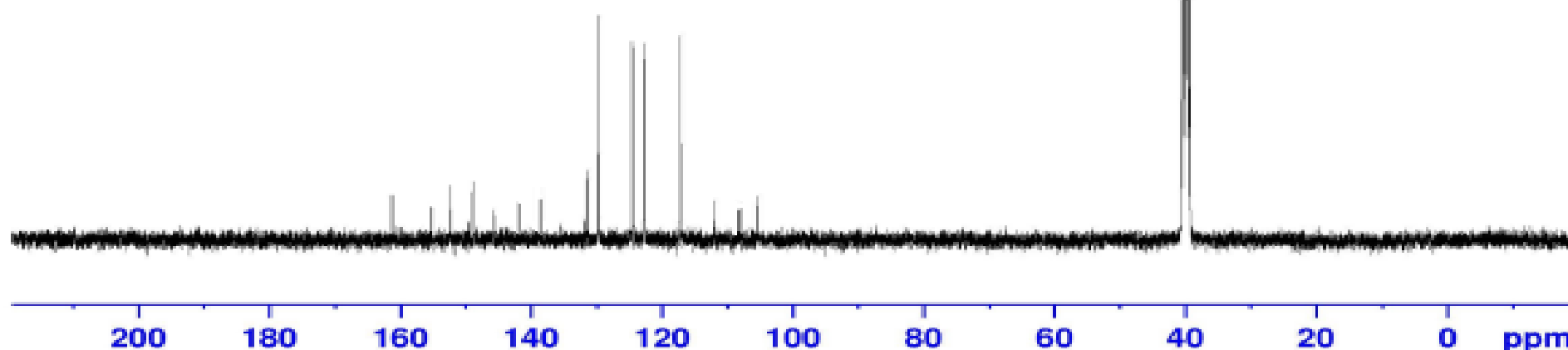
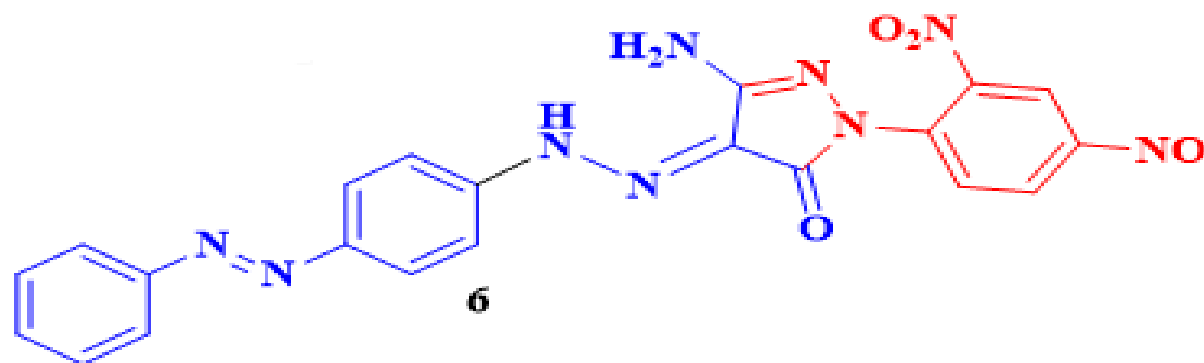
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG(2) waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

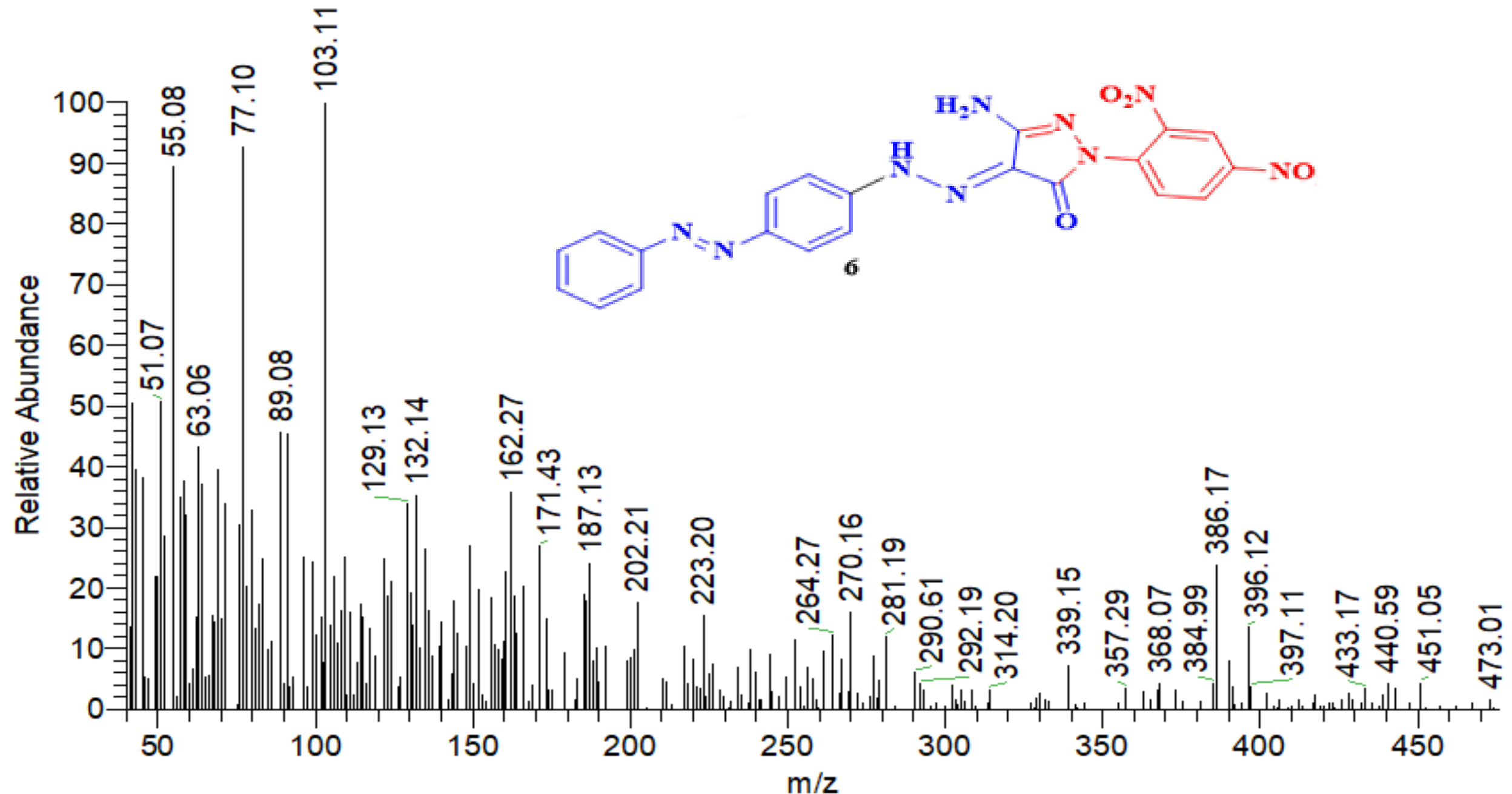
F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

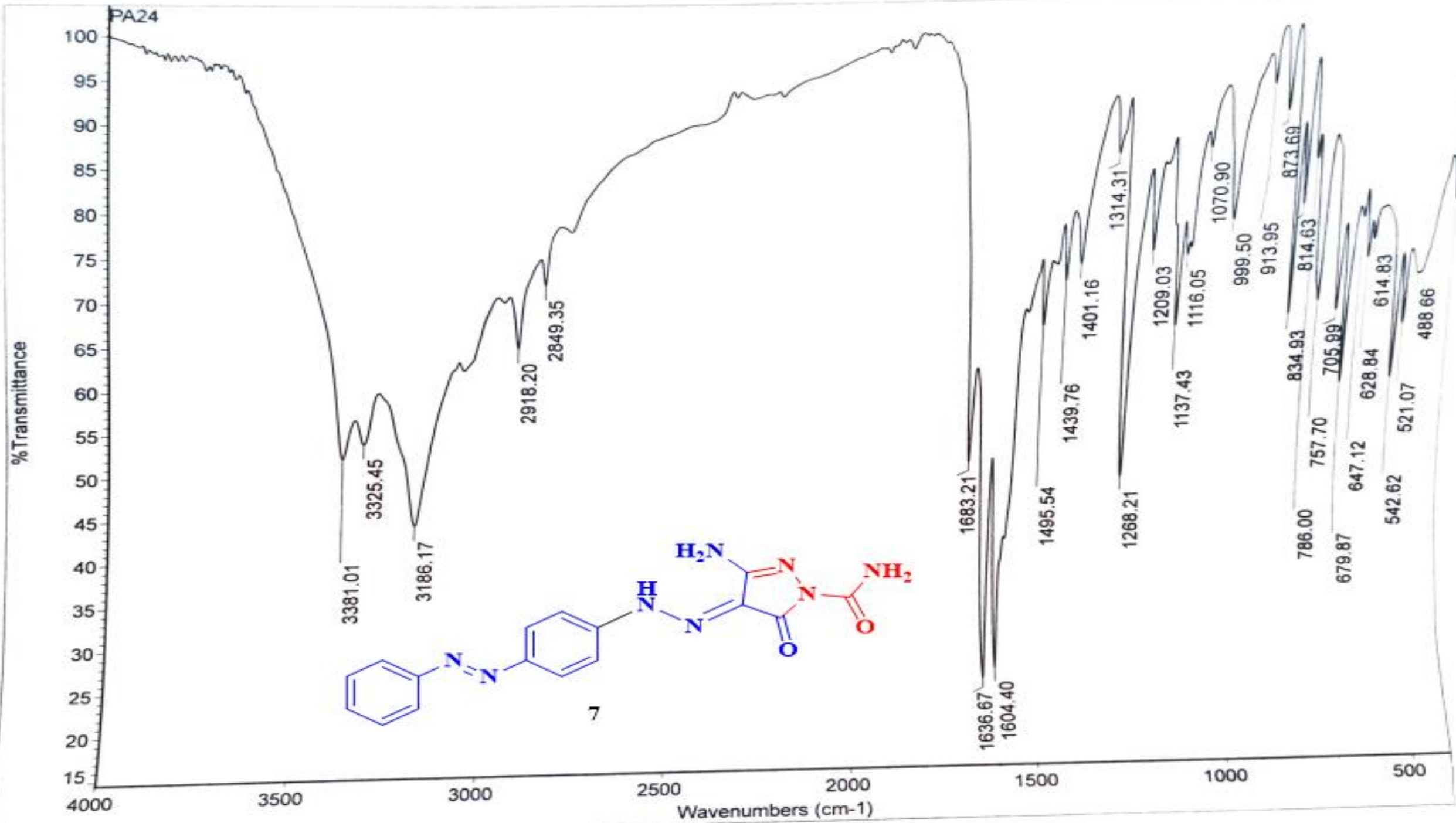
161.44
155.31
152.52
149.04
145.81
141.96
138.52
131.63
129.88
124.67
122.94
122.86
117.31
112.13
108.46
105.52

40.60
40.39
40.19
39.98
39.77
39.56
39.35



Kerles-PA23 #36-40 RT: 0.62-0.69 AV: 5 SB: 26 1.21-1.34 , 0.87-1.14 NL: 4.01E3
T: {0,0} + c EI Full ms [40.00-1000.00]





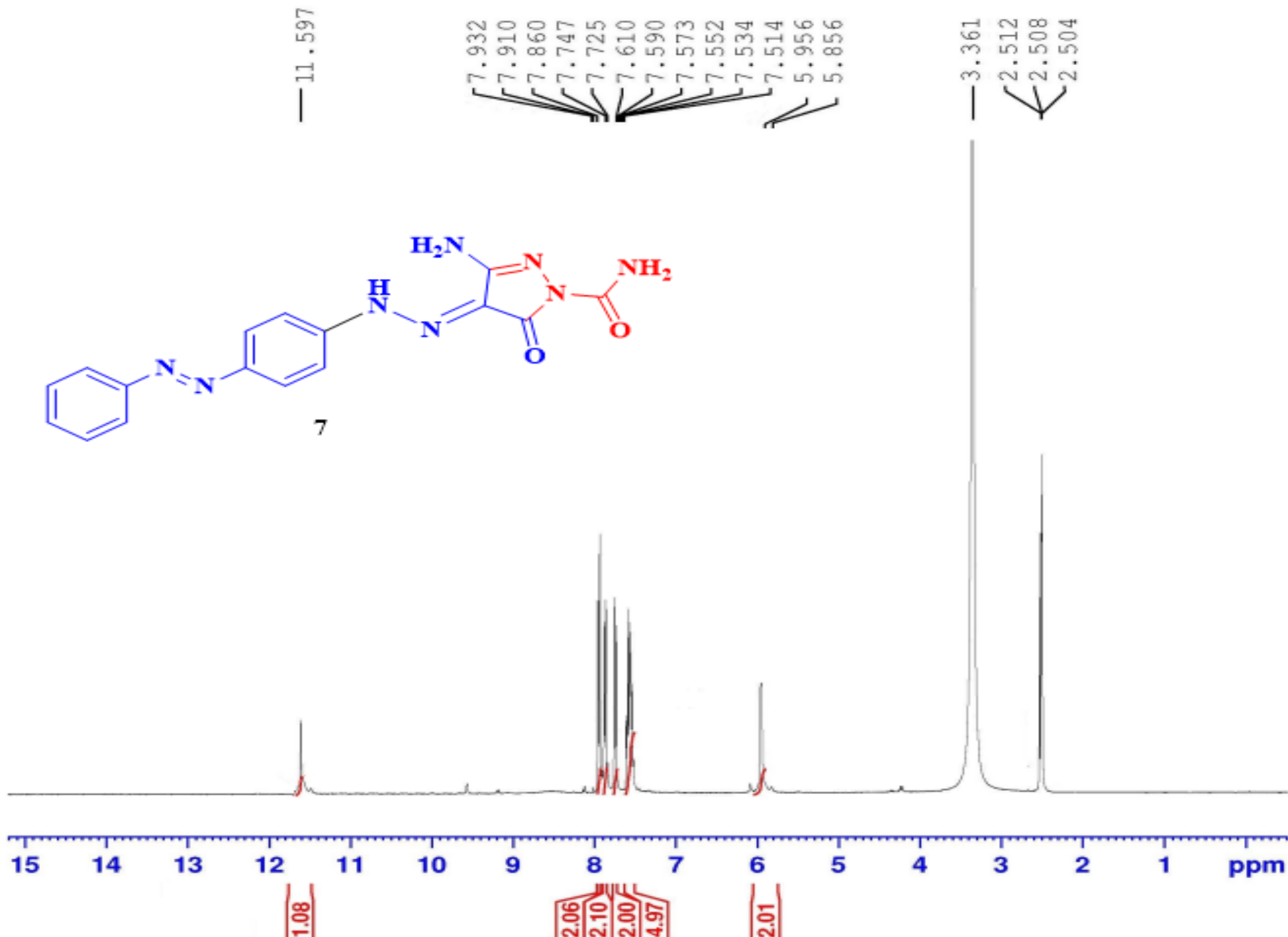
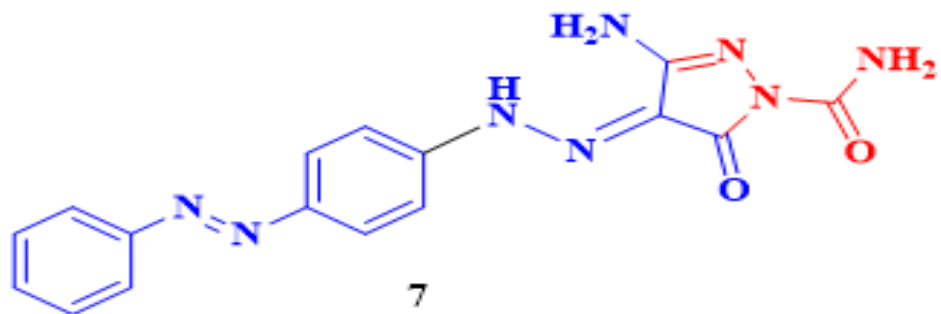


Current Data Parameters
NAME nour eldin-PA24
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 13.28
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 83
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 205.37
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TDO 1

----- CHANNEL f1 -----
SFO1 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00





Current Data Parameters
NAME neur eldin-PA24
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 15.27
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
ID 65536
SOLVENT DMSO
NS 2000
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
ID0 1

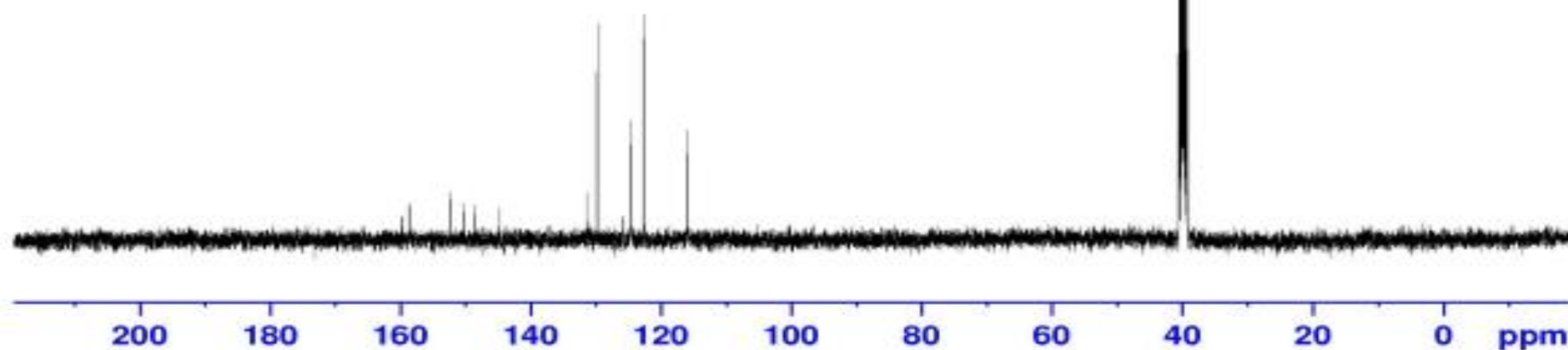
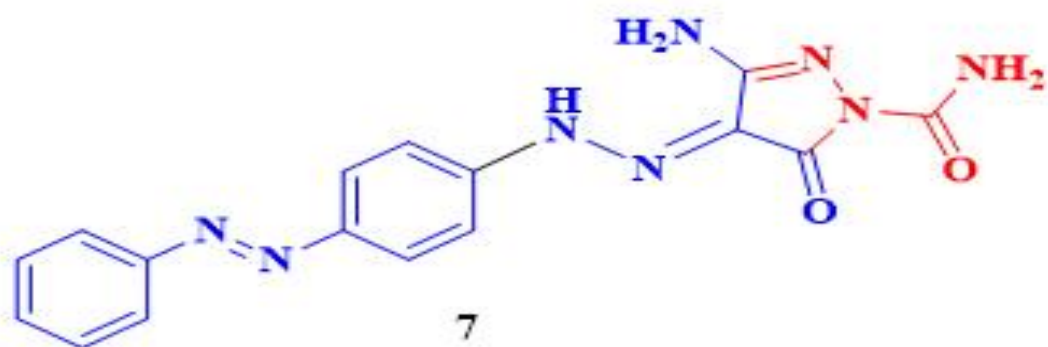
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG(2) waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

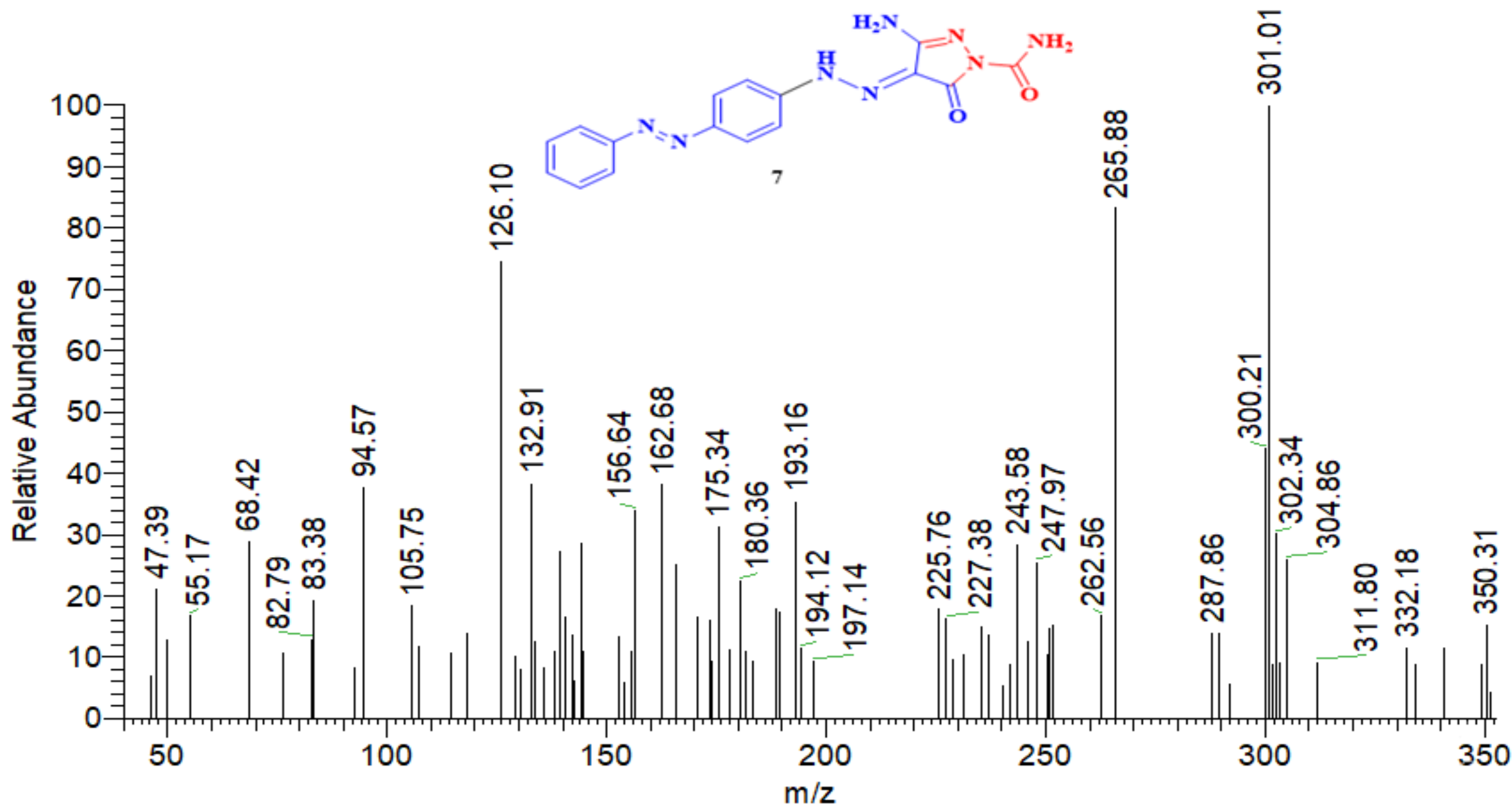
159.99
158.81
152.55
150.30
148.74
145.09
131.88
129.91
125.93
124.73
122.85
116.15

40.59
40.39
40.18
39.97
39.76
39.55
39.34

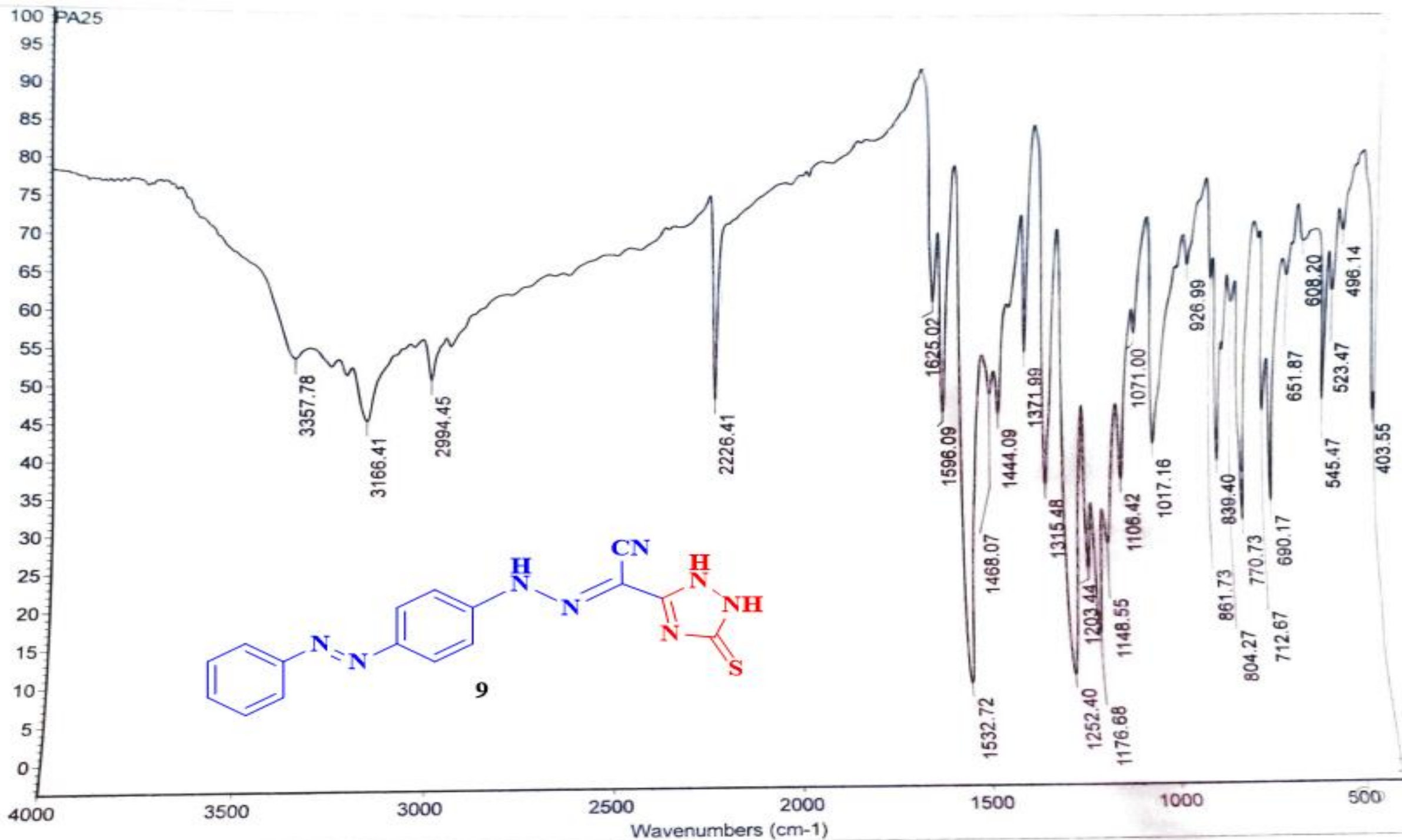


kerles-PA24 #296 RT: 4.97 AV: 1 SB: 26 1.21-1.34 , 0.87-1.14 NL: 7.20E2

T: {0,0} + c EI Full ms [40.00-1000.00]



% Transmittance





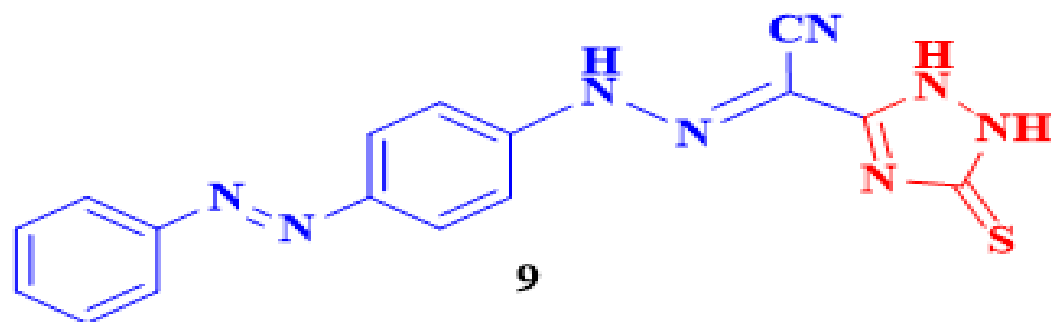
Current Data Parameters
NAME nour eldin-PA25
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 17.29
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
ID 65536
SOLVENT DMSO
NS 128
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 205.37
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

----- CHANNEL f1 -----
SFO1 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

8.618
7.987
7.968
7.946
7.912
7.899
7.882
7.864
7.844
7.757
7.734
7.655
7.633
7.616
7.610
7.599
7.580
7.565
7.548
7.185
— 4.492
— 3.344
2.511
2.507
2.503



2.00
2.02
3.97
2.95

1.02



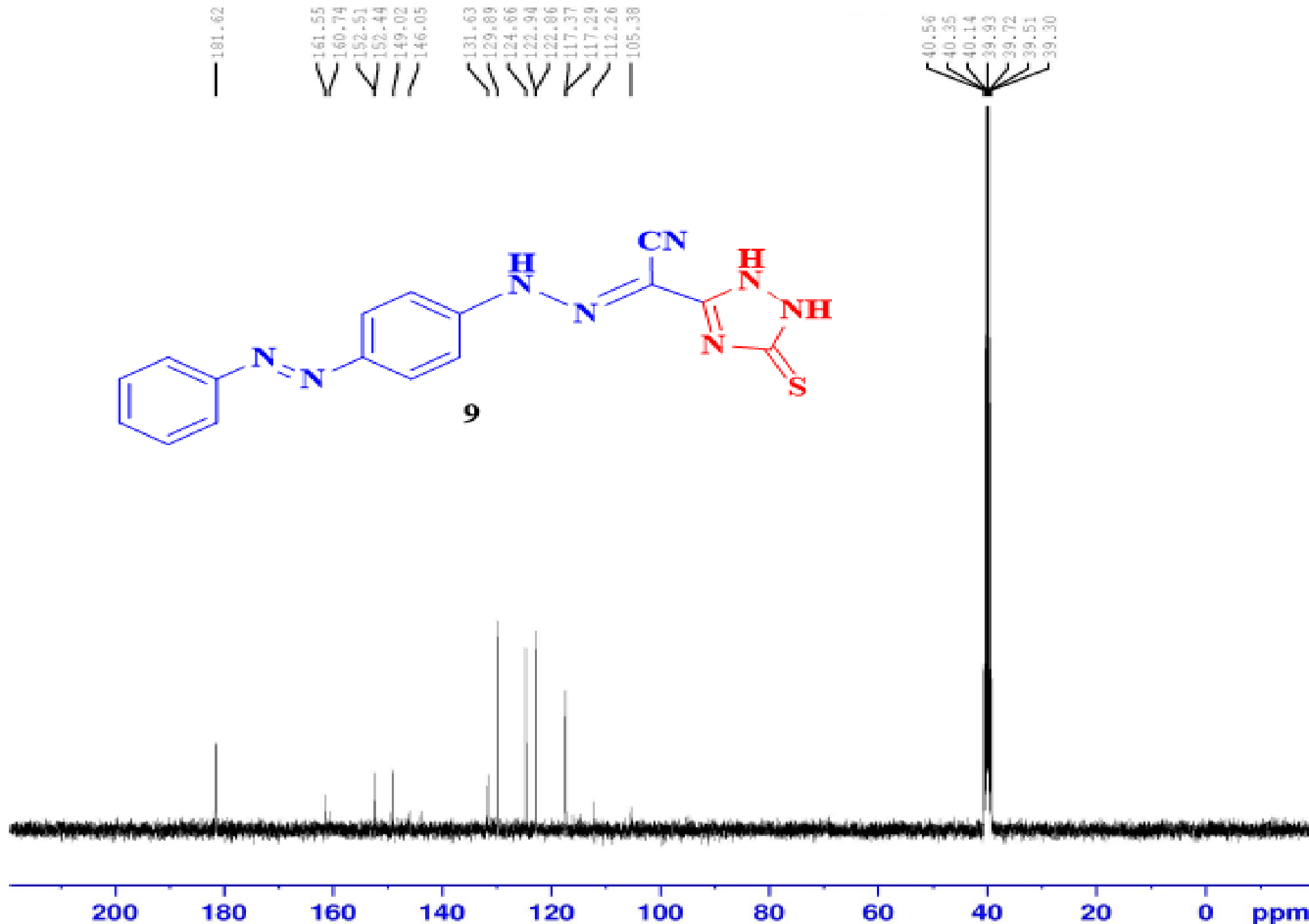
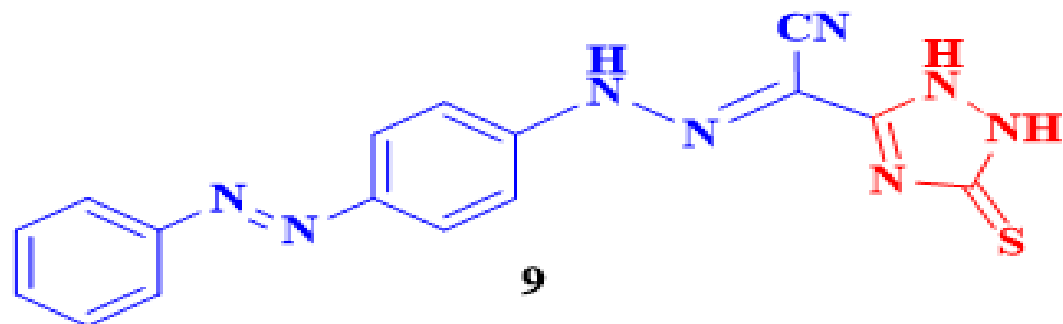
Current Data Parameters
NAME nour eldin-PA25
EXPNO 2
PROCNO 1

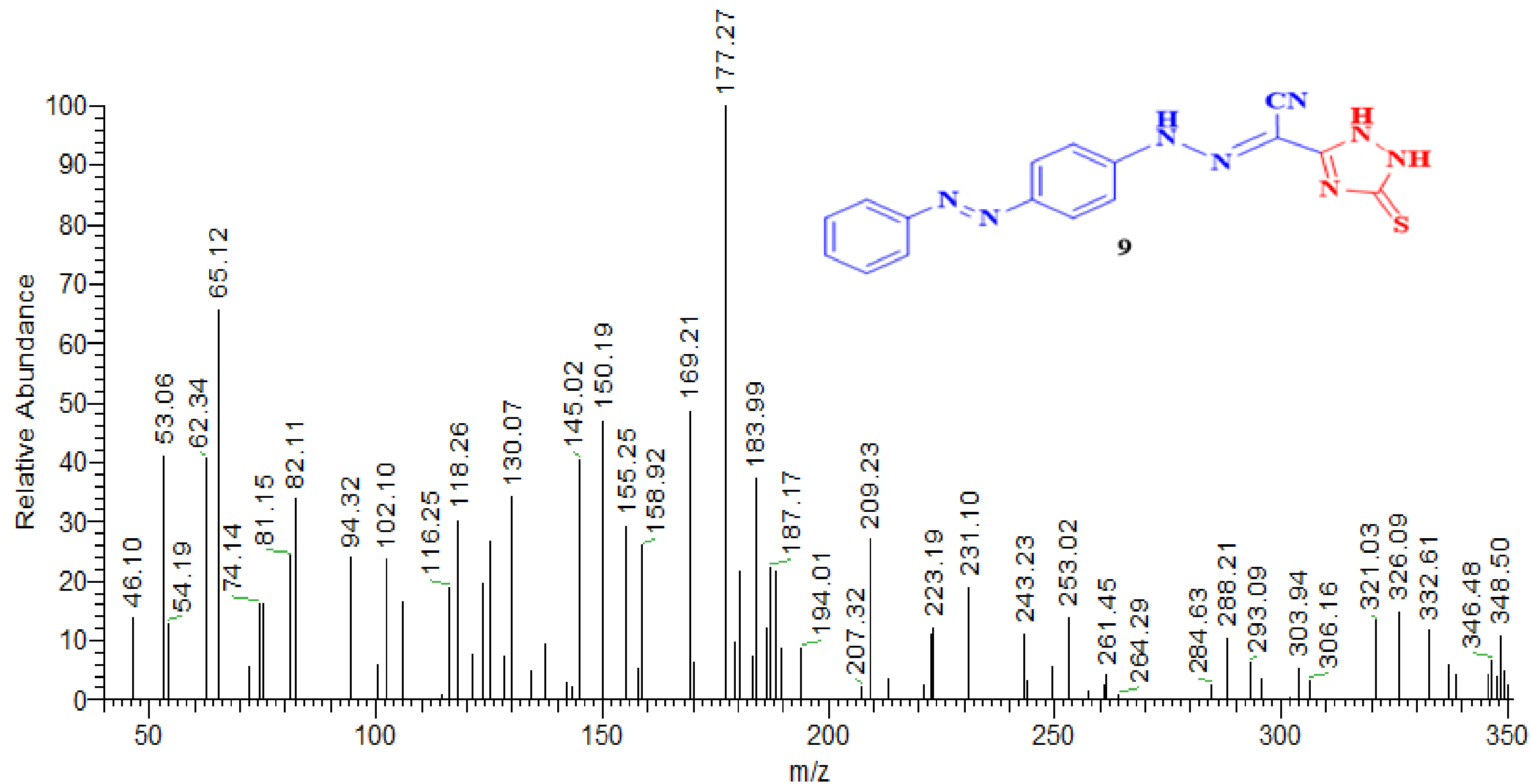
F2 - Acquisition Parameters
Date_ 20230316
Time 9.22
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 954
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TDO 1

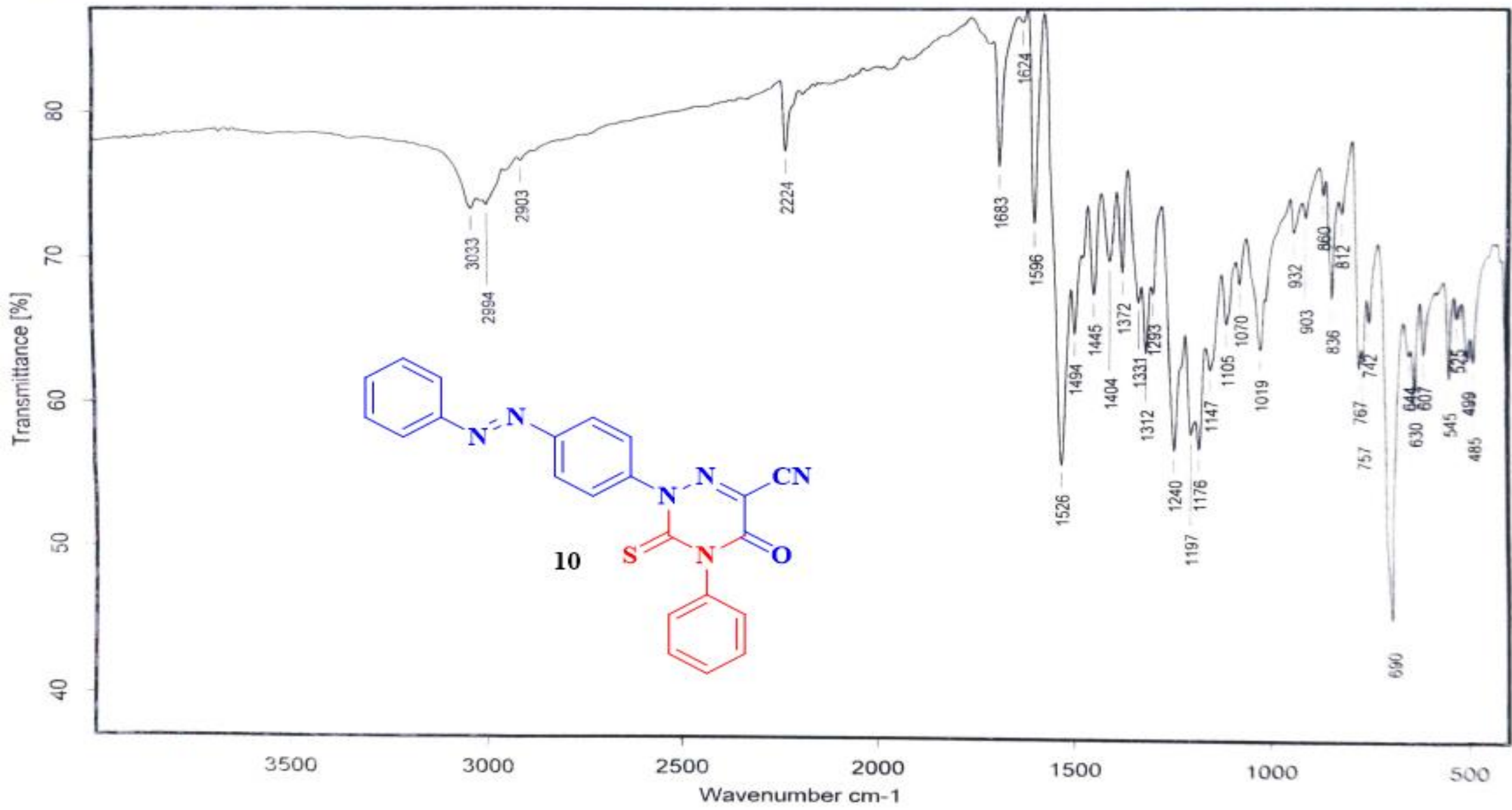
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40







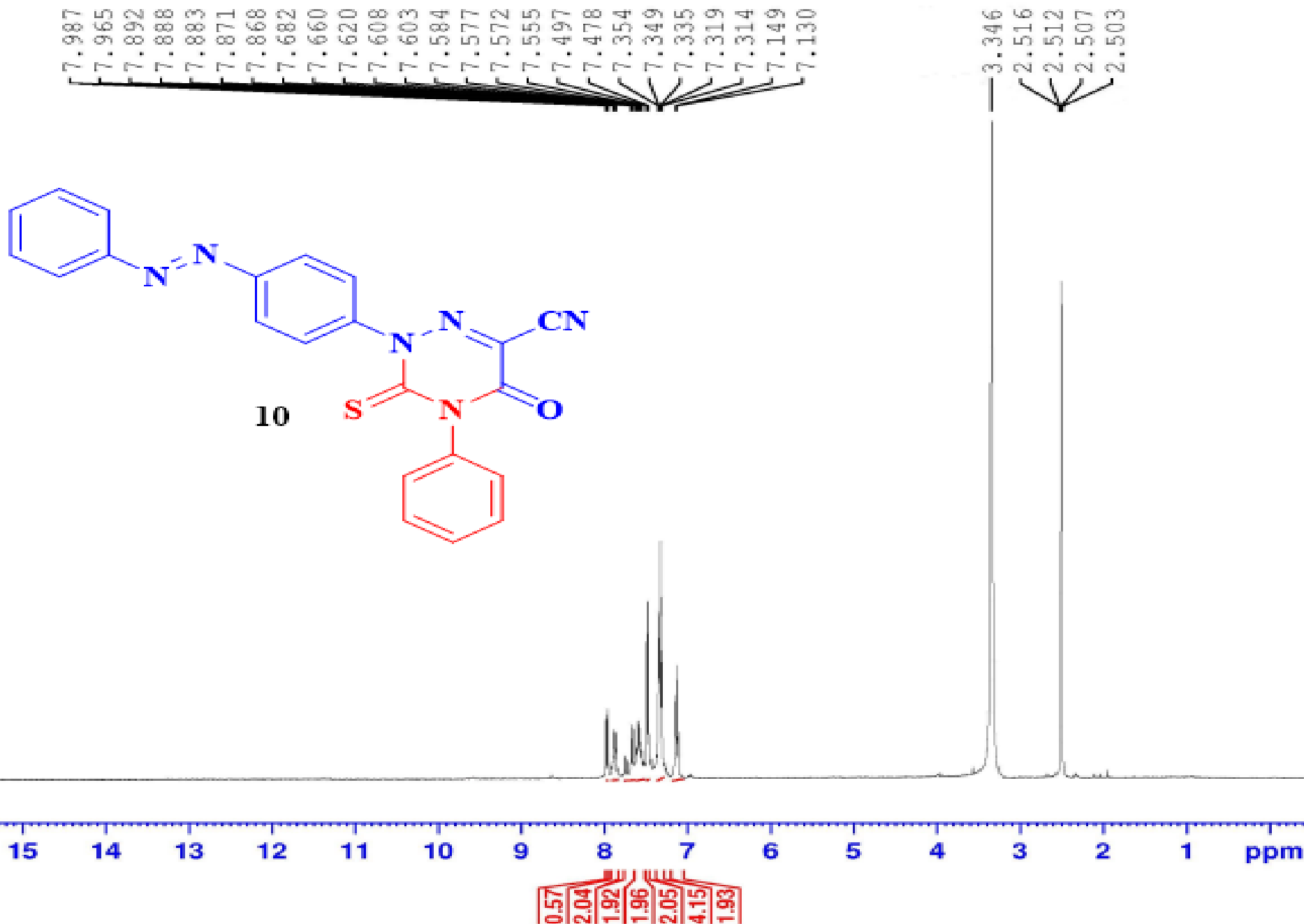


Current Data Parameters
NAME: nour eldin-PA31
EXPNO: 1
PROCNO: 1

F2 - Acquisition Parameters
Date_: 20230313
Time: 16.15
INSTRUM: spect
PROBHD: 5 mm PABBO BB/
PULPROG: zg30
ID: 65536
SOLVENT: DMSO
NS: 128
DS: 2
SWH: 8012.820 Hz
FIDRES: 0.122266 Hz
AQ: 4.0894465 sec
RG: 205.37
DW: 62.400 usec
DE: 6.50 usec
TE: 300.0 K
D1: 1.00000000 sec
TDO: 1

----- CHANNEL f1 -----
SFO1: 400.1524711 MHz
NUC1: 1H
P1: 12.00 usec
PLW1: 18.00000000 W

F2 - Processing parameters
SI: 65536
SF: 400.1500000 MHz
WDW: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 1.00





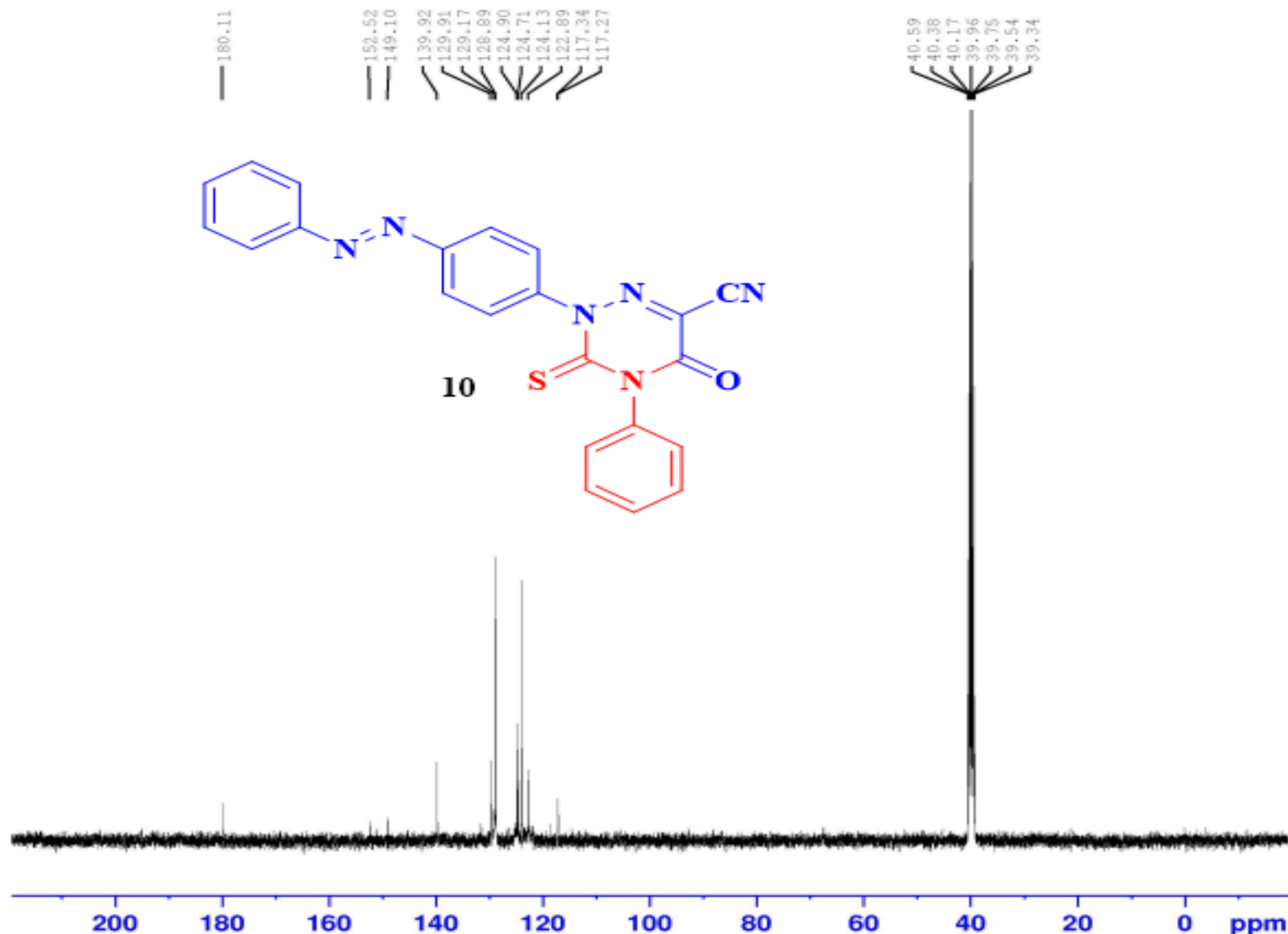
Current Data Parameters
NAME nour eldin-PA31
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230315
Time 11.45
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
ID 65536
SOLVENT DMSO
NS 1431
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.0000000 sec
D11 0.0300000 sec
TDO 1

===== CHANNEL f1 =====
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

===== CHANNEL f2 =====
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG(2) waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



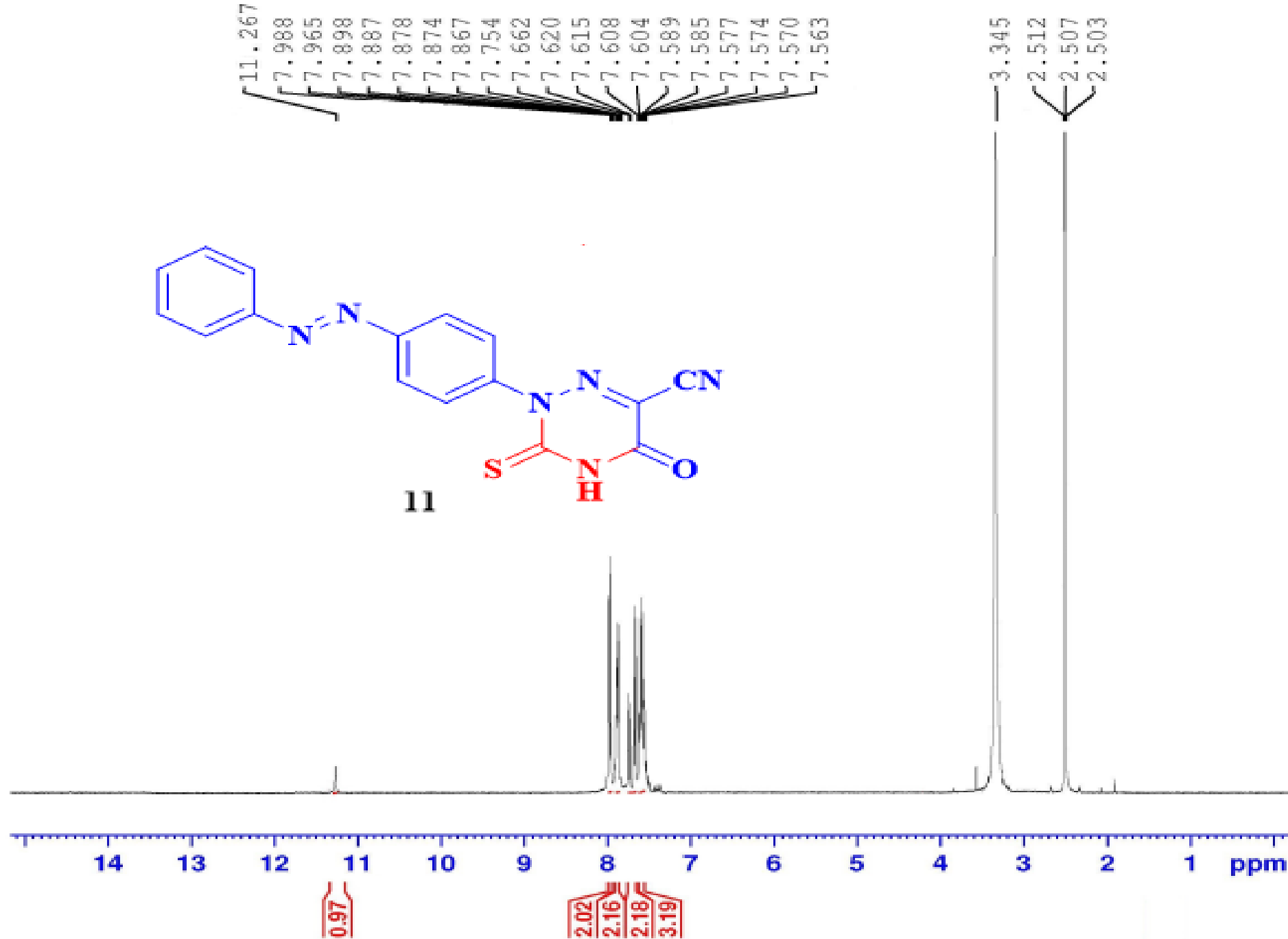
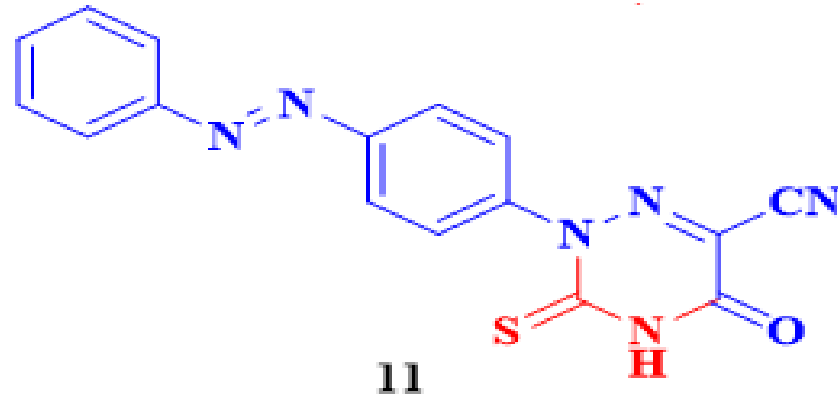


Current Data Parameters
NAME nour eldin-PA28
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 17.42
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
ID 65536
SOLVENT DMSO
NS 128
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 205.37
DW 62.400 usec
DE 6.50 usec
IE 300.0 K
D1 1.00000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00





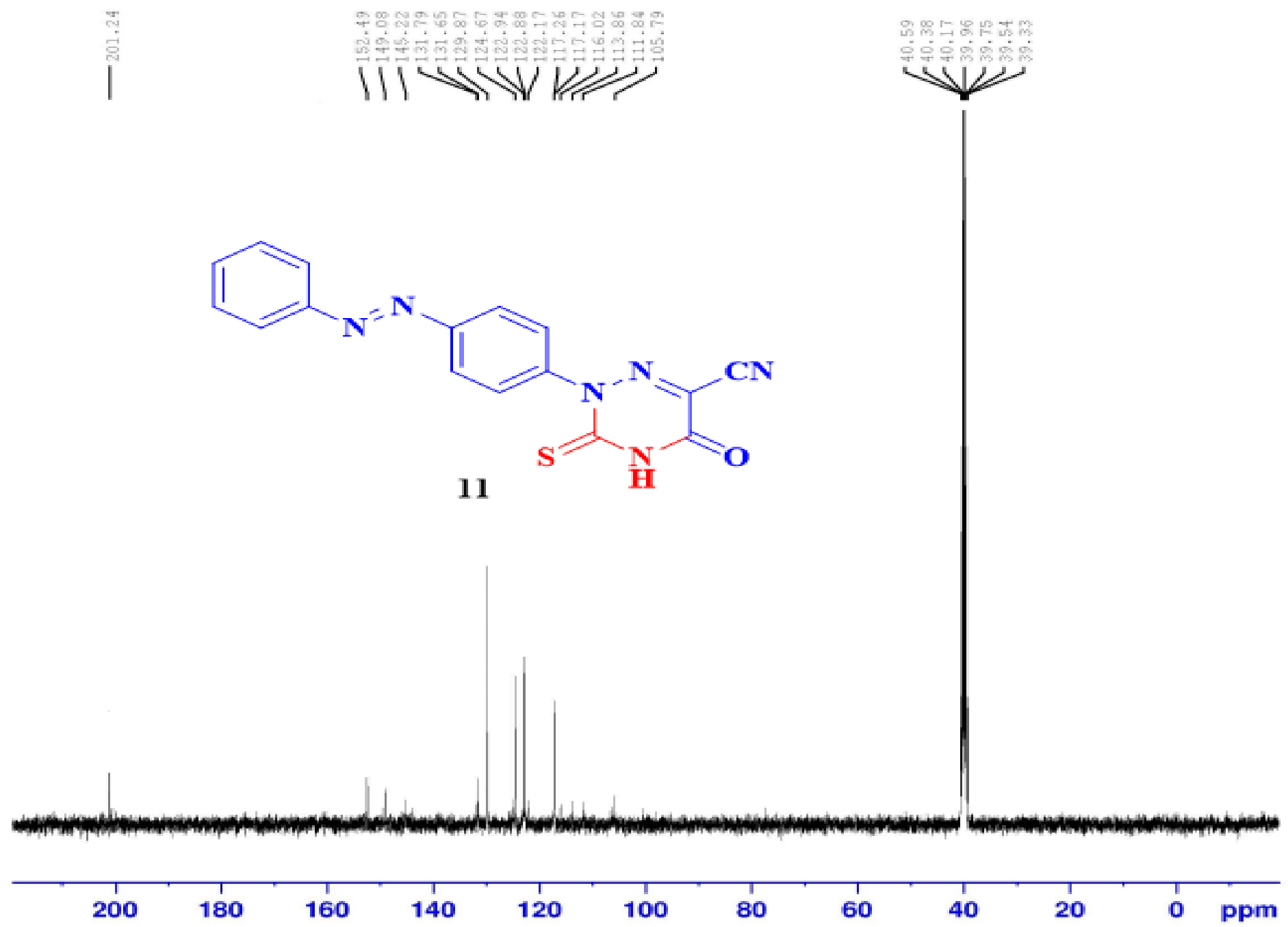
Current Data Parameters
NAME neur eldin-PA28
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230315
Time 13.49
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
ID 65536
SOLVENT DMSO
NS 1000
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
ID0 1

----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1816006 MHz
NUC2 1H
CPDPRG(2) waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



152.49
149.08
145.22
131.79
131.65
129.87
124.67
122.94
122.88
122.17
117.26
117.17
116.02
113.86
111.84
105.79

40.59
40.38
40.17
39.96
39.75
39.54
39.33

11



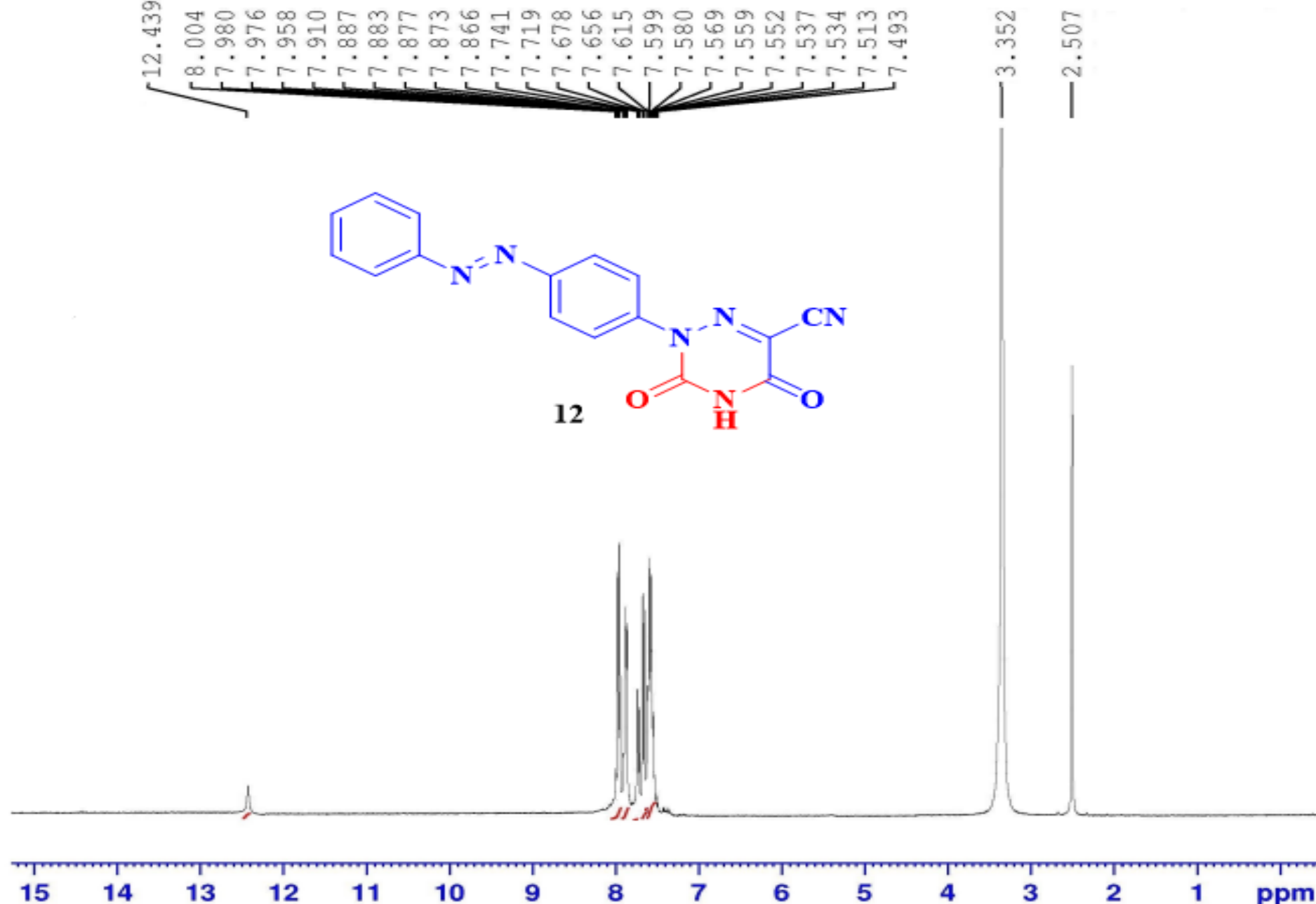
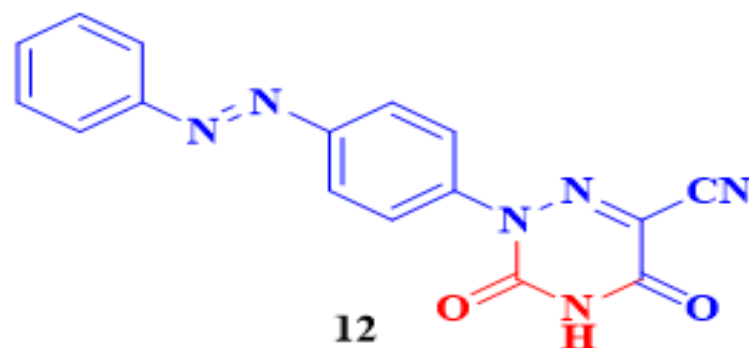
Current Data Parameters
NAME nour eldin-PA27
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 16.37
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 94
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 205.37
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

----- CHANNEL f1 -----
SF01 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.150000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

12.439
8.004
7.980
7.976
7.958
7.910
7.887
7.883
7.877
7.873
7.866
7.741
7.719
7.678
7.656
7.615
7.599
7.580
7.569
7.559
7.552
7.537
7.534
7.513
7.493



1.03

2.04
2.03
0.42
2.00
3.01



Current Data Parameters
NAME neur eldin-PA27
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230314
Time 12.30
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
ID 65536
SOLVENT DMSO
NS 1376
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631468 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

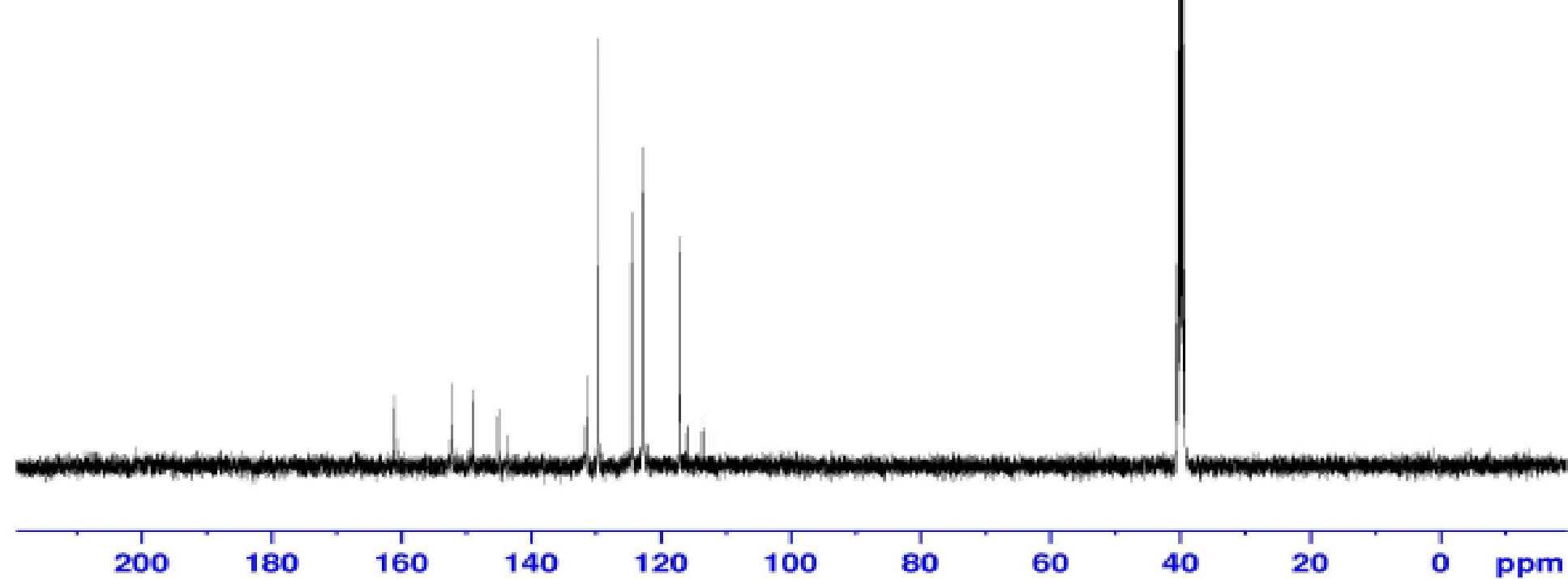
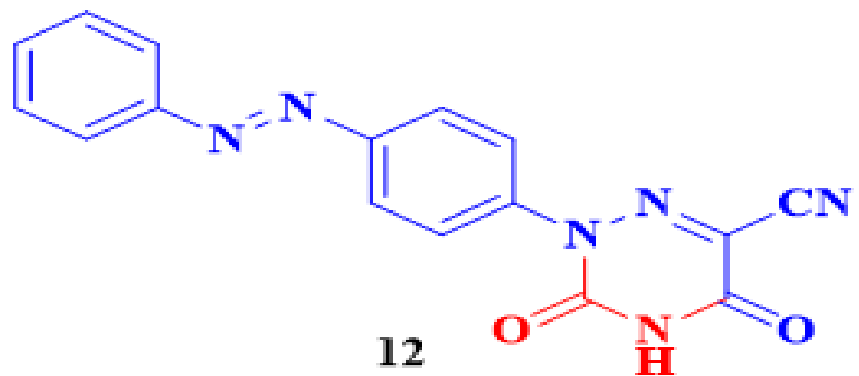
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

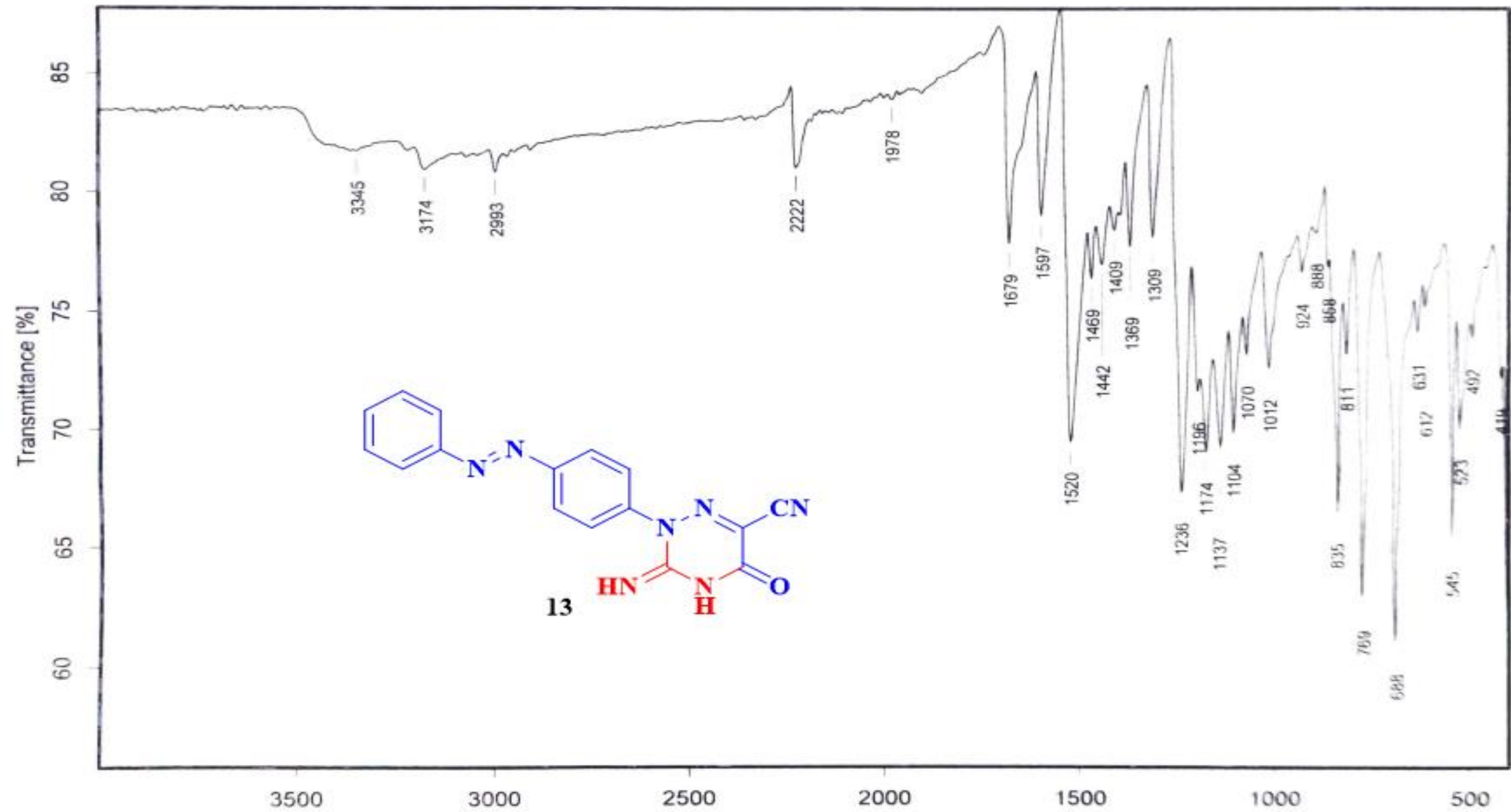
----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

161.21
160.74
152.49
149.08
145.19
143.91
131.77
131.64
129.86
124.66
122.94
122.88
117.26
117.16
116.01
113.87

40.60
40.39
40.18
39.97
39.76
39.56
39.35







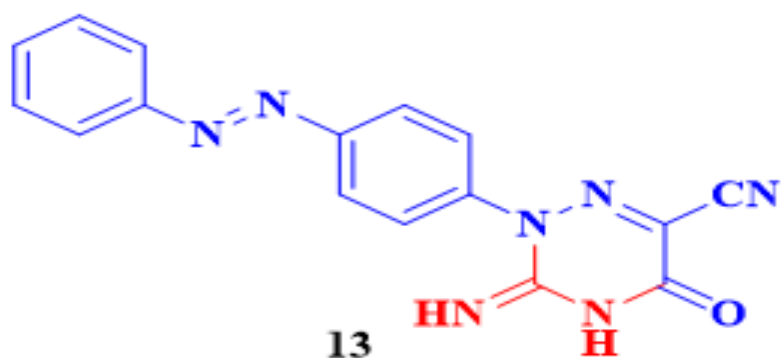
Current Data Parameters
NAME nour eldin-PA29
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 15.39
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 112
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 31.47
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TDO 1

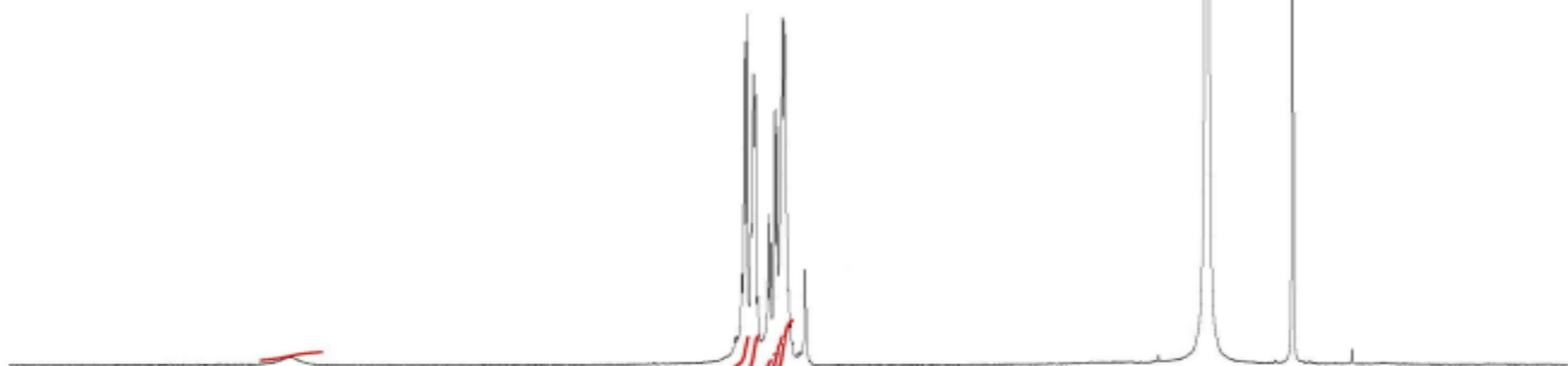
----- CHANNEL f1 -----
SFO1 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

12.644
8.064
8.041
8.000
7.970
7.948
7.908
7.883
7.861
7.840
7.733
7.711
7.669
7.647
7.594
7.574
7.547
7.531
7.513
7.492
7.378
7.356



3.352
2.507



15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

2.03

2.01
2.08
0.54
2.03
3.03



Current Data Parameters
NAME: nour eldin-PA29
EXPNO: 2
PROCNO: 1

F2 - Acquisition Parameters
Date_: 20230314
Time: 10.13
INSTRUM: spect
PROBHD: 5 mm PABBO BB/
PULPROG: zgpg30
TD: 65536
SOLVENT: DMSO
NS: 1500
DS: 4
SWH: 24038.461 Hz
FIDRES: 0.366798 Hz
AQ: 1.3631488 sec
RG: 205.37
DW: 20.800 usec
DE: 6.50 usec
TE: 300.0 K
D1: 2.00000000 sec
D11: 0.03000000 sec
TDO: 1

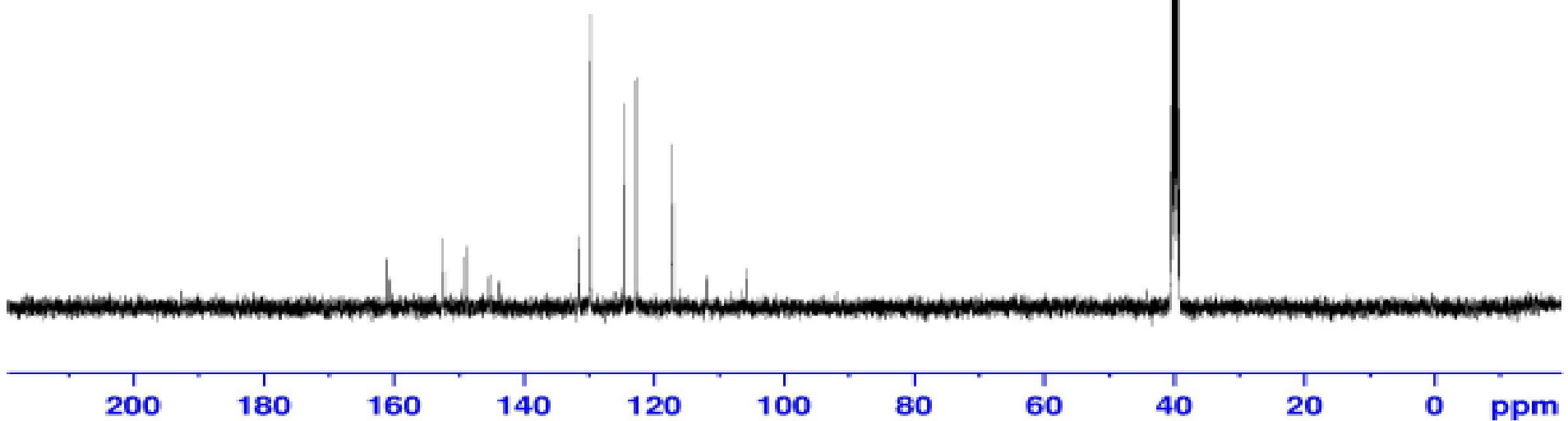
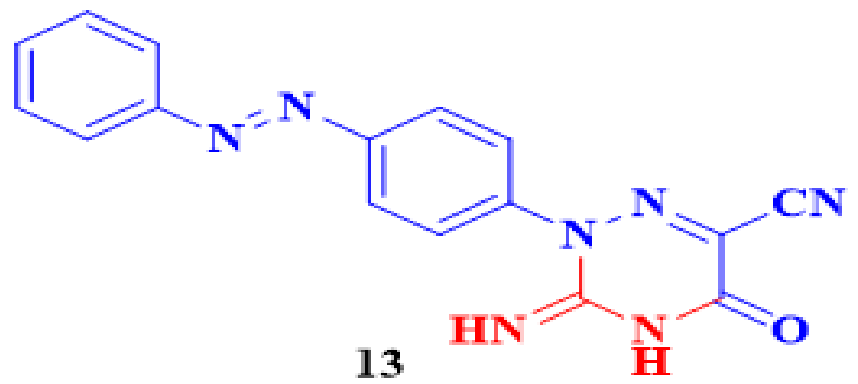
----- CHANNEL f1 -----
SFO1: 100.6278588 MHz
NUC1: 13C
P1: 10.00 usec
PLW1: 47.00000000 W

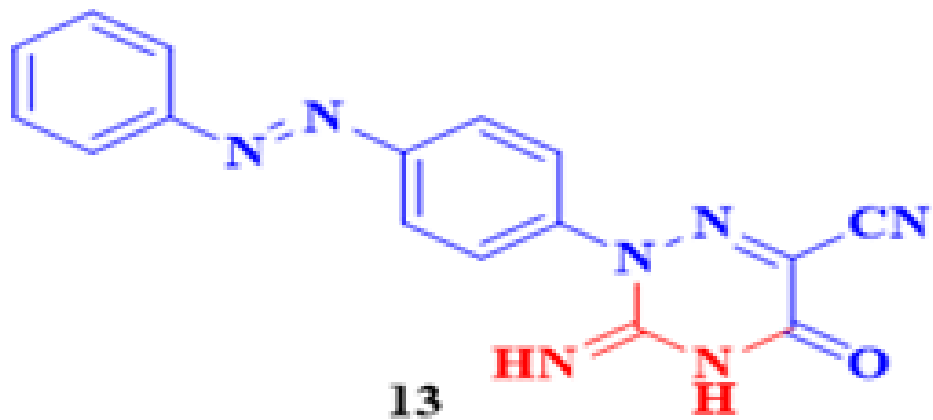
----- CHANNEL f2 -----
SFO2: 400.1516006 MHz
NUC2: 1H
CPDPRG[2]: waltz16
PCPD2: 90.00 usec
PLW2: 18.00000000 W
PLW12: 0.34722000 W
PLW13: 0.28125000 W

F2 - Processing parameters
SI: 32768
SF: 100.6177975 MHz
WDW: EM
SSB: 0
LB: 1.00 Hz
GB: 0
PC: 1.40

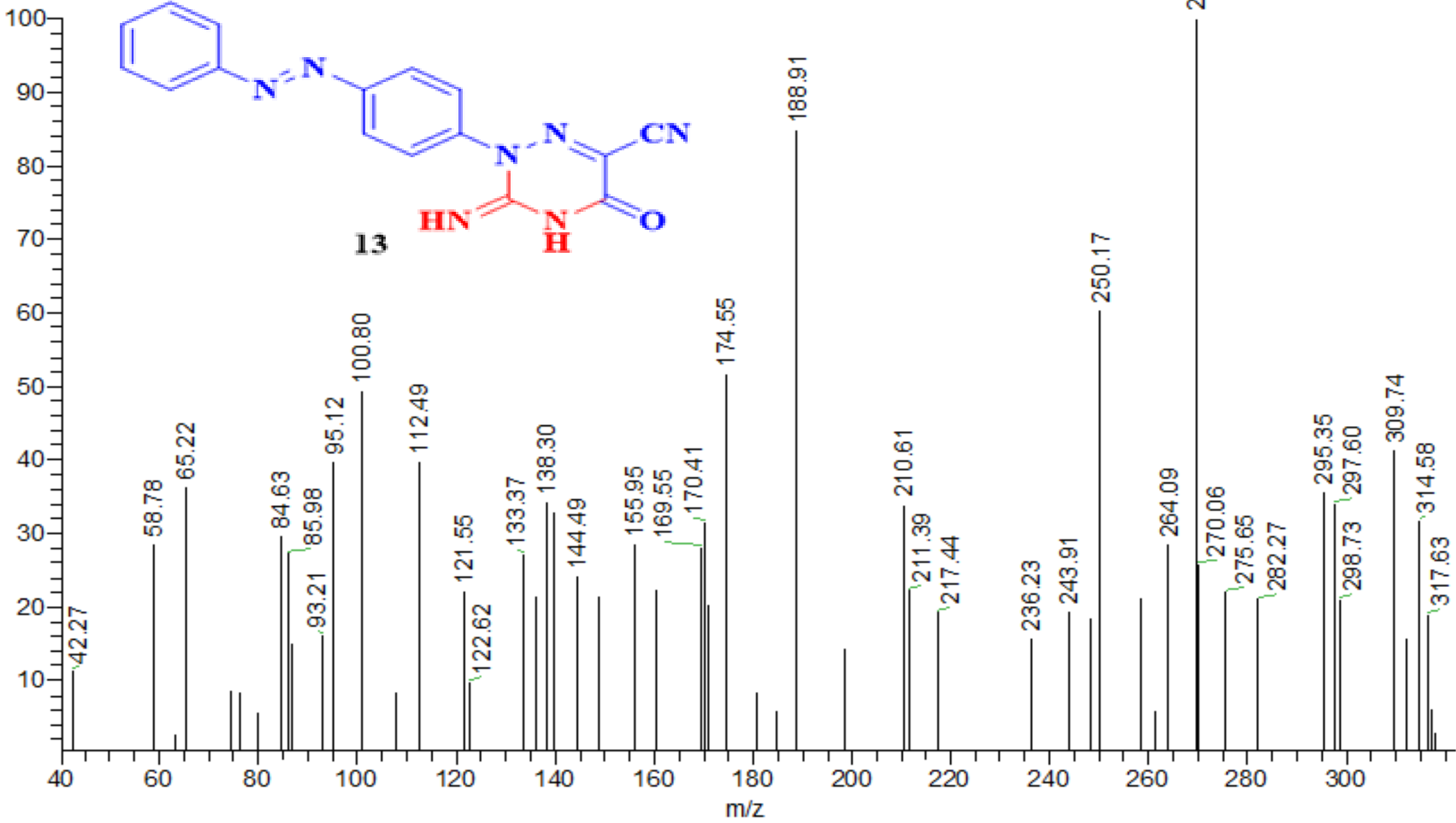
161.30
160.72
152.51
149.08
145.42
143.97
131.81
131.66
129.89
124.69
122.95
122.88
117.30
117.22
111.93
105.74

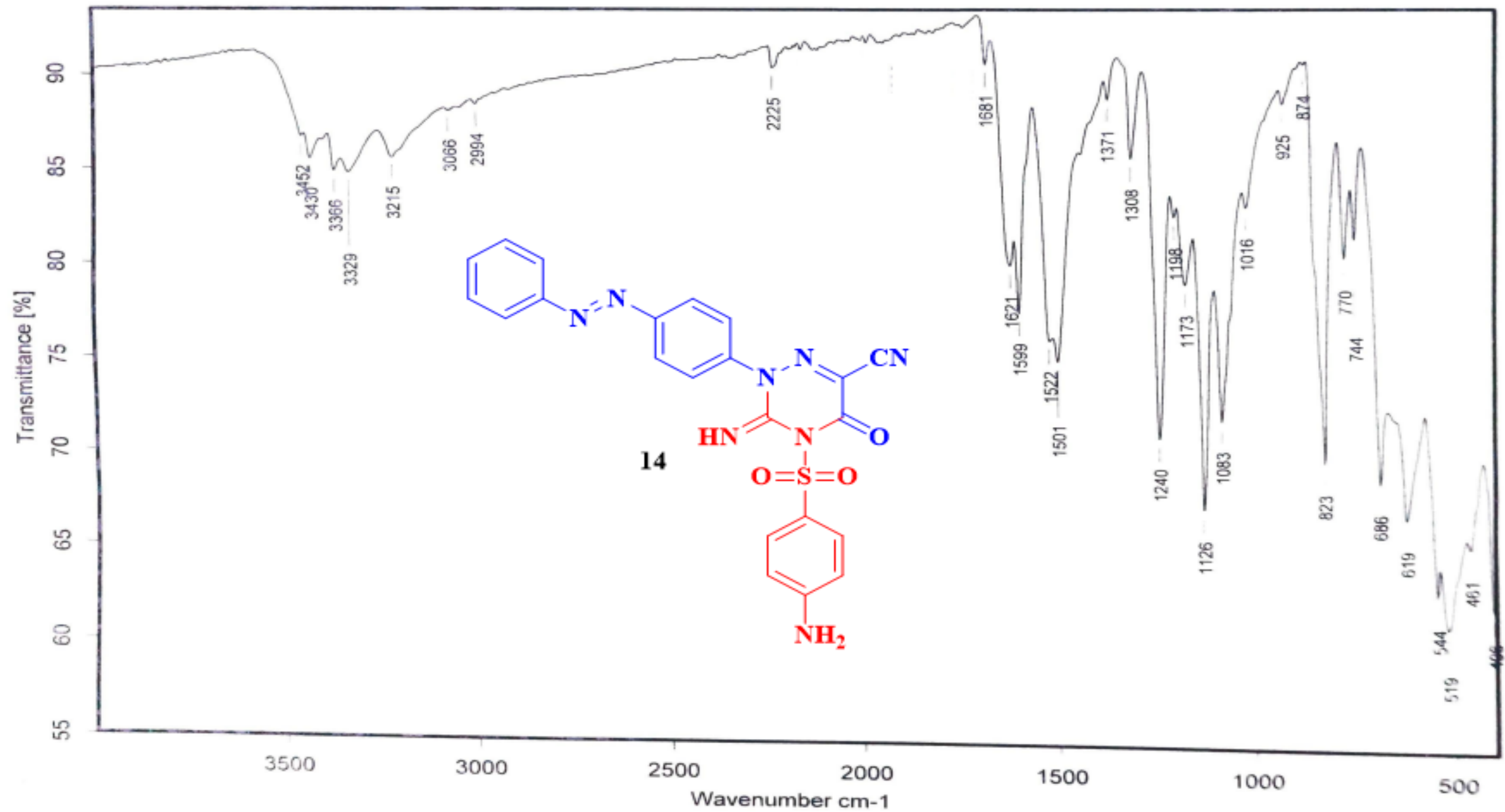
40.61
40.40
40.19
39.98
39.77
39.56
39.36



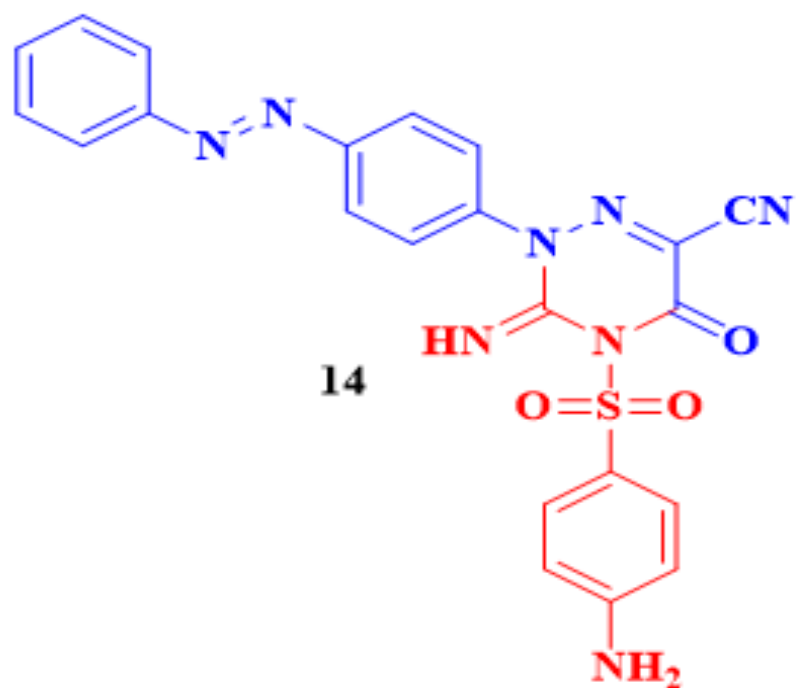


Relative Abundance





9.679
7.988
7.981
7.966
7.958
7.898
7.894
7.890
7.886
7.869
7.866
7.672
7.657
7.650
7.619
7.609
7.602
7.583
7.570
7.403
7.396
7.391
7.379
7.375
7.368
6.559
6.553
6.548
6.536
6.531
6.525
5.674



15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

1.08
4.01
5.08
4.08
2.20



Current Data Parameters
NAME nour eldin-PA30
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230313
Time 17.16
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 106
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 205.37
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TDO 1

----- CHANNEL f1 -----
SFO1 400.1524711 MHz
NUC1 1H
P1 12.00 usec
PLW1 18.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



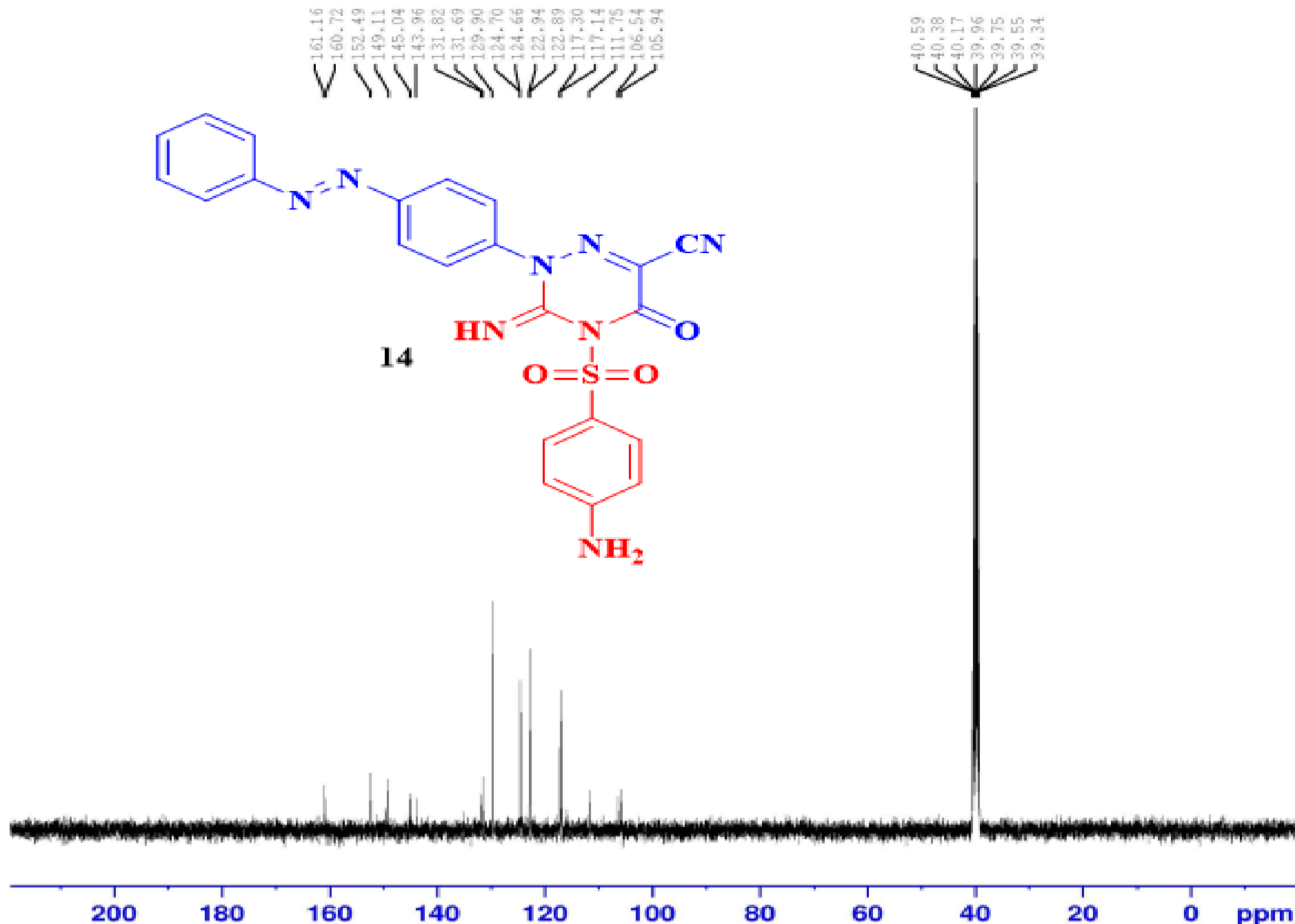
Current Data Parameters
NAME nour eldin-PA30
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230314
Time 12.49
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
ID 65536
SOLVENT DMSO
NS 285
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631468 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 299.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



kerles-PA30 #204 RT: 3.43 AV: 1 SB: 26 1.21-1.34, 0.87-1.14 NL: 5.41E3

T: {0,0} + c EI Full ms [40.00-1000.00]

