Rational Experimental Design and Computational insights into Novel Heteroleptic Mixed-Ligand Ru(II) Complexes possessing Derivatized Bipyridines and Phendione for Anti-cancer Activities

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Supplementary Section

Figure S1: ^{1}H NMR (400 MHz, ($DMSO_4$) spectrum of **V2**

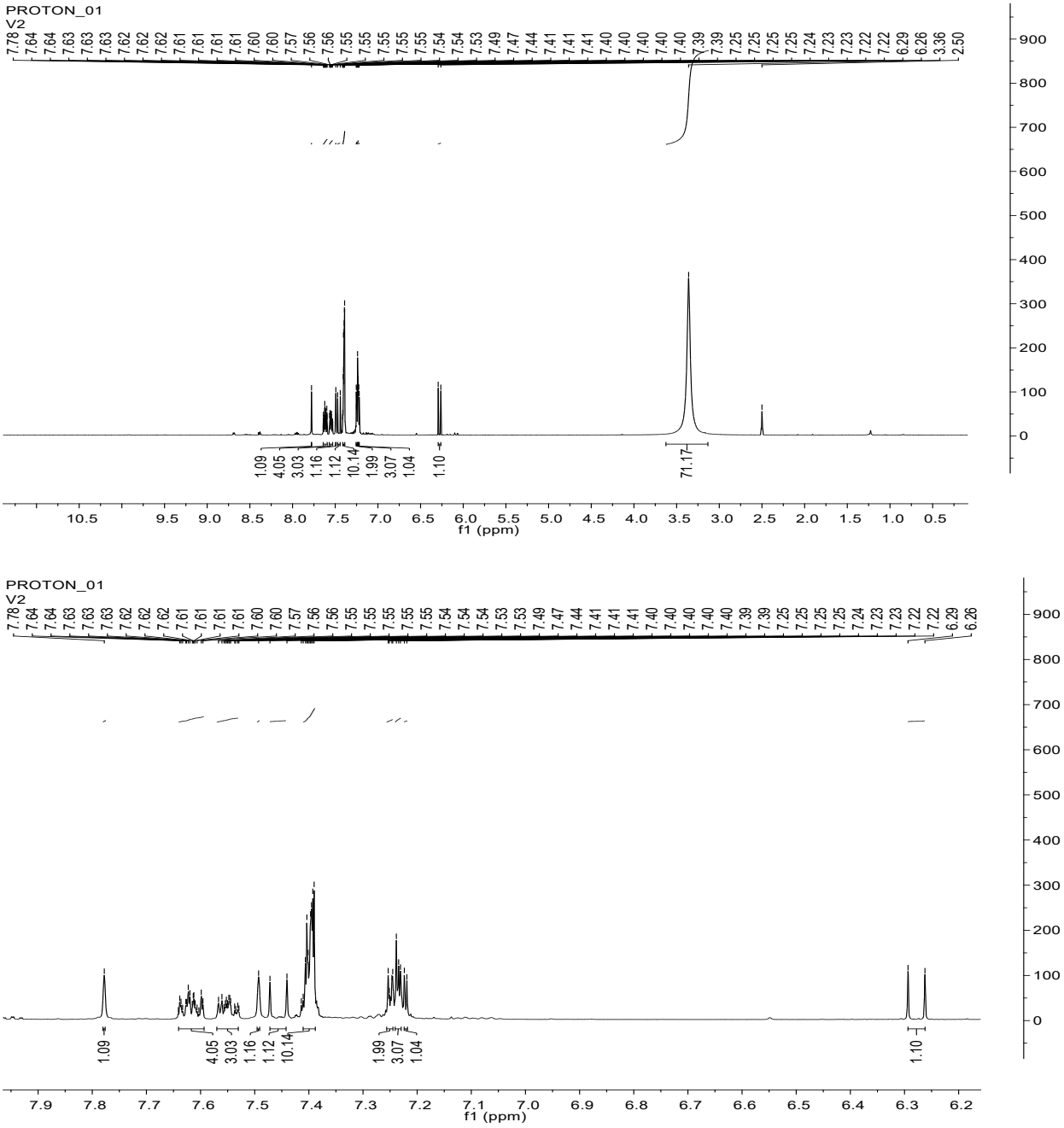
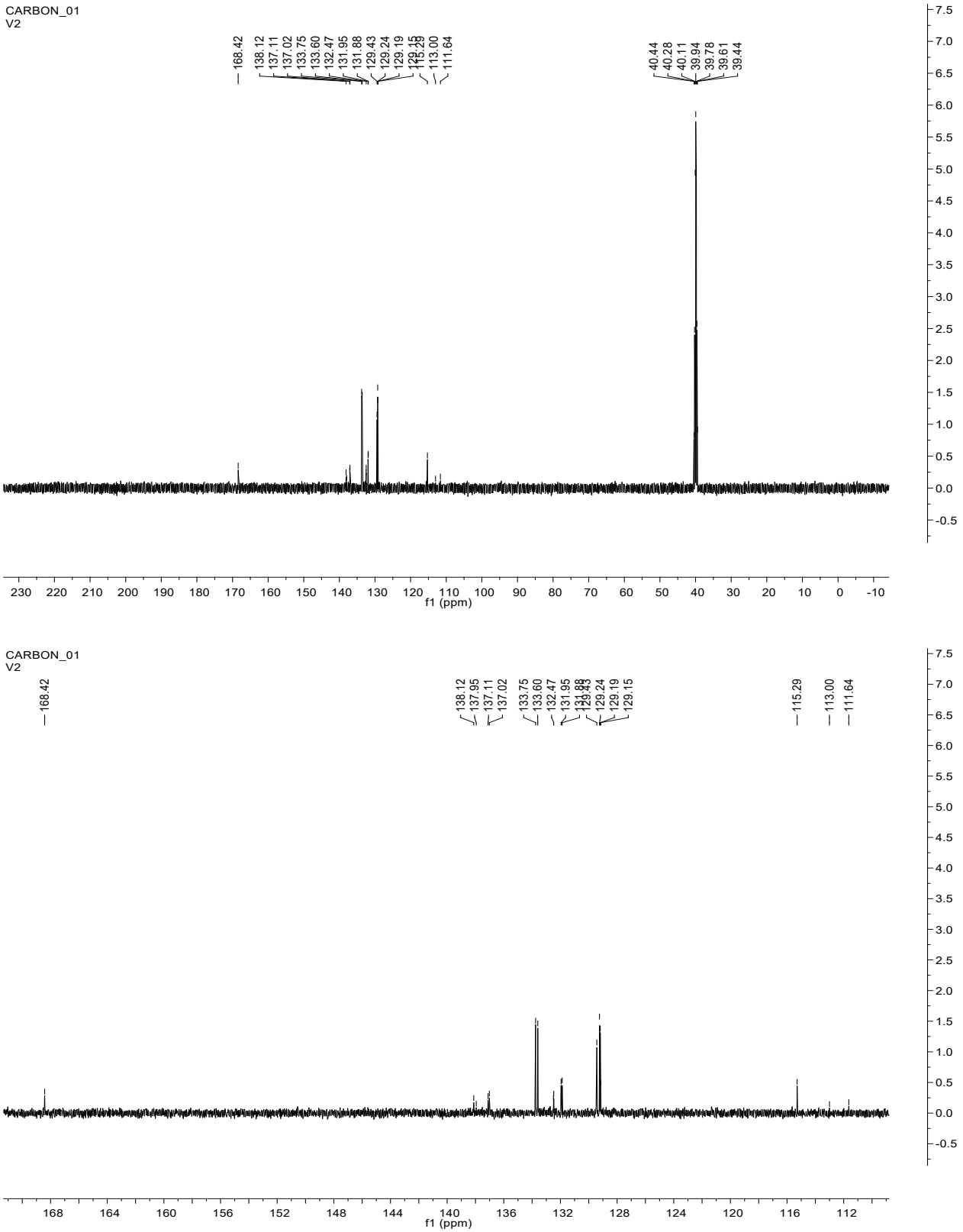
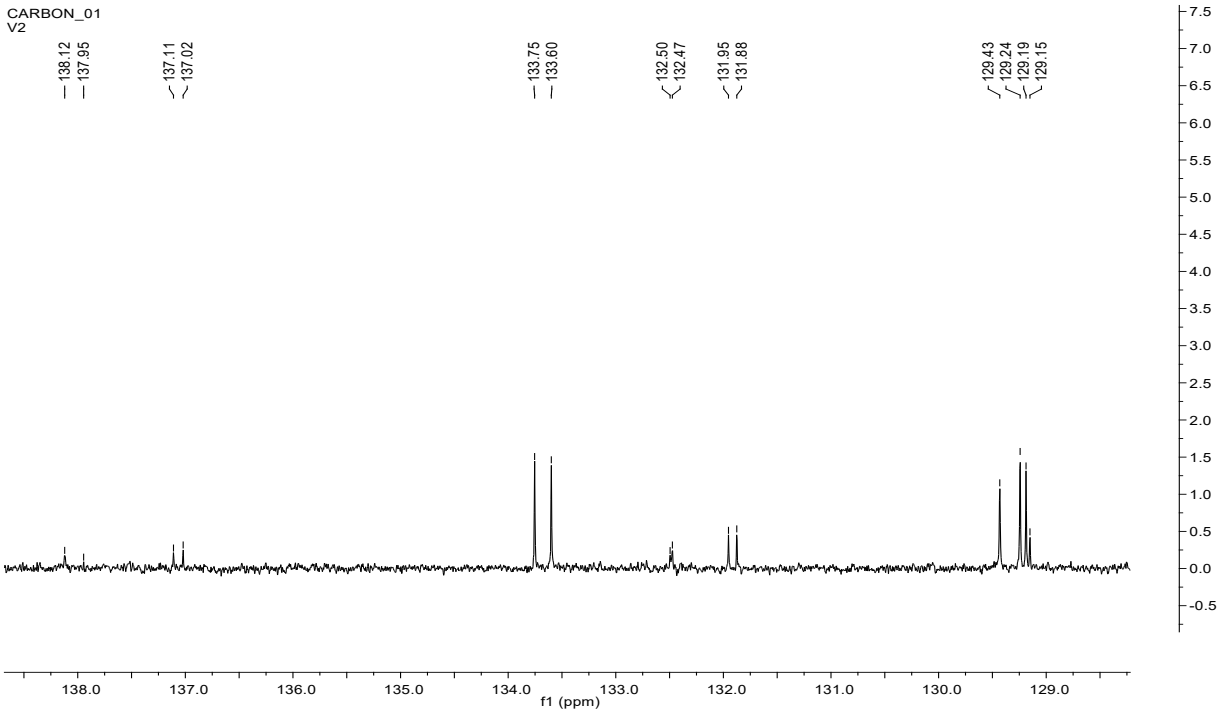


Figure S2: ^{13}C NMR (400 MHz, ($DMSO_4$) spectrum of **V2**




CARBON_01
V2
138.12
137.95
137.11
137.02
133.75
133.60
132.50
132.47
131.95
131.88
129.43
129.24
129.19
129.15
f1 (ppm)

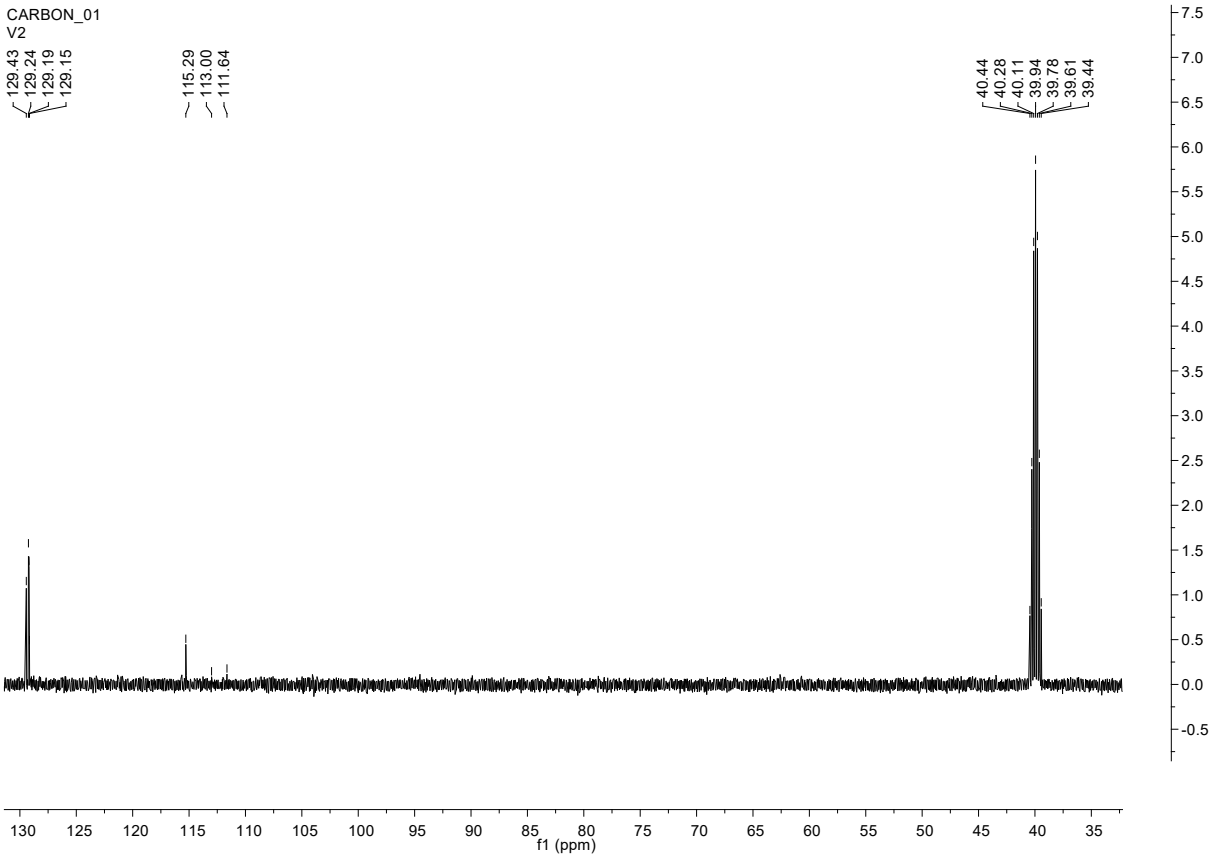

CARBON_01
V2
129.43
129.24
129.19
129.15
115.29
113.00
111.64
40.44
40.28
40.11
39.94
39.78
39.61
39.44
f1 (ppm)

Figure S3: ^{31}P NMR (400 MHz, ($DMSO_4$) spectrum of **V2**

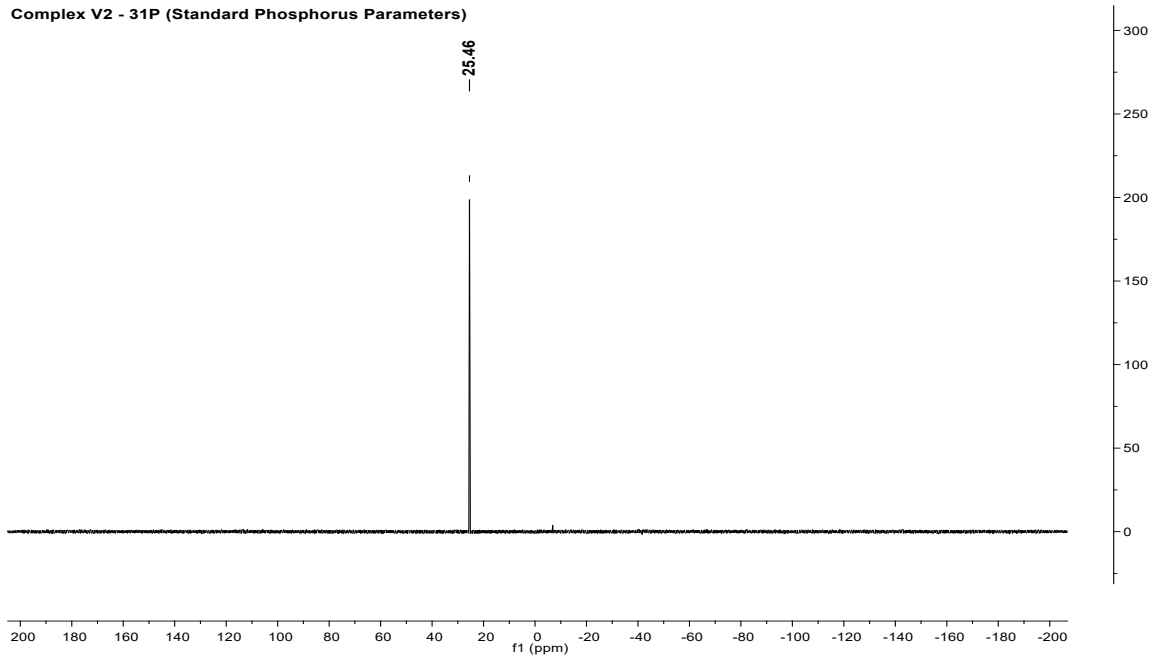
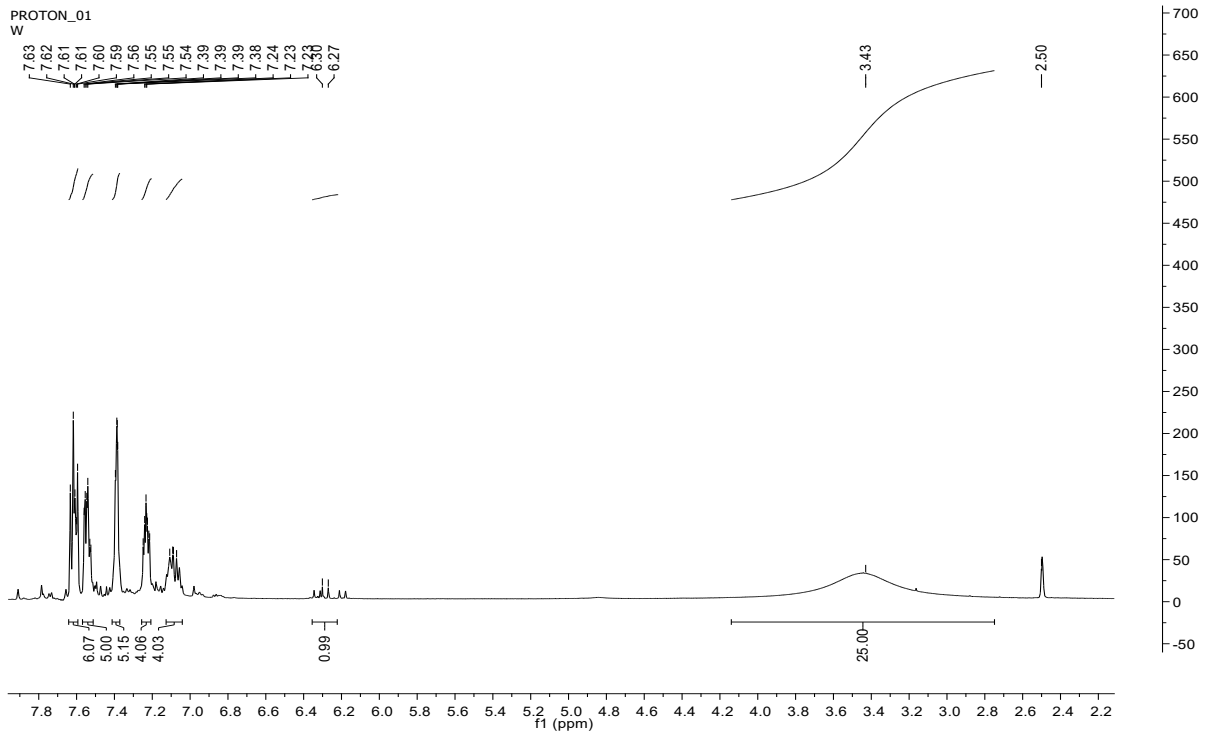
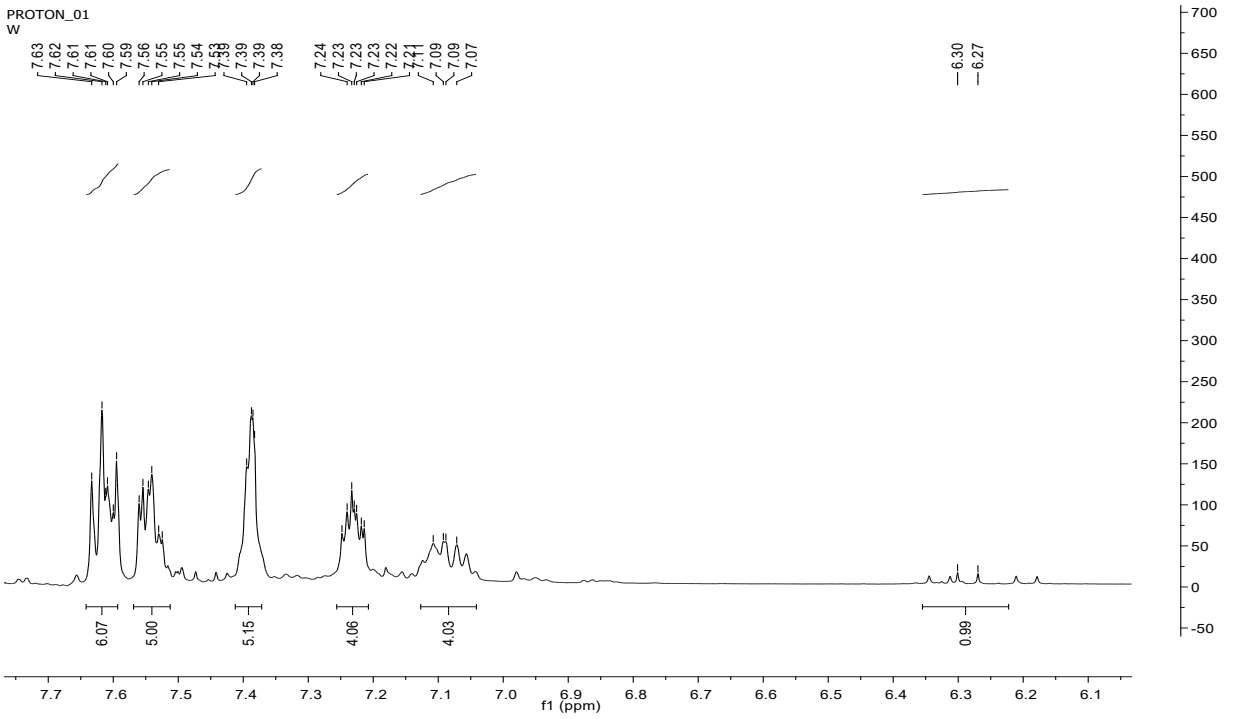


Figure S4: ^{1}H NMR (400 MHz, ($DMSO_4$) spectrum of **W**




PROTON_01
W
7.63
7.62
7.61
7.61
7.60
7.59
7.56
7.55
7.55
7.54
7.39
7.39
7.38
7.24
7.23
7.23
7.23
7.22
7.21
7.09
7.09
7.07
6.30
6.27
6.07
5.00
5.15
4.06
4.03
0.99
f1 (ppm)

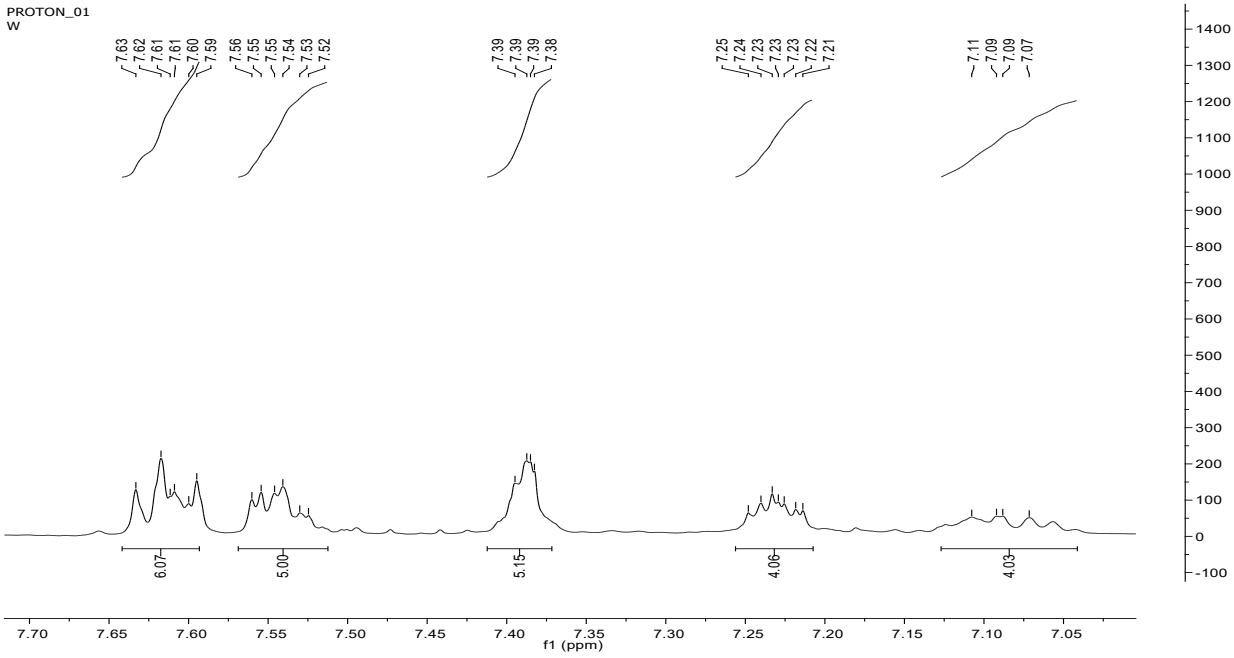
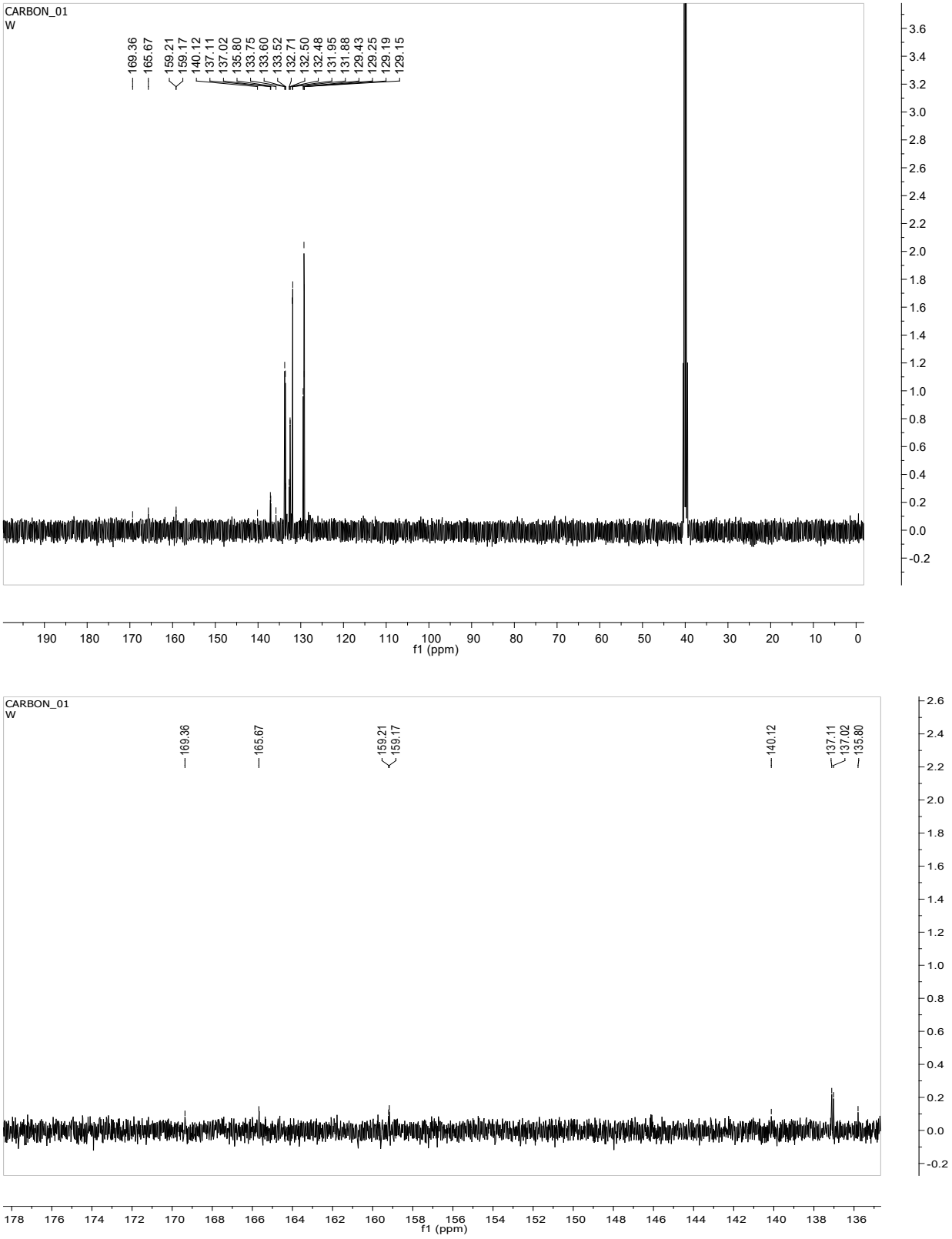
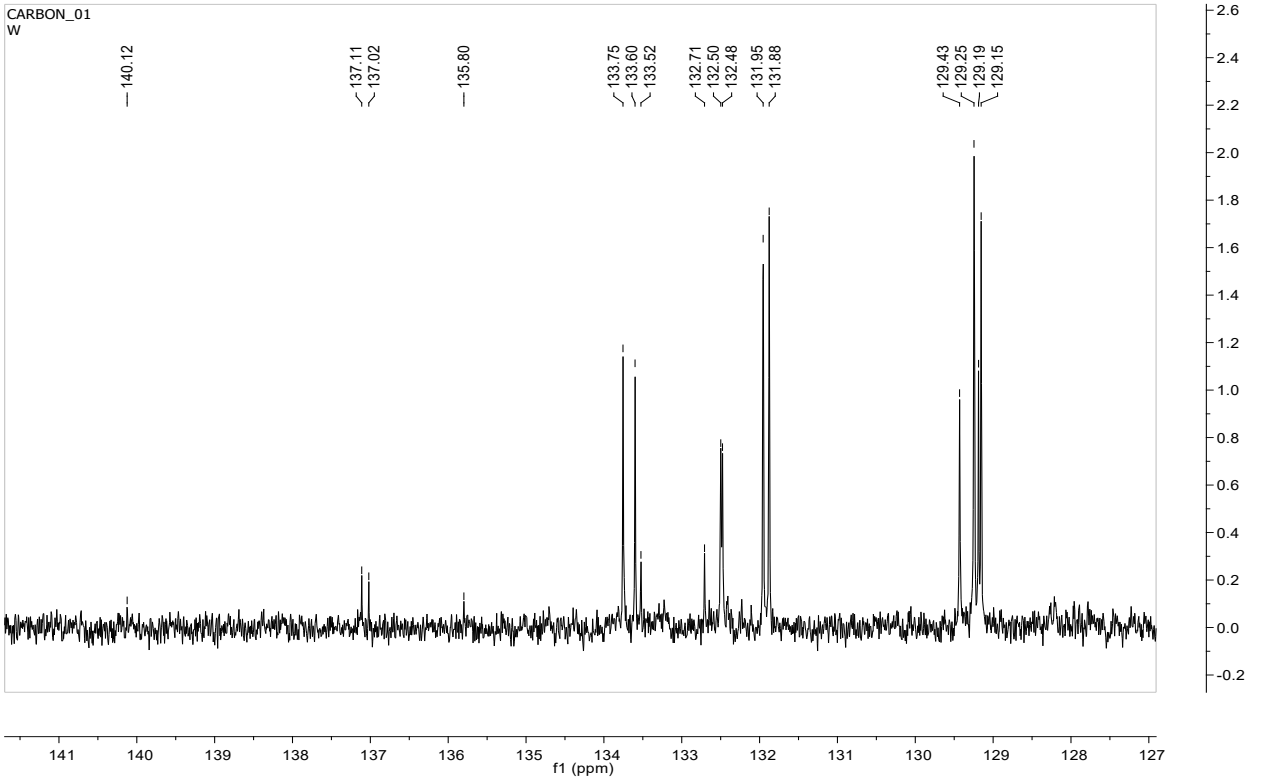

PROTON_01
W
7.63
7.62
7.61
7.61
7.60
7.59
7.56
7.55
7.55
7.54
7.53
7.52
7.39
7.39
7.39
7.38
7.25
7.24
7.23
7.23
7.23
7.22
7.21
7.11
7.09
7.09
7.07
6.07
5.00
5.15
4.06
4.03
f1 (ppm)

Figure S5: ^{13}C NMR (400 MHz, ($DMSO_4$) spectrum of **W**.




CARBON_01
W
140.12
137.11
137.02
135.80
133.75
133.60
133.52
132.71
132.50
132.48
131.95
131.88
129.43
129.25
129.19
129.15
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
141
140
139
138
137
136
135
134
133
132
131
130
129
128
127
f1 (ppm)

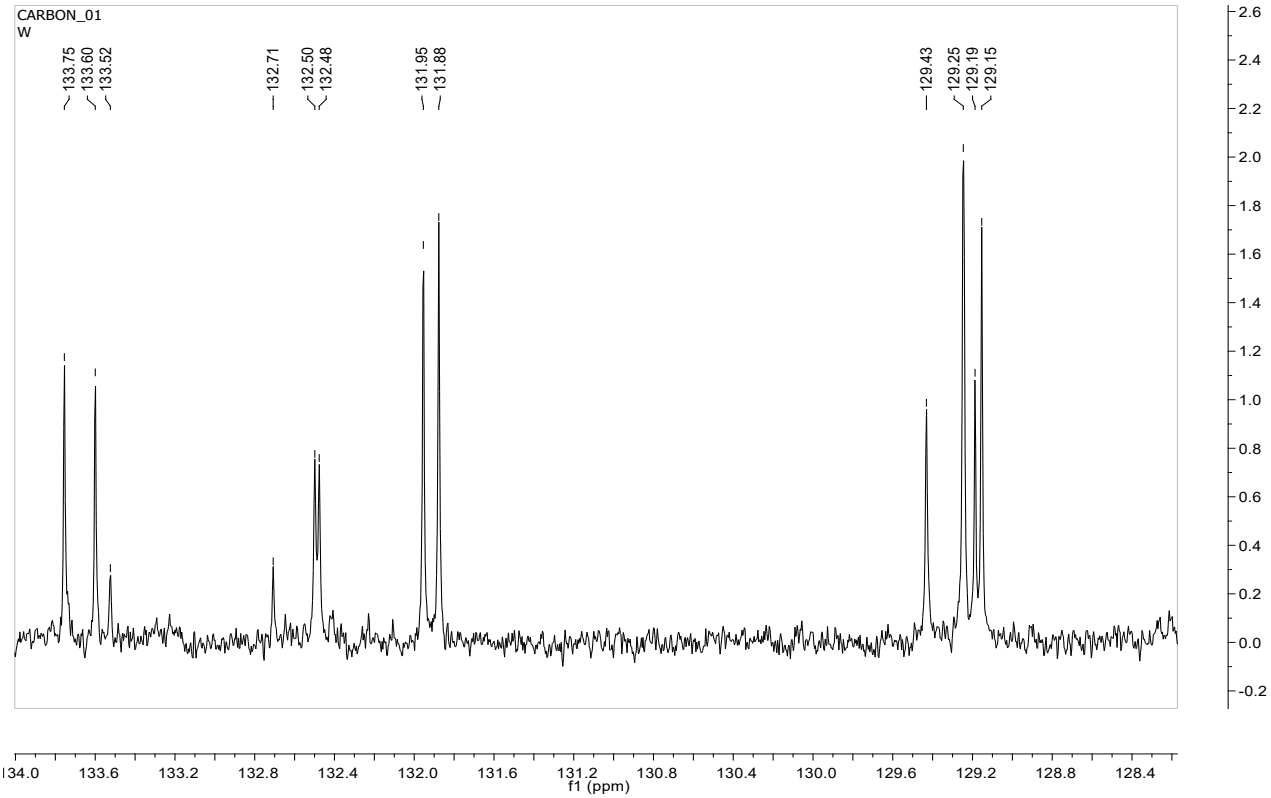

CARBON_01
W
133.75
133.60
133.52
132.71
132.50
132.48
131.95
131.88
129.43
129.25
129.19
129.15
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
134.0
133.6
133.2
132.8
132.4
132.0
131.6
131.2
130.8
130.4
130.0
129.6
129.2
128.8
128.4
f1 (ppm)

Figure S6: ^{31}P NMR (400 MHz, ($DMSO_4$) spectrum of **W**.

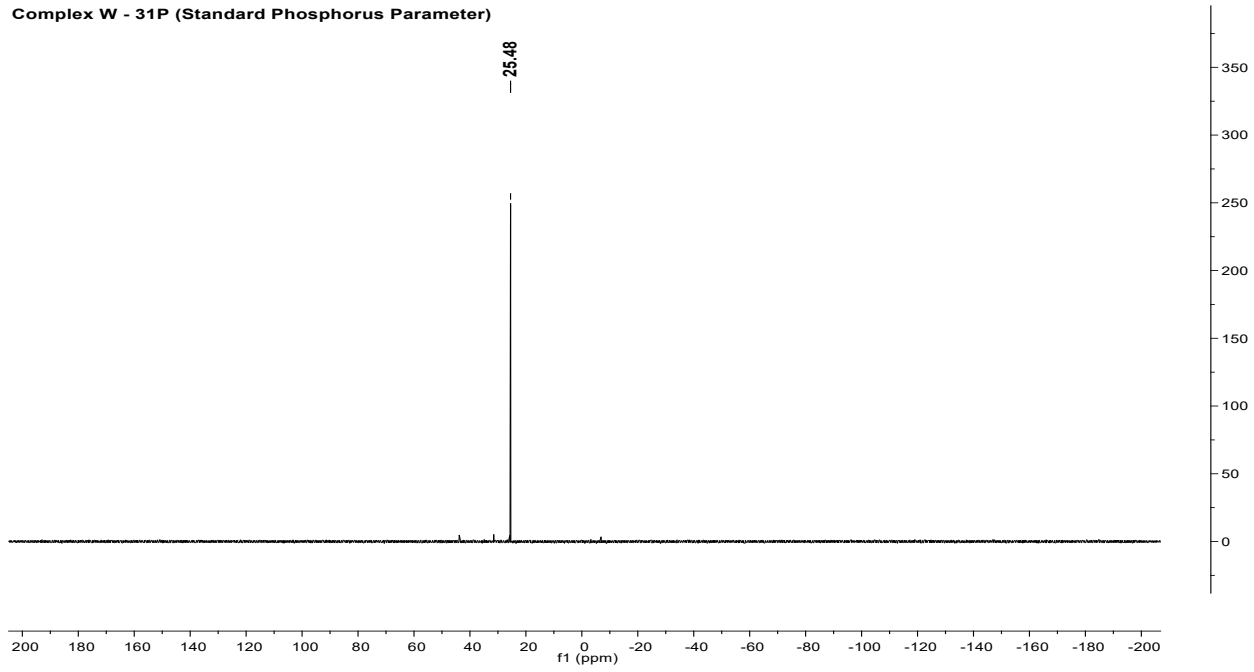
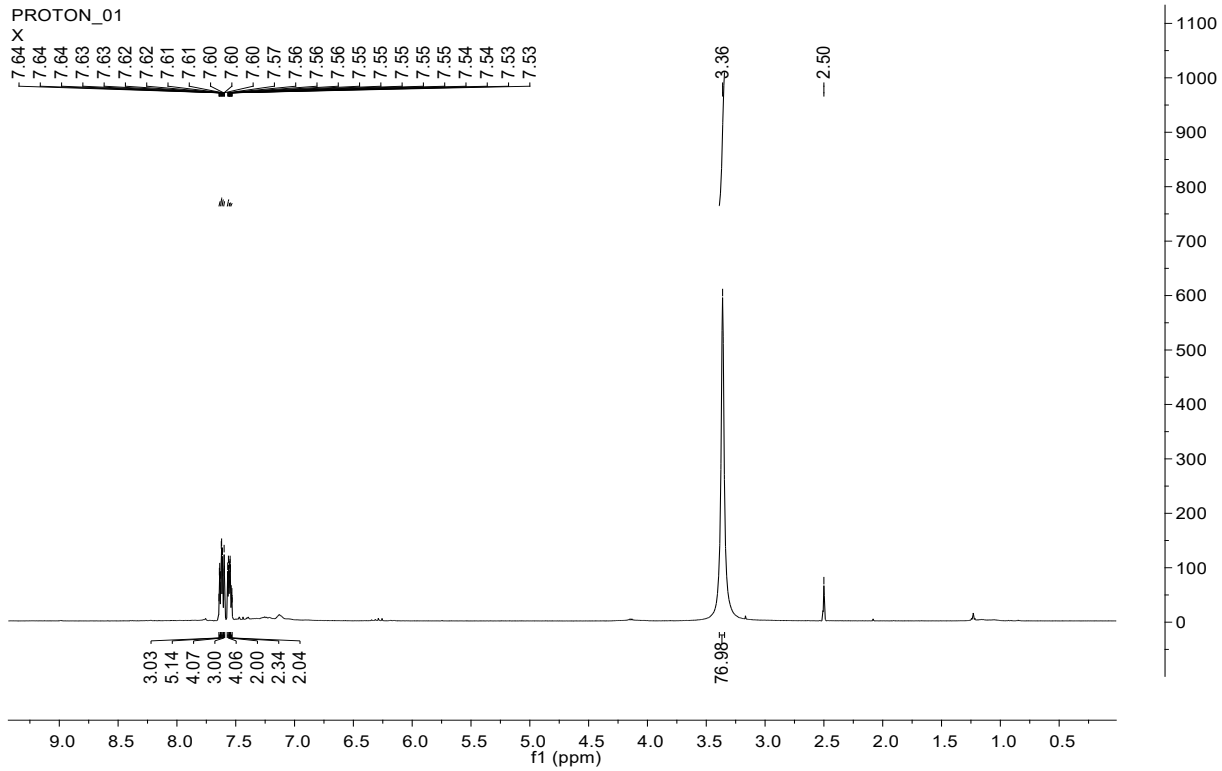


Figure S7: ^{1}H NMR (400 MHz, ($DMSO_4$) spectrum of **X**.



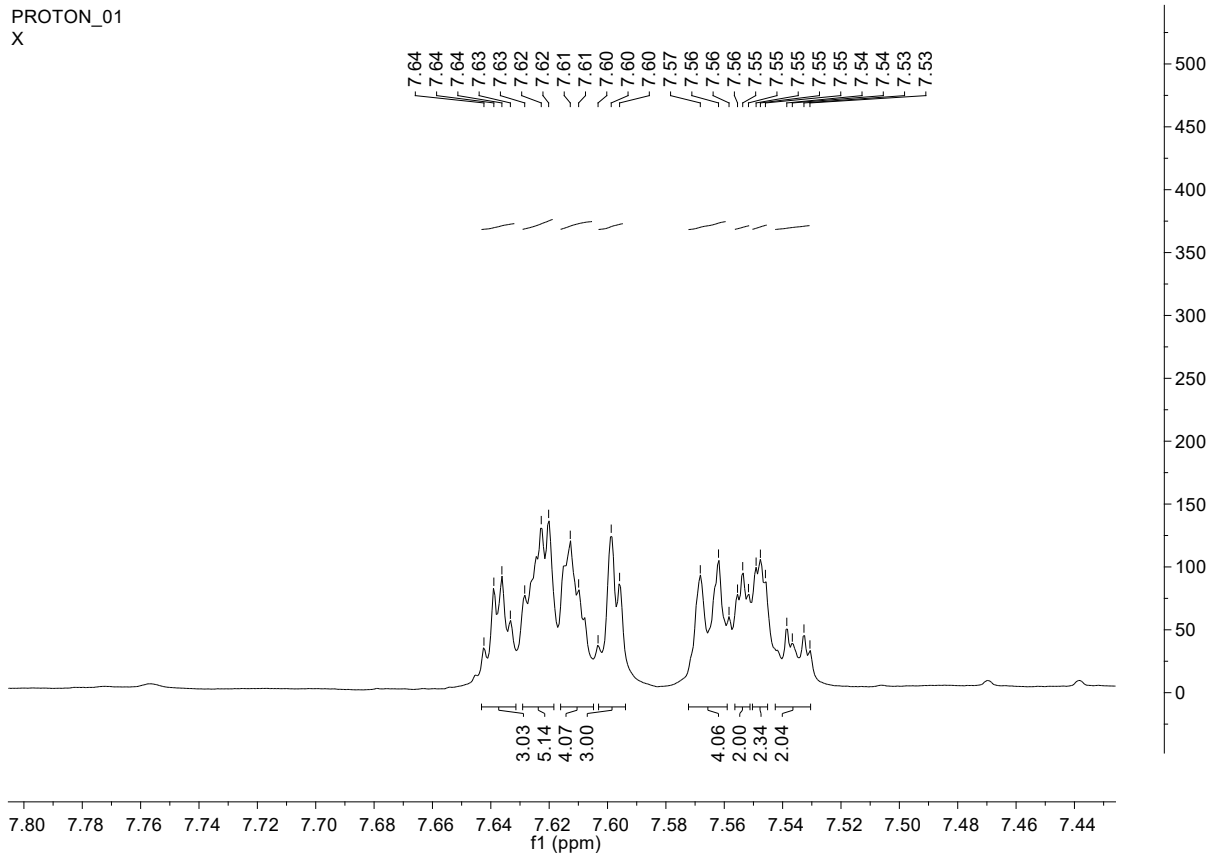
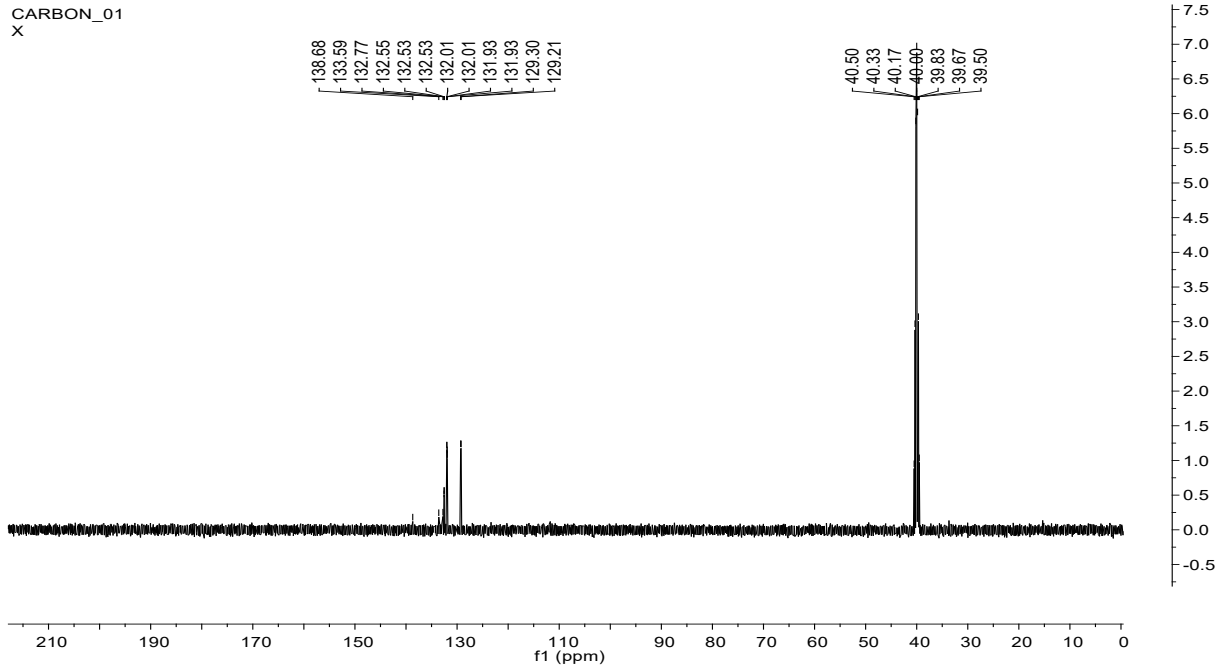
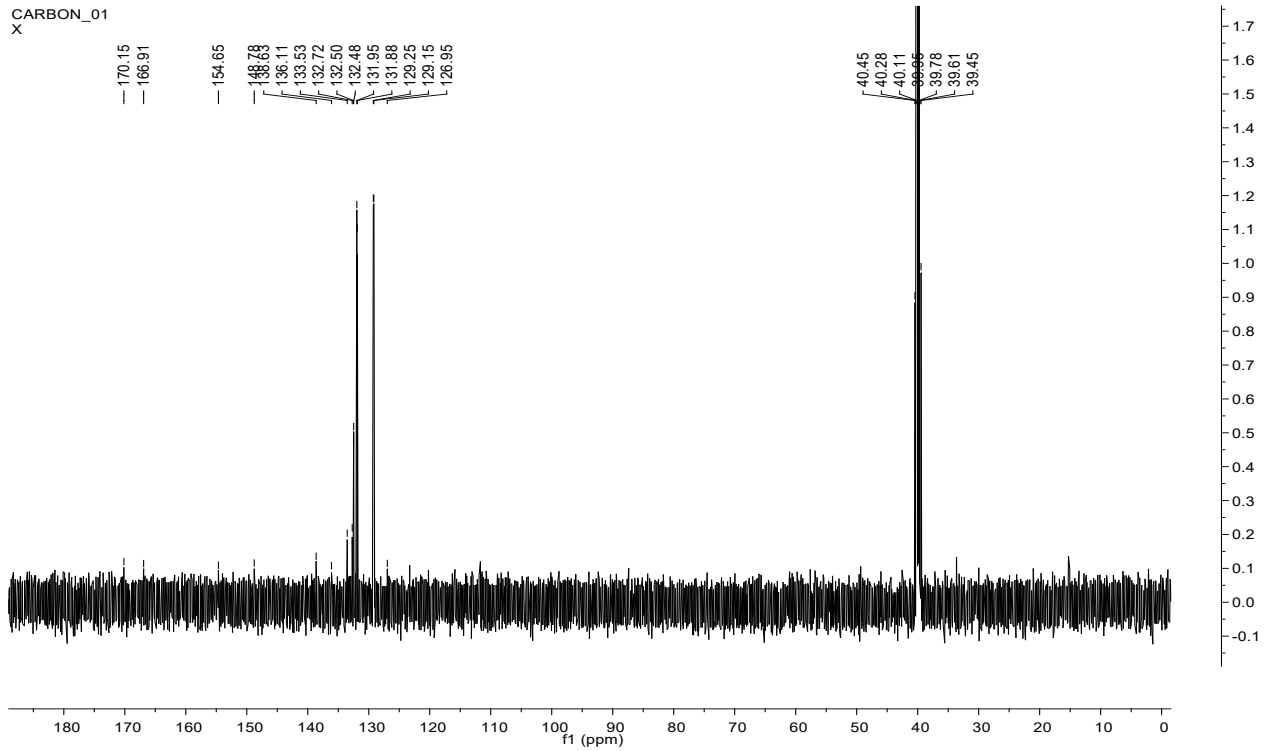


Figure S8: Aromatic region of ^{13}C NMR (400 MHz, ($DMSO_4$) spectrum of **X**.




CARBON_01
X
170.15
166.91
154.65
148.78
138.63
136.11
133.53
132.72
132.50
132.48
131.95
131.88
129.25
129.15
126.95
40.45
40.28
40.11
39.78
39.61
39.45
f1 (ppm)

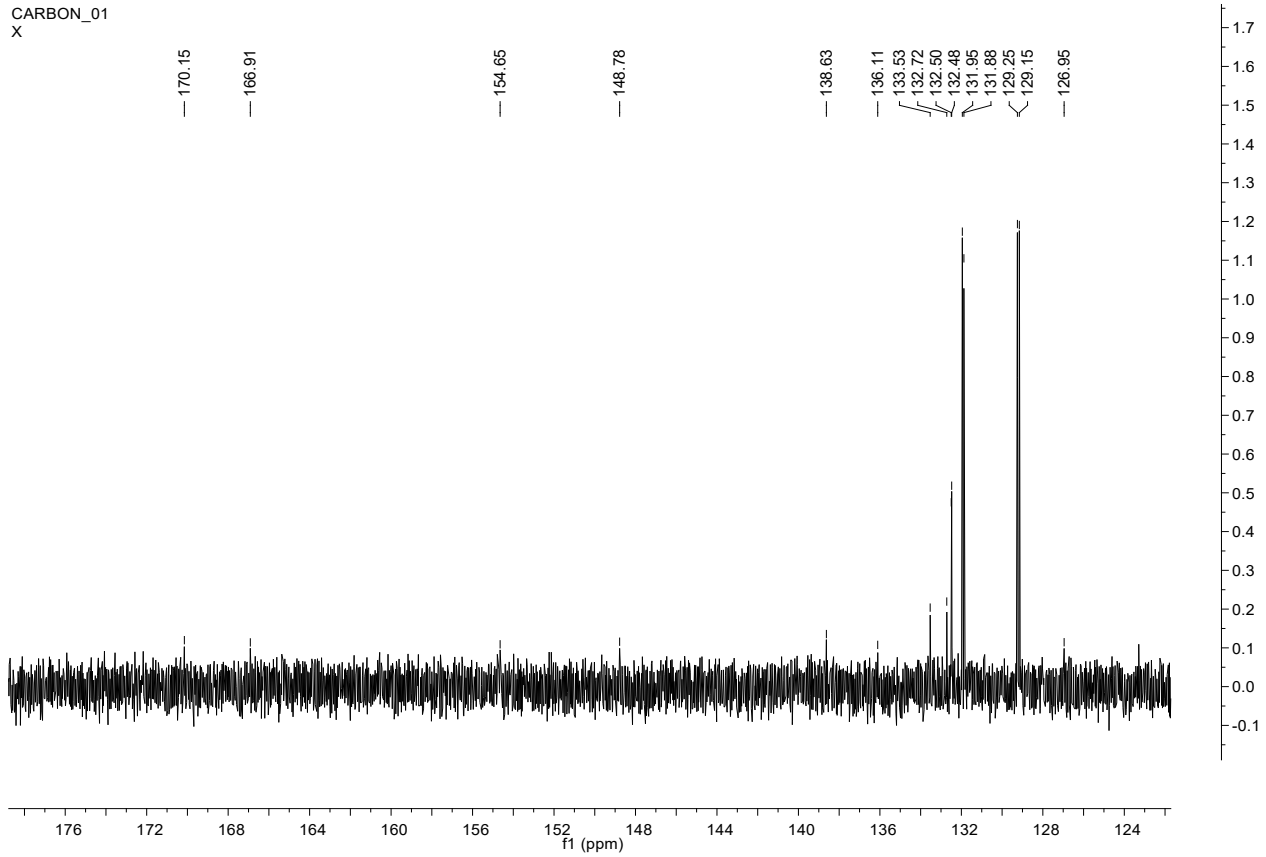

CARBON_01
X
170.15
166.91
154.65
148.78
138.63
136.11
133.53
132.72
132.50
132.48
131.95
131.88
129.25
129.15
126.95
f1 (ppm)

Figure S9: Expanded Aromatic region of ^{13}C NMR 400 MHz, ($DMSO_4$) spectrum of **X**.

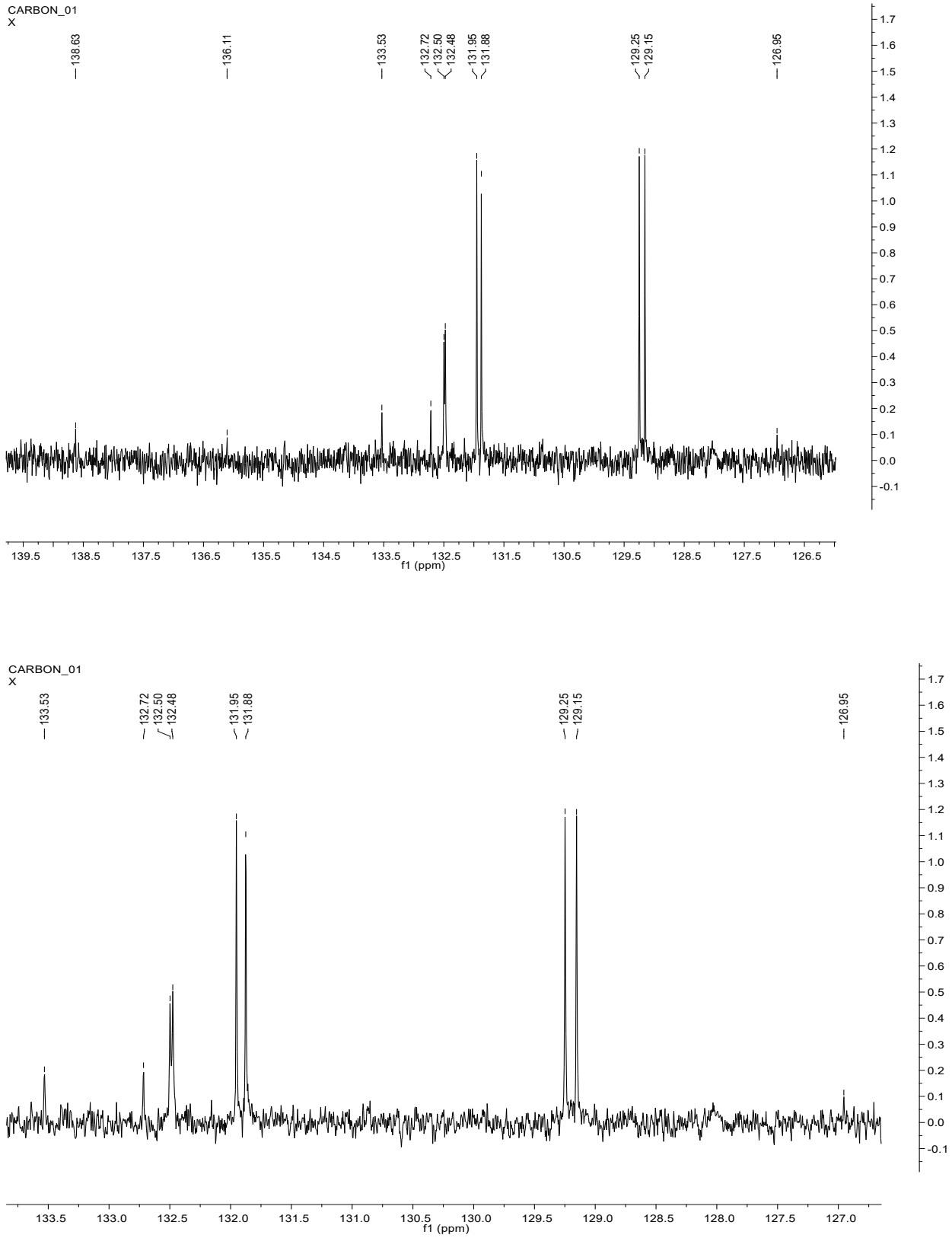


Figure S10: ^{31}P NMR (400 MHz, ($DMSO_4$) spectrum of **X**.

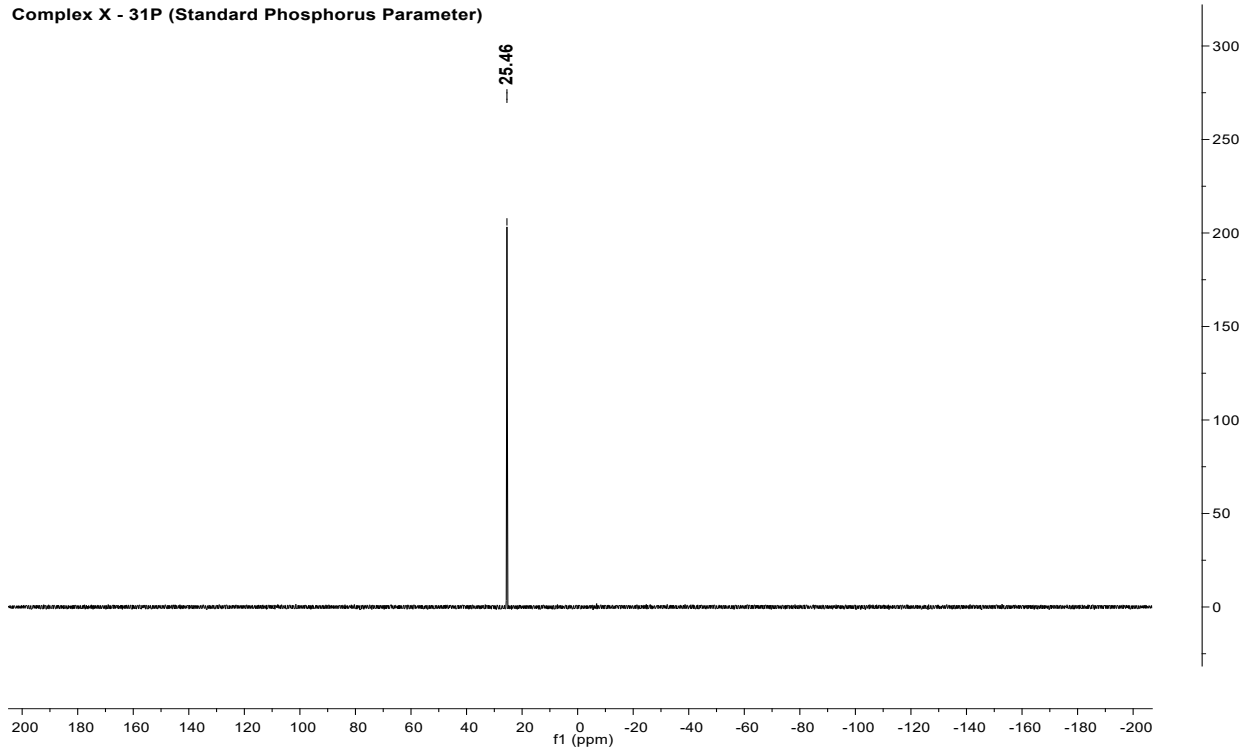


Figure S11: Mass Spectrometry of complex **V2**.

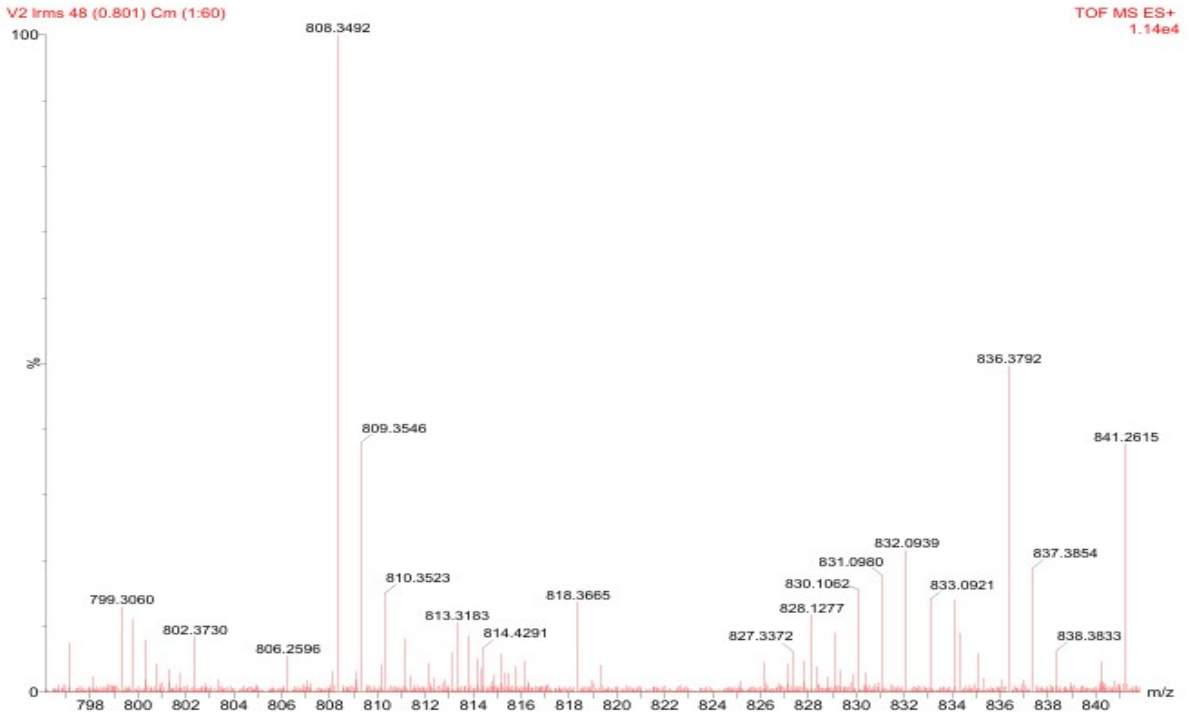


Figure S12: Mass Spectrometry of complex **W**.

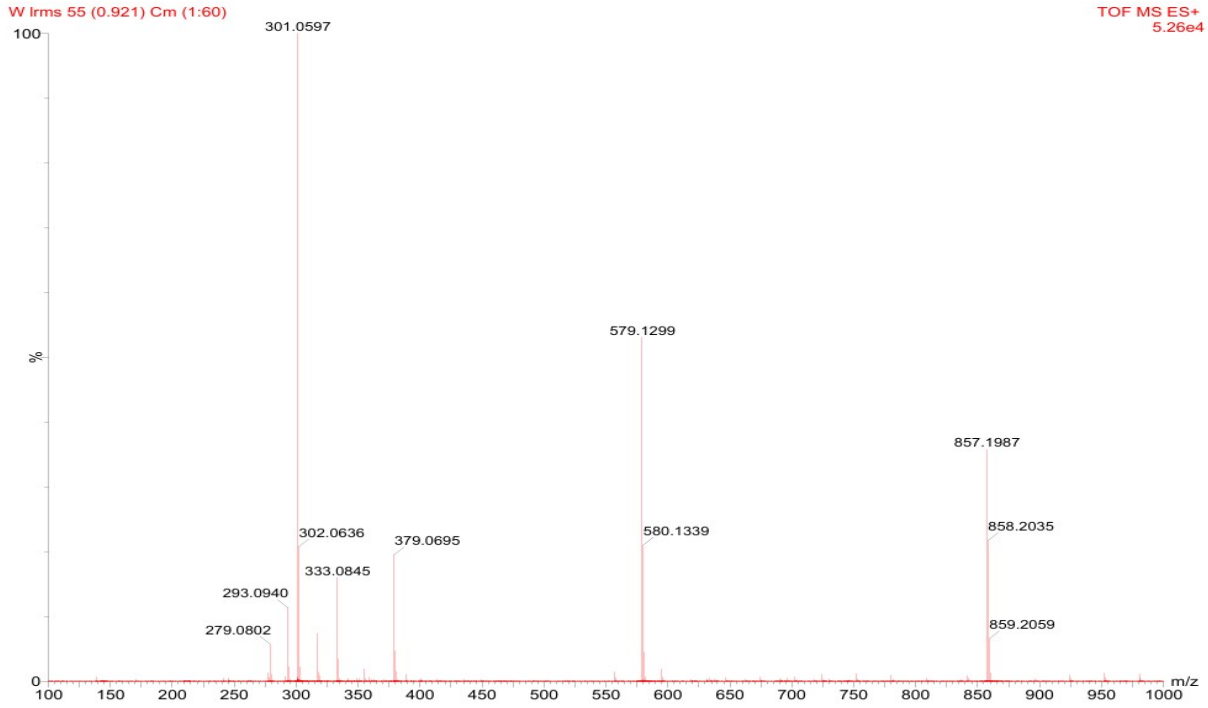


Figure S13: Mass Spectrometry of complex **X**

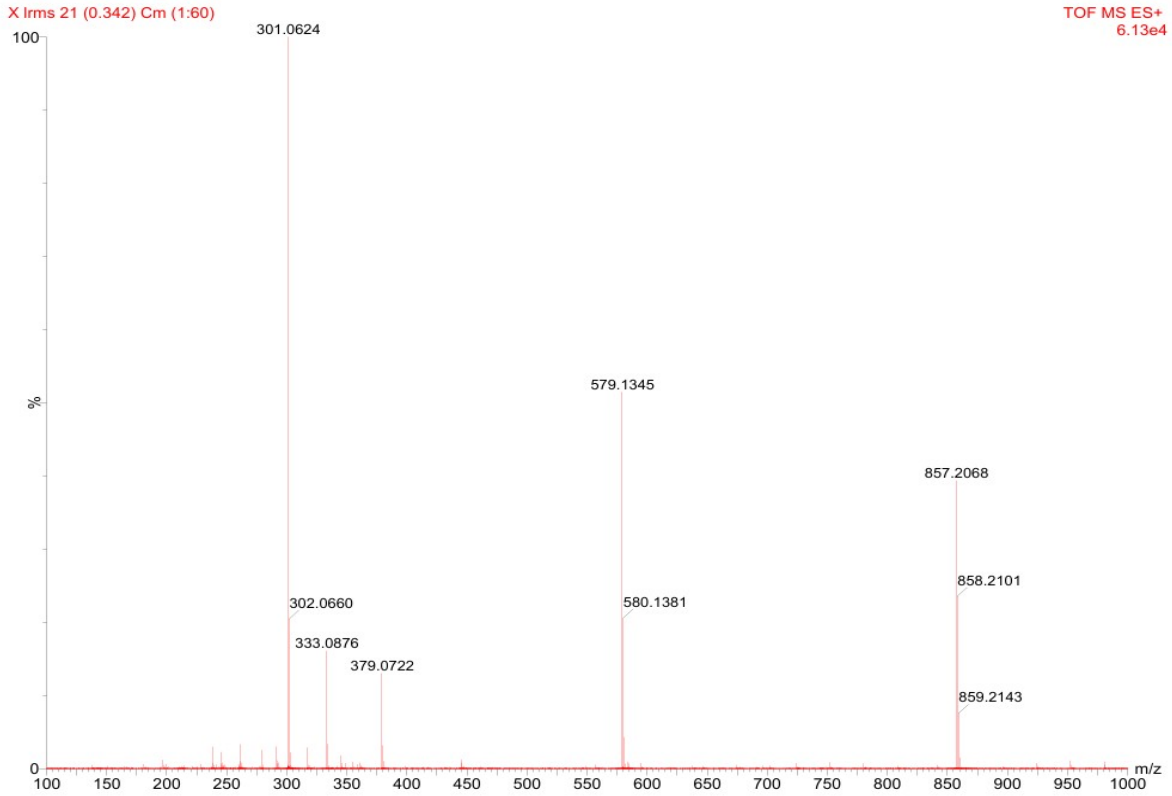
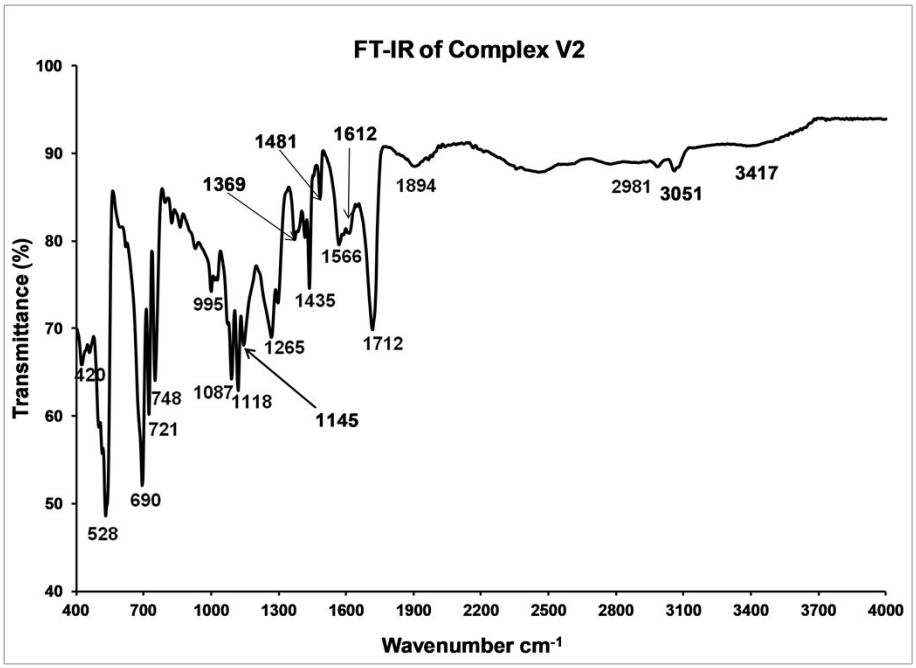
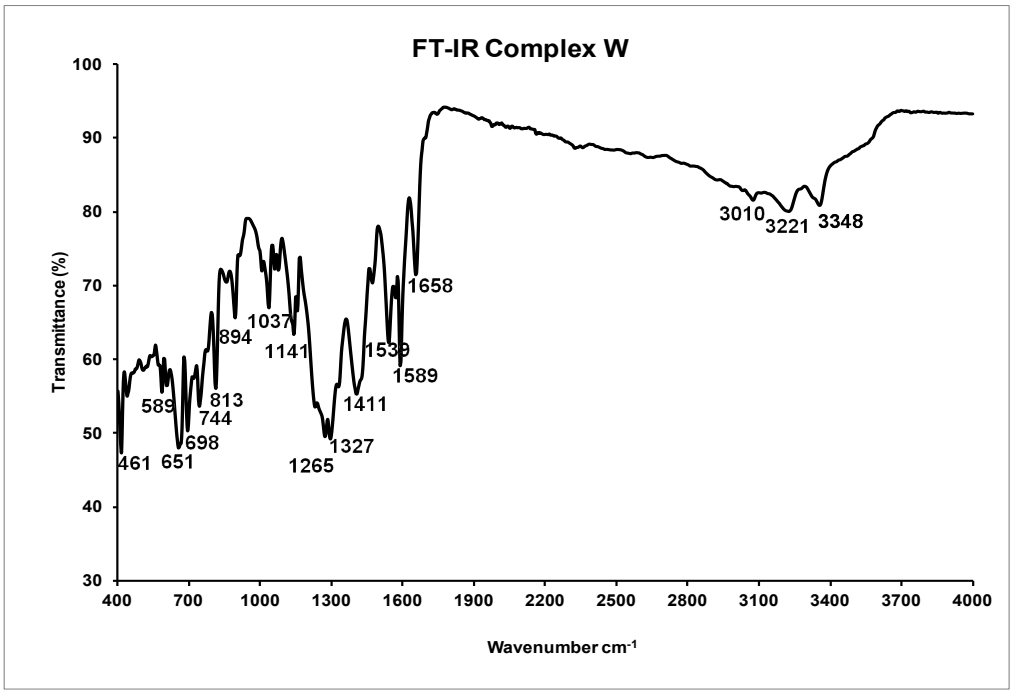


Figure S14: FT-IR Spectra of complexes (V2, W and X)




FT-IR Complex W
Transmittance (%)
Wavenumber cm-1
100
90
80
70
60
50
40
30
400
700
1000
1300
1600
1900
2200
2500
2800
3100
3400
3700
4000
3010
3221
3348
1658
1589
1539
1411
1327
1265
1141
1037
894
813
744
698
651
589
461

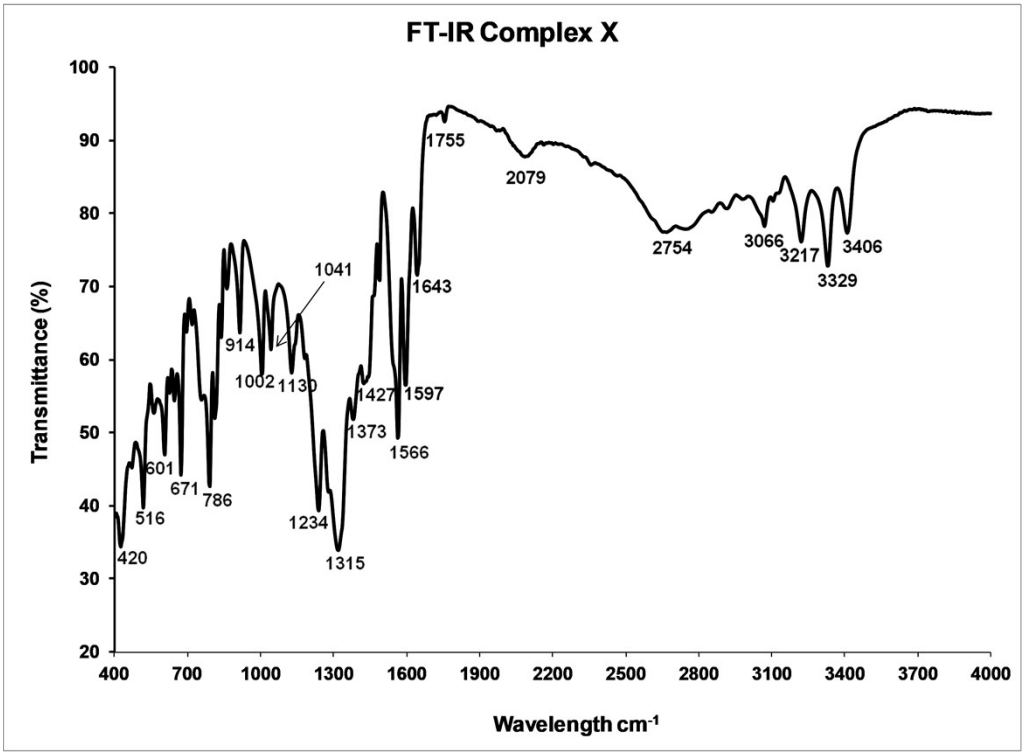

FT-IR Complex X
Transmittance (%)
Wavelength cm-1
100
90
80
70
60
50
40
30
20
400
700
1000
1300
1600
1900
2200
2500
2800
3100
3400
3700
4000
1755
2079
2754
3066
3217
3329
3406
1643
1597
1566
1427
1373
1315
1234
1130
1041
1002
914
786
671
601
516
420

Figure S15. 3D and 2D representation of the molecular interaction between ERα+ (8DU6) and (**A**) V2; (**B**) W; and (**C**) X.

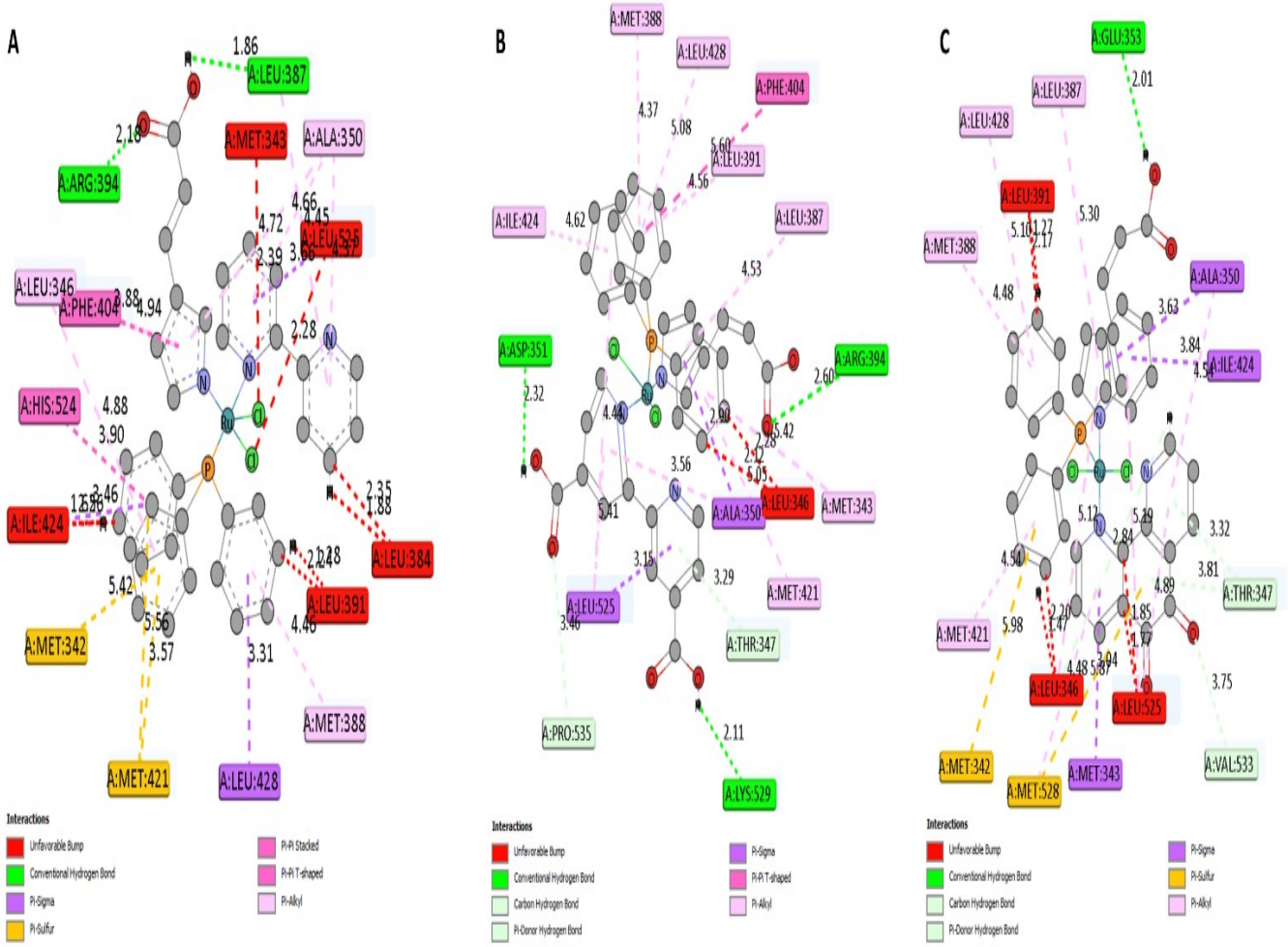


Figure S16. 2D representation of the molecular interaction between ERα+ (8DU6) and (**A**) Crizotinib; (**B**) Doxorubicin; (**C**) Gemcitabine; (**D**) Lorlatinib.

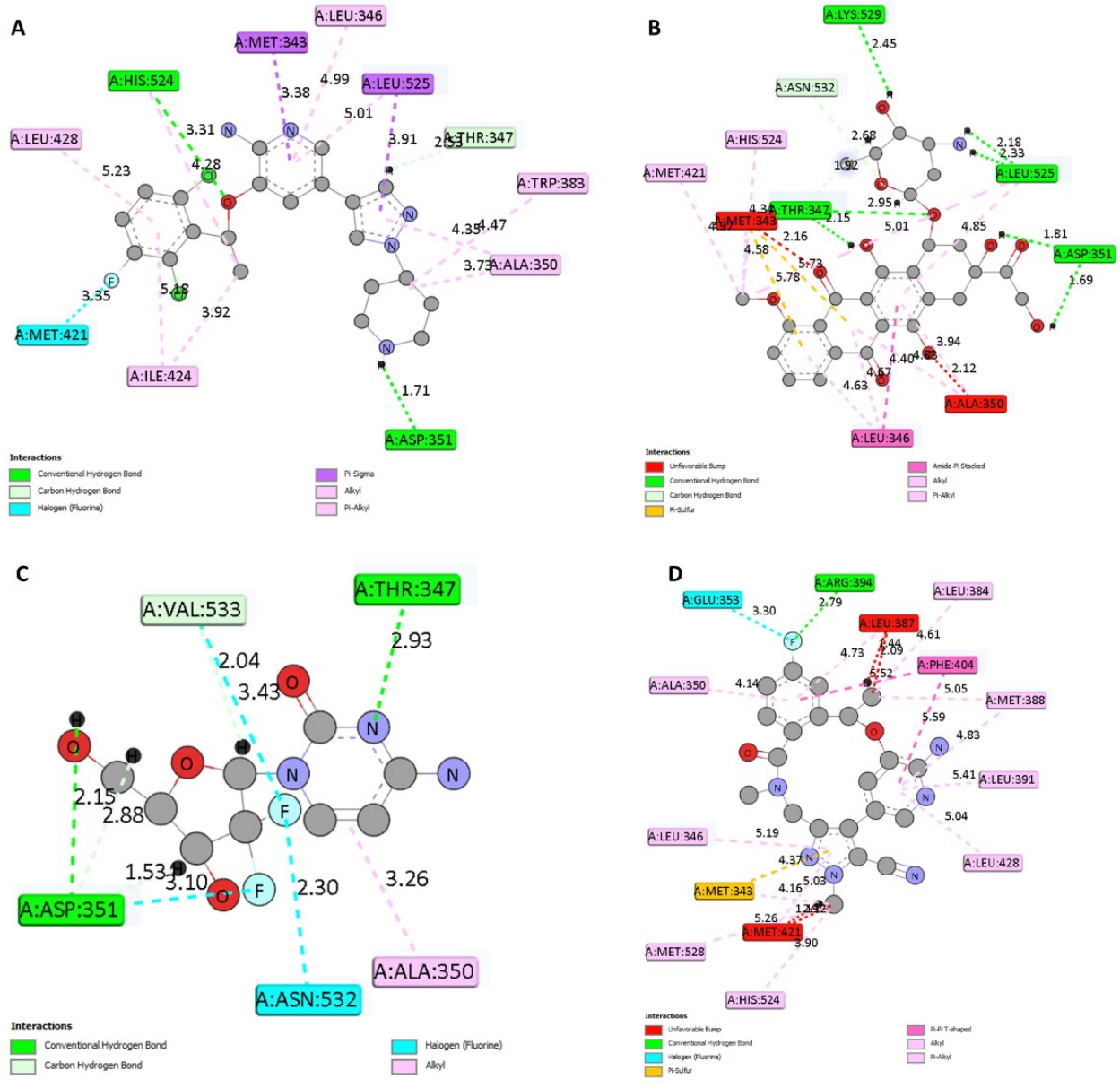


Figure S17. 2D representation of the molecular interaction between WT-EGFR (8PO4) and (**A**) V2; (**B**) W; (**C**) X.

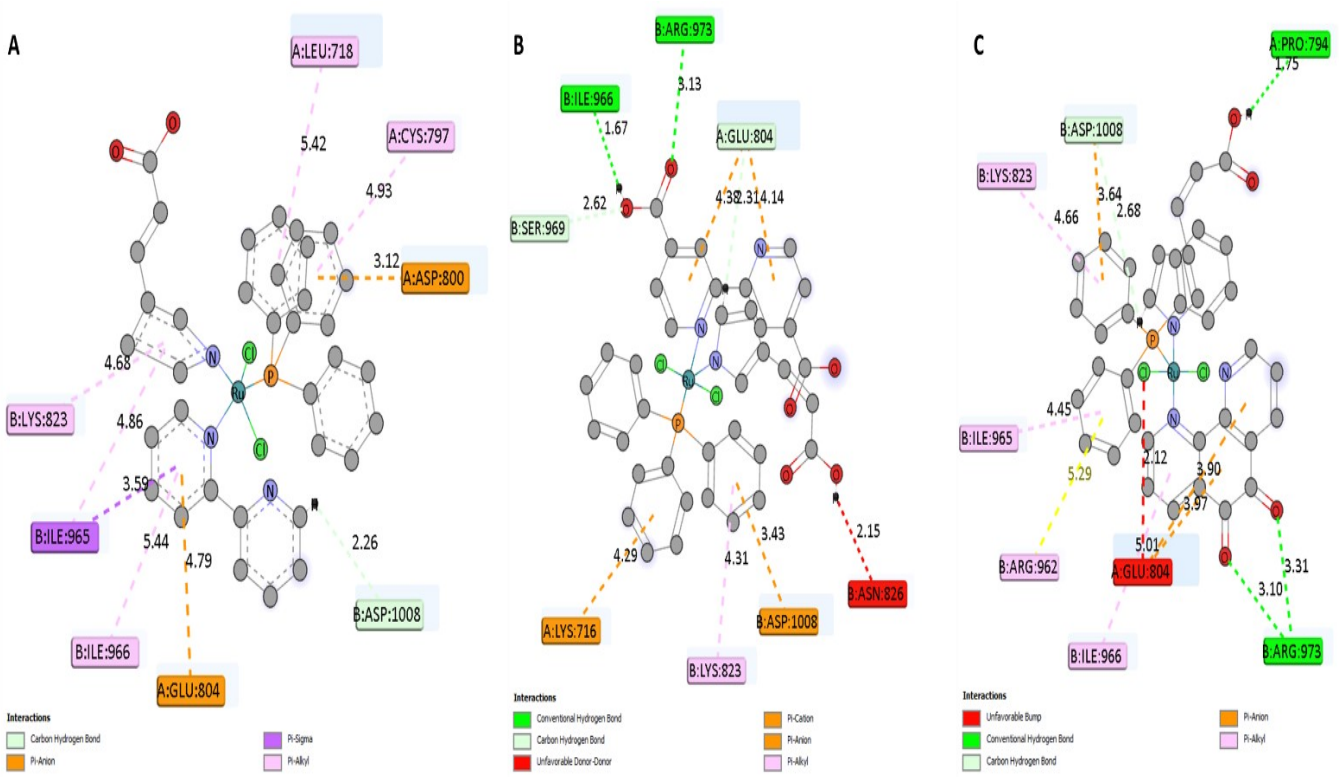


Figure S18. 2D representation of the molecular interaction between WT EGFR (8PO4) and (**A**) Crizotinib; (**B**) Doxorubicin; (**C**) Gemcitabine; (**D**) Lorlatinib.

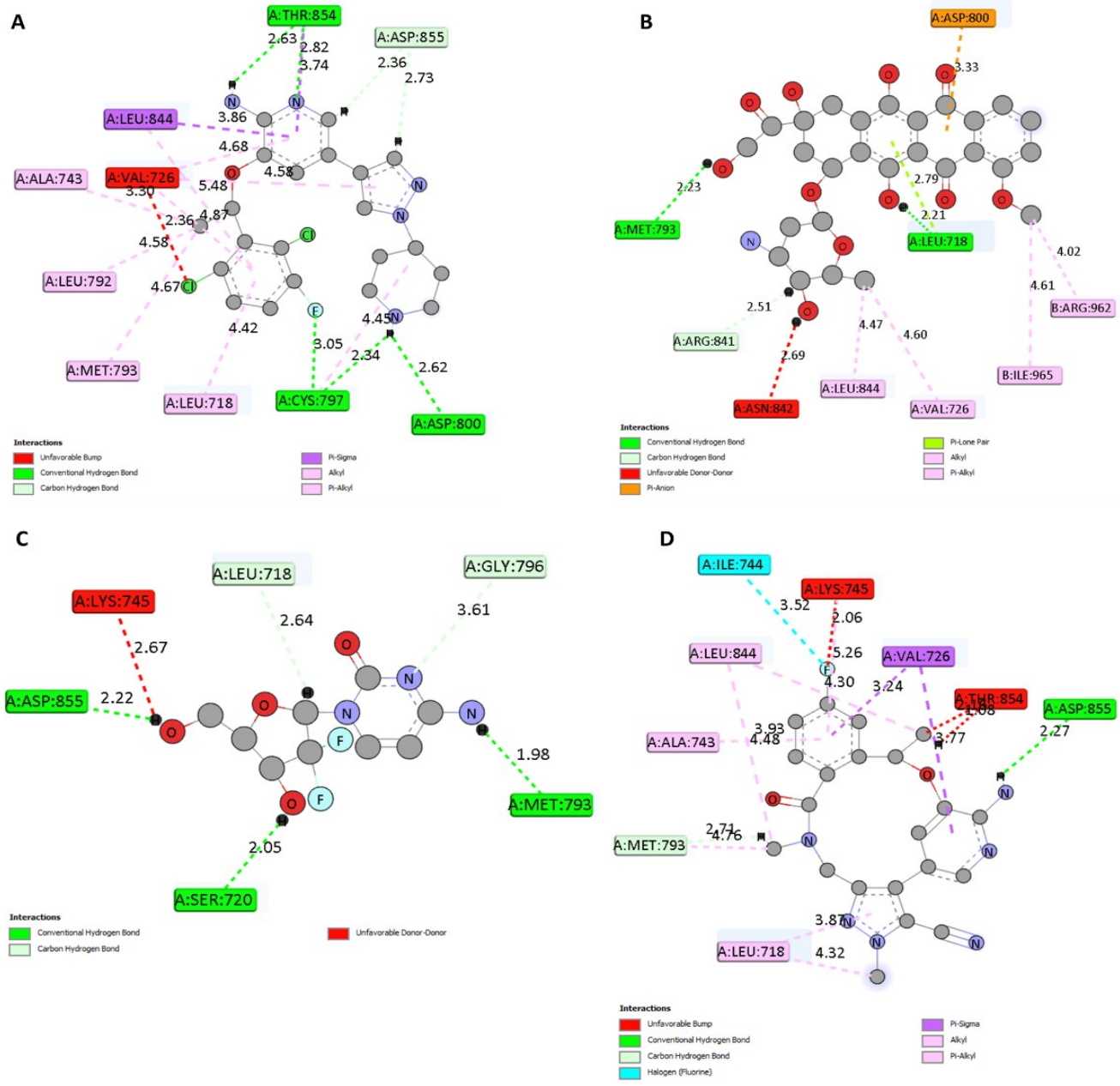
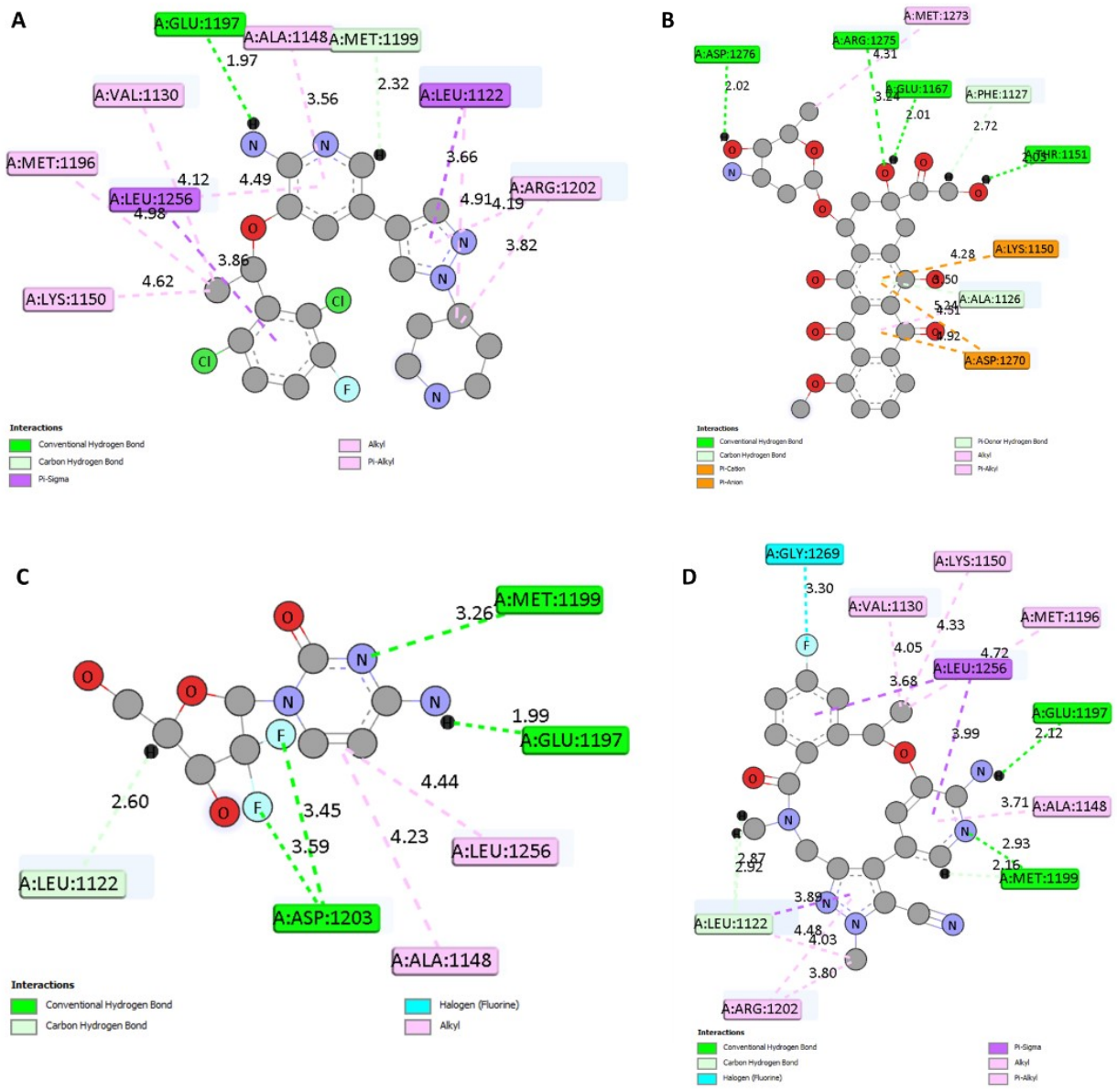


Figure S19. 2D representation of the molecular interaction between ALK (9GBE) and (**A**) Crizotinib; (**B**) Doxorubicin; (**C**) Gemcitabine; (**D**) Lorlatinib.



V2 Optimized XYZ Coordinates:

Electronic Energy = -1795.992176 Hartree

73

V2

C	0.44400	4.27300	-1.06600
C	-0.08900	5.56300	-1.19000
C	-1.30300	5.86500	-0.54700
C	-1.92100	4.87600	0.23200
C	-1.32000	3.60900	0.34800
N	-0.17000	3.30600	-0.33300
N	-3.27500	2.55800	1.31000
C	-1.91600	2.57900	1.24200
C	-1.10900	1.69400	1.99600
C	-1.73800	0.72200	2.79900
C	-3.14200	0.67100	2.83500
C	-3.86600	1.62200	2.08700
N	-1.04700	0.64400	-1.14700
C	1.09700	-1.52800	4.11700
C	1.55800	-1.07000	2.86900
C	1.05300	-1.63400	1.67400
C	0.06600	-2.64000	1.74600
C	-0.39900	-3.09100	2.99700
C	0.11700	-2.54000	4.18500
C	6.35100	-1.22000	0.27200
C	5.55800	-2.08500	1.04900
C	4.15500	-1.99000	1.00200

C	3.53600	-1.02300	0.18100
C	4.33100	-0.15300	-0.59300
C	5.73400	-0.25600	-0.54600
P	1.65600	-0.93800	0.03000
C	0.68000	-1.94500	-2.46500
C	1.28900	-2.28200	-1.24000
C	1.68600	-3.61800	-1.00400
C	1.46000	-4.60700	-1.97600
C	0.84500	-4.26900	-3.19800
C	0.46100	-2.93800	-3.44000
Ru	0.62900	1.31700	-0.26900
Cl	2.38500	2.26900	1.16100
C	-2.84300	0.50000	-2.53800
C	-1.66700	1.18300	-2.29100
C	-1.85300	-0.38300	-0.68000
C	-2.98500	-0.51000	-1.49800
Cl	1.73200	1.58800	-2.38400
C	-4.09100	-1.43200	-1.35800
C	-4.26300	-2.33400	-0.34500
O	-5.58500	-3.91500	0.86900
O	-6.30900	-3.41000	-1.22700
C	-5.39600	-3.26200	-0.17000
H	1.36100	3.98300	-1.56200
H	0.43900	6.30100	-1.78500
H	-1.75000	6.85100	-0.64100
H	-2.85300	5.05200	0.75500

H	-0.02900	1.83900	2.06000
H	-1.14000	0.03400	3.38800
H	-3.66700	-0.06700	3.43300
H	-4.95300	1.63800	2.10900
H	1.50200	-1.09700	5.02900
H	2.30500	-0.28200	2.82500
H	-0.32900	-3.08800	0.83800
H	-1.15500	-3.87100	3.03800
H	-0.23500	-2.89700	5.15000
H	7.43600	-1.29300	0.30900
H	6.02500	-2.83000	1.68900
H	3.55900	-2.65800	1.61900
H	3.86600	0.60200	-1.21700
H	6.33800	0.42300	-1.14300
H	0.39100	-0.92000	-2.67000
H	2.17500	-3.89300	-0.07300
H	1.76700	-5.63200	-1.78300
H	0.67300	-5.03400	-3.95200
H	-0.00700	-2.66600	-4.38200
H	-3.53600	0.68400	-3.34900
H	-1.20200	1.98500	-2.84100
H	-1.58500	-0.94700	0.20000
H	-4.84800	-1.35200	-2.14400
H	-3.54400	-2.38800	0.46800
H	-6.02400	-2.96900	-2.05500

W Optimized XYZ Coordinates

Electronic Energy = -2173.053801 Hartree

79

W

C	-1.59800	2.62500	-0.70600
C	-2.75200	3.39600	-0.84600
C	-3.93900	2.77300	-1.26800
C	-3.91000	1.38900	-1.49000
C	-2.71300	0.65700	-1.32000
N	-1.55300	1.27600	-0.94400
N	-2.12200	-1.35800	-2.56600
C	-2.79500	-0.82100	-1.52100
C	-3.63200	-1.57000	-0.66700
C	-3.75600	-2.95300	-0.88600
C	-3.05500	-3.52000	-1.97000
C	-2.25800	-2.69100	-2.77700
N	0.17100	1.05900	1.32800
C	5.61400	2.01800	2.23100
C	4.76200	1.01200	1.73600
C	4.02600	1.22200	0.54900
C	4.15500	2.45300	-0.13500
C	5.01000	3.45300	0.36300
C	5.74200	3.24100	1.54800
C	4.67500	-1.58300	-4.20200
C	3.41800	-2.03700	-3.75900
C	2.89400	-1.58800	-2.53400

C	3.63200	-0.68100	-1.73900
C	4.89200	-0.23000	-2.18200
C	5.41000	-0.68100	-3.41100
P	2.87300	-0.11700	-0.11600
C	2.42400	-1.62300	2.26600
C	3.16200	-1.55100	1.06500
C	4.12600	-2.53800	0.78000
C	4.35400	-3.58800	1.68900
C	3.62200	-3.65600	2.88900
C	2.65800	-2.67000	3.17500
Ru	0.51400	0.49800	-0.53200
Cl	-0.03800	-1.81800	-0.14200
C	0.19100	1.97500	3.40500
C	0.87600	1.91200	2.19900
C	-0.94600	0.59300	1.98900
C	-0.98400	1.12600	3.28800
Cl	1.25000	2.29300	-1.99100
C	-1.93000	0.77800	4.33600
C	-3.12300	0.11000	4.22900
O	-4.29300	-1.40500	2.74600
O	-3.93200	0.68100	1.97600
C	-3.79900	-0.28500	2.97100
C	-4.64500	-3.85800	-0.05800
O	-4.96700	-4.98100	-0.47800
O	-5.11300	-3.41000	1.14100
C	-5.18400	3.60800	-1.41200

O	-5.35900	4.66300	-0.79700
O	-6.15800	3.13900	-2.28100
H	-0.67200	3.08800	-0.39900
H	-2.73100	4.46000	-0.63500
H	-4.80100	0.83200	-1.76200
H	-4.15100	-1.06800	0.14300
H	-3.15100	-4.58100	-2.17300
H	-1.71000	-3.09700	-3.62200
H	6.17500	1.84100	3.14600
H	4.68000	0.07400	2.27500
H	3.58800	2.63500	-1.04100
H	5.10000	4.39400	-0.17400
H	6.40100	4.01600	1.93100
H	5.07600	-1.92700	-5.15300
H	2.84300	-2.73300	-4.36500
H	1.92600	-1.95100	-2.19700
H	5.46900	0.46700	-1.58200
H	6.38200	-0.32700	-3.74600
H	1.66200	-0.88300	2.48800
H	4.69400	-2.50000	-0.14600
H	5.09600	-4.34900	1.45700
H	3.79400	-4.47100	3.58900
H	2.07800	-2.72200	4.09300
H	0.47700	2.56000	4.26900
H	1.78000	2.41000	1.88700
H	-1.56800	-0.15700	1.53400

H	-1.61100	1.02100	5.35100
H	-3.61700	-0.25200	5.12600
H	-3.51800	1.53800	2.21900
H	-4.74000	-2.59800	1.58400
H	-5.87400	2.39000	-2.84800

X Optimized XYZ Coordinates

Electronic Energy = -2021.441324 Hartree

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X

C	-2.32500	1.91500	-1.22600
C	-3.51600	2.56200	-1.60600
C	-4.74400	1.93600	-1.35800
C	-4.74500	0.65500	-0.76800
C	-3.51200	0.06700	-0.42000
N	-2.32000	0.70500	-0.61600
N	-2.18600	-1.79700	0.30900
C	-3.43800	-1.30300	0.08600
C	-4.59400	-2.09500	0.24600
C	-4.44600	-3.44400	0.62400
C	-3.15300	-3.95800	0.79400
C	-2.04500	-3.11000	0.62400
N	0.77500	-1.68700	0.86000
C	3.66900	3.10700	3.02500
C	2.92300	2.86800	1.85800
C	2.19400	1.66500	1.70700

C	2.22400	0.70800	2.73800
C	2.97200	0.95000	3.90700
C	3.69600	2.14600	4.05500
C	4.59900	0.56800	-3.09600
C	3.26000	0.73400	-3.49500
C	2.26100	0.99300	-2.54000
C	2.59400	1.10100	-1.17100
C	3.94000	0.93900	-0.77500
C	4.93400	0.67200	-1.73400
P	1.23300	1.37100	0.10600
C	0.97600	3.88300	-1.35100
C	0.61400	3.13100	-0.21500
C	-0.24700	3.70500	0.75100
C	-0.73700	5.01100	0.57700
C	-0.37800	5.75900	-0.56400
C	0.47900	5.19100	-1.52500
Ru	-0.62900	-0.39400	0.15700
Cl	-0.30800	-1.11000	-2.16200
C	1.81000	-3.19200	2.22100
C	0.68500	-2.39800	2.07200
C	1.96000	-2.05400	0.24700
C	2.64100	-2.99800	1.04700
Cl	-1.30500	0.47800	2.35200
C	3.94500	-3.63100	0.89300
C	4.79400	-3.79000	-0.16800
O	5.59600	-3.30300	-2.36900

O	3.34100	-3.35600	-2.12700
C	4.62900	-3.45100	-1.60300
C	-5.94600	-1.52000	0.00300
C	-6.02500	-0.06700	-0.53200
O	-6.99200	-2.16800	0.20400
O	-7.13500	0.45300	-0.76200
H	-1.36400	2.37300	-1.40800
H	-3.46100	3.53500	-2.08000
H	-5.69000	2.39800	-1.62200
H	-5.33200	-4.05800	0.75400
H	-2.98800	-4.99800	1.05300
H	-1.03200	-3.47000	0.74200
H	4.22400	4.03600	3.12700
H	2.90900	3.61900	1.07300
H	1.66300	-0.21300	2.65000
H	2.98200	0.20300	4.69700
H	4.27000	2.33100	4.96000
H	5.36400	0.33300	-3.83000
H	2.98400	0.62800	-4.54100
H	1.22600	1.05100	-2.86100
H	4.21600	1.00000	0.27200
H	5.96200	0.52500	-1.41300
H	1.65500	3.46900	-2.08900
H	-0.53200	3.13300	1.63100
H	-1.39100	5.44400	1.33000
H	-0.75300	6.77100	-0.69600

H	0.77200	5.76300	-2.40200
H	2.03900	-3.83600	3.06100
H	-0.13600	-2.22400	2.75200
H	2.25100	-1.60200	-0.68800
H	4.32300	-4.04000	1.83300
H	5.77500	-4.21600	0.03000
H	2.63100	-3.53200	-1.47000