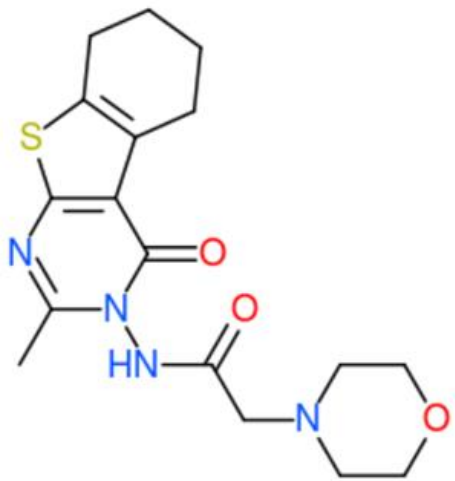
In-Silico Screening of Novel Synthesized Thienopyrimidines Targeting Fms Related Receptor Tyrosine Kinase-3 and Their *In-Vitro* Biological Evaluation

Elshaymaa I. Elmongy 1,2,*, Najla Altwaijry 1, Nashwah G. M. Attallah 1,3, Manal Mubarak AlKahtani 4 and Hanan Ali Henidi 4

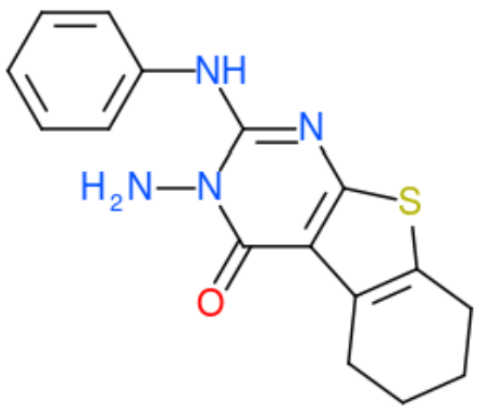


Molecular Properties and Drug-likeness.

Molecular formula: C17 H22 N4 O3 S
Molecular weight: 362.14
Number of HBA: 6
Number of HBD: 1
MolLogP : 0.94
MolLogS : -1.40 (in Log(moles/L)) 14550.50 (in mg/L)
MolPSA : 62.31 A^2
MolVol : 385.55 A^3
pKa of most Basic/Acidic group : 4.76 / 10.80

$$pK_{\mathrm{a}} = -\log_{10} K_a = \log_{10} \frac{[\mathrm{HA}]}{[\mathrm{A}^-][\mathrm{H}^+]}$$

BBB Score : 3.60 The Blood-Brain Barrier (BBB) Score: 6-High,0-Low *(DOI: 10.1021/acs.jmedchem.9b01220)*
Number of stereo centers: 0



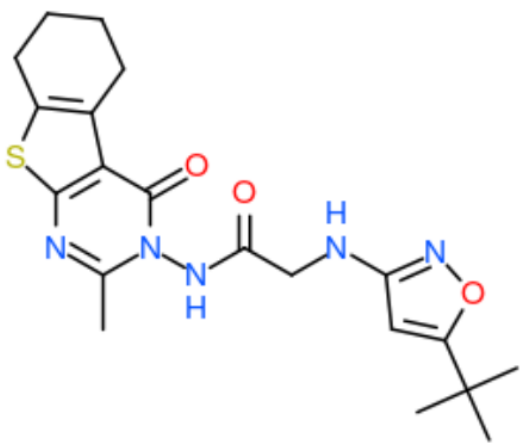
Molecular Properties and Drug-likeness.

Molecular formula: C16 H16 N4 O S
Molecular weight: 312.10
Number of HBA: 4
Number of HBD: 3
MolLogP : 3.14
MolLogS : -3.71 (in Log(moles/L)) 60.86 (in mg/L)
MolPSA : 50.87 A^2
MolVol : 307.14 A^3
pKa of most Basic/Acidic group : -2.07 / 15.42

$$pK_{\mathrm{a}} = -\log_{10} K_a = \log_{10} \frac{[\mathrm{HA}]}{[\mathrm{A}^-][\mathrm{H}^+]}$$

BBB Score : 4.01 The Blood-Brain Barrier (BBB) Score: 6-High,0-Low *(DOI: 10.1021/acs.jmedchem.9b01220)*
Number of stereo centers: 0

Molecular Properties and Drug-likeness.



Molecular formula: C20 H25 N5 O3 S
Molecular weight: 415.17
Number of HBA: 6
Number of HBD: 2
MolLogP : 3.23
MolLogS : -3.75 (in Log(moles/L)) 73.61 (in mg/L)
MolPSA : 83.28 A^2
MolVol : 443.53 A^3
pKa of most Basic/Acidic group : 3.09 / 11.69

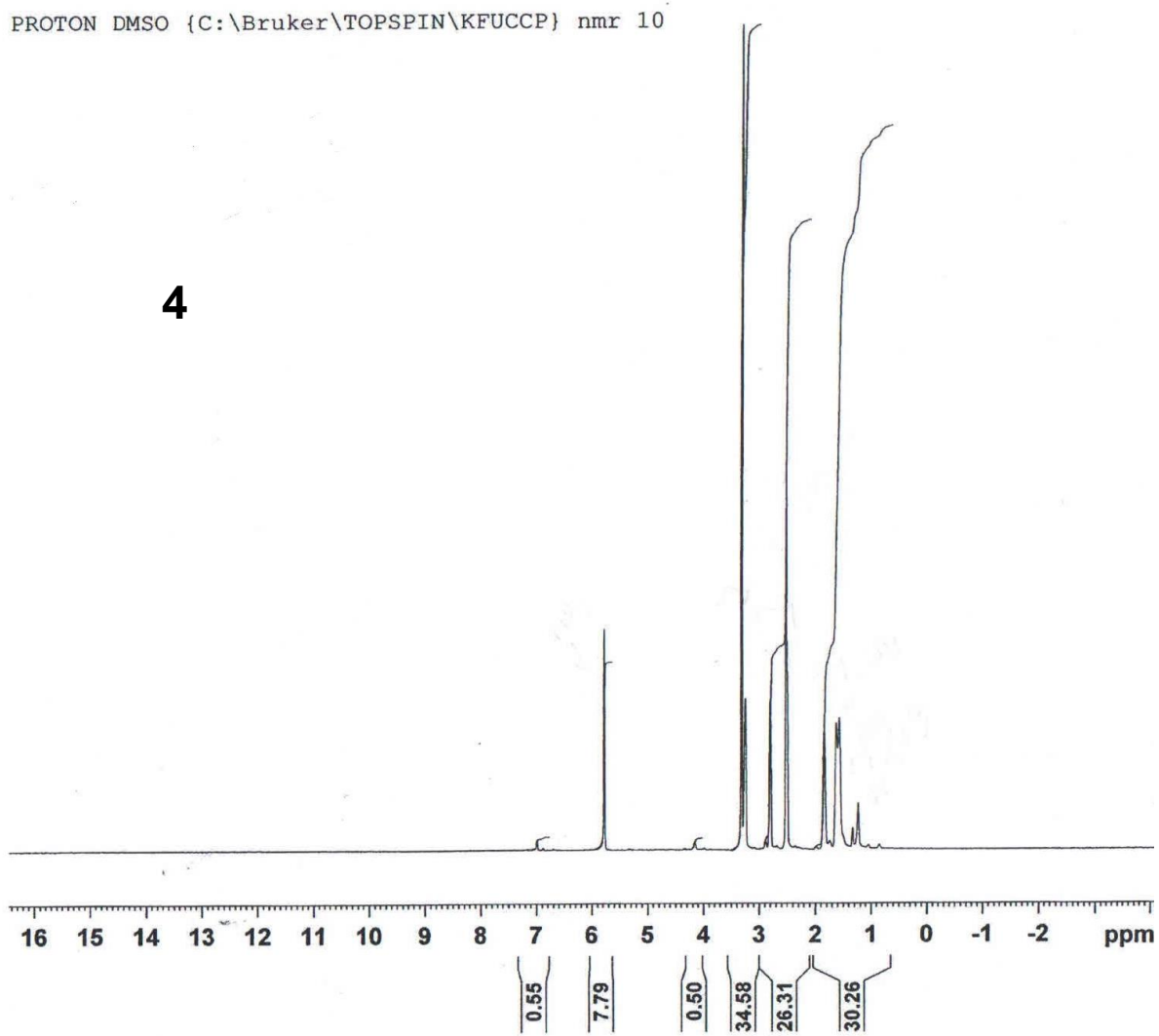
$$pK_{\mathrm{a}} = -\log_{10} K_a = \log_{10} \frac{[\mathrm{HA}]}{[\mathrm{A}^-][\mathrm{H}^+]}$$

BBB Score : 3.10 The Blood-Brain Barrier (BBB) Score: 6-High,0-Low *(DOI: 10.1021/acs.jmedchem.9b01220)*
Number of stereo centers: 0

H-NMR

PROTON DMSO {C:\Bruker\TOPSPIN\KFUCCP} nmr 10

4



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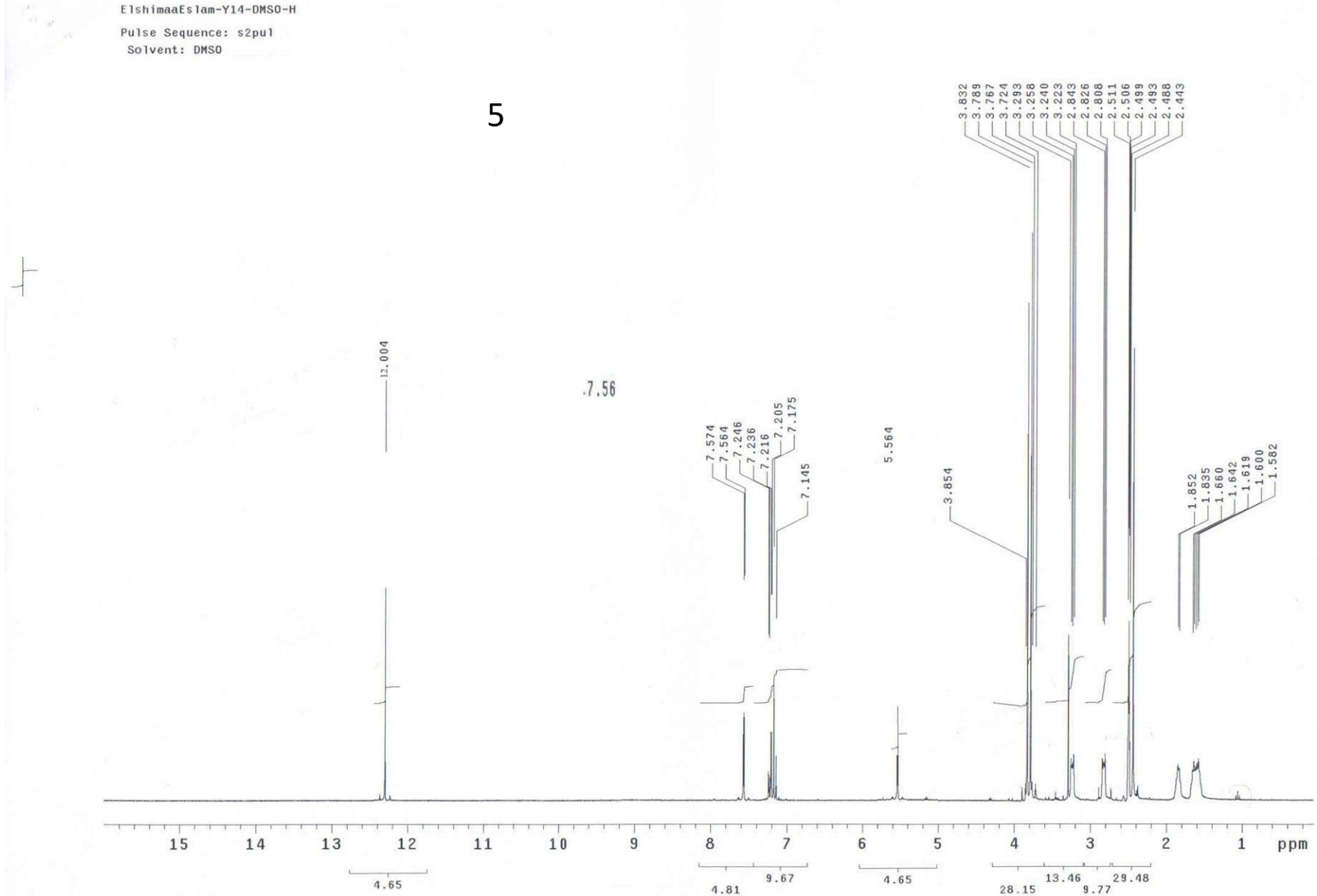
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Pulse Sequence: s2pul
Solvent: DMSO
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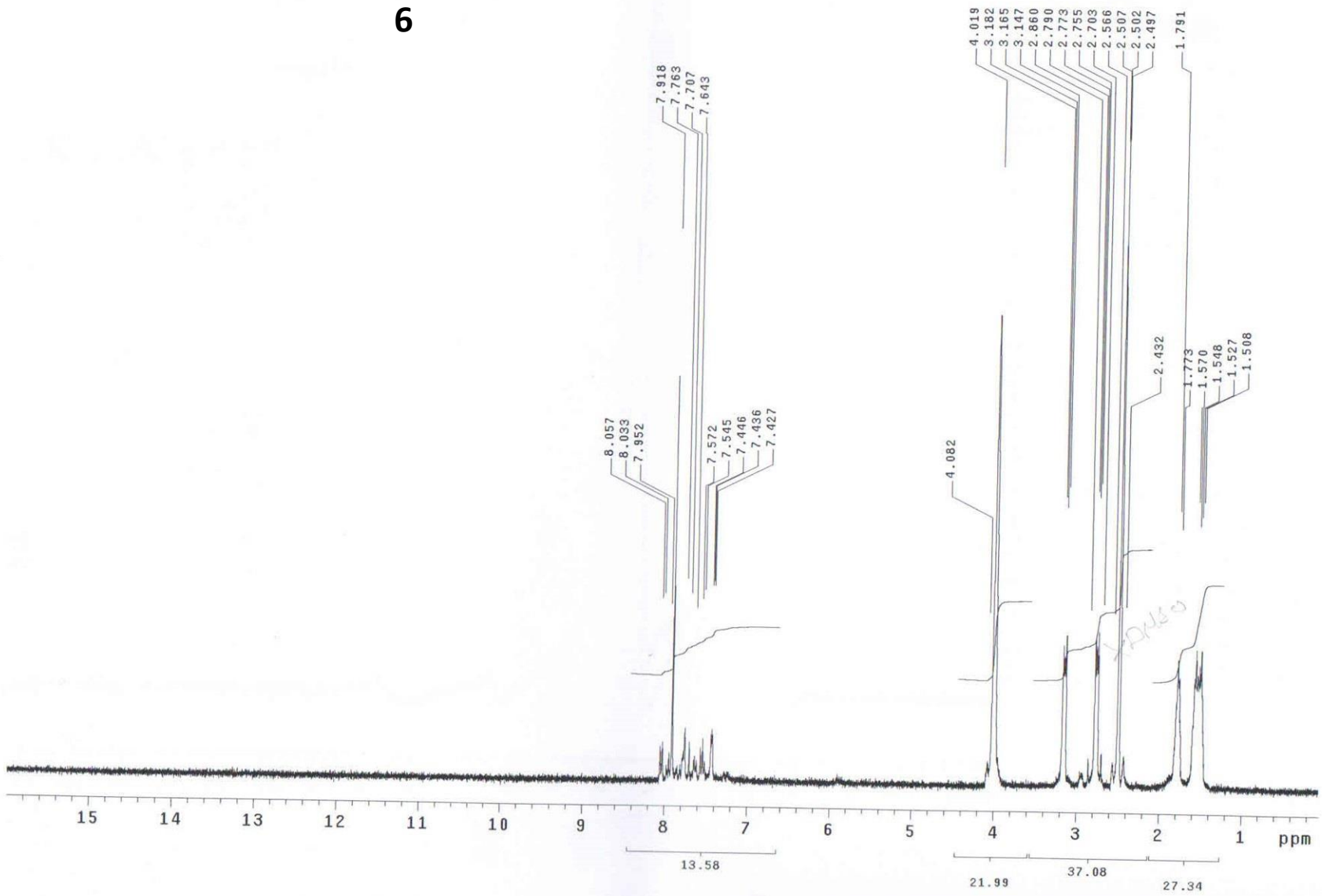
7.56
7.574
7.564
7.246
7.236
7.216
7.205
7.175
7.145
5.564
3.854
3.832
3.789
3.767
3.724
3.293
3.258
3.240
3.223
2.843
2.826
2.808
2.511
2.506
2.499
2.493
2.488
2.443
1.852
1.835
1.660
1.642
1.619
1.600
1.582
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
4.65
4.81
9.67
4.65
28.15
9.77
13.46
29.48

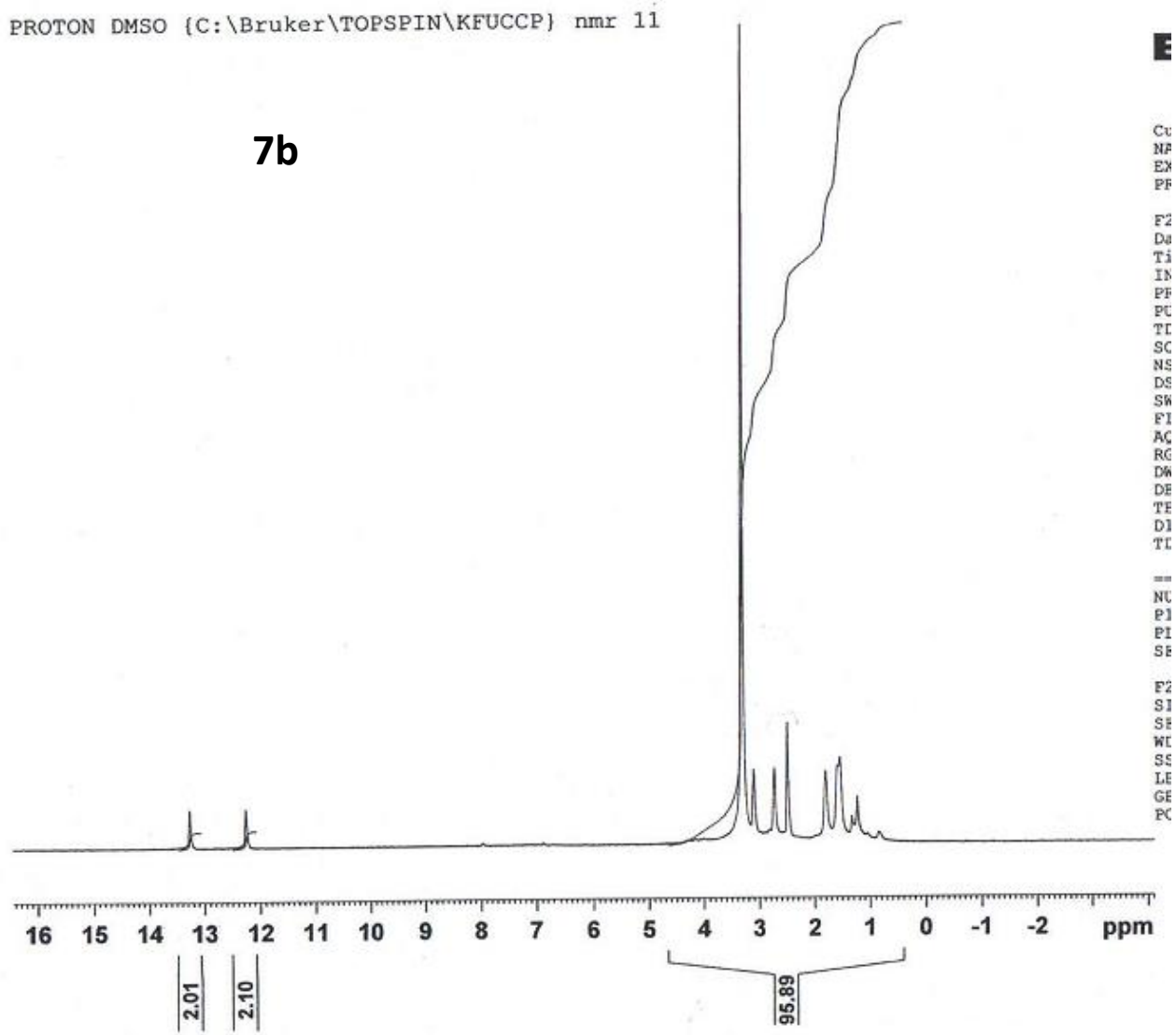
ElshimaaEslam-T8-DMSO-D2O-H

Pulse Sequence: s2pul

Solvent: DMSO

6

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7b
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 ppm
2.01
2.10
95.89

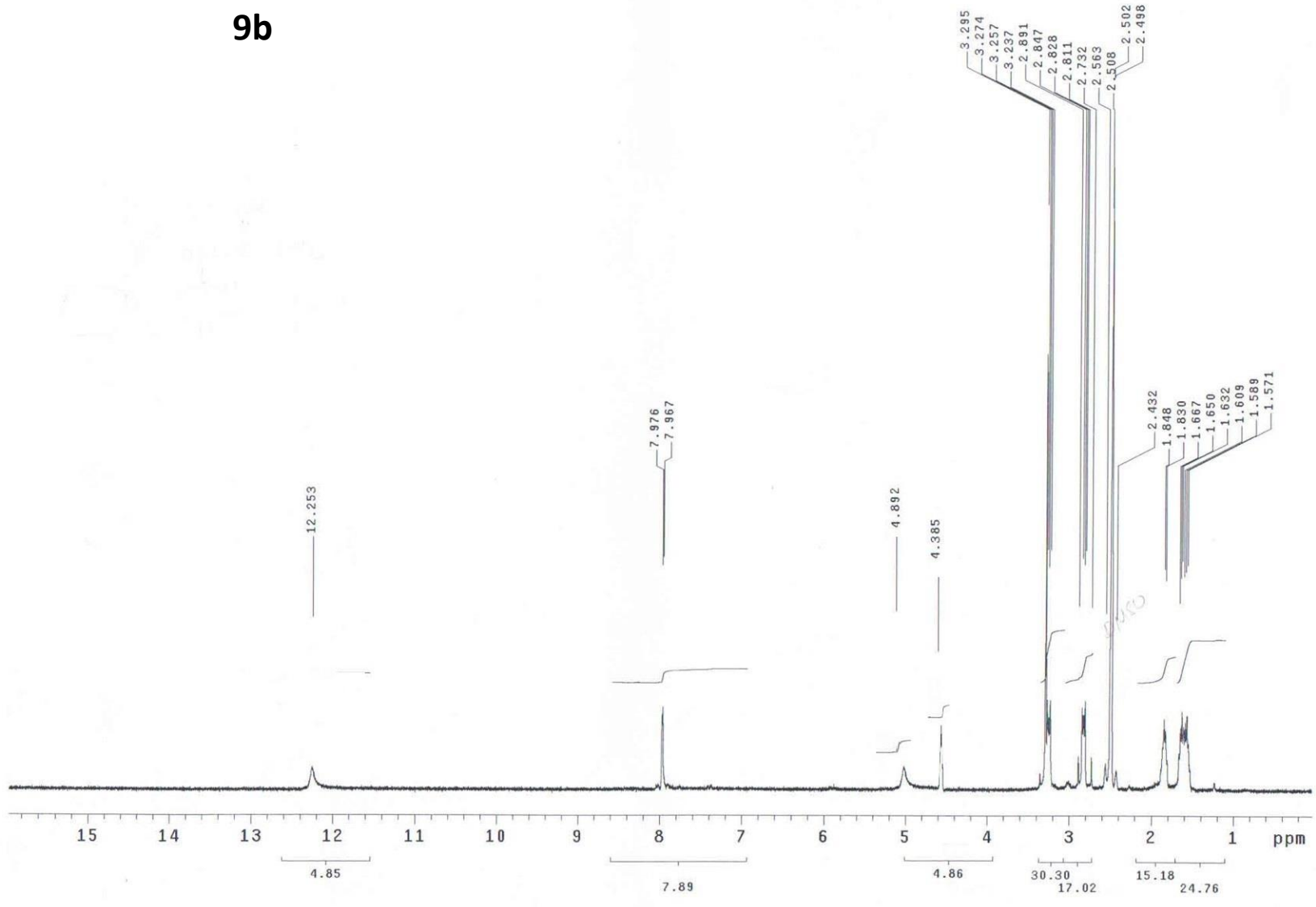
ElshimaaEslam-T7-DMSO-H

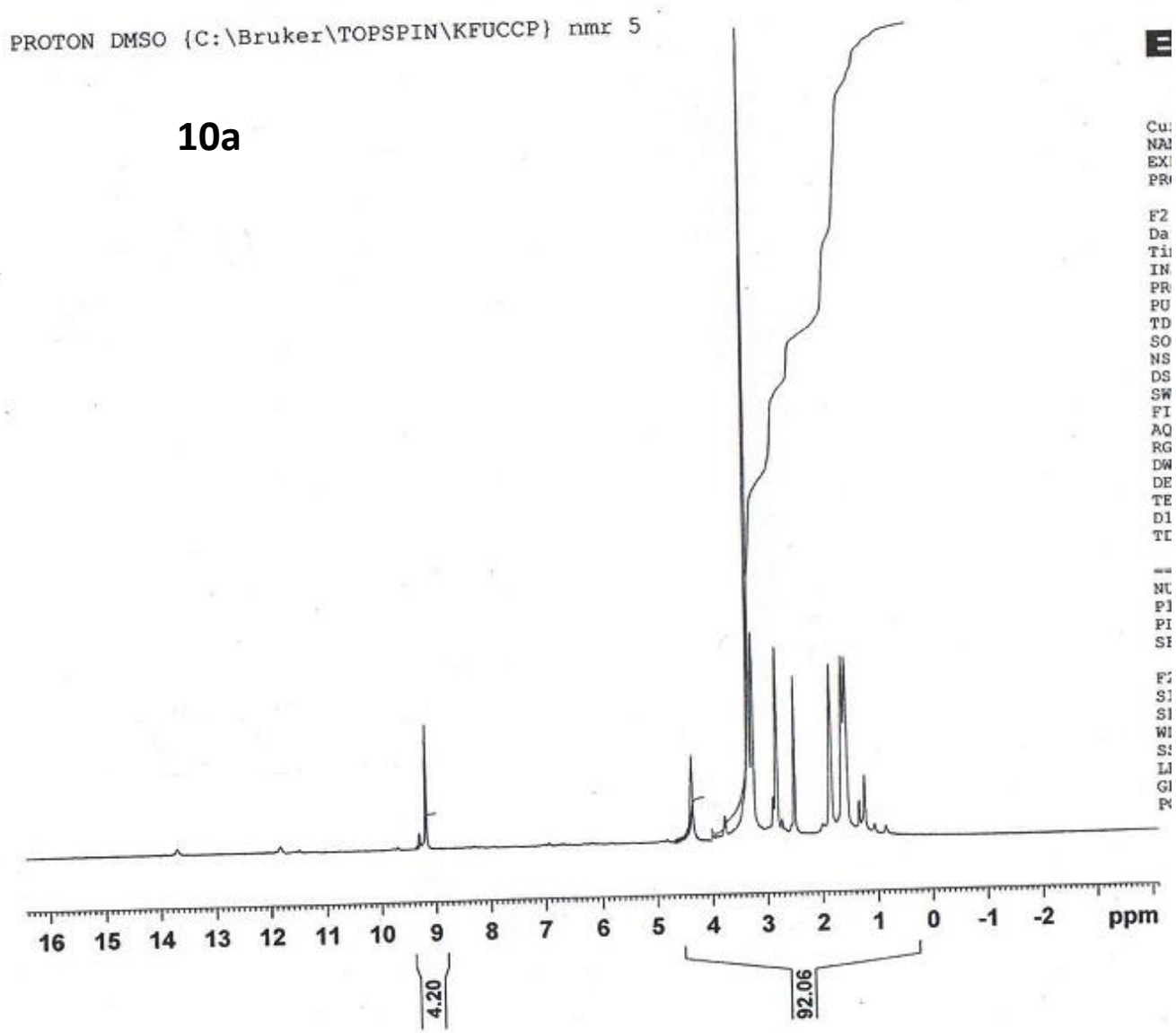
Pulse Sequence: s2pul

Solvent: DMSO

Temp. 30.0 C / 303.1 K

9b



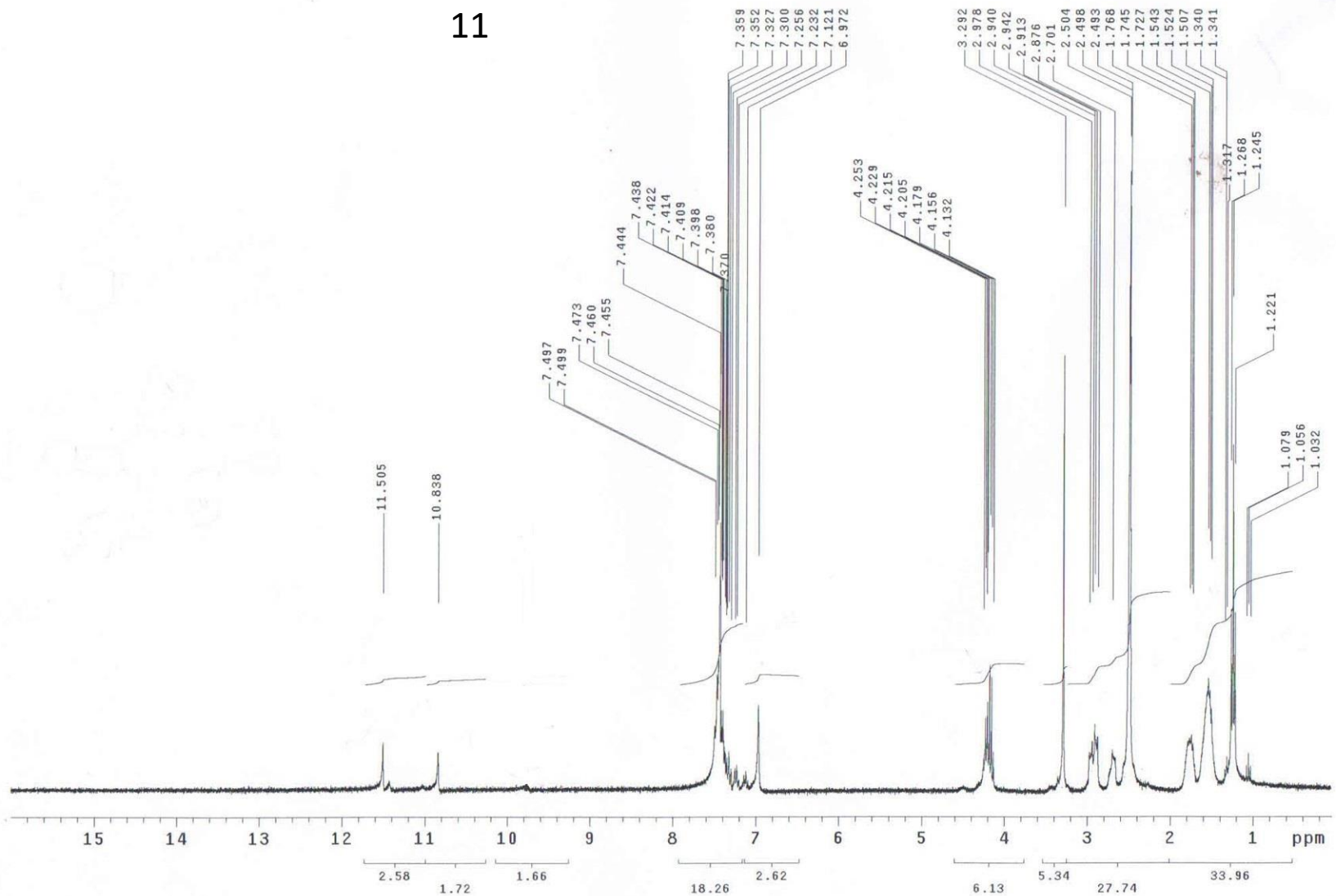

PROTON DMSO {C:\Bruker\TOPSPIN\KFUCCP} nmr 5
10a
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 ppm
4.20
92.06

ElshimaaEslam-YB-DMSO-H

Pulse Sequence: s2pul

Solvent: DMSO

11

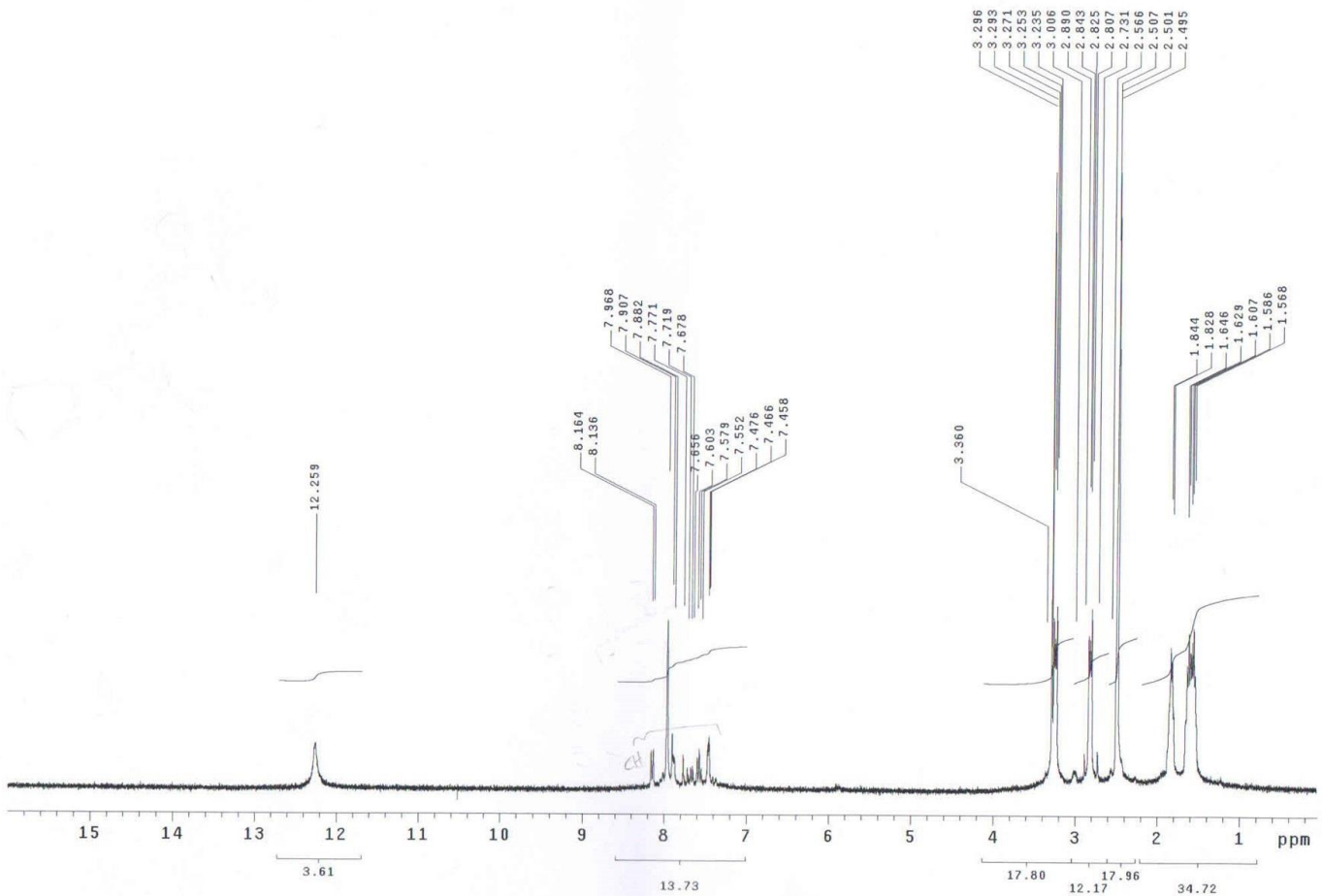


ElshimaaEslam-T8-DMSO-H

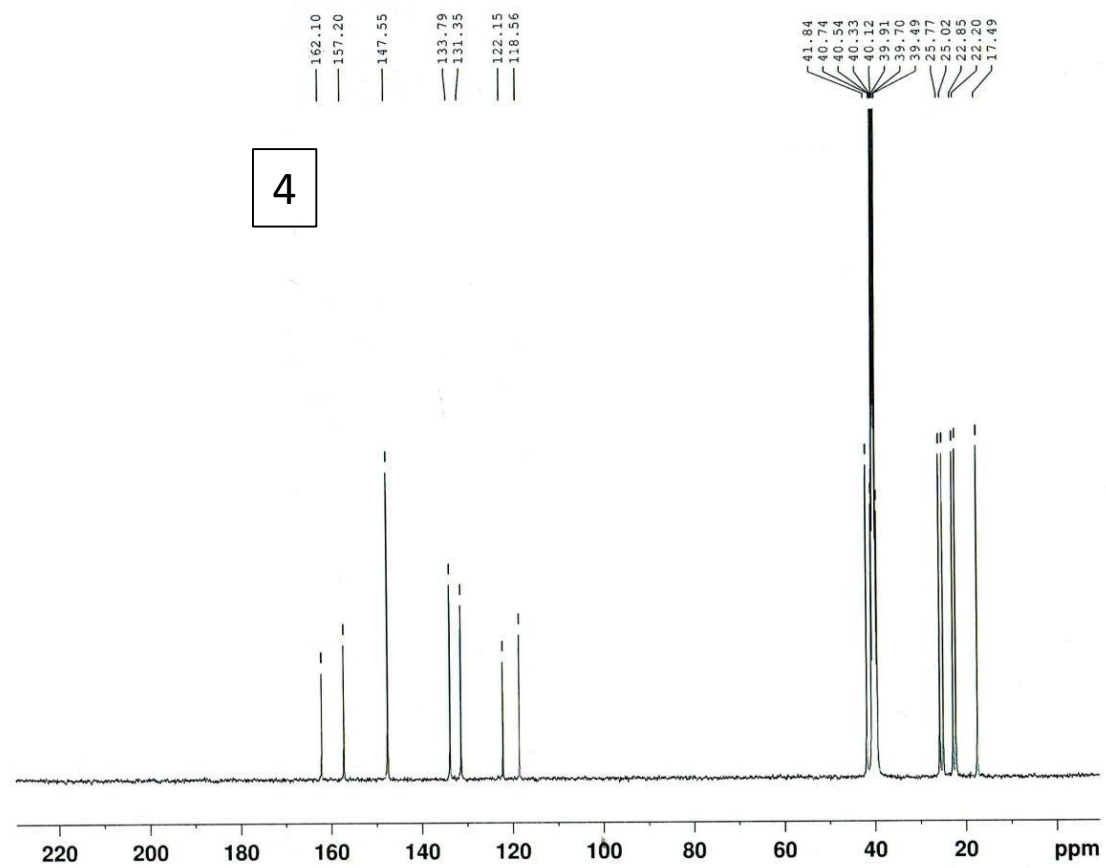
Pulse Sequence: s2pul

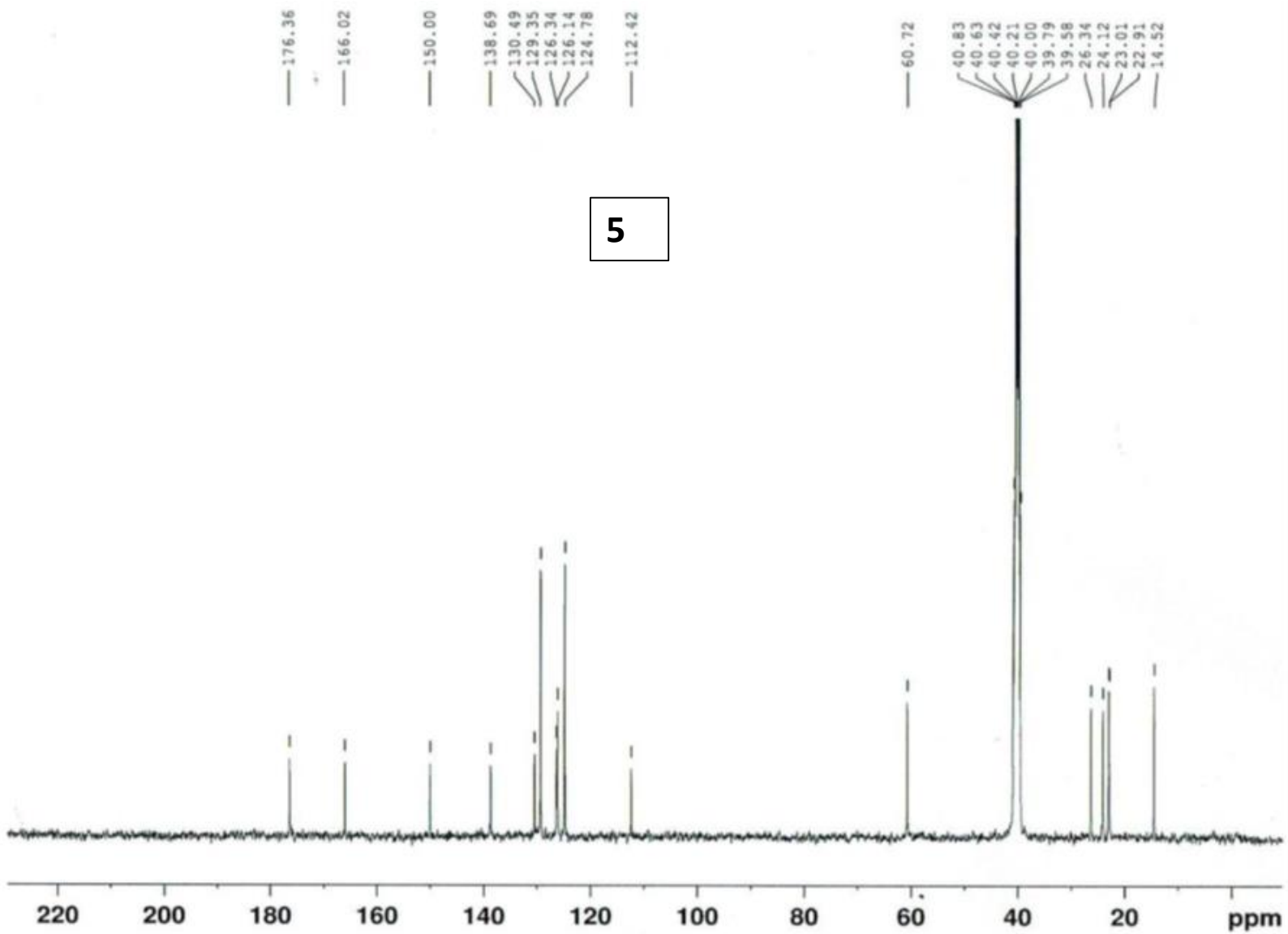
Solvent: DMSO

12

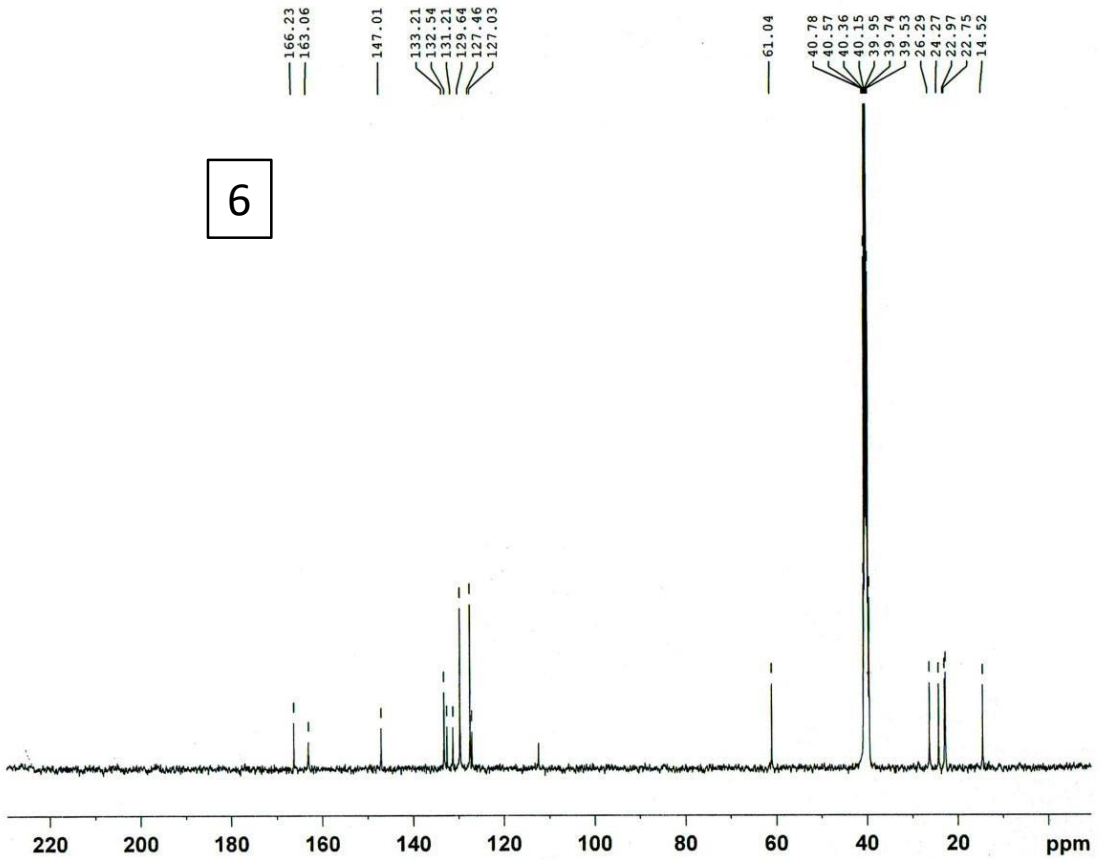


C-13-NMR


4
162.10
157.20
147.55
133.79
131.35
122.15
118.56
41.84
40.74
40.54
40.33
40.12
39.91
39.70
39.49
25.77
25.02
22.85
22.20
17.49
220
200
180
160
140
120
100
80
60
40
20
ppm


176.36
166.02
150.00
138.69
130.49
129.35
126.34
126.14
124.78
112.42
60.72
40.83
40.63
40.42
40.21
40.00
39.79
39.58
26.34
24.12
23.01
22.91
14.52
5
220
200
180
160
140
120
100
80
60
40
20
ppm

6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163.06
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133.21
132.54
131.21
129.64
127.46
127.03
61.04
40.78
40.57
40.36
40.15
39.95
39.74
39.53
26.29
24.27
22.97
22.75
14.52
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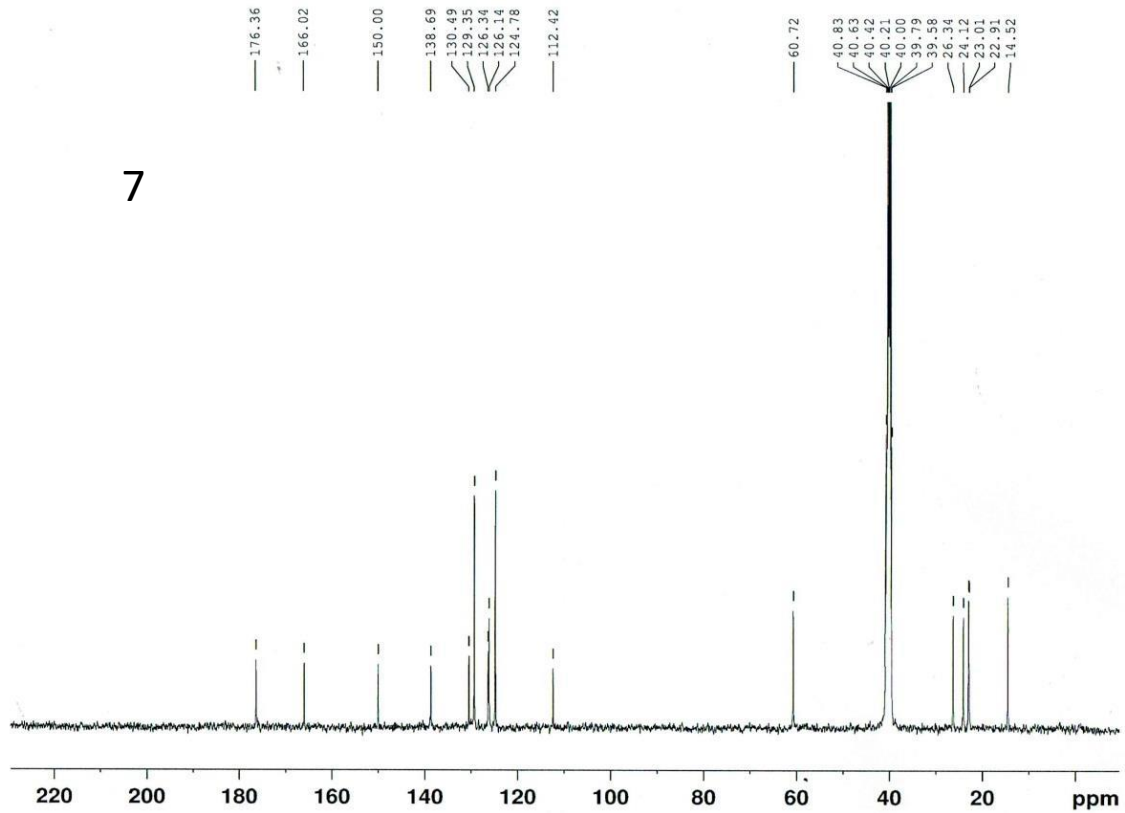
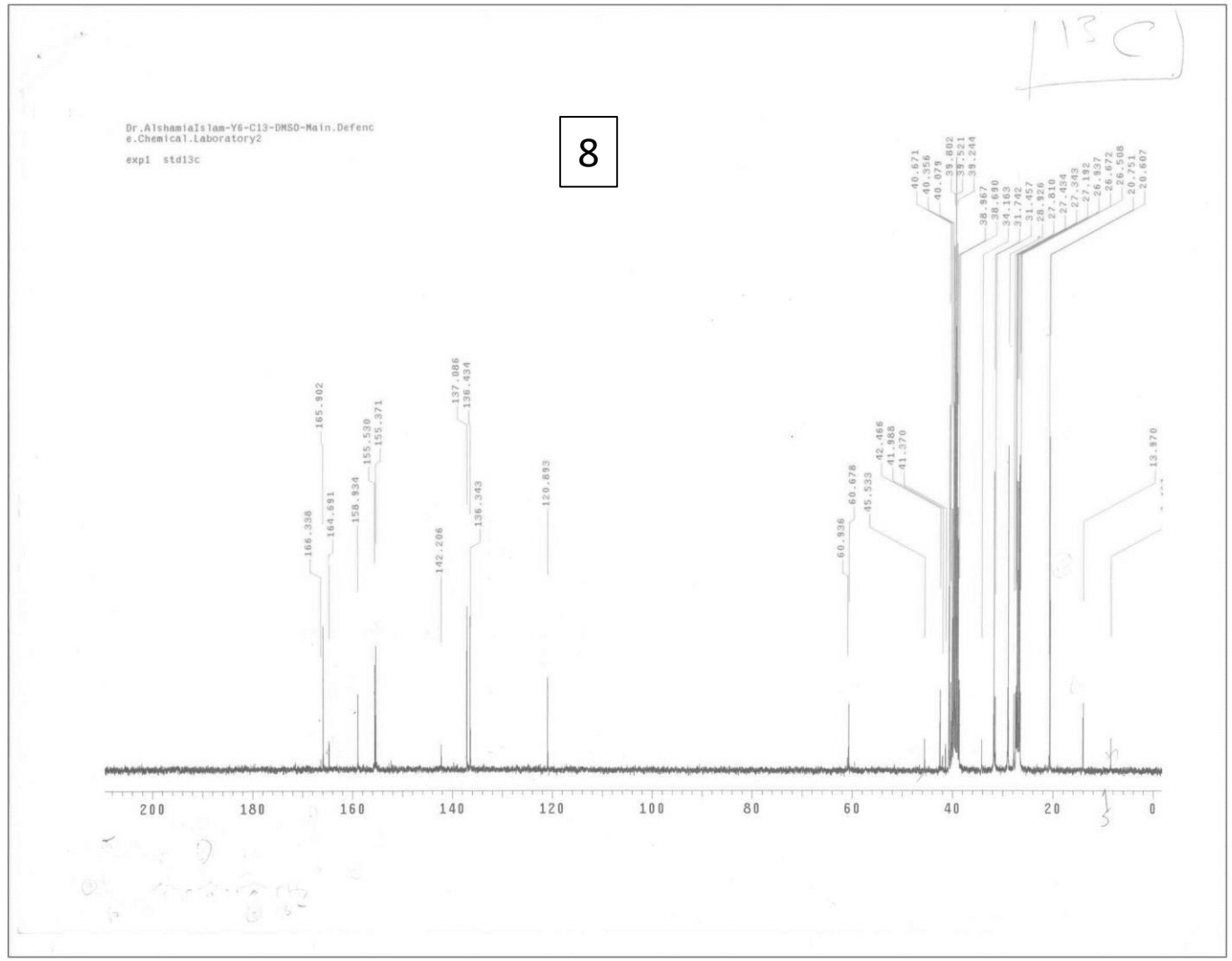
200
180
160
140
120
100
80
60
40
20
ppm

7


176.36
166.02
150.00
138.69
130.49
129.35
126.34
126.14
124.78
112.42
60.72
40.83
40.63
40.42
40.21
40.00
39.79
39.58
26.34
24.12
23.01
22.91
14.52
220
200
180
160
140
120
100
80
60
40
20
ppm

8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45.533
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41.988
41.370
40.671
40.356
40.079
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38.967
38.690
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31.742
31.457
28.926
27.810
27.434
27.343
27.132
26.837
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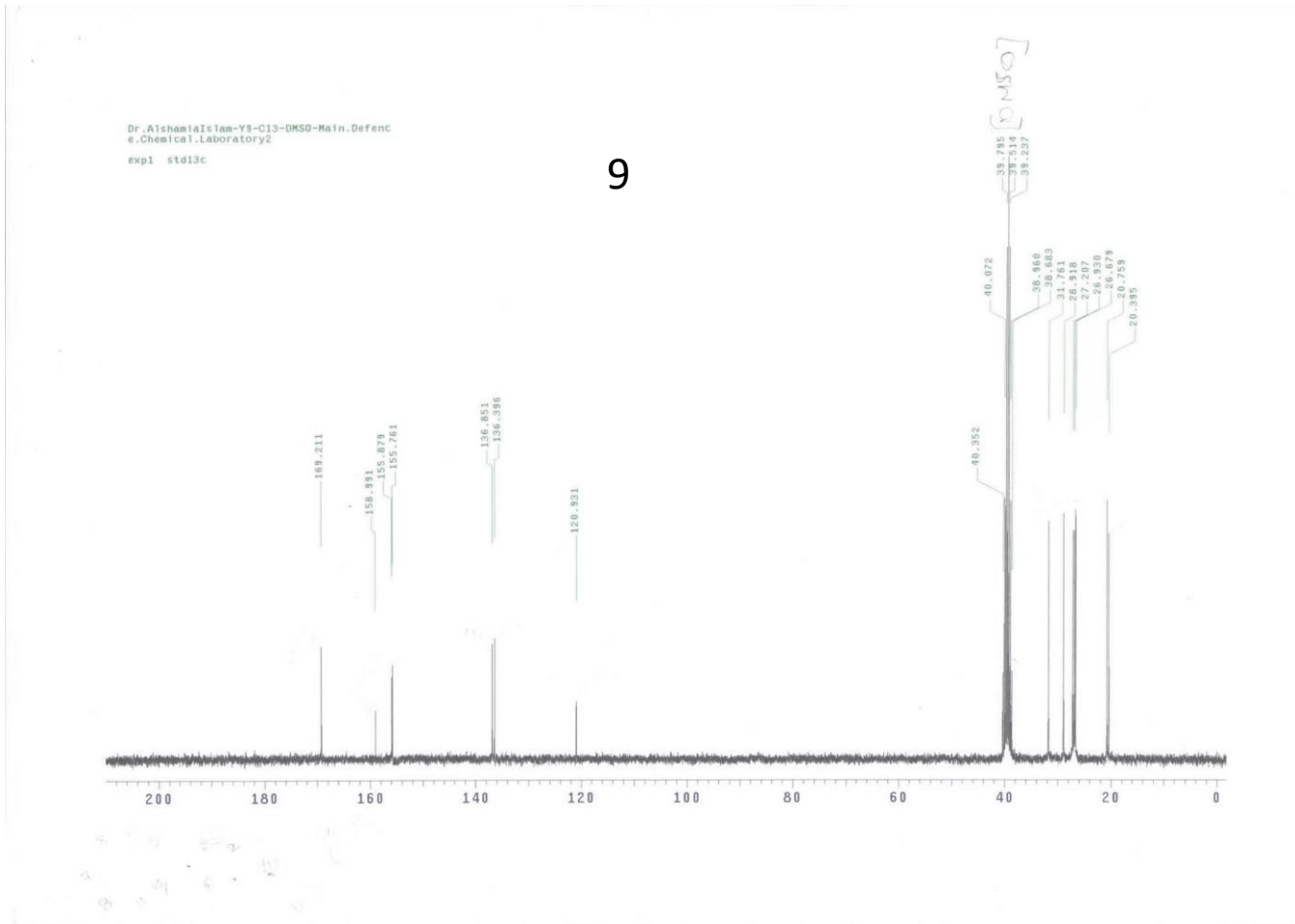
9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40
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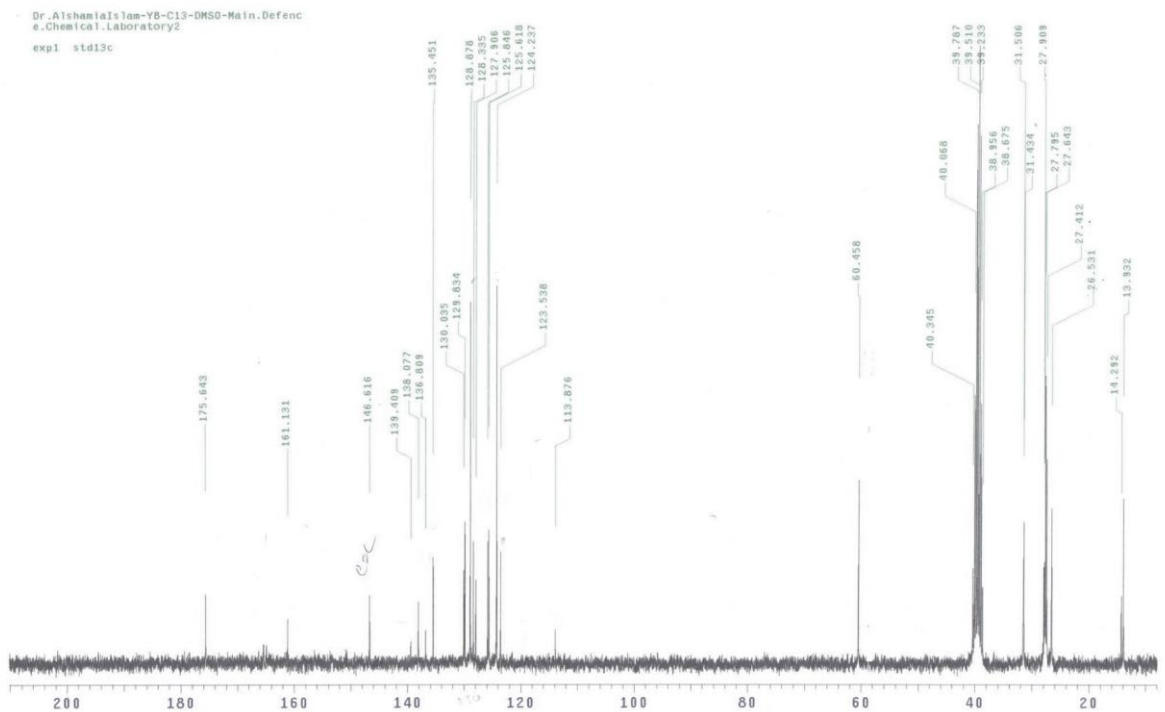
0

10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exp1 std13c
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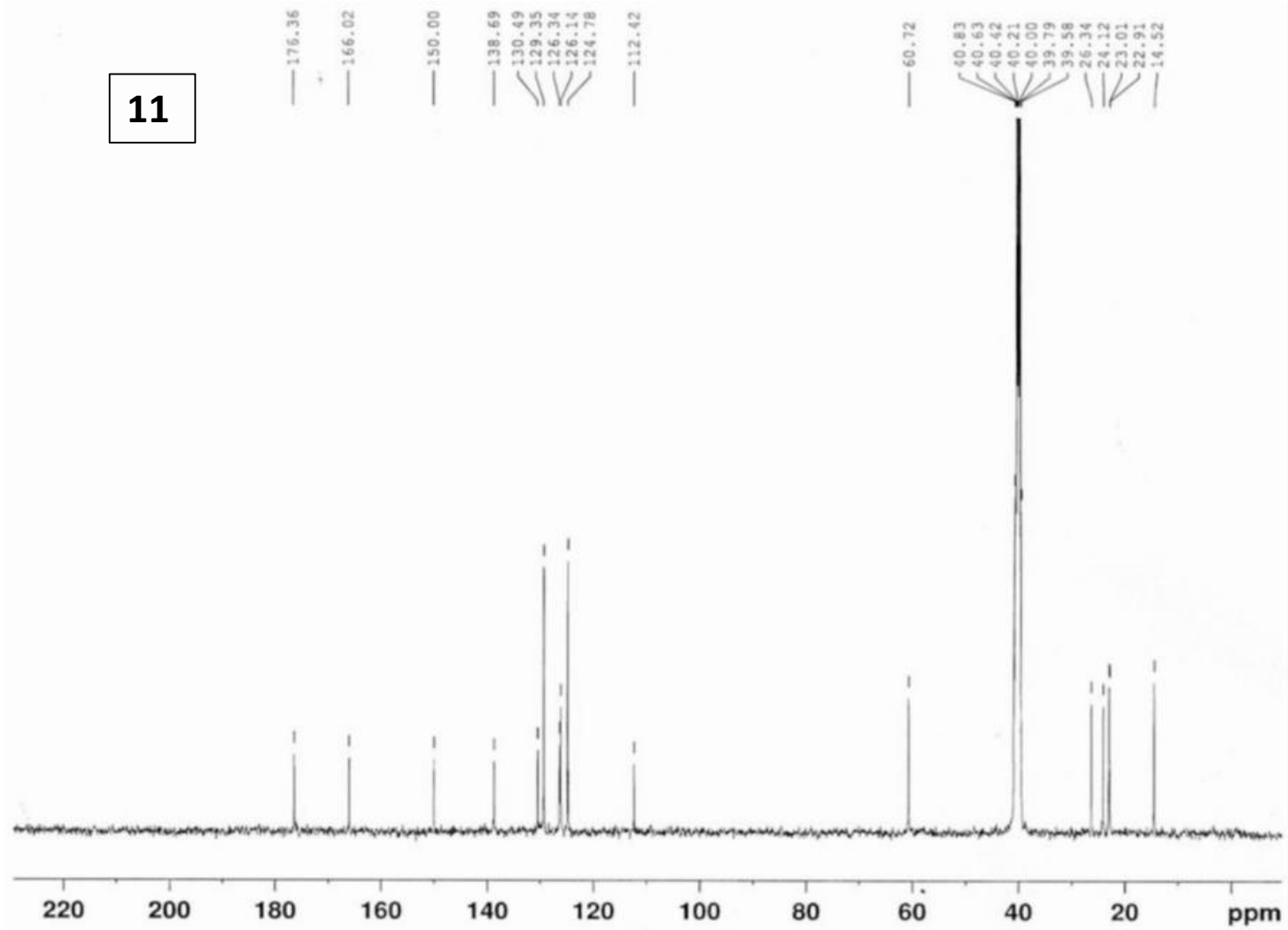
130.035
129.834
128.676
128.335
127.906
125.846
125.610
124.237
123.538
113.876
60.458
40.668
40.345
39.767
39.510
39.233
38.956
38.675
31.586
31.434
27.909
27.795
27.643
27.412
26.531
14.292
13.932
200
180
160
140
120
100
80
60
40
20

11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166.02
150.00
138.69
130.49
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40.63
40.42
40.21
40.00
39.79
39.58
26.34
24.12
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14.52
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120
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80
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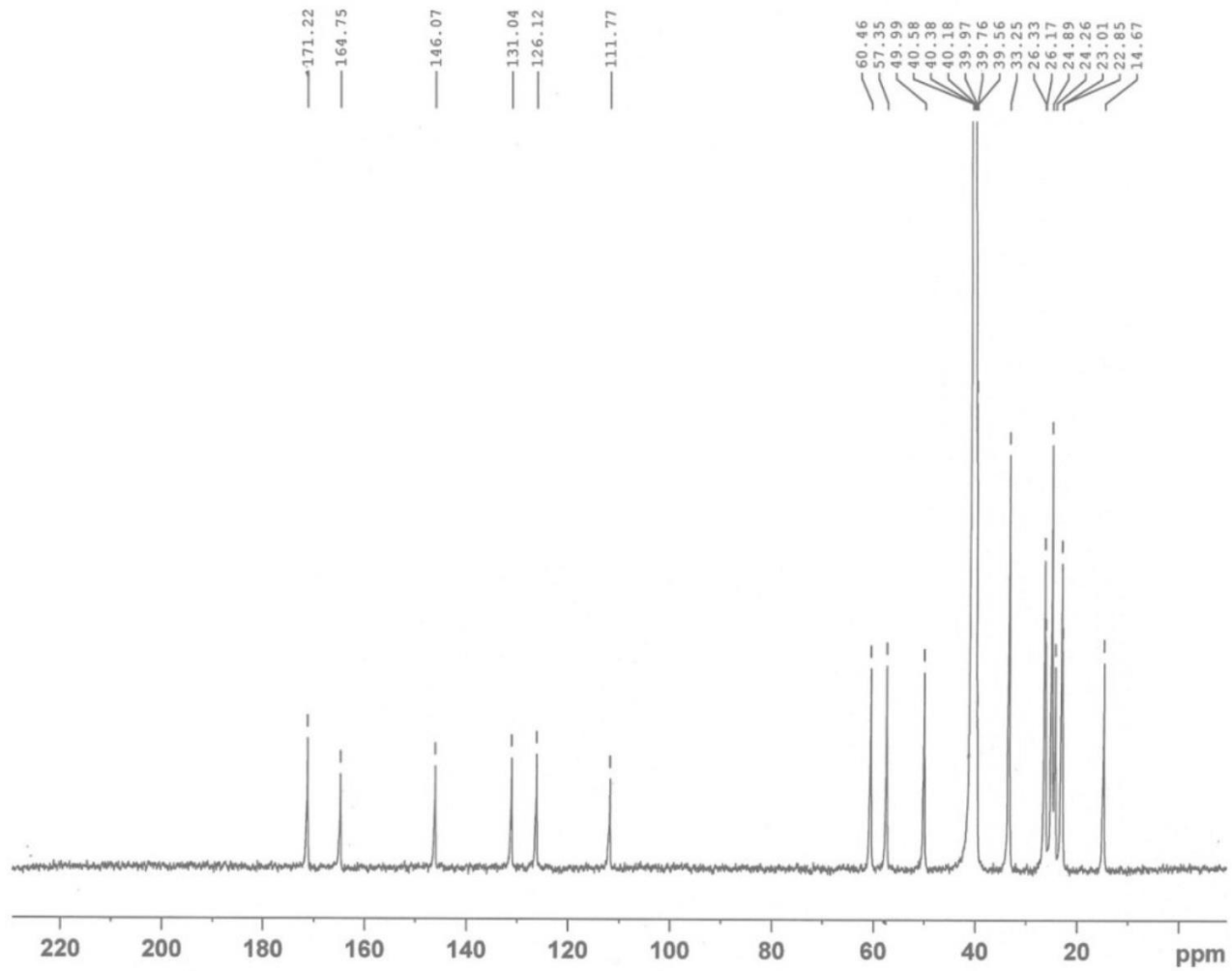
ppm

12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131.04
126.12
111.77
60.46
57.35
49.99
40.58
40.38
40.18
39.97
39.76
39.56
33.25
26.33
26.17
24.89
24.26
23.01
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14.67
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180
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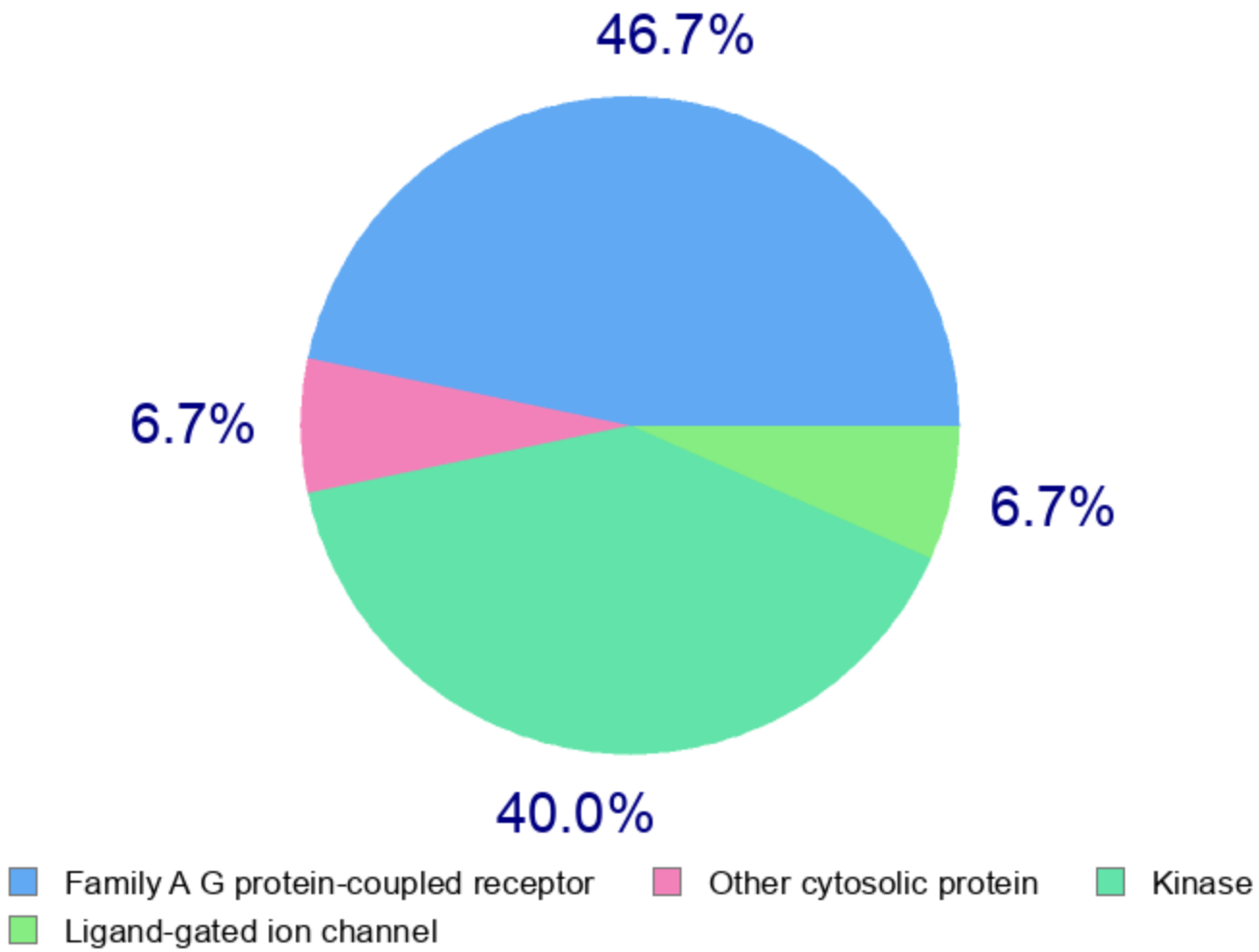
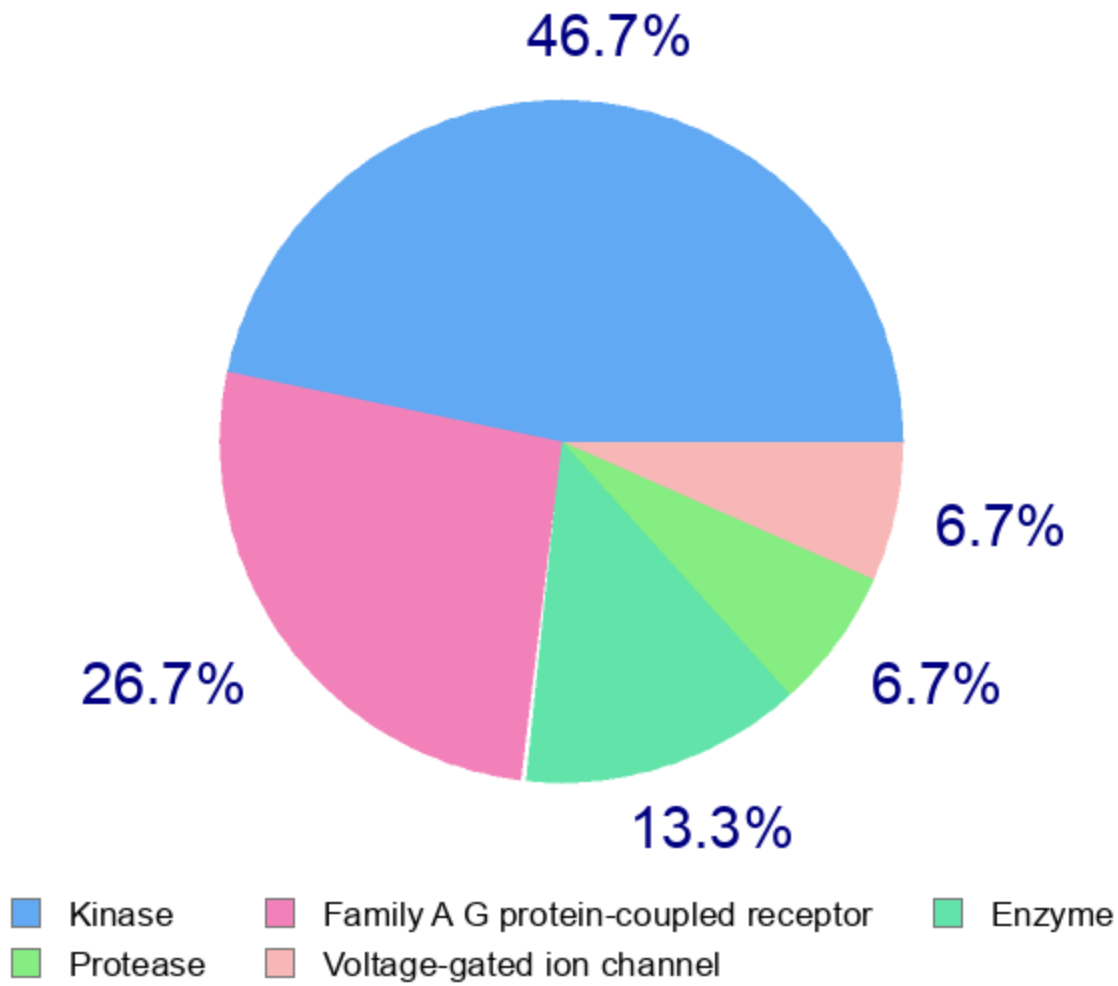
140
120
100
80
60
40
20
ppm

Target prediction

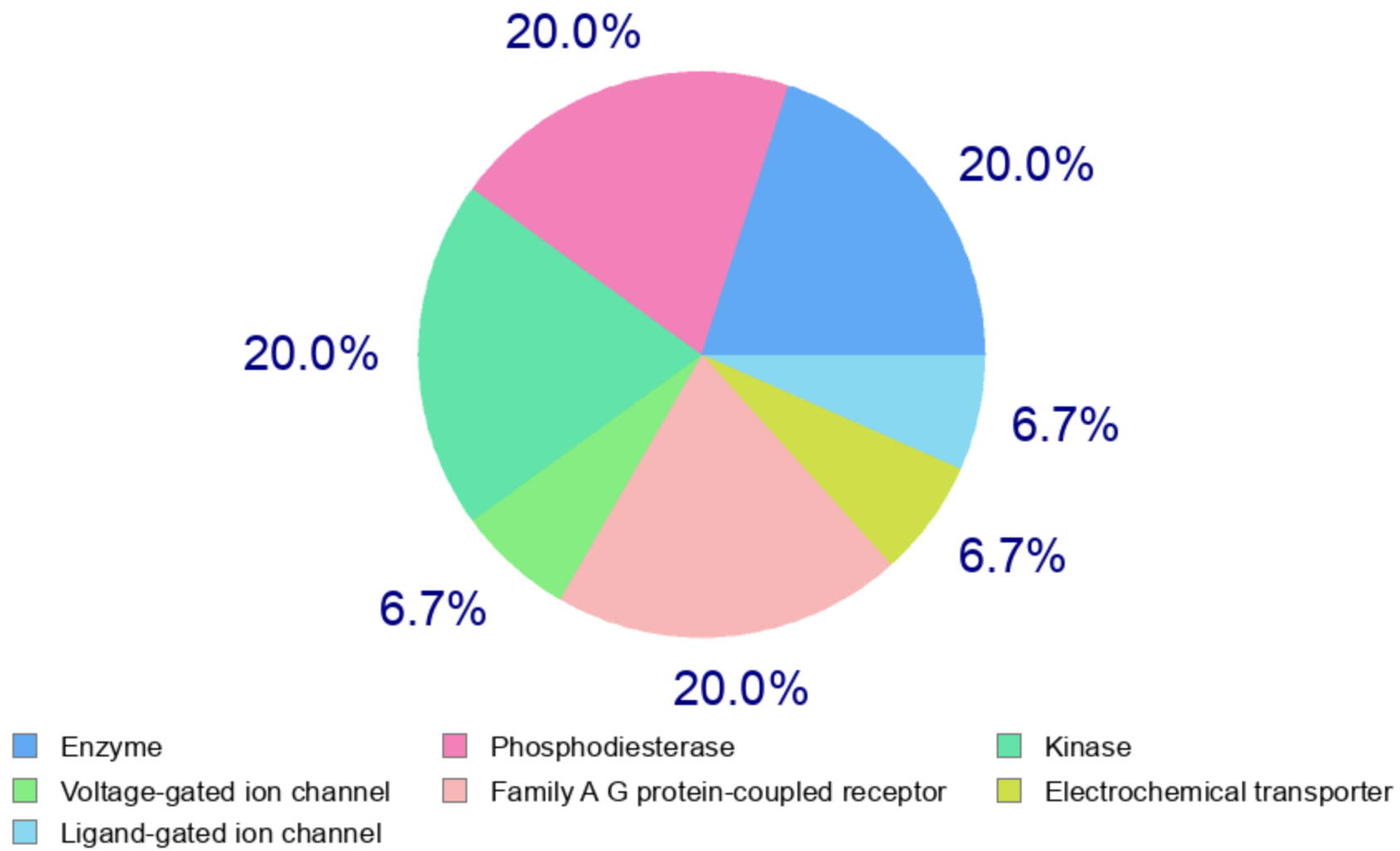
9a


46.7%
6.7%
6.7%
40.0%
Family A G protein-coupled receptor
Other cytosolic protein
Kinase
Ligand-gated ion channel

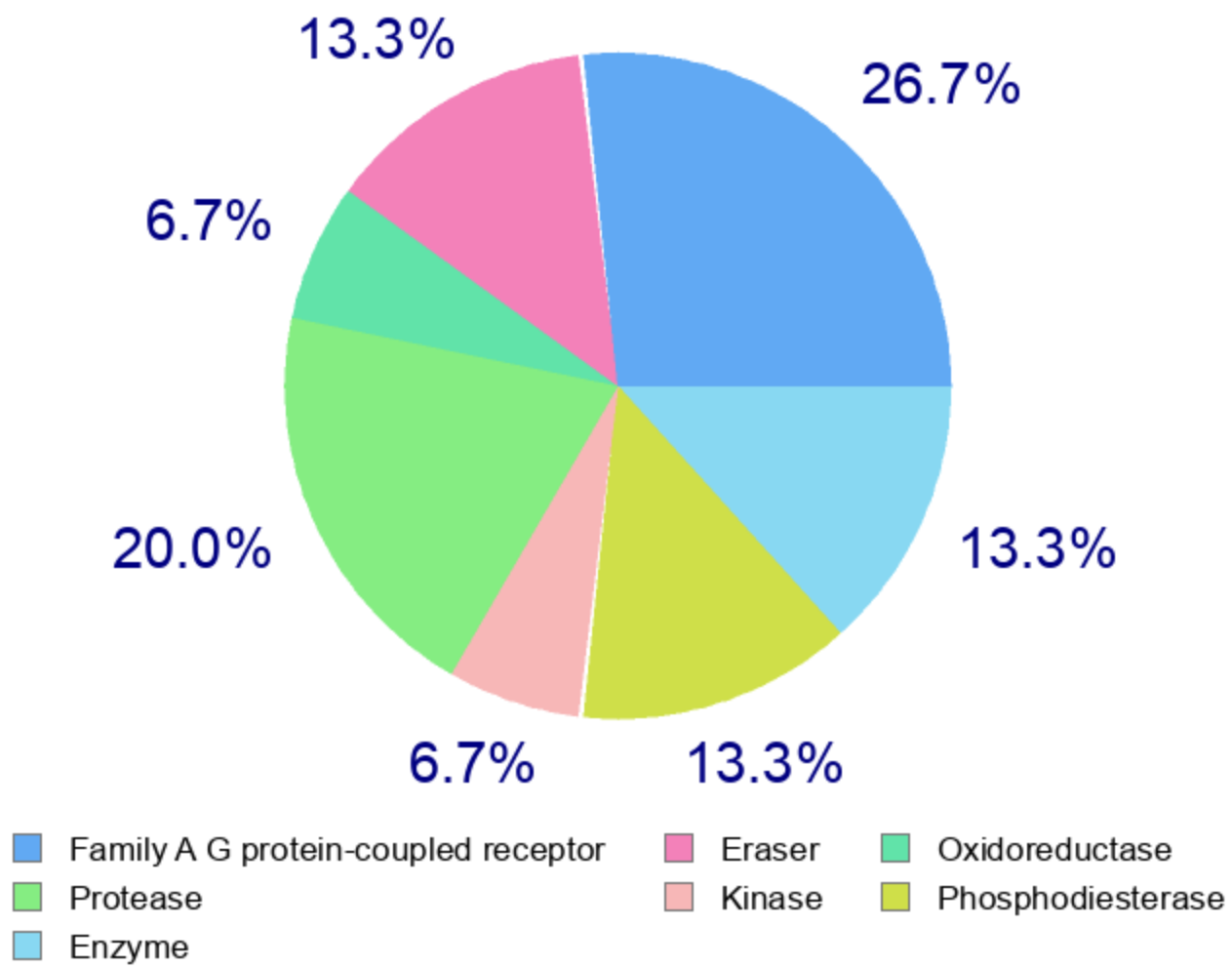
9b


46.7%
6.7%
26.7%
6.7%
13.3%
Kinase
Family A G protein-coupled receptor
Enzyme
Protease
Voltage-gated ion channel

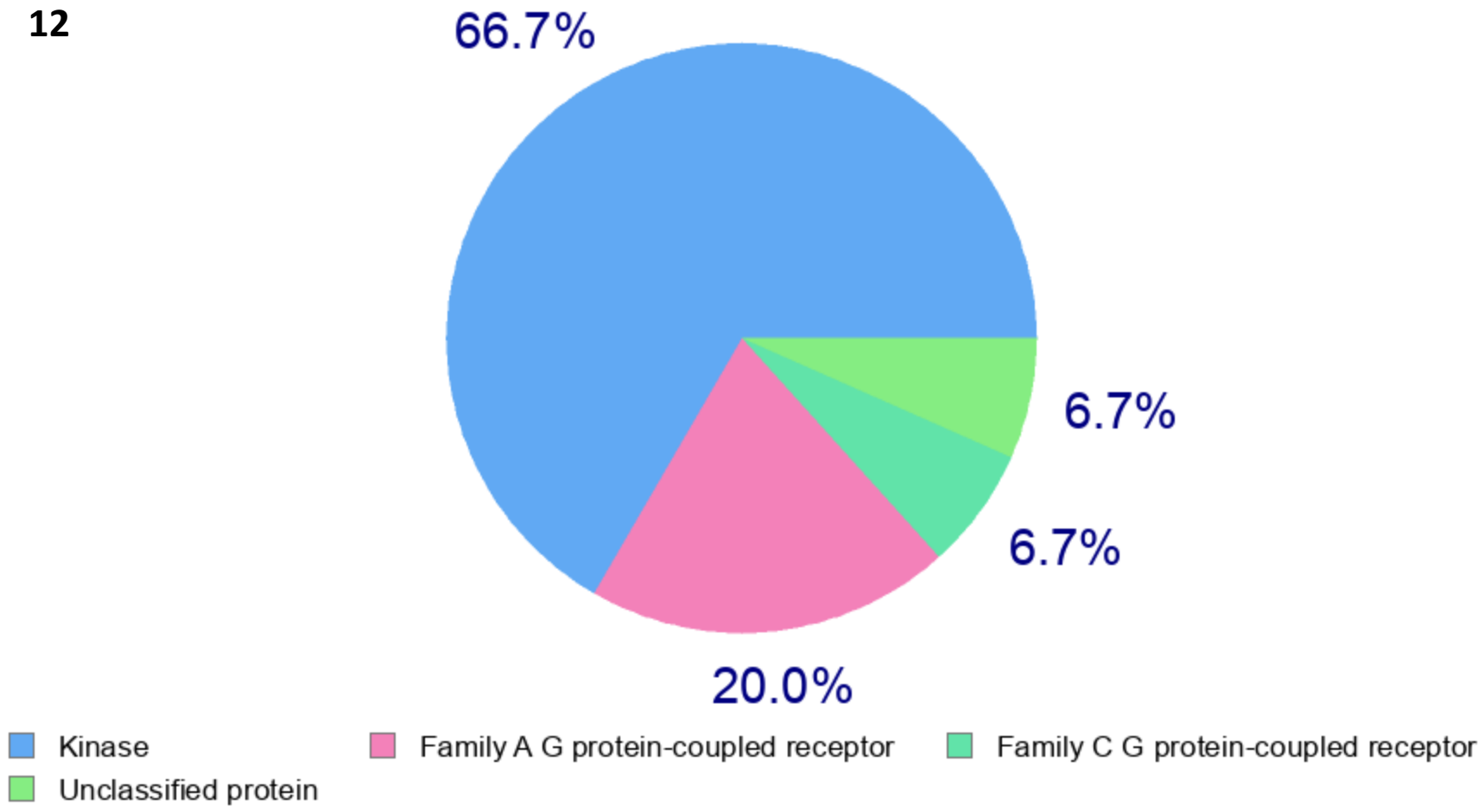
10a


20.0%
20.0%
20.0%
6.7%
6.7%
6.7%
20.0%
Enzyme
Phosphodiesterase
Kinase
Voltage-gated ion channel
Family A G protein-coupled receptor
Electrochemical transporter
Ligand-gated ion channel

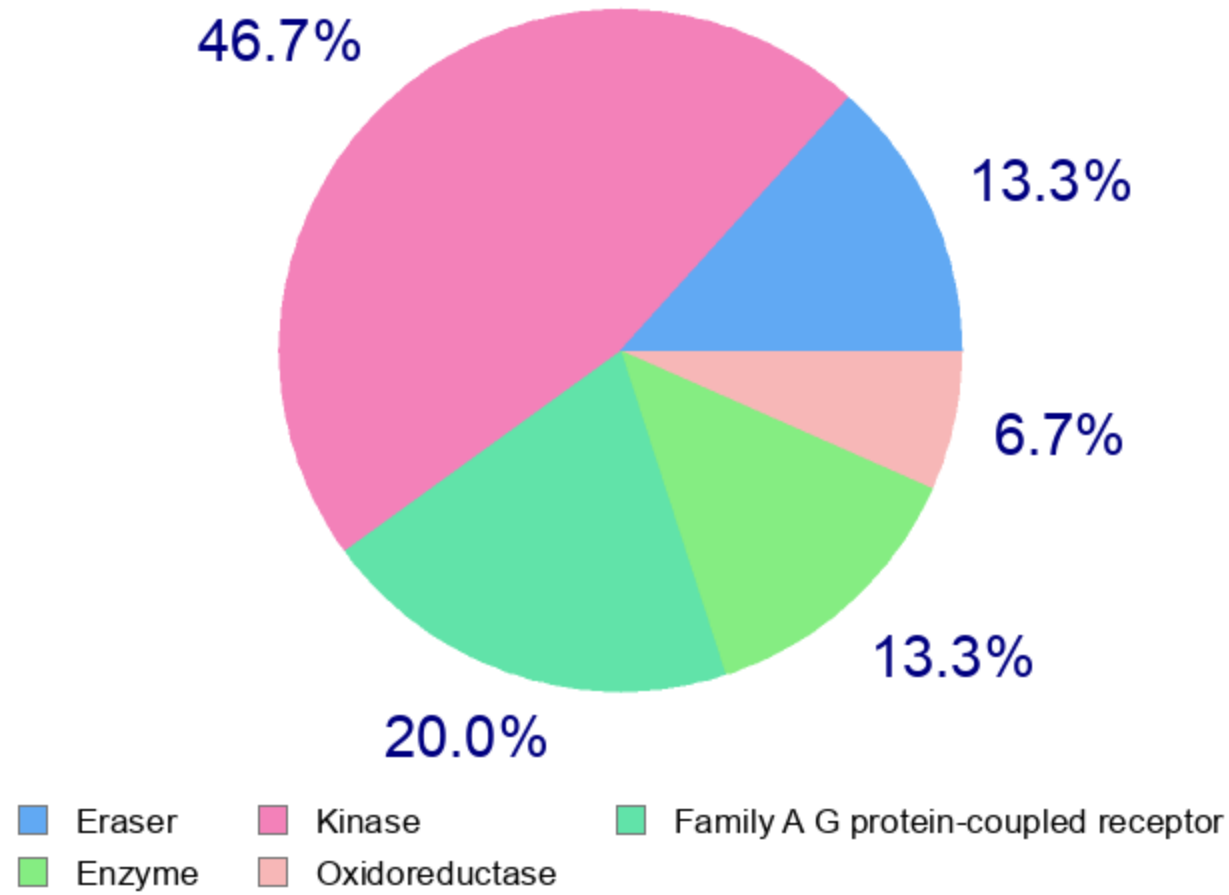
10b


13.3%
26.7%
6.7%
20.0%
13.3%
6.7%
13.3%
Family A G protein-coupled receptor
Eraser
Oxidoreductase
Protease
Kinase
Phosphodiesterase
Enzyme

12


66.7%
6.7%
6.7%
20.0%
Kinase
Family A G protein-coupled receptor
Family C G protein-coupled receptor
Unclassified protein

8


46.7%
13.3%
6.7%
13.3%
20.0%
Eraser
Kinase
Family A G protein-coupled receptor
Enzyme
Oxidoreductase