Supplementary Information (SI) for New Journal of Chemistry.

Supporting Information

Investigation of enzyme and serum protein protective effects, along with molecular docking studies of mixed ligand ruthenium(II) polypyridyl complexes

Sunita Khatkar[a], Santosh Kumar Dubey [a*], Manoj Trivedi[b*], Chanchal Vashisth[c], Neeru Devi[a], Neera Raghav[c*], Meenakshi Sharma[d], Jagan Rajamoni[e]

[a]Department of Chemistry, Institute of Integrated and Honors Studies, Kurukshetra University, Kurukshetra 136119, India Email: santoshkdubey@kuk.ac.in

[b]Department of Chemistry, Daulat Ram College, University of Delhi, Delhi-110007, India

Email:manojtrivedi@dr.du.ac.in

[c]Department of Chemistry, Kurukshetra University, Kurukshetra-136119, India

[d]Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi, 110007, India

[e]Department of Chemistry and Biochemistry, University of Missouri-St. Louis, MO 63121, USA

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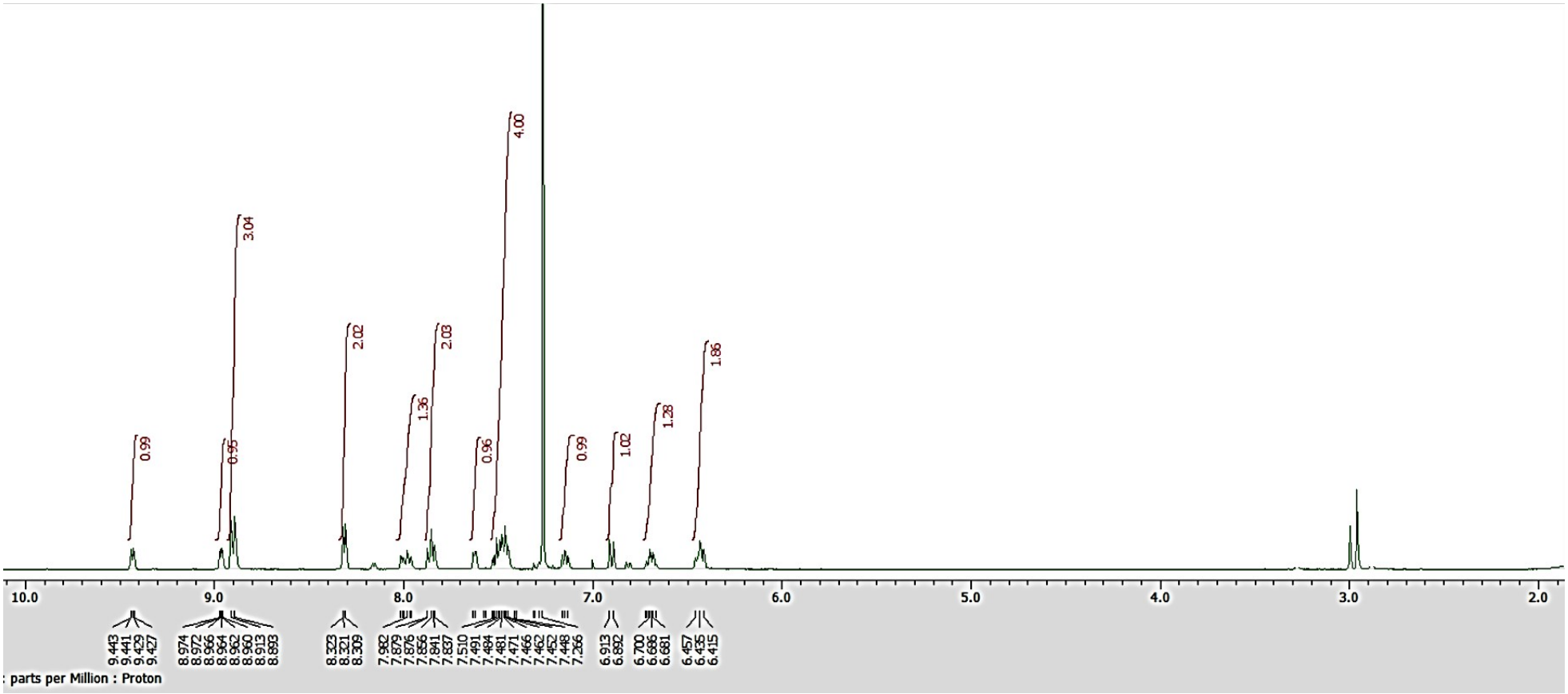


Fig. S1.^{1}H NMR spectrum of [Ru(η^2-N,S-mpy)(η^1-S-mpy)(tptz)]**(Ru1)** in $CDCl_3$ at 298K.

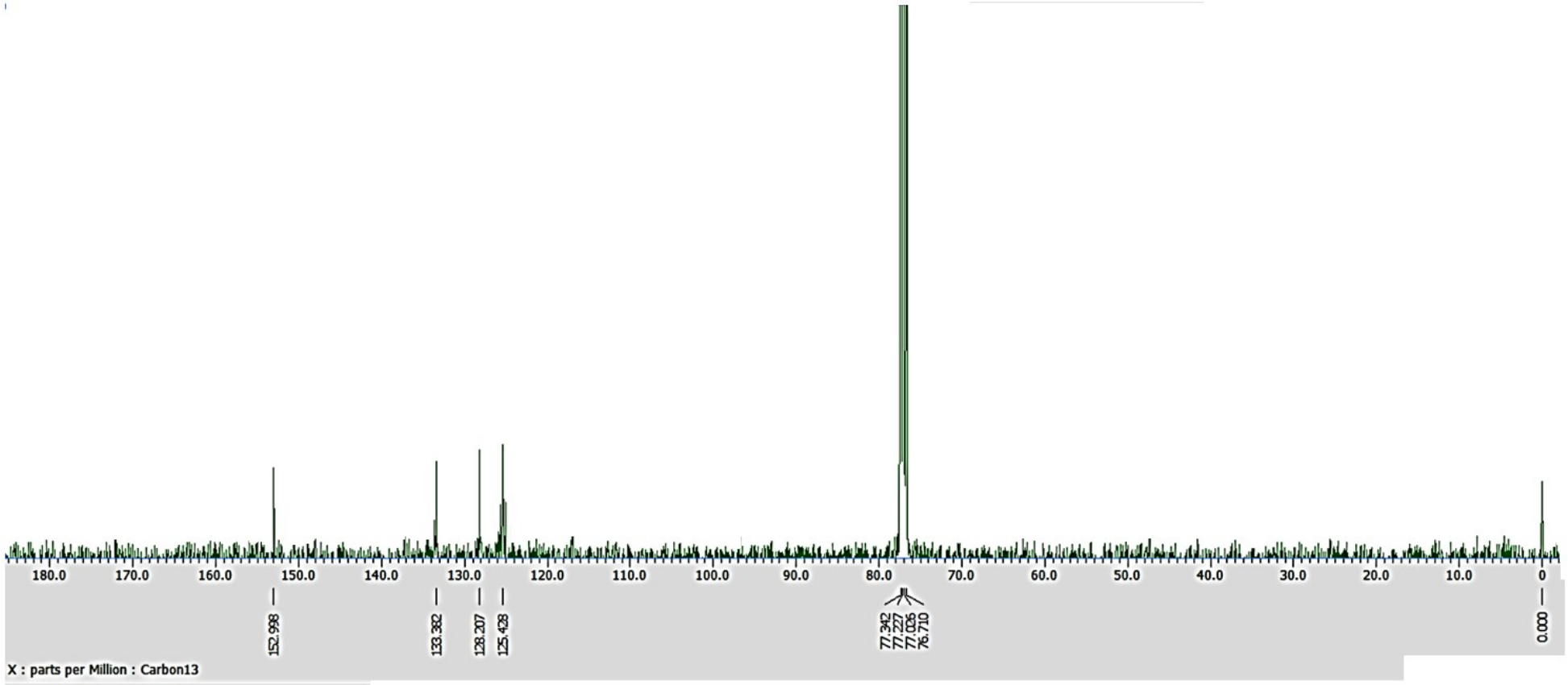


Fig. S2. ^{13}C NMR spectrum of [Ru $(mpy)_2(tptz)$]**(Ru1)** in $CDCl_3$ at 298K.

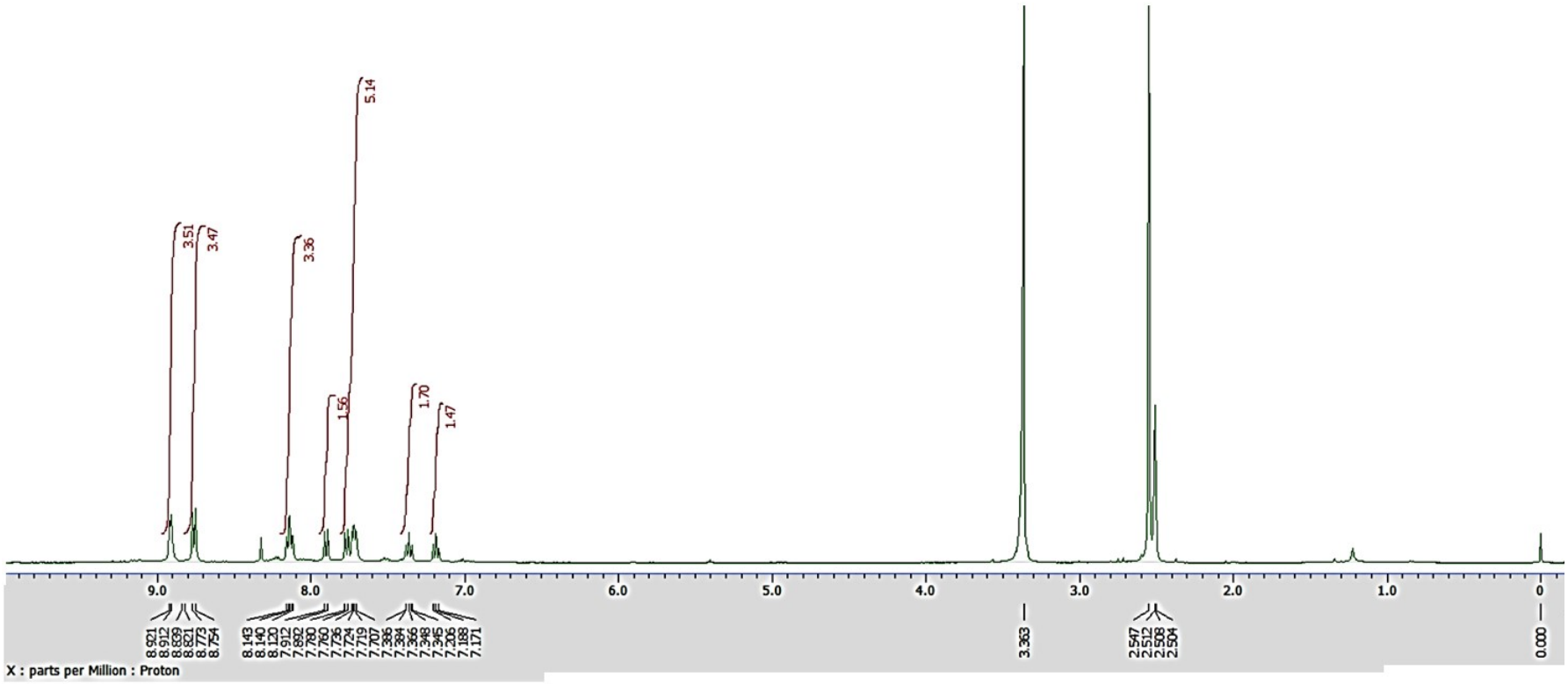


Fig. S3.^{1}H NMR spectrum of [Ru(η^2-N,S-mbtz)(η^1-S-mbtz)(tptz)] (**Ru2**) in DMSO-d_6 at 298K.

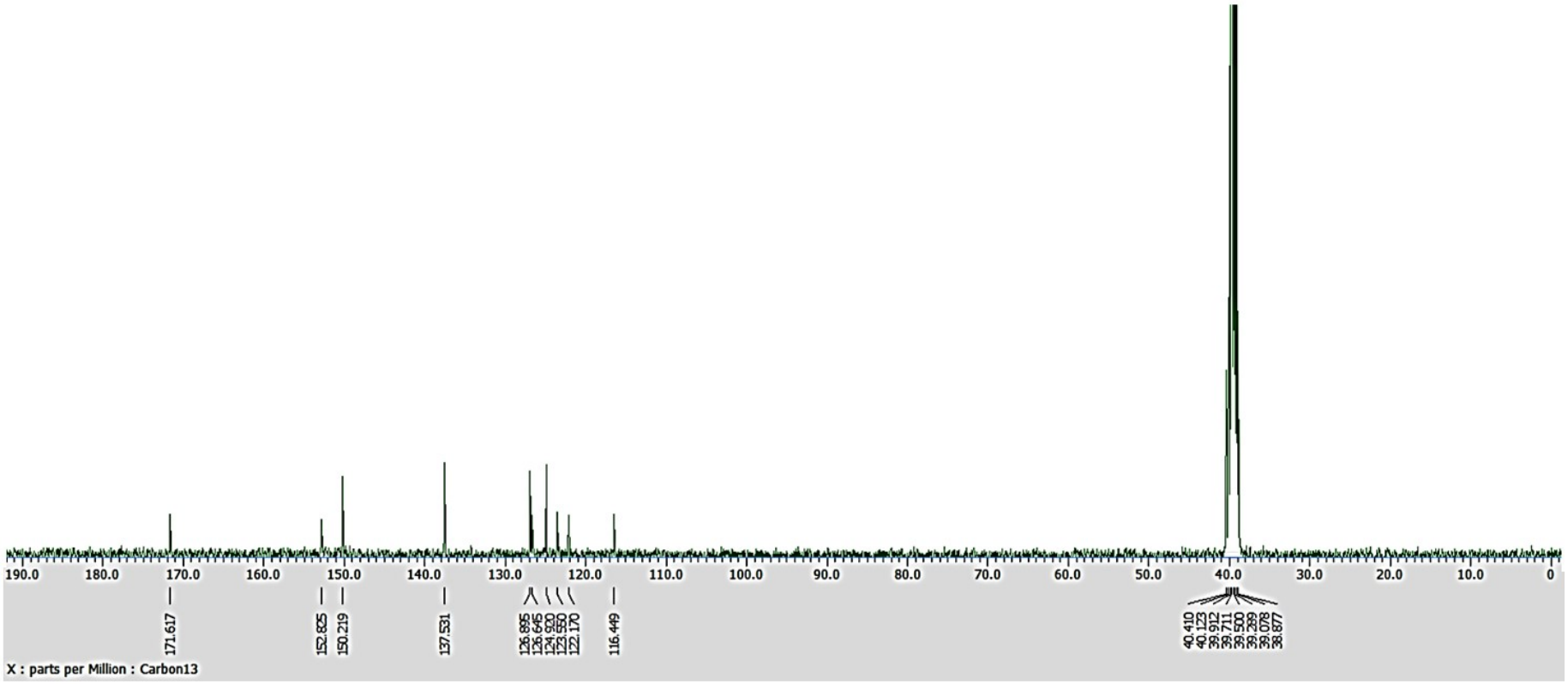


Fig. S4.^{13}C NMR spectrum of [Ru(η^2-N,S-mbtz)(η^1-S-mbtz)(tptz)] (**Ru2**) in DMSO-d_6 at 298K.

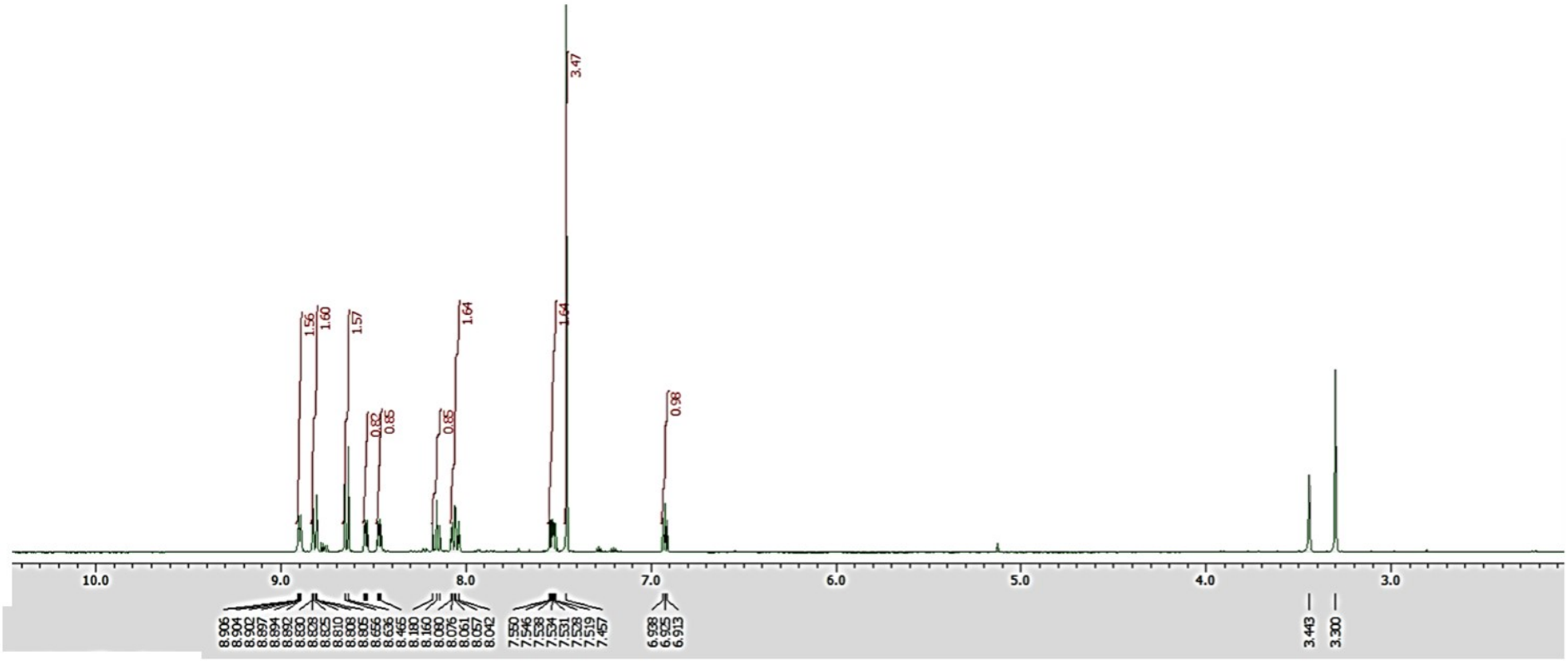


Fig. S5.^{1}H NMR spectrum of [Ru(η^2-N,S-mpt)(η^1-S-mpt)(tpy)] (**Ru3**) in $CDCl_3$ at 298K.

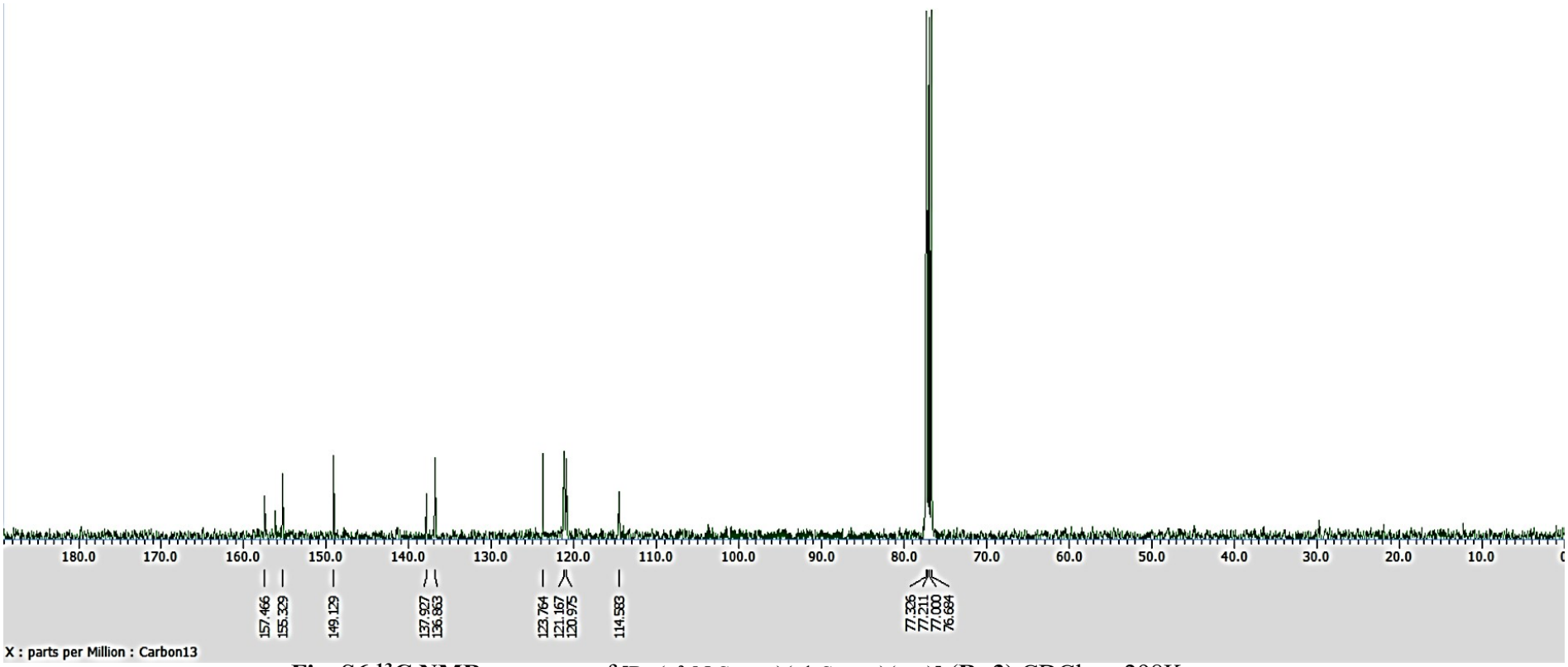


Fig. S6.^{13}C NMR spectrum of [Ru(η^2-N,S-mpt)(η^1-S-mpt)(tpy)] (**Ru3**) $CDCl_3$ at 298K.

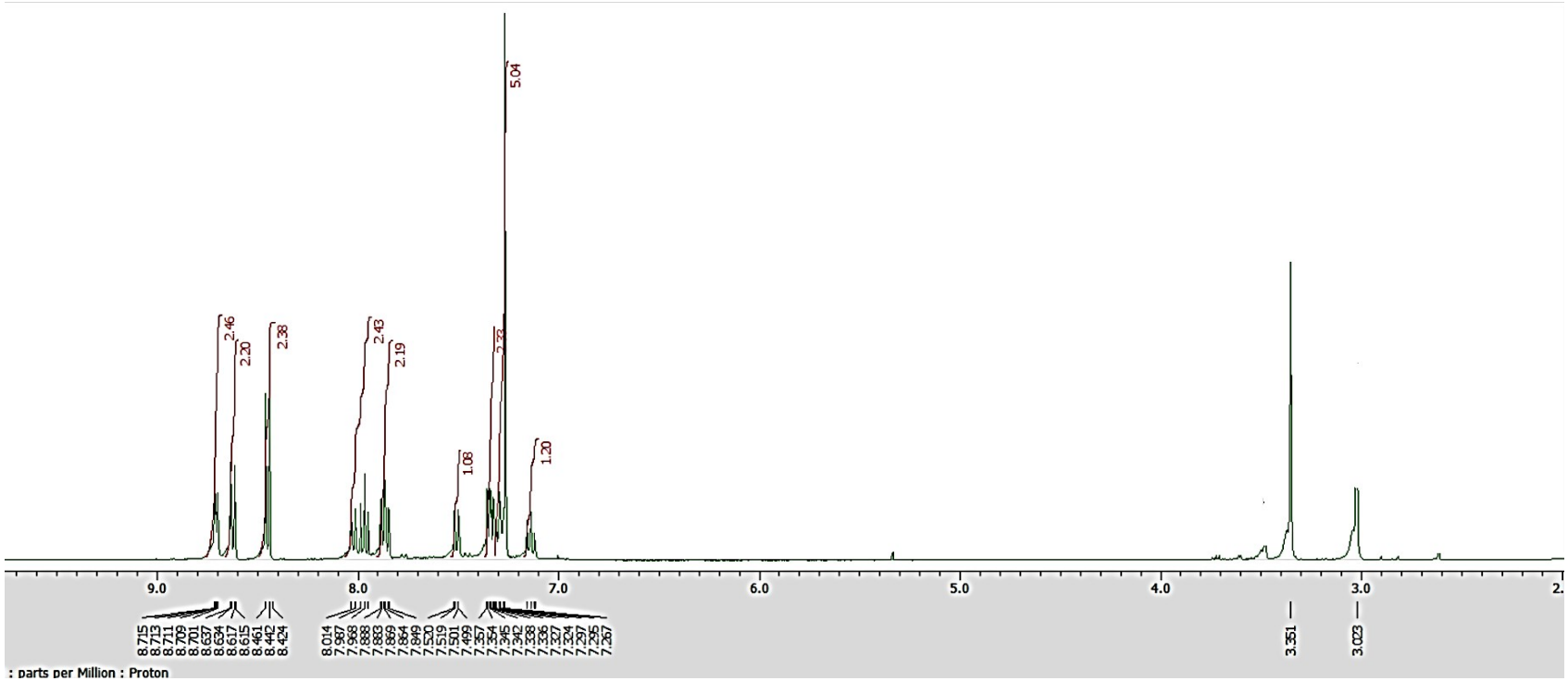
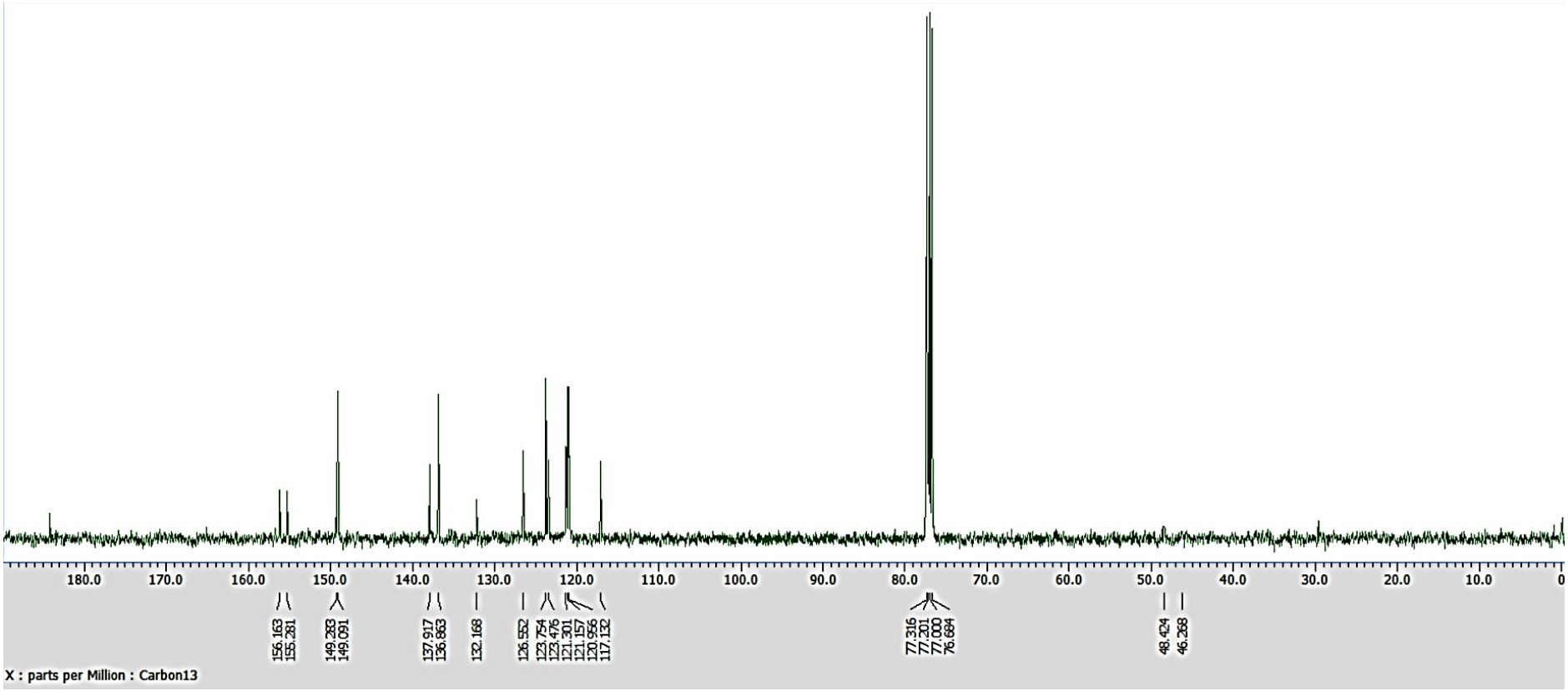


Fig. S7.^{1}H NMR spectrum of [Ru(η^2-N,S-mbtz)(η^1-S-mbtz)(tpy)] (**Ru4**) in $CDCl_3$ at 298K.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170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.163
155.281
149.283
149.091
137.917
136.863
132.168
126.552
123.754
123.476
121.301
121.157
120.956
117.132
77.316
77.301
77.000
76.684
48.424
46.288
X : parts per Million : Carbon13

Fig. S8.^{13}C NMR spectrum of [Ru(η^2-N,S-mbtz)(η^1-S-mbtz)(tpy)] (**Ru4**) in $CDCl_3$ at 298K.

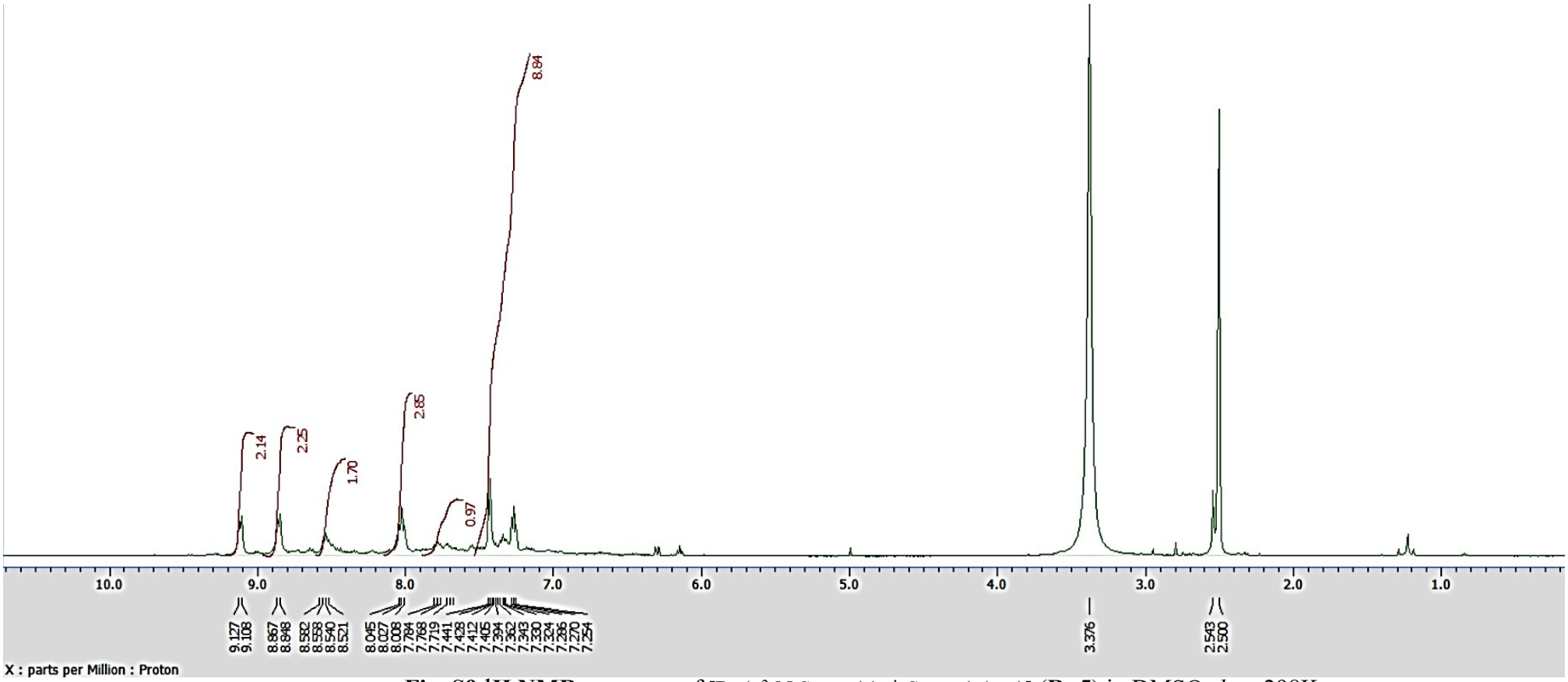


Fig. S9.^{1}H NMR spectrum of [Ru(η^2-N,S-mpy)(η^1-S-mpy) (tpy)] (**Ru5**) in DMSO-d_6 at 298K.

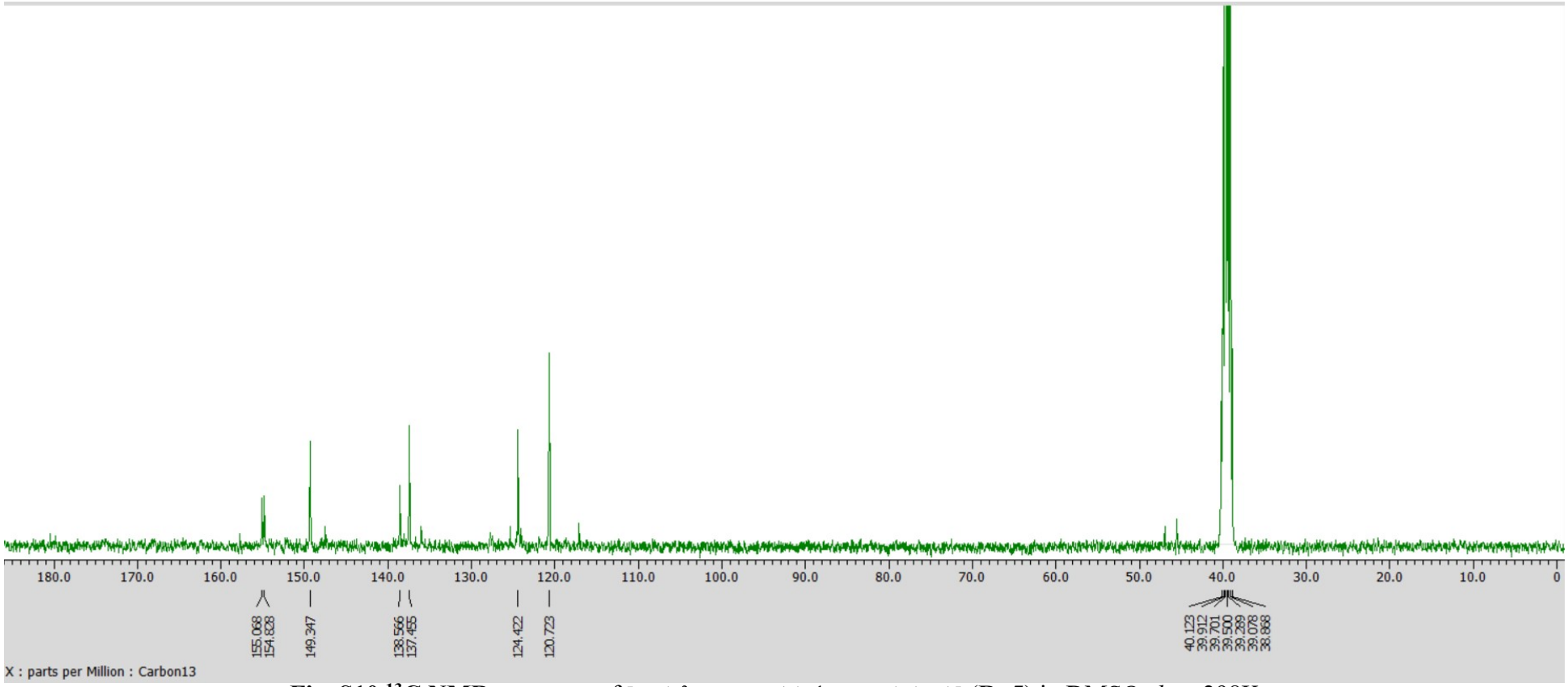


Fig. S10.^{13}C NMR spectrum of [Ru(η^2-N,S-mpy)(η^1-S-mpy) (tpy)] (**Ru5**) in DMSO-d_6 at 298K.

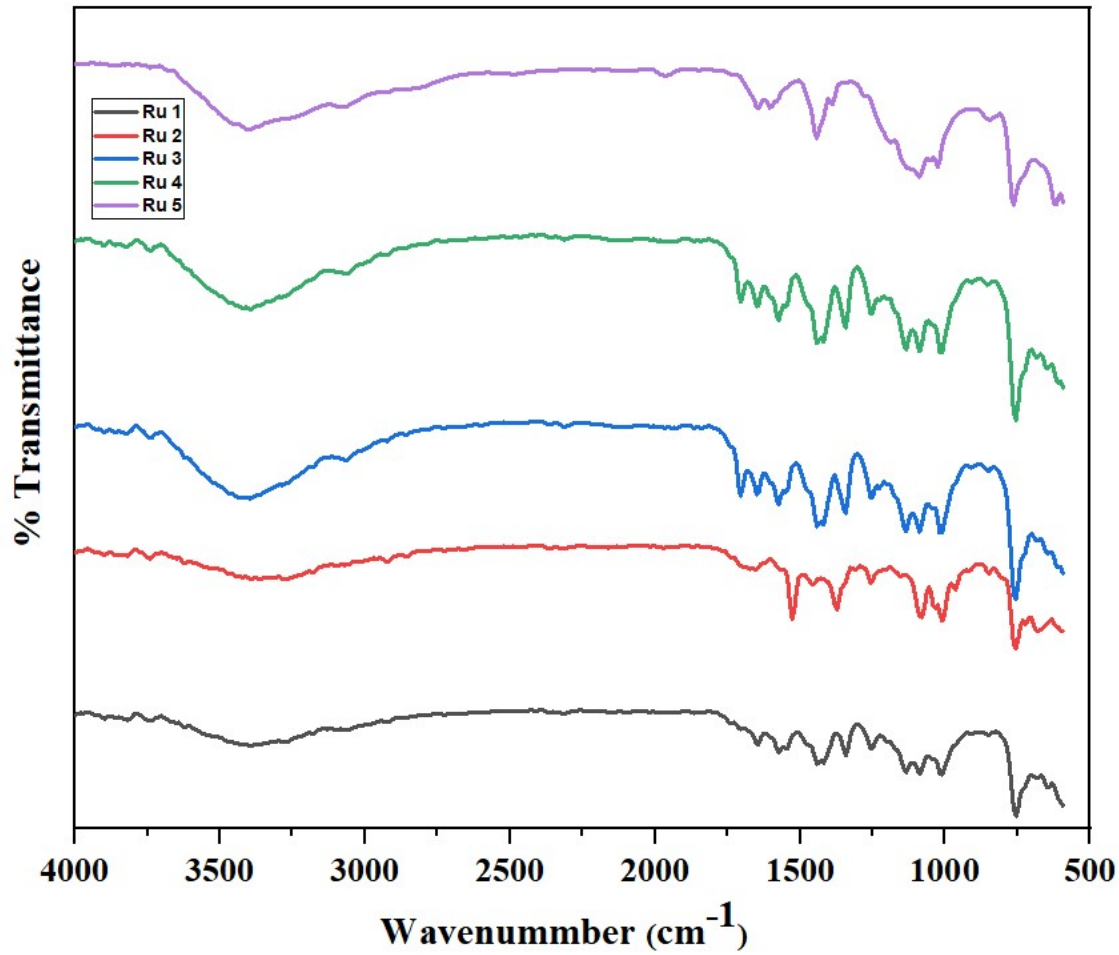


Fig. S11. IR spectrum of complexes **Ru1**-**Ru5** at 298K.

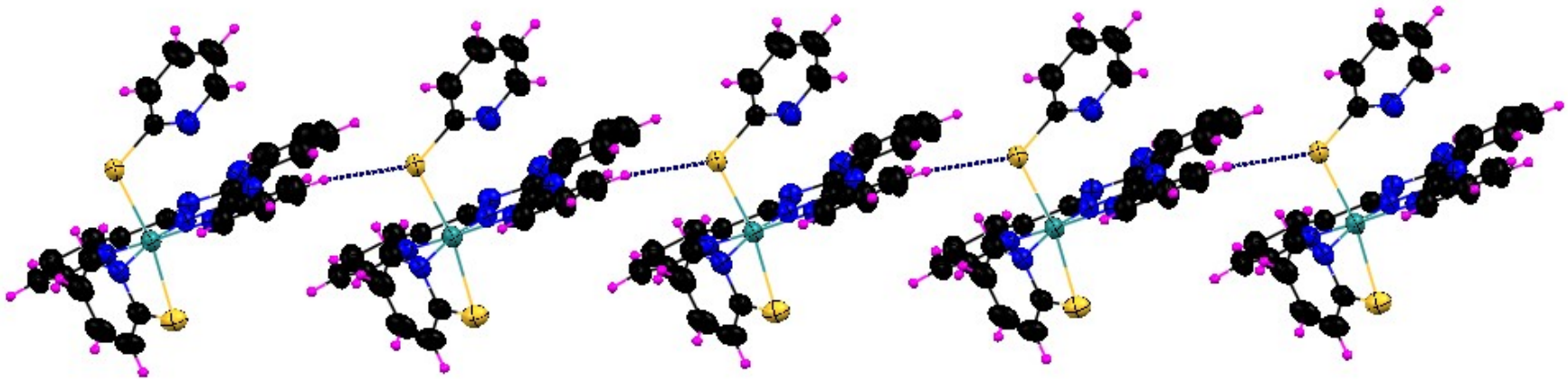


Fig. S12. Single helical motif in **Ru1** resulting from intermolecular C–H···S interactions.

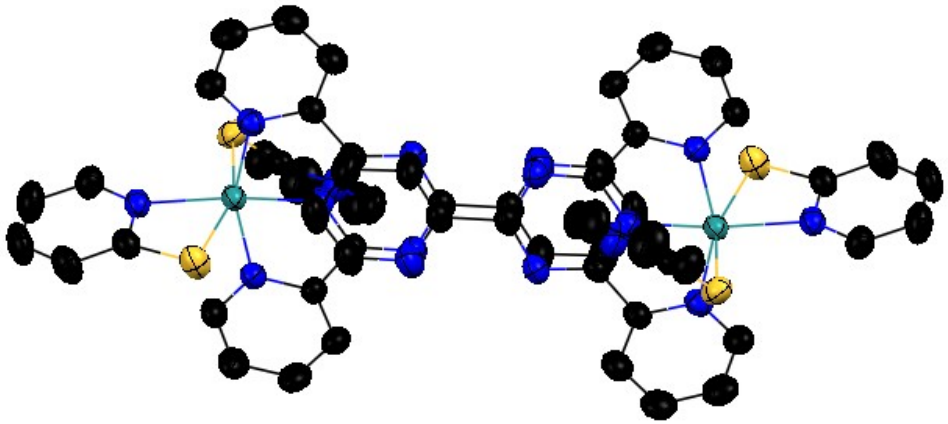
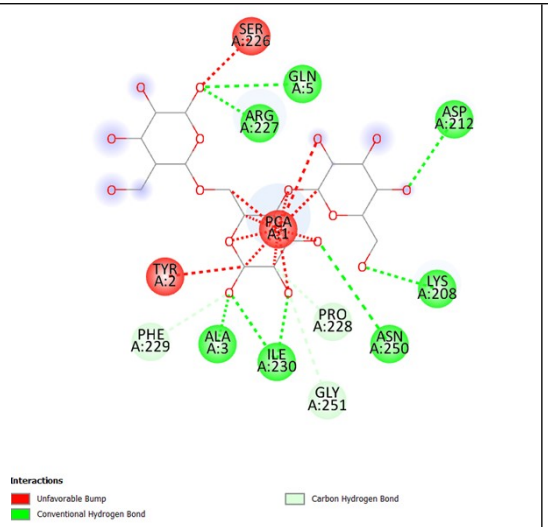
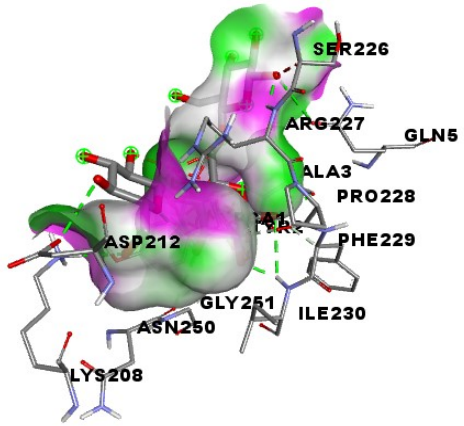
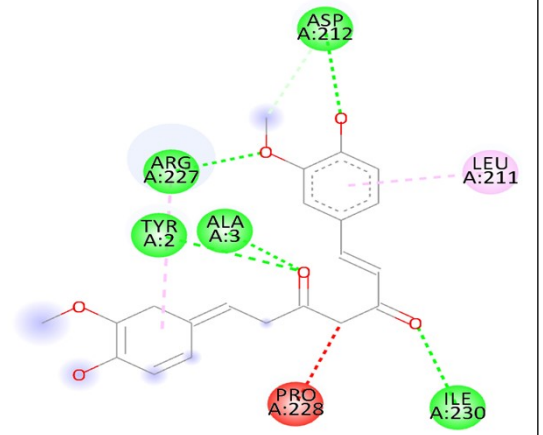
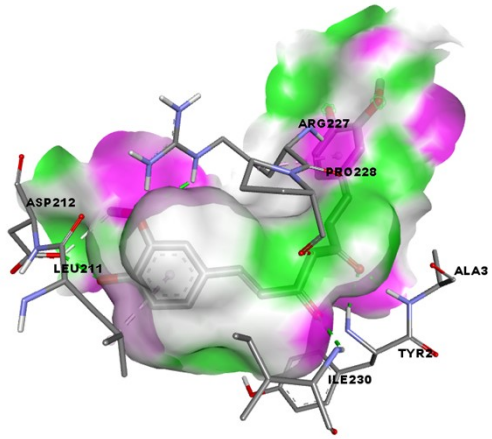
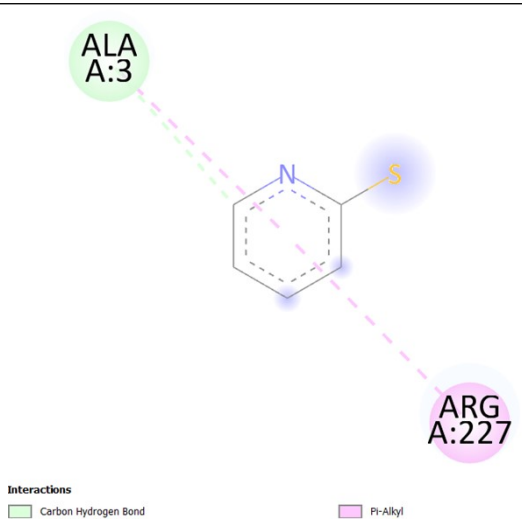
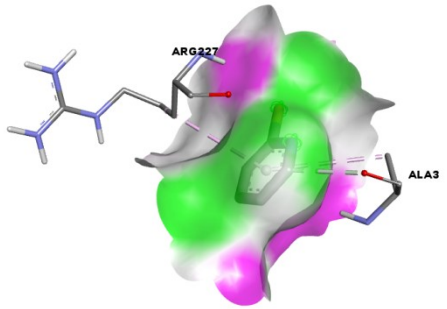
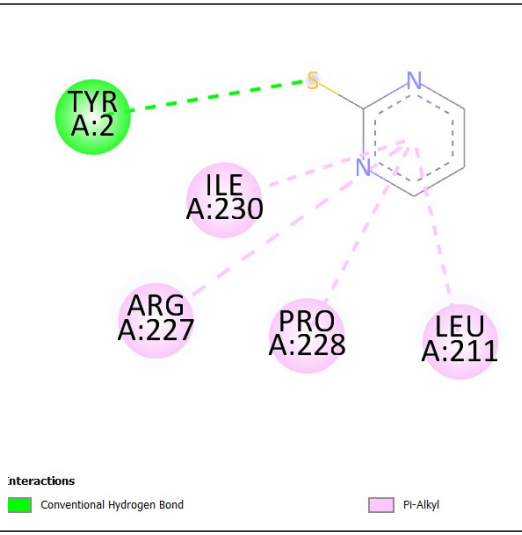
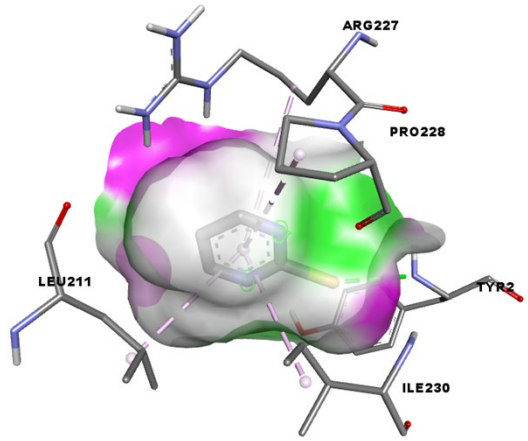


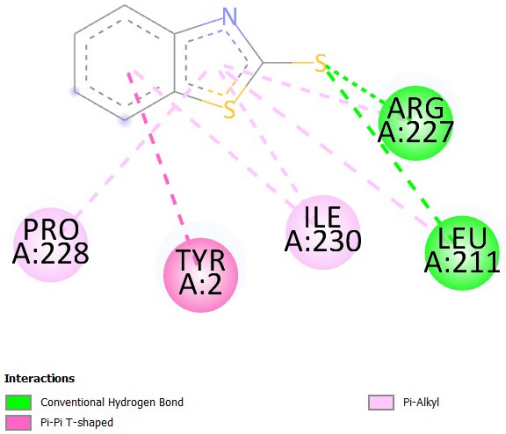
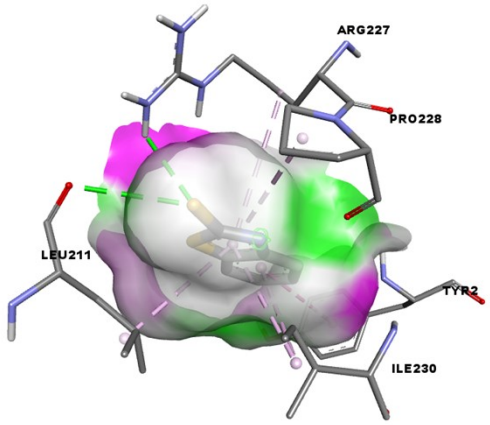
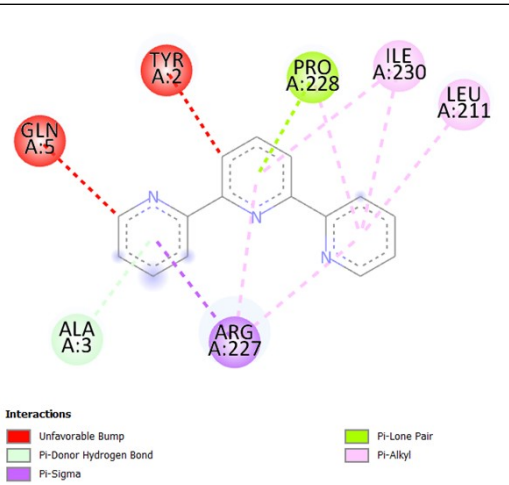
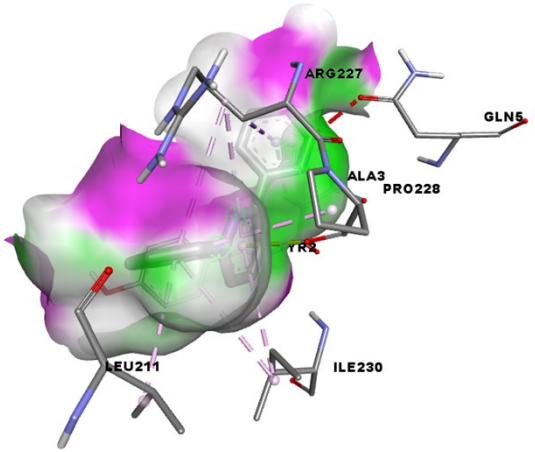
Fig. S13. Face to Face and Edge to Face π–π stacking interactions in **Ru1**.

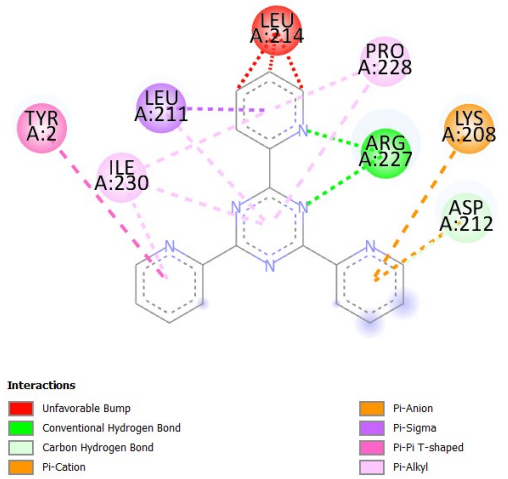
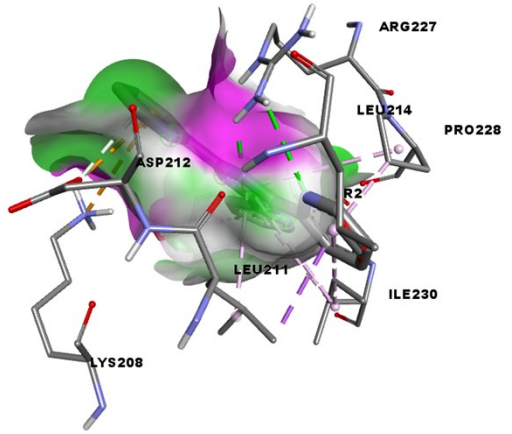
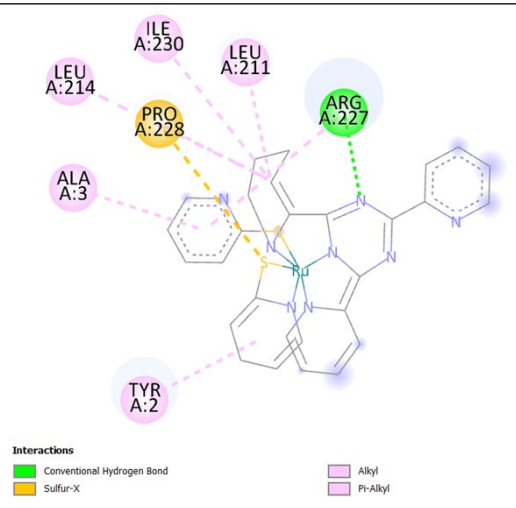
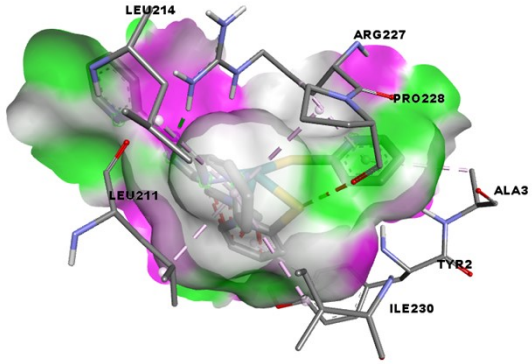
Table S1. Docking data of ligands and complexes with different enzymes.

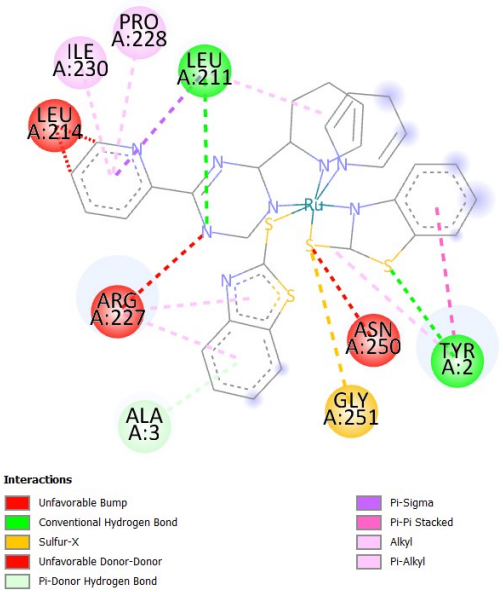
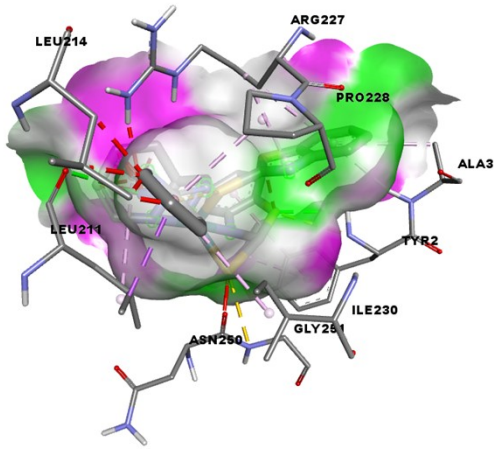
Ligand	Energy (Kcal/mol)			Total no. of interactions	No. of H-bonds	No. of Hydrophobic bonds	2D image	3D image
	Total	VDW	H- bond					
Amylase								

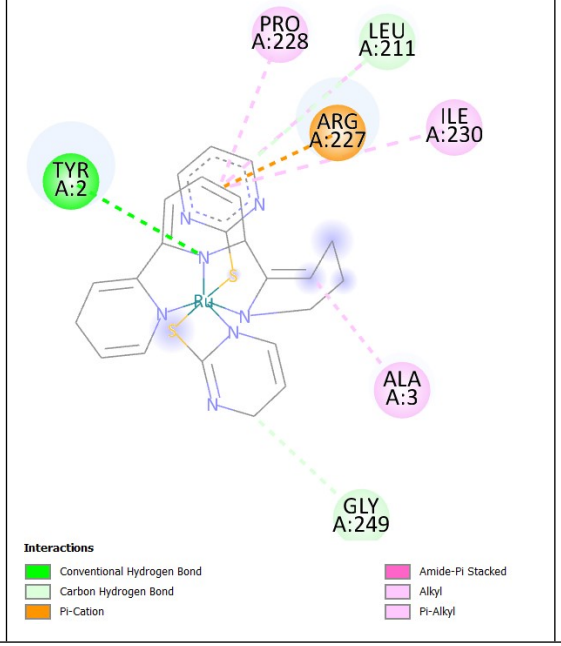
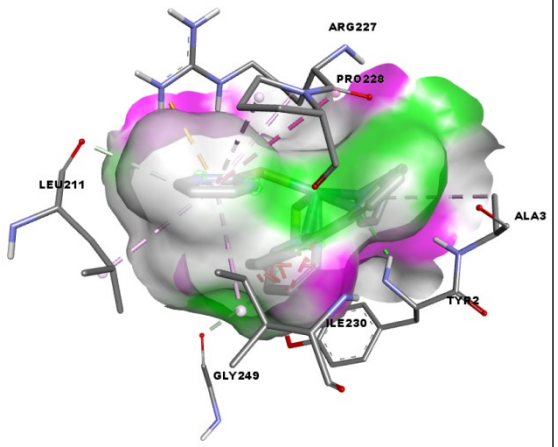
Starch	-103.978	-58.911	-45.066	12	12	0		
Curcumin	-95.3669	-71.4793	-23.8876	9	7	2		

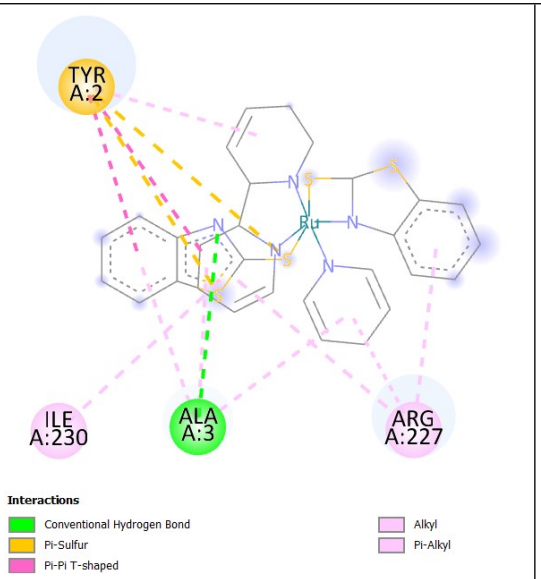
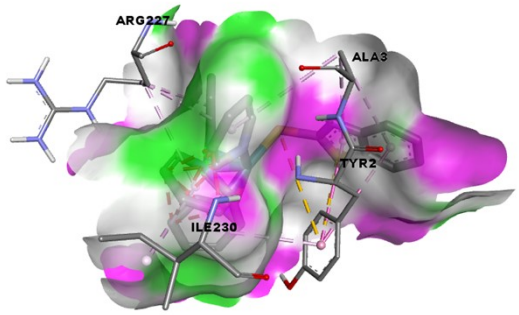
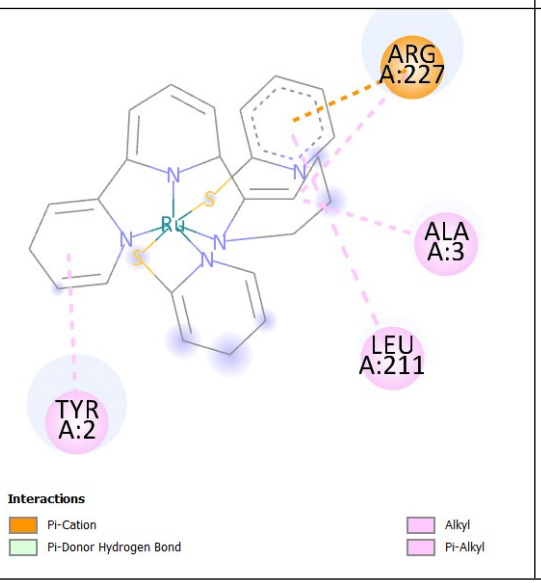
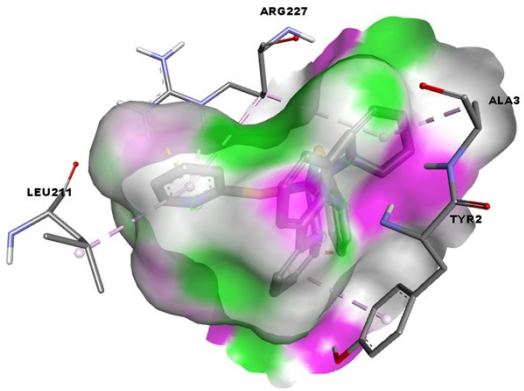
MPY	-41.5854	-31.1001	-10.4853	3	1	2		
MPT	-43.1972	-36.1972	-7	5	1	4		

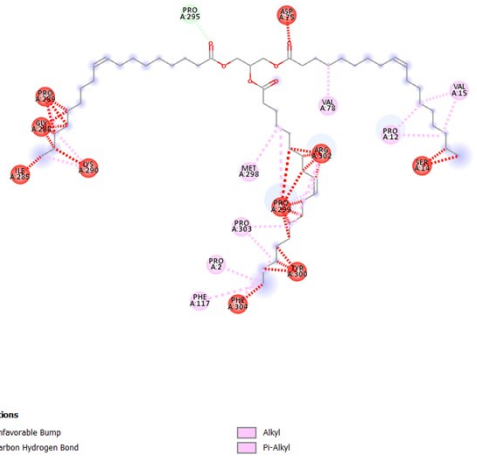
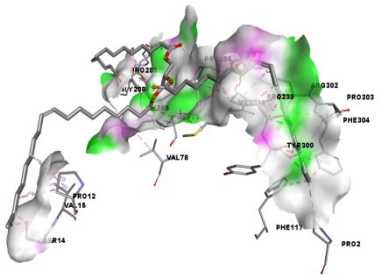
MBTZ	-49.5214	-46.0214	-3.5	8	2	6		
TPY	-82.9624	-67.3116	-15.6508	10	1	8		

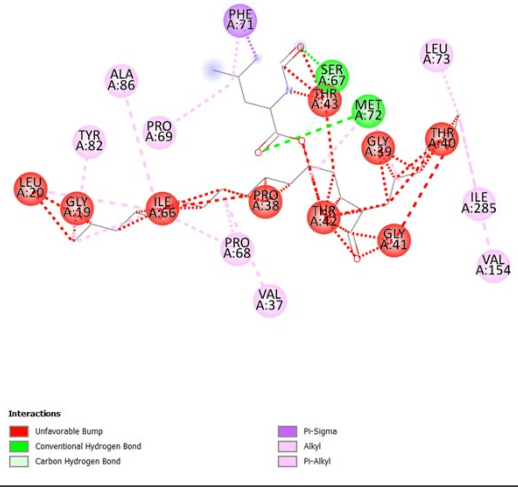
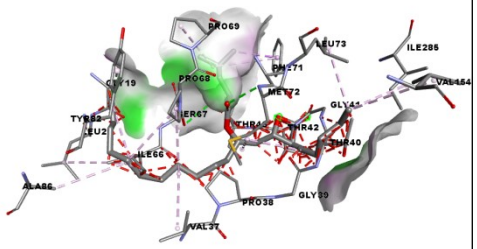
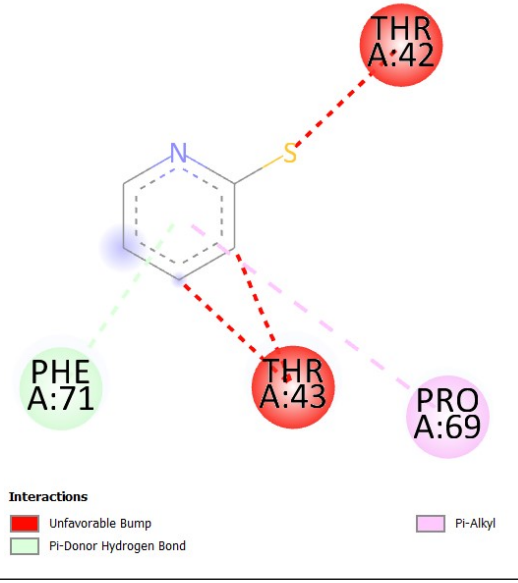
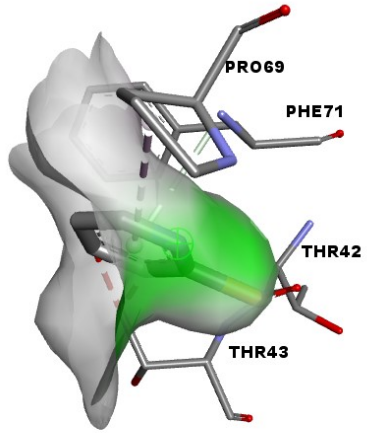
TPTZ	-99.9655	-81.7204	-18.2451	13	3	8		
Ru1	-112.995	-105.457	-7.53777	9	1	7		

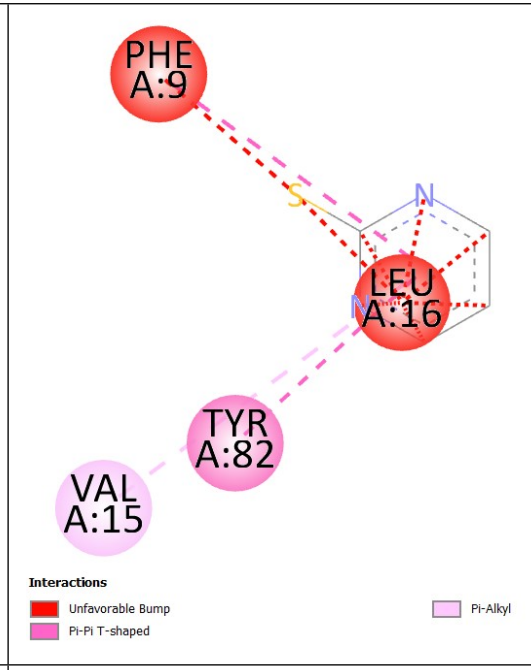
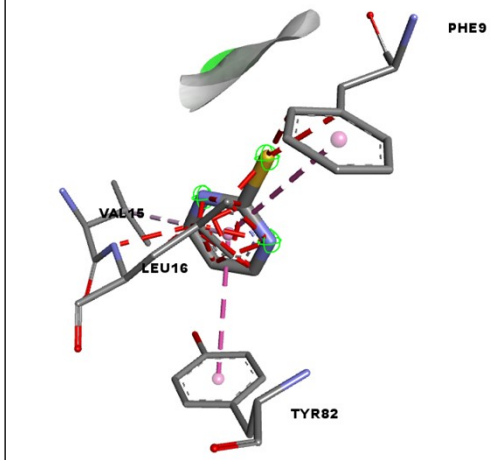
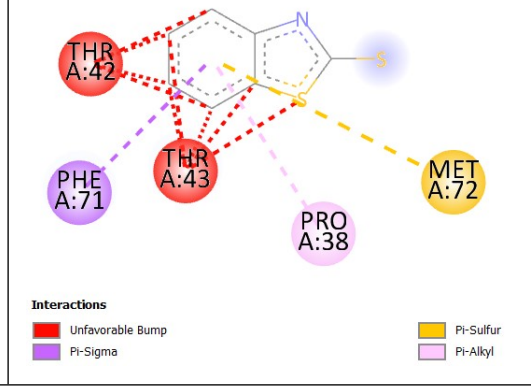
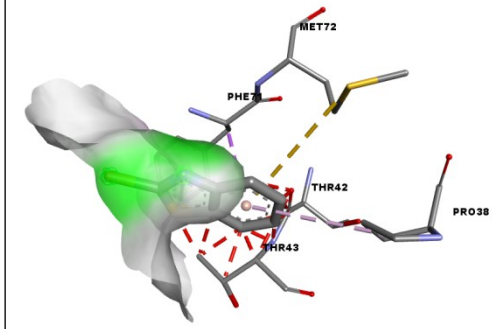
Ru2	-111.032	-97.0934	-13.9381	15	2	10		

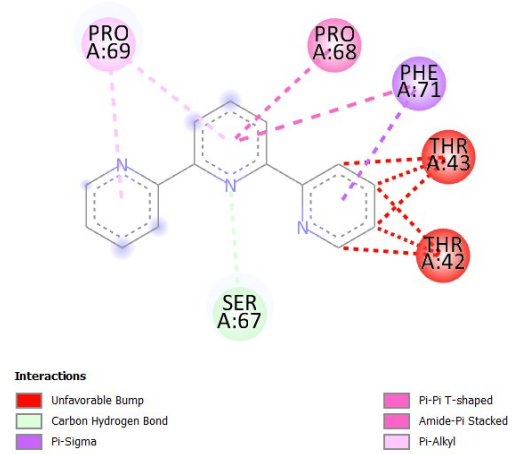
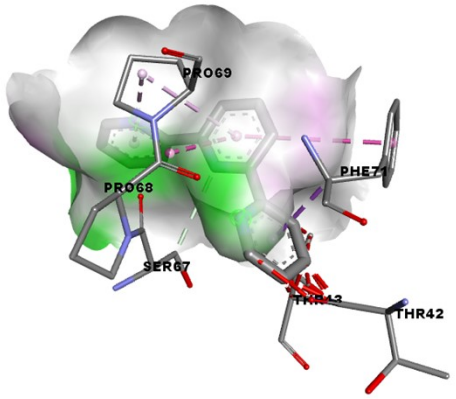
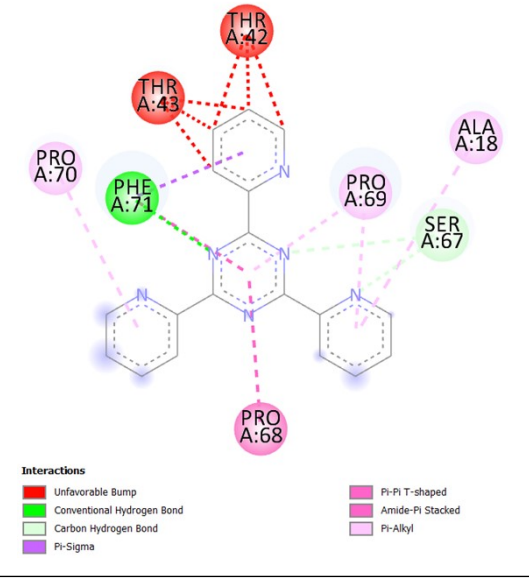
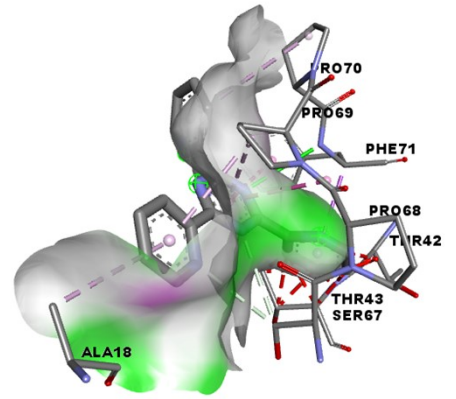
Ru3	-104.377	-95.0537	-9.32352	10	3	7		

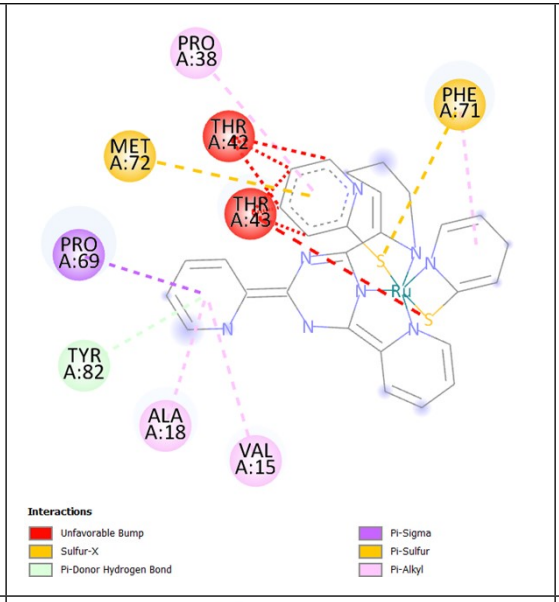
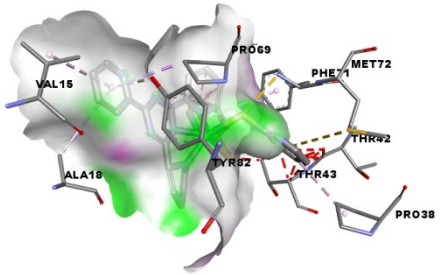
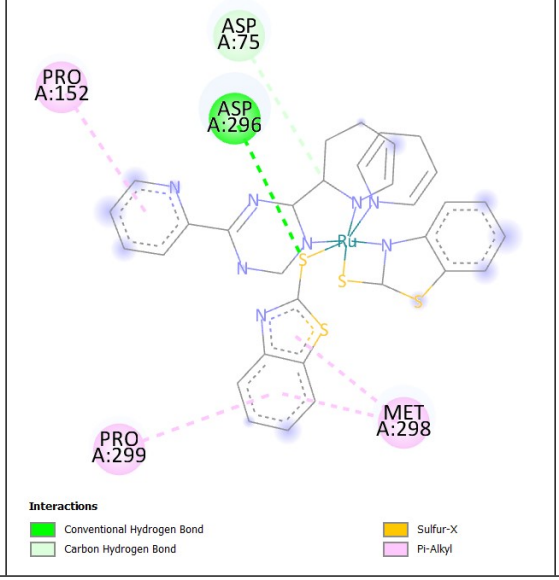
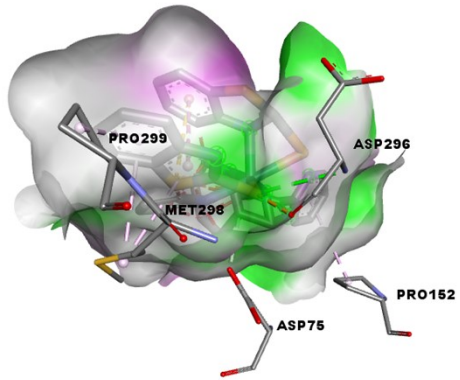
Ru4	-101.462	-98.962	-2.5	13	1	10		
Ru5	-93.6391	-91.1391	-2.5	7	2	5		

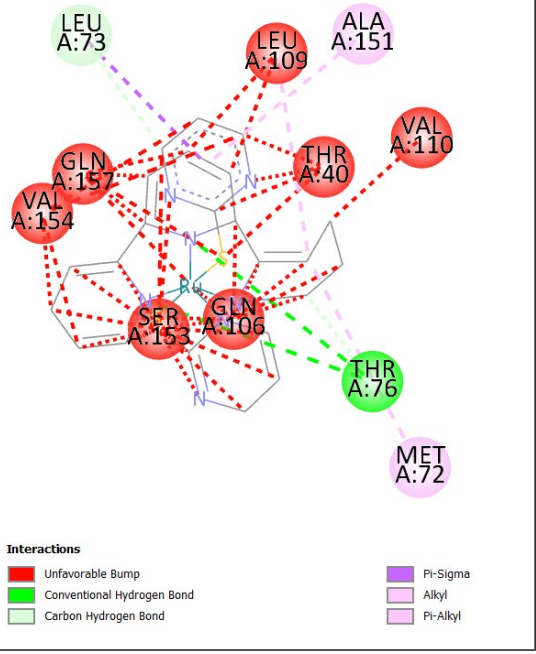
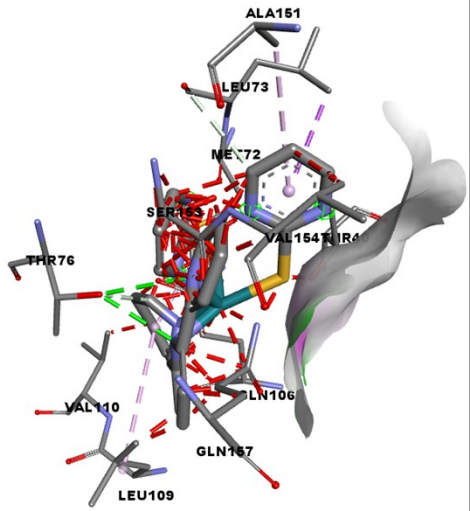
Ligand	Energy (Kcal/mol)			Total no. of interactions	No. of H-bonds	No. of Hydrophobic bonds	2D image	3D image
	Total	VDW	H- bond					
Lipase								
Olive oil	-79.737	-56.107	-23.629	21	1	20		

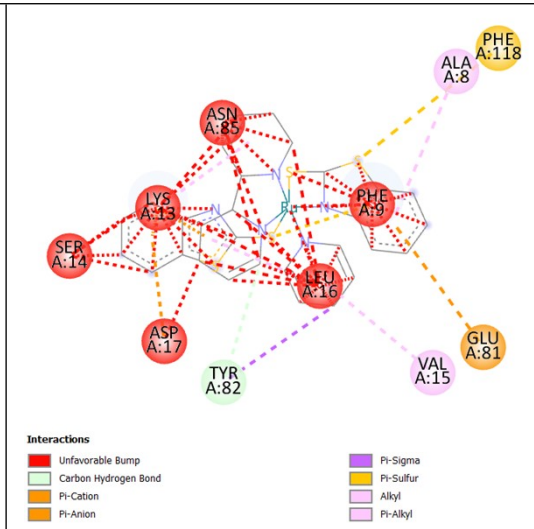
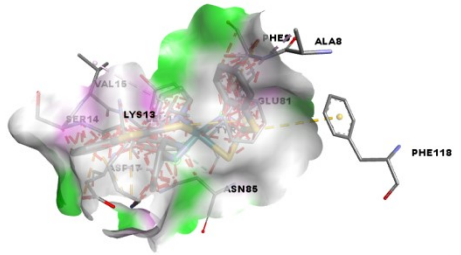
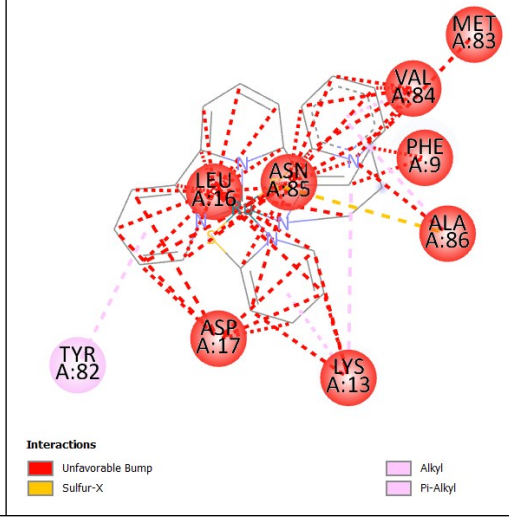
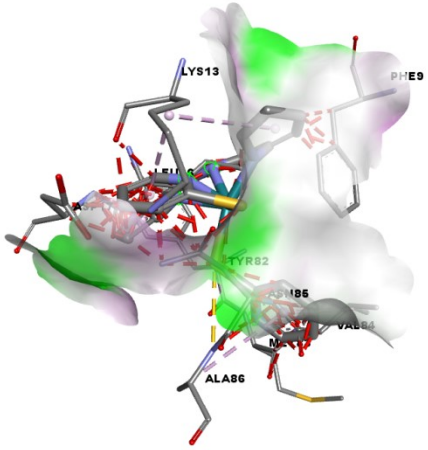
Orlistat	-85.796	-63.415	-22.380	18	3	15		
MPY	-45.3098	-38.3098	-7	2	1	1		

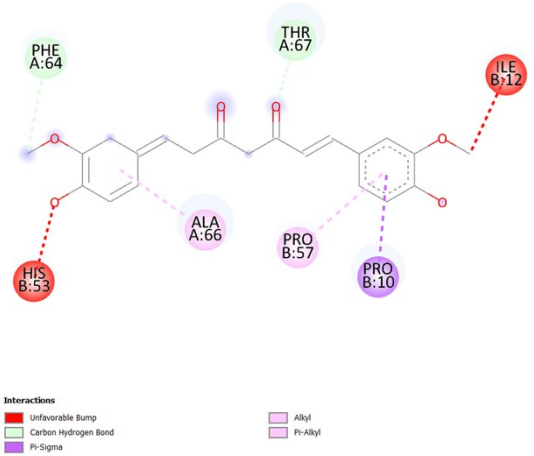
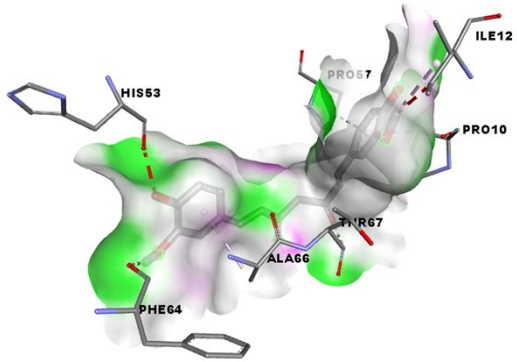
MPT	-45.2622	-35.9828	-9.27941	3	0	3		
MBTZ	-57.3685	-51.0175	-6.35096	3	0	2		

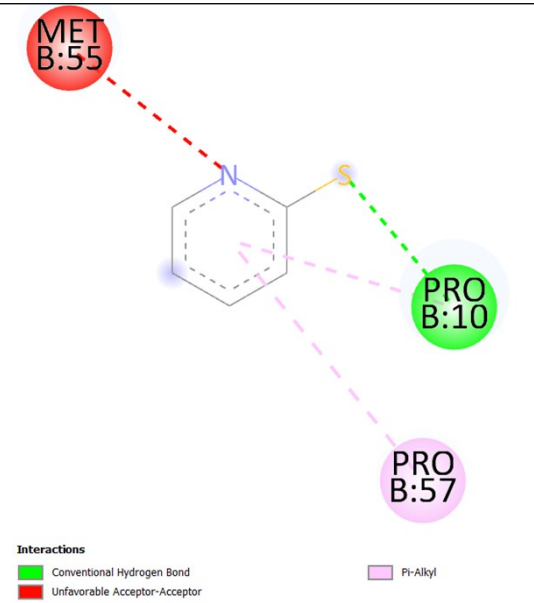
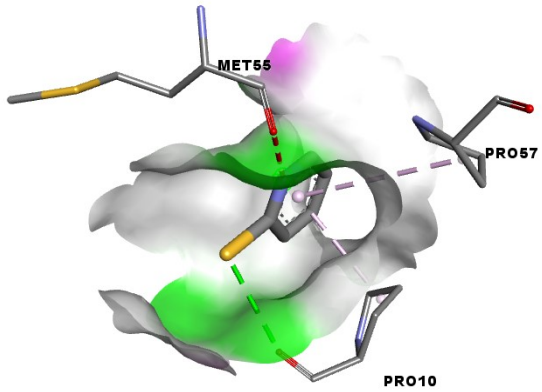
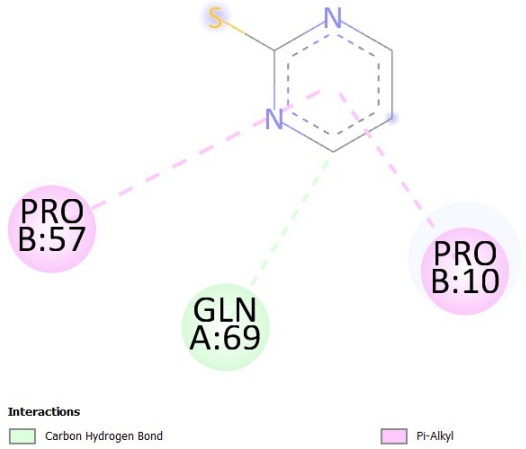
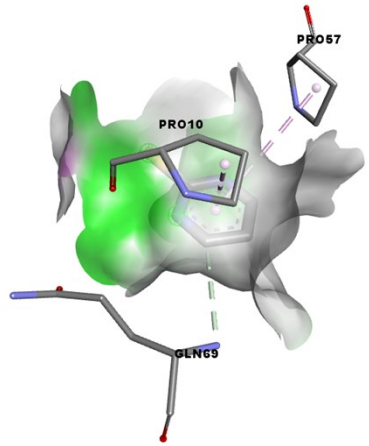
TPY	-82.3868	-70.8311	-11.55	6	1	5		
TPTZ	-98.8317	-87.5853	-11.2464	10	3	7		

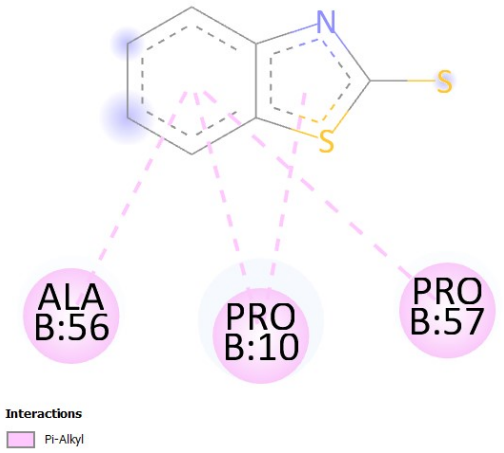
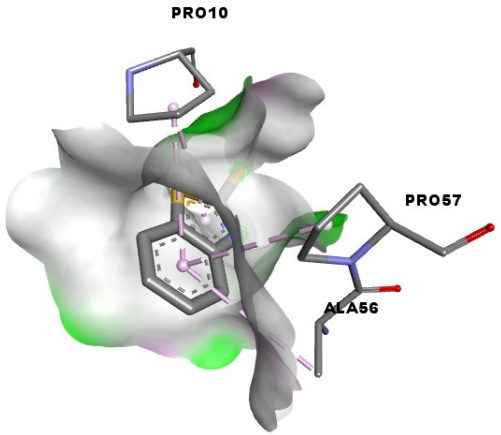
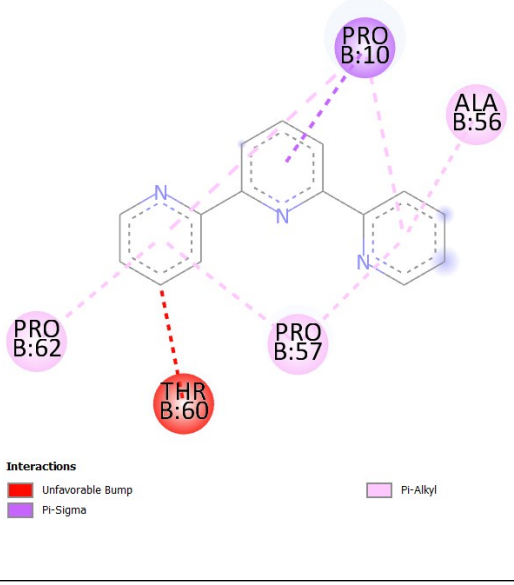
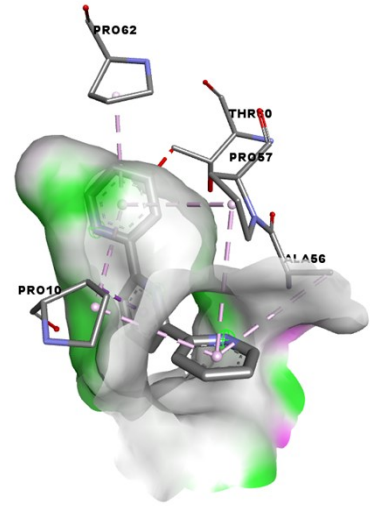
Ru1	-92.5807	-88.849	-3.73155	8	1	5		
Ru2	-96.2066	-83.0782	-13.1284	9	2	5		

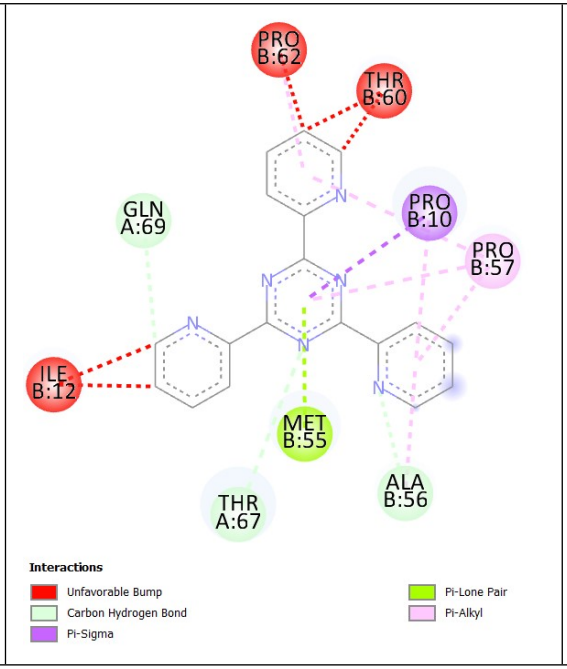
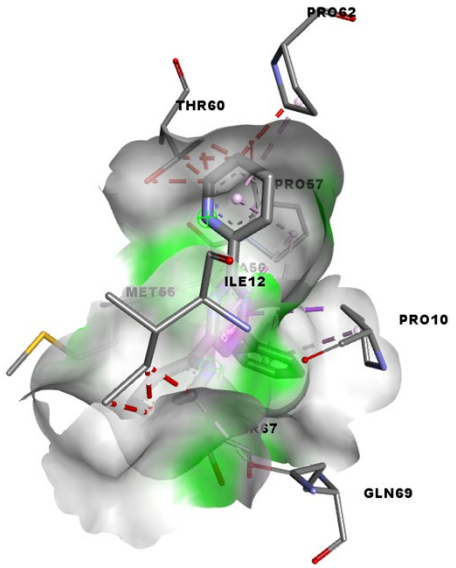
Ru3	-84.3377	-65.2409	-19.0968	8	4	4		

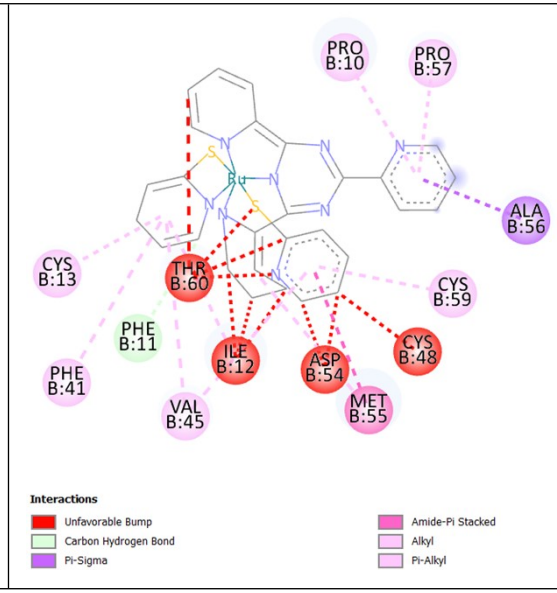
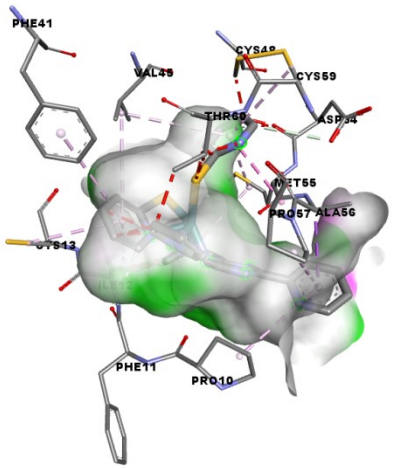
Ru4	-88.1961	-85.8076	-2.38855	13	3	5		
Ru5	-80.9755	-73.99	-6.98552	6	0	5		

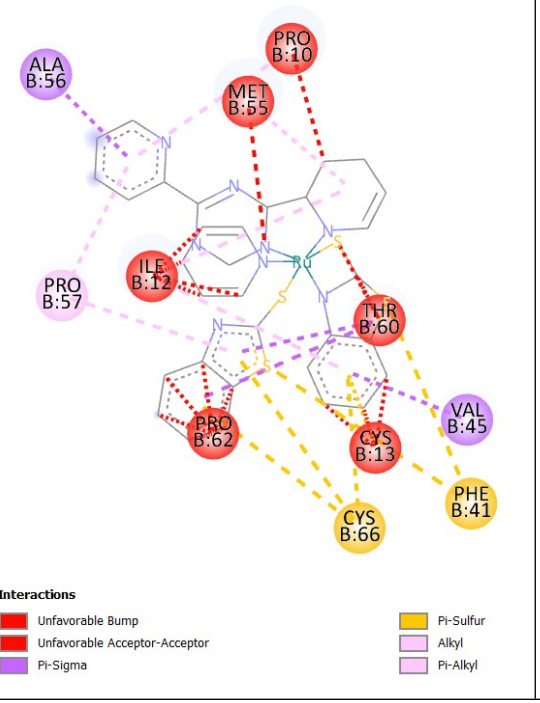
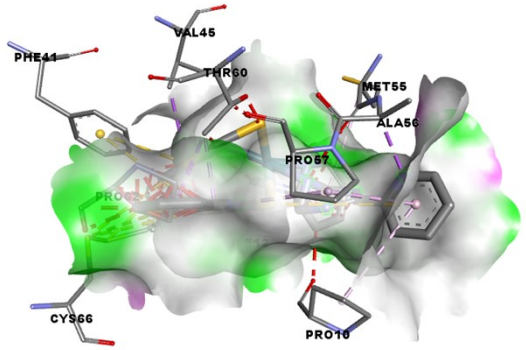
Ligand	Energy (Kcal /mol)			Total no. of interactions	No. of H-bonds	No. of Hydrophobic bonds	2D image	3D image
	Total	VDW	H- bond					
Pepsin								
Curcumin	-98.564	-75.434	-23.129	5	3	2		

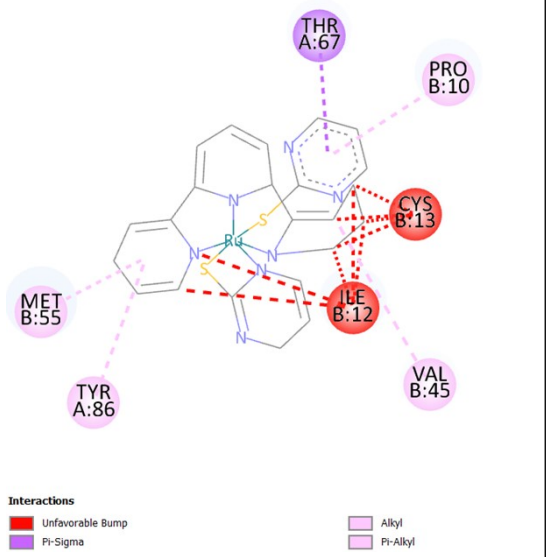
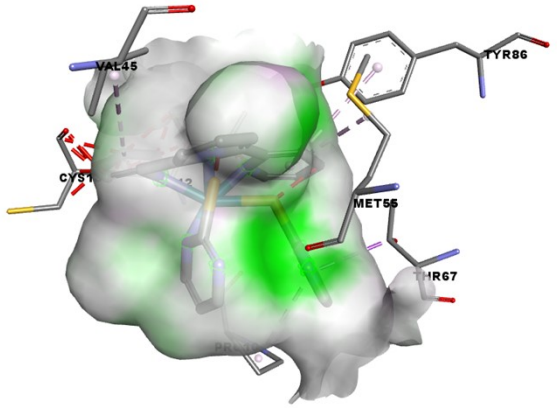
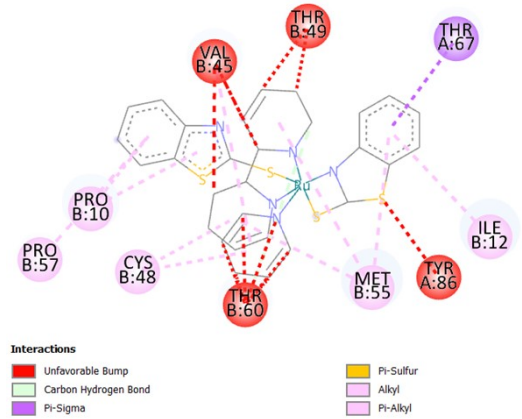
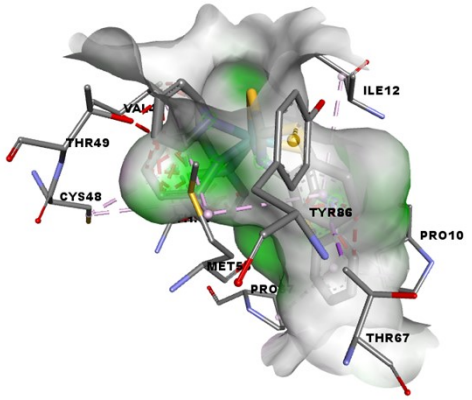
MPY	-40.9173	-37.4173	-3.5	3	1	2		
MPT	-44.8596	-37.8596	-7	3	1	2		

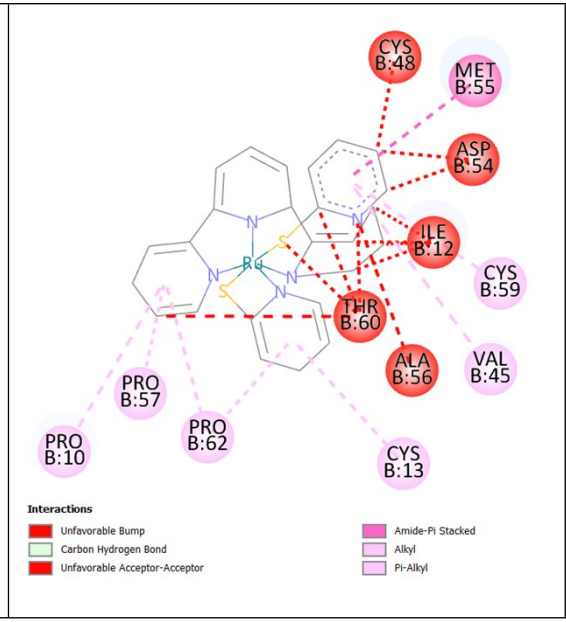
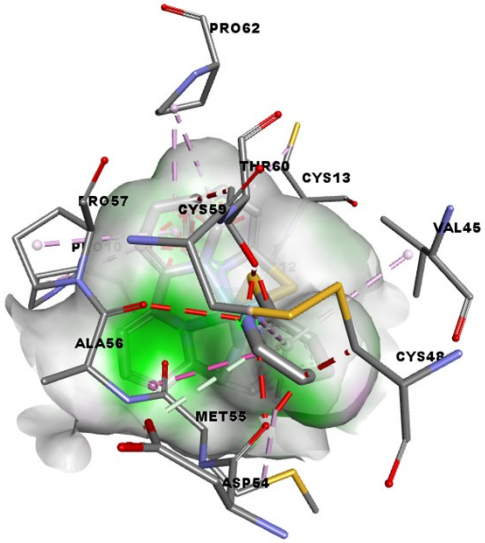
MBTZ	-52.1587	-48.6587	-3.5	4	0	4		
TPY	-85.0769	-74.7123	-10.364	7	0	7		

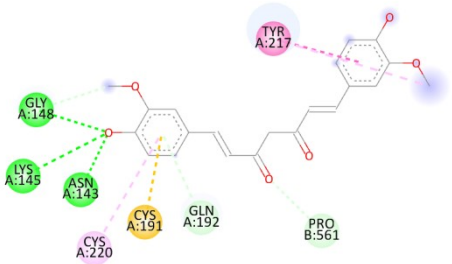
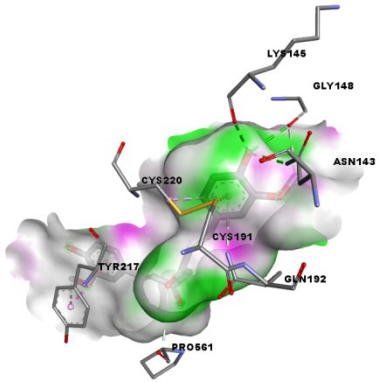
TPTZ	-105.317	-82.0323	-23.2849	11	3	7		

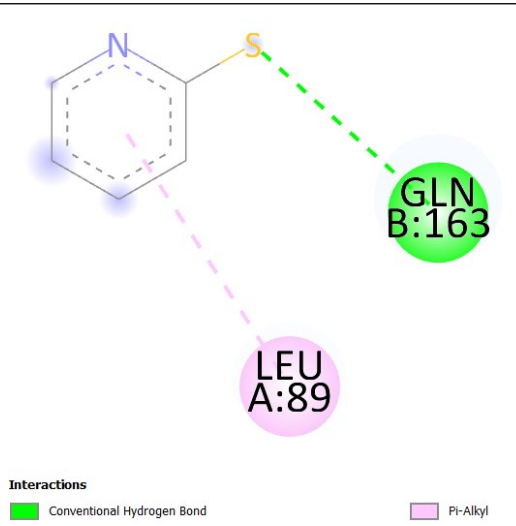
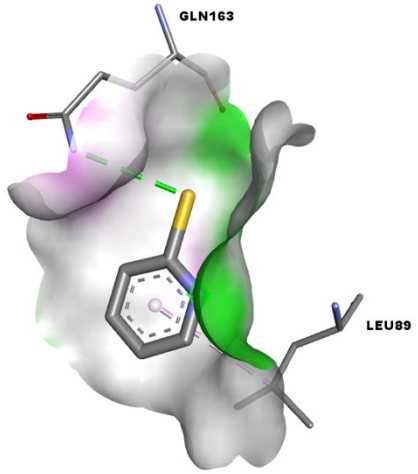
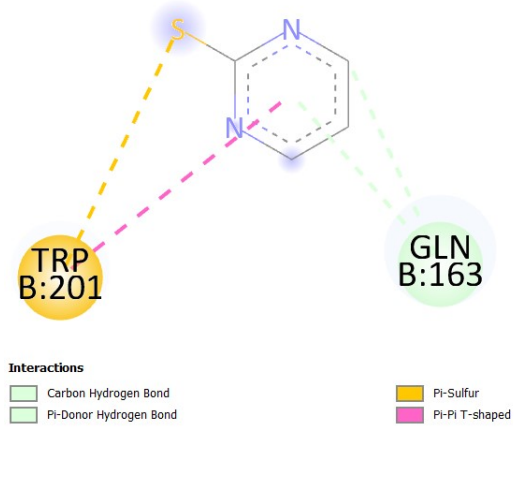
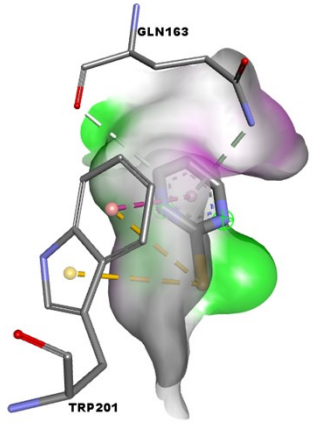
Ru1	-113.912	-101.548	-12.3644	14	2	12		

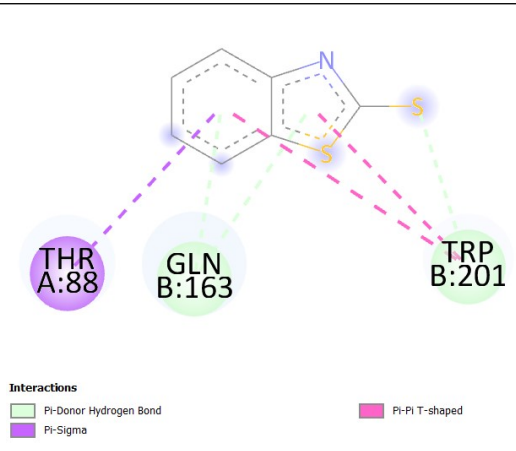
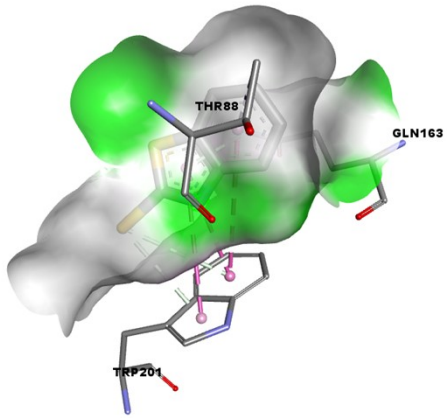
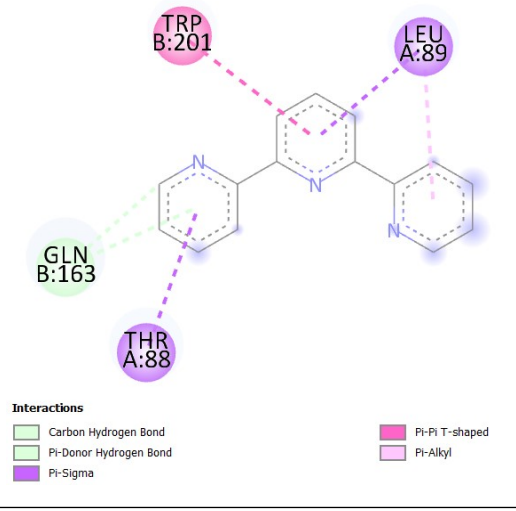
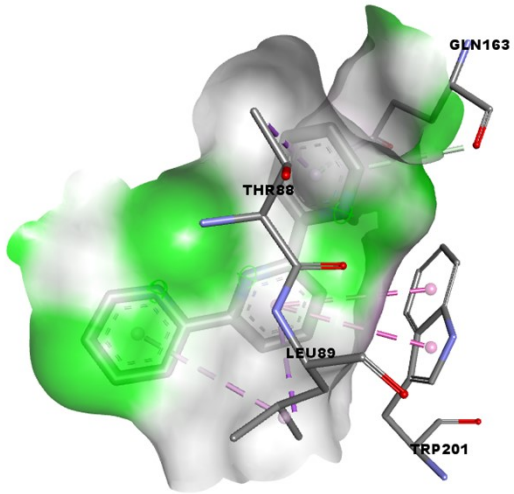
Ru2	-106.213	-92.5386	-13.6746	17	0	10		

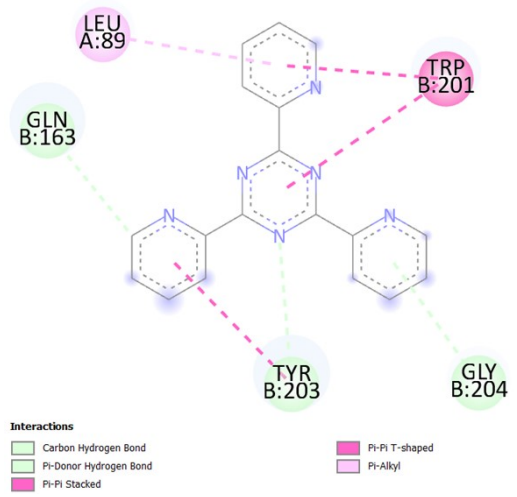
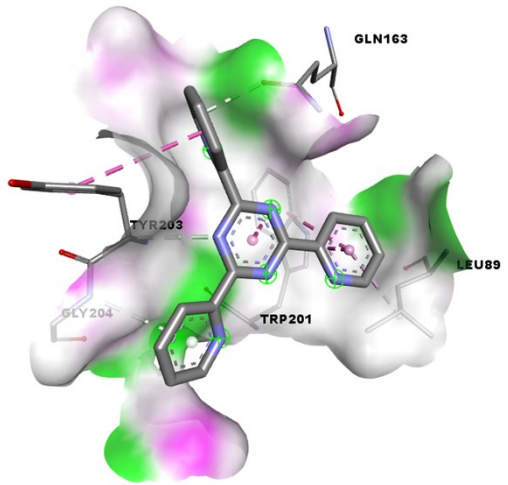
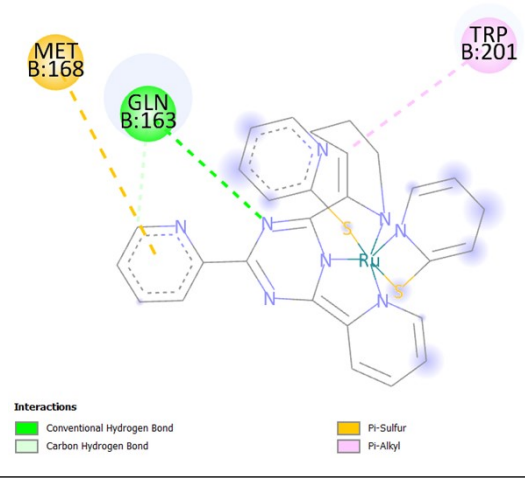
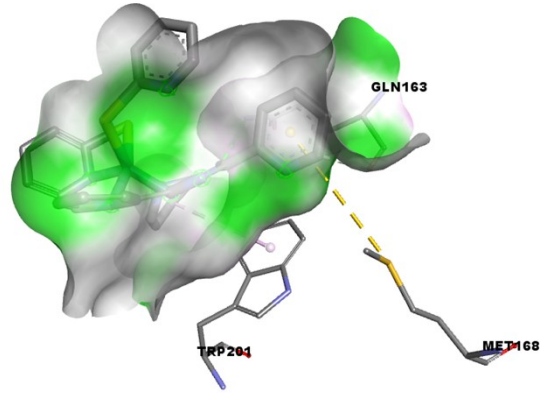
Ru3	-90.9276	-78.7789	-12.1487	5	0	5		
Ru4	-88.998	-85.498	-3.5	13	0	13		

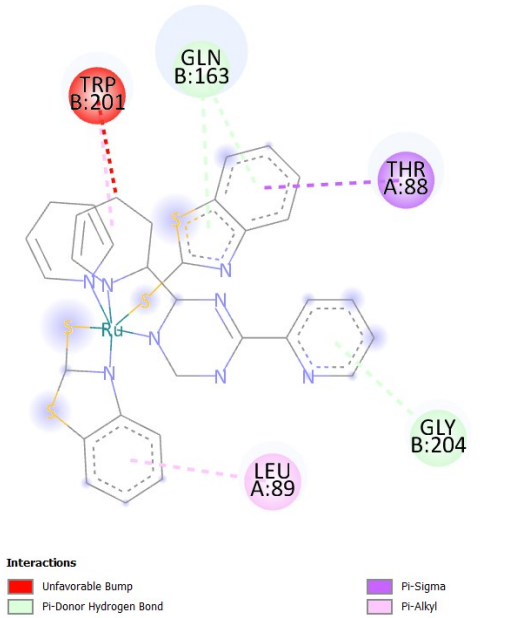
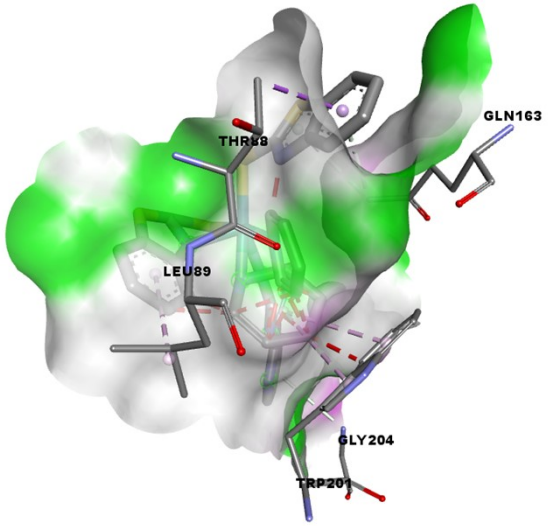
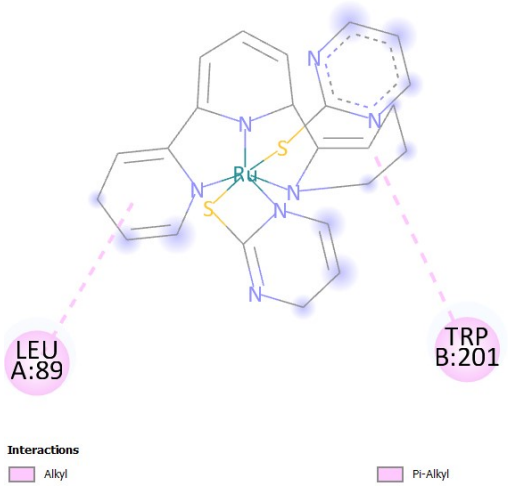
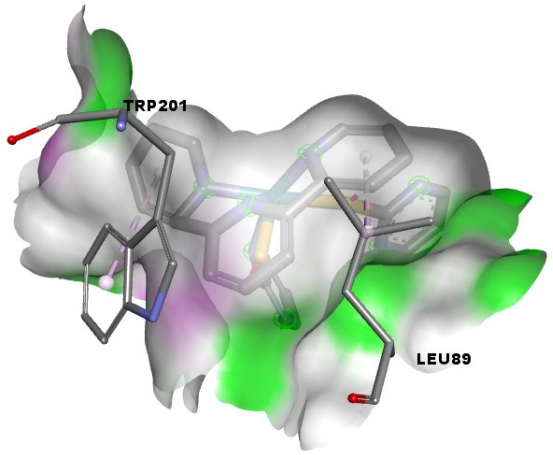
Ru5	-87.0109	-80.9652	-6.04571	10	1	9		

Ligand	Energy (Kcal/mol)			Total no. of interactions	No. of H-bonds	No. of Hydrophobic bonds	2D image	3D image
	Total	VDW	H- bond					
Trypsin								
Curcumin	-106.636	-86.6059	-20.03	6	5	1		

MPY	-43.4387	-36.4387	-7	2	1	1		
MPT	-44.3987	-37.3996	-6.9991	5	2	1		

MBTZ	-53.2579	-49.7579	-3.5	8	4	4		
TPY	-86.0795	-75.5795	-10.5	7	2	5		

TPTZ	-97.4857	-85.6194	-11.8663	8	3	5		
Ru1	-99.1708	-82.9575	-16.2133	4	2	1		

Ru2	-109.9	-104.454	-5.44594	7	3	4		
Ru3	-92.8516	-85.0167	-7.83485	2	0	2		

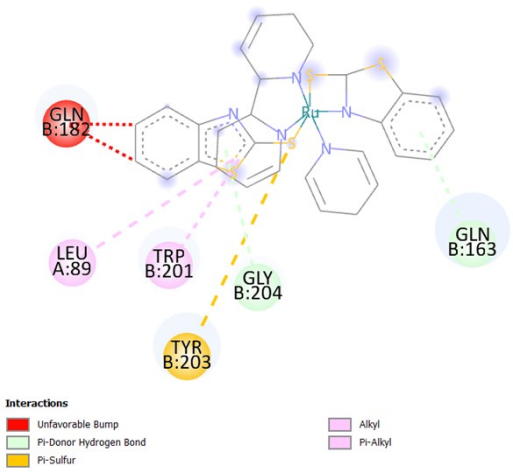
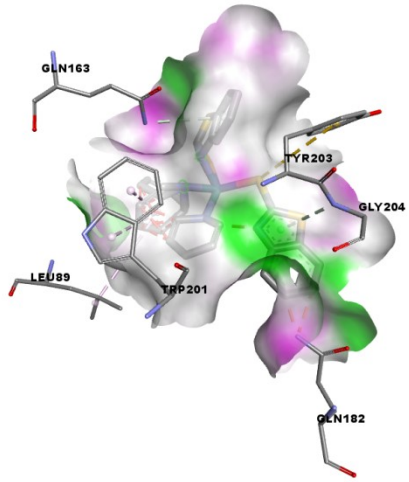
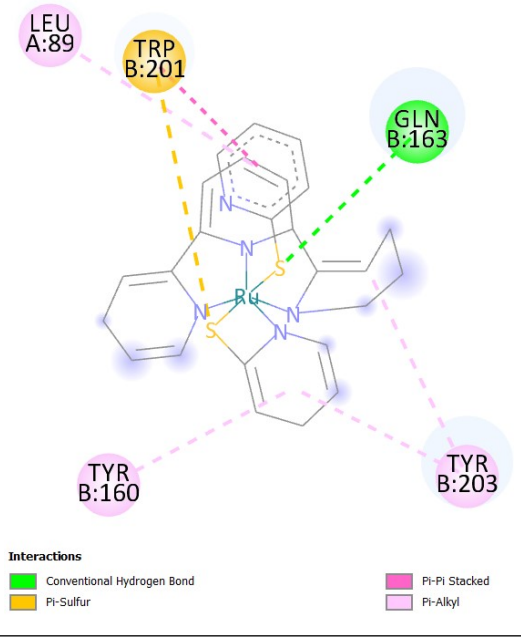
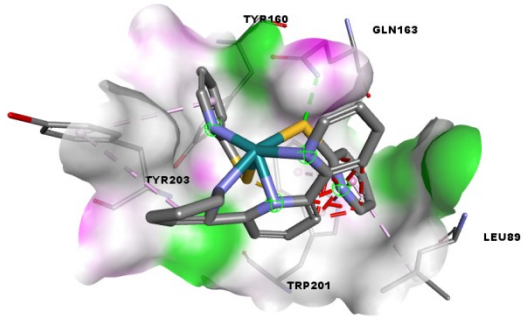
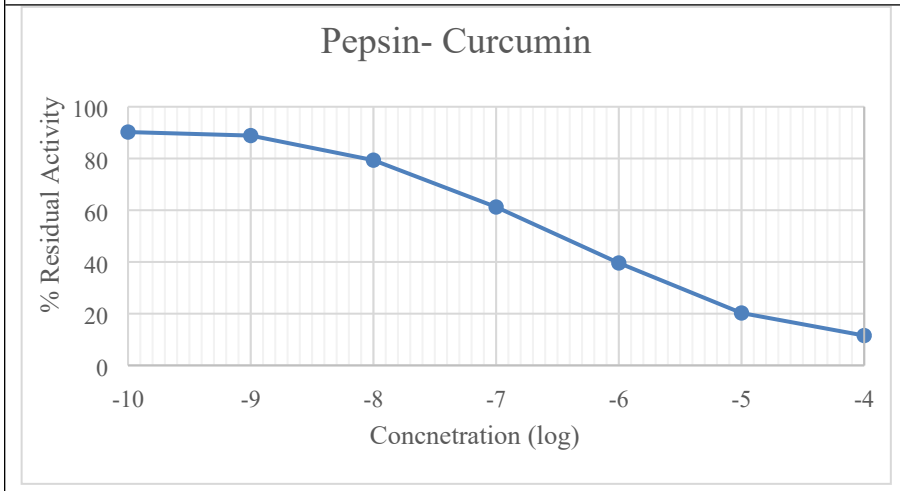
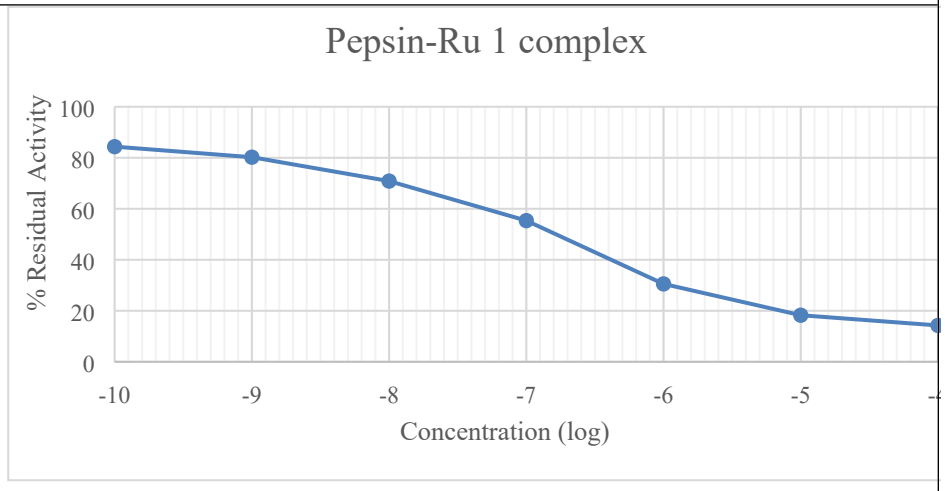
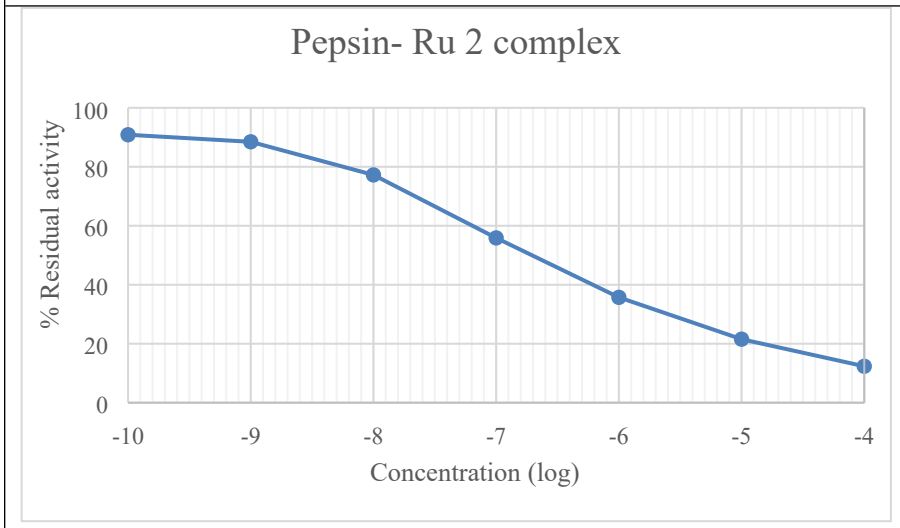
Ru4	-93.3025	-87.8408	-5.46175	6	2	3		
Ru5	-84.4582	-84.4582	0	8	1	6		

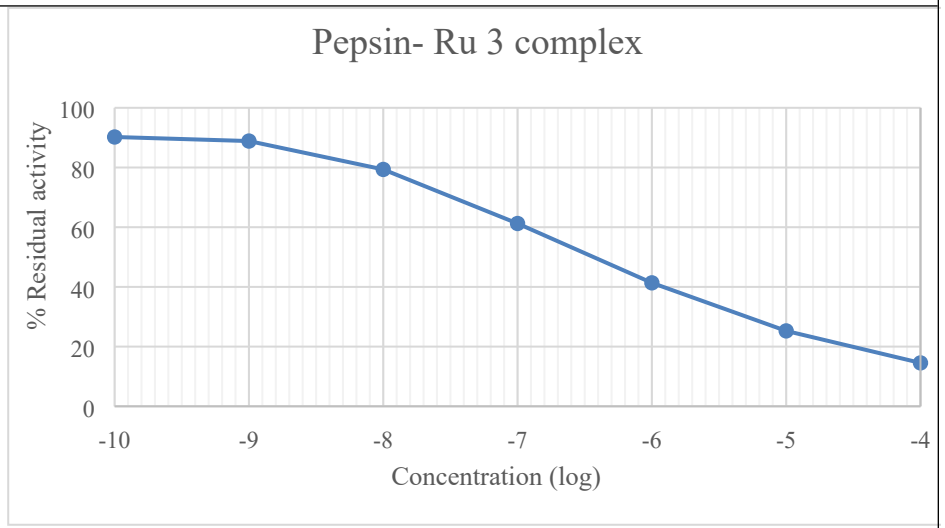
Table S2. IC_{50} curves of Ru-based complexes and different ligands for the enzyme pepsin, trypsin and lipase.

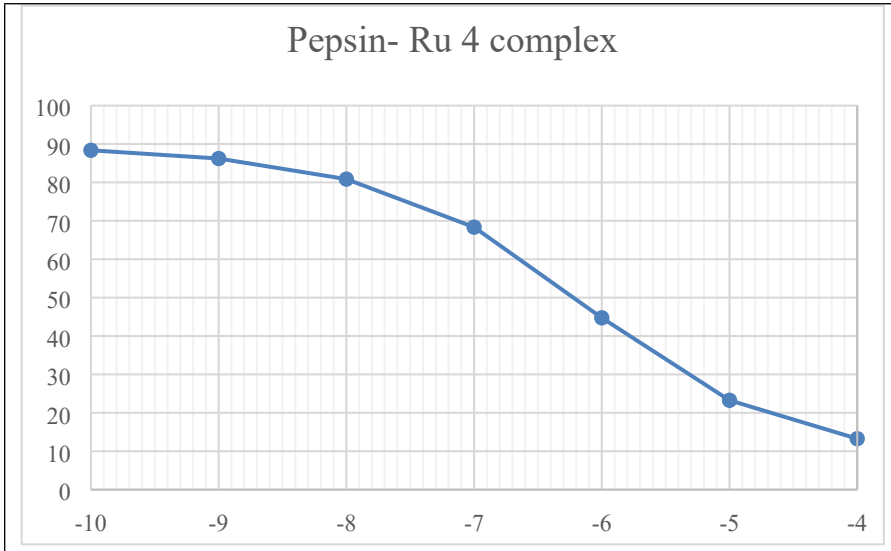
Pepsin

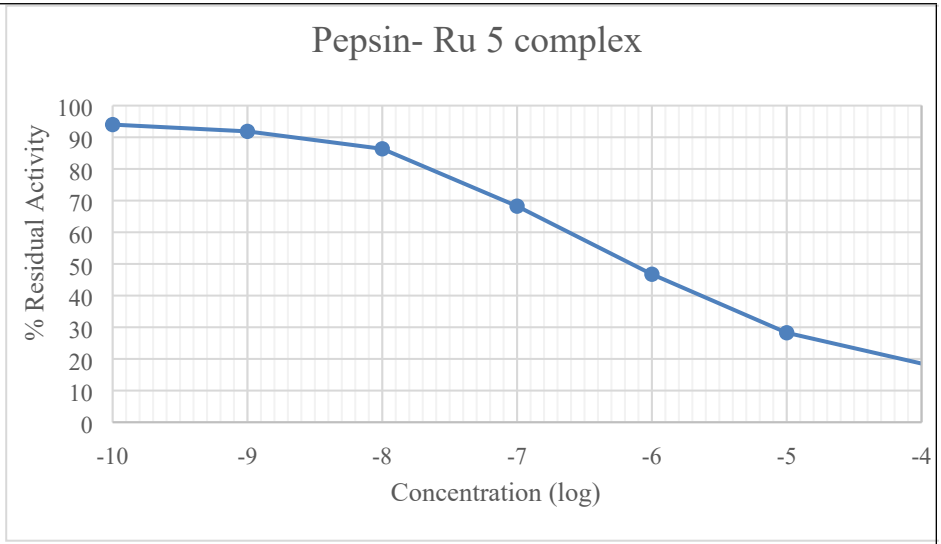


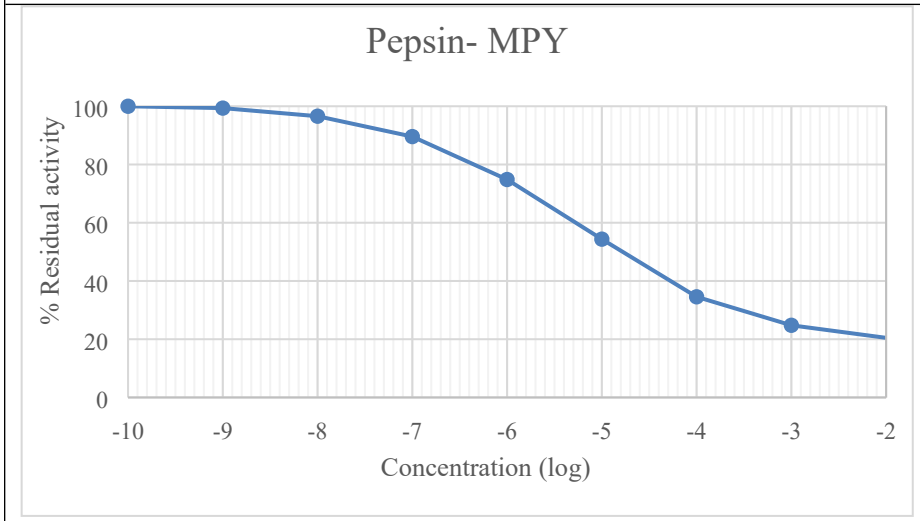


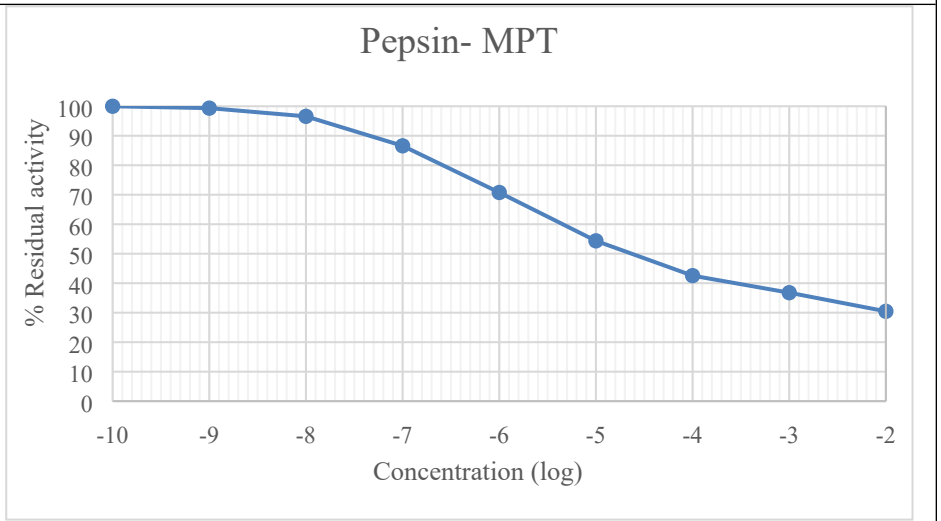


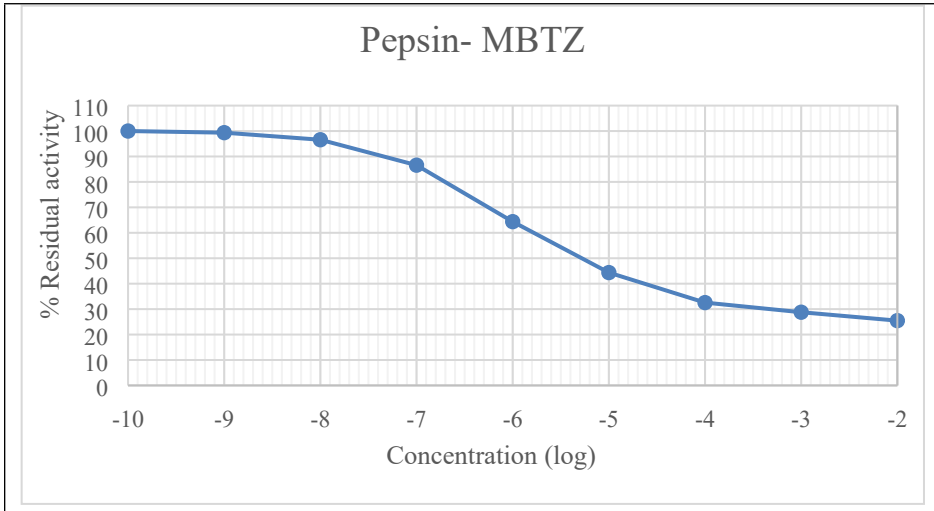


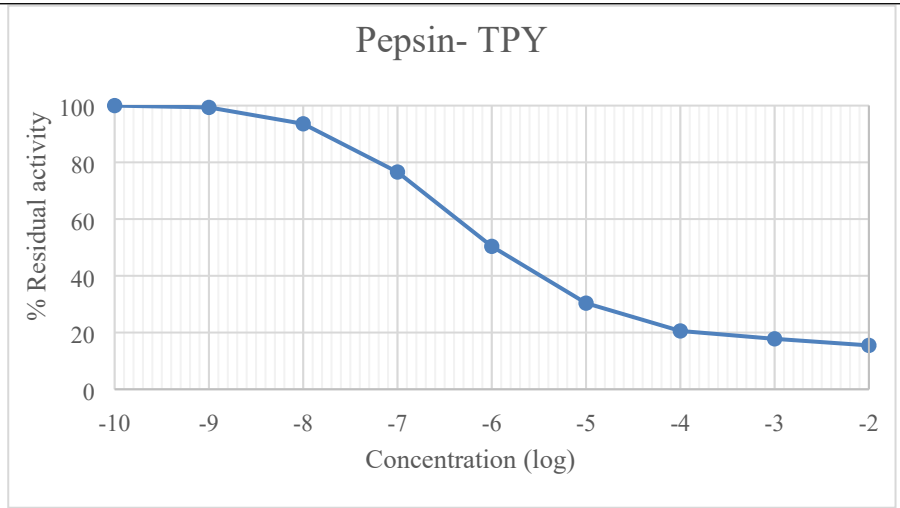

Pepsin- Ru 4 complex
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4

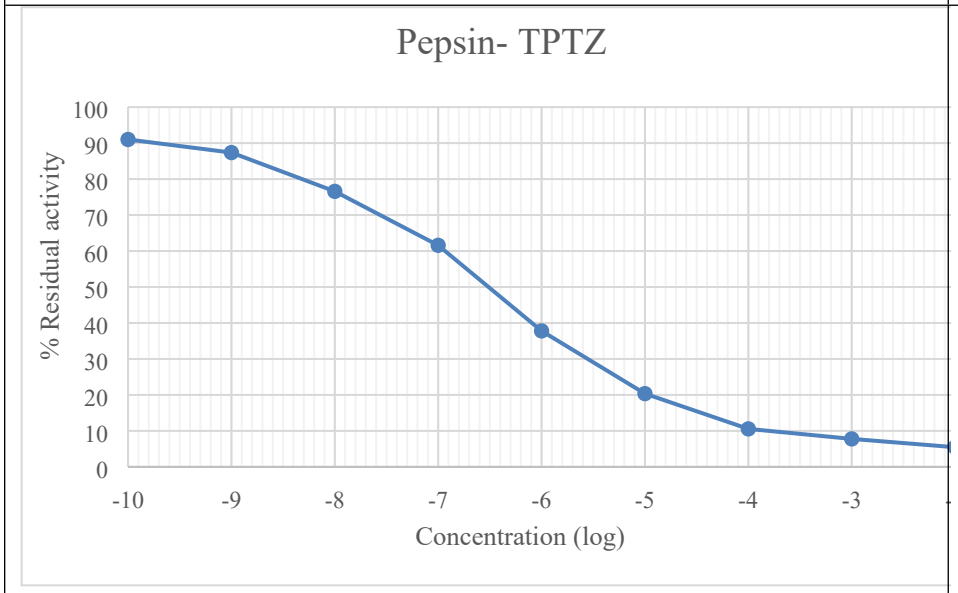

Pepsin- Ru 5 complex
% Residual Activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)


Pepsin- MPY
% Residual activity
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

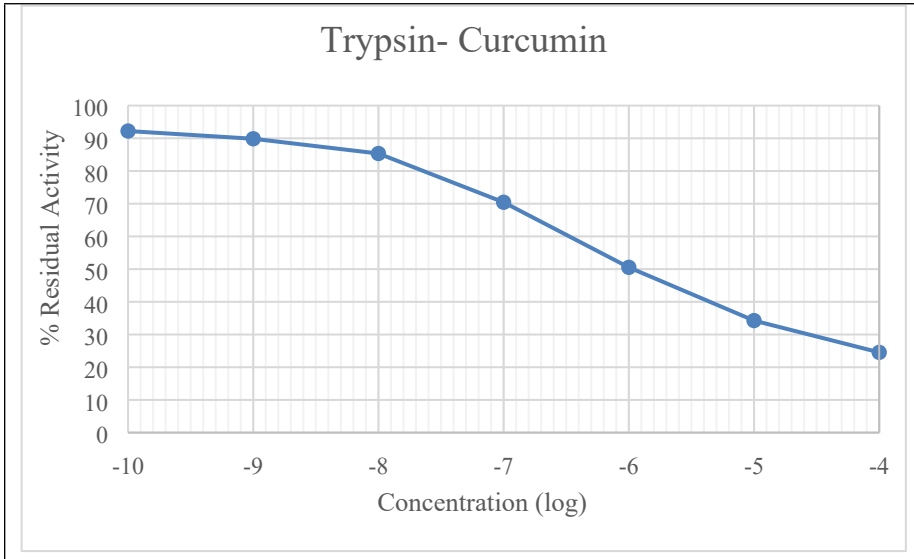

Pepsin- MPT
% Residual activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

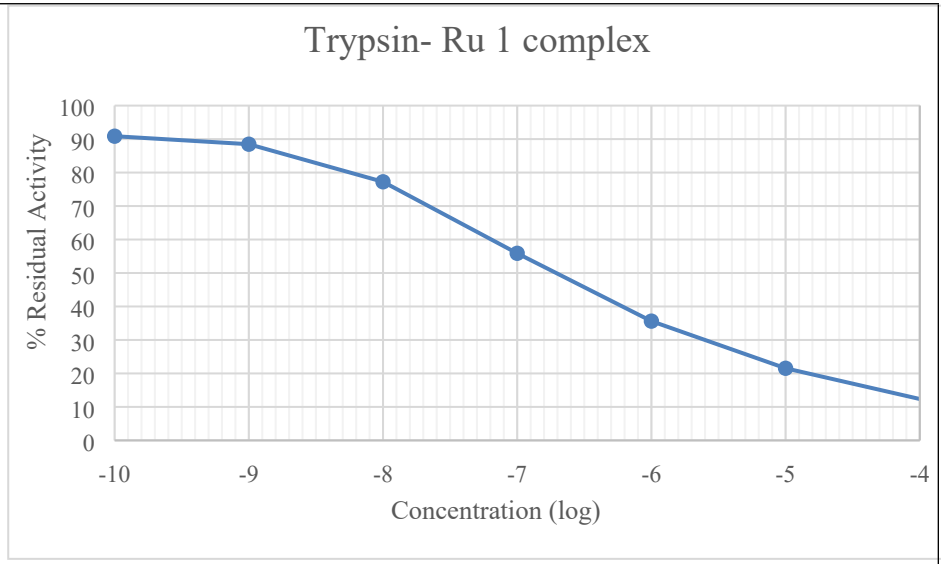

Pepsin- MBTZ
% Residual activity
110
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

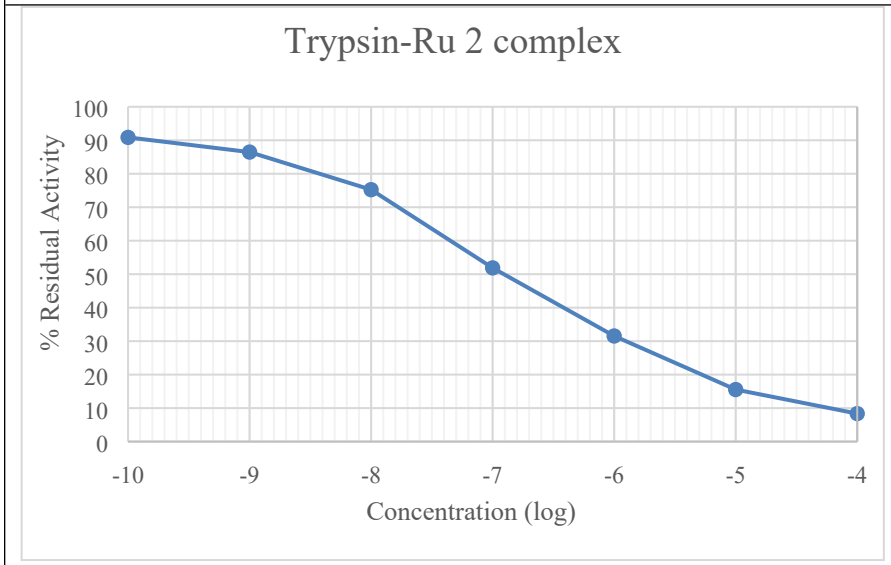

Pepsin- TPY
% Residual activity
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

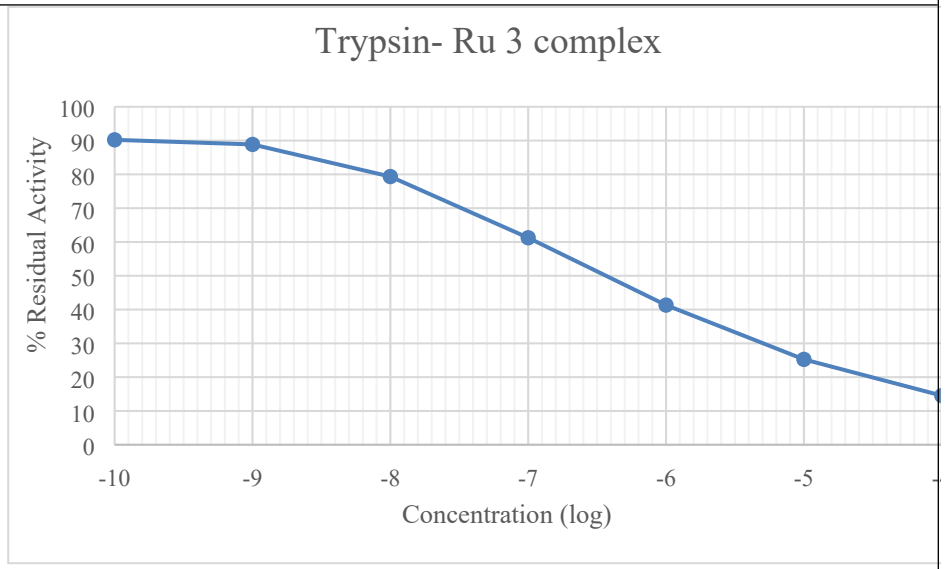

Pepsin- TPTZ
% Residual activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
Concentration (log)

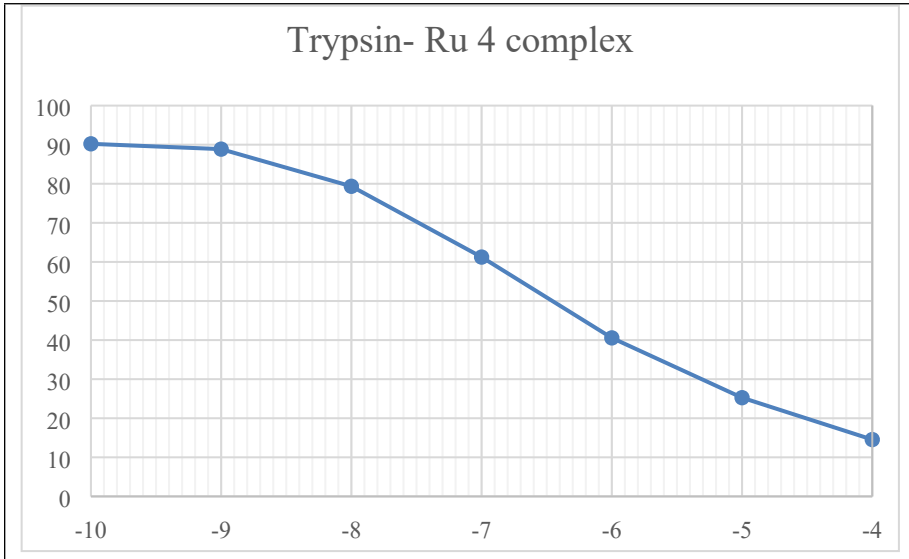
Trypsin

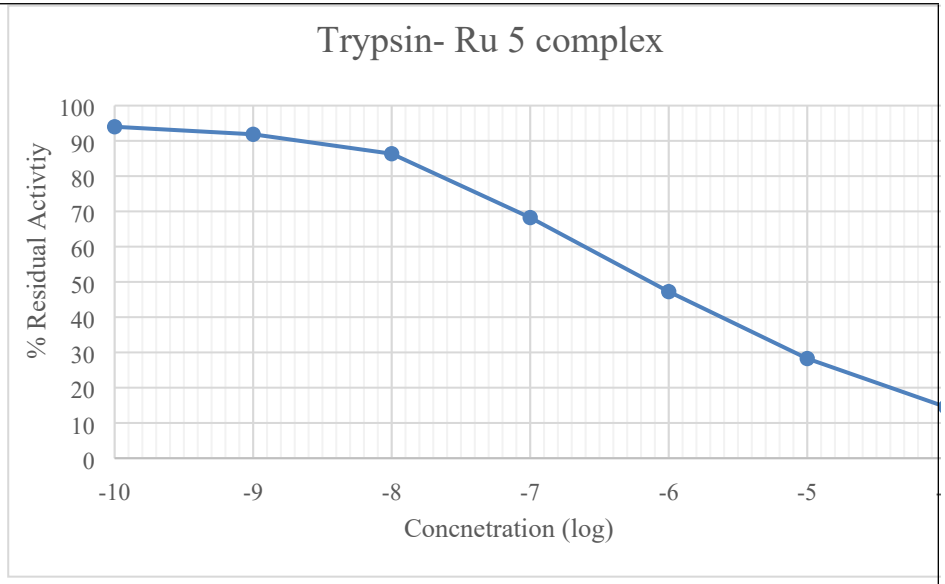

Trypsin- Curcumin
% Residual Activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)

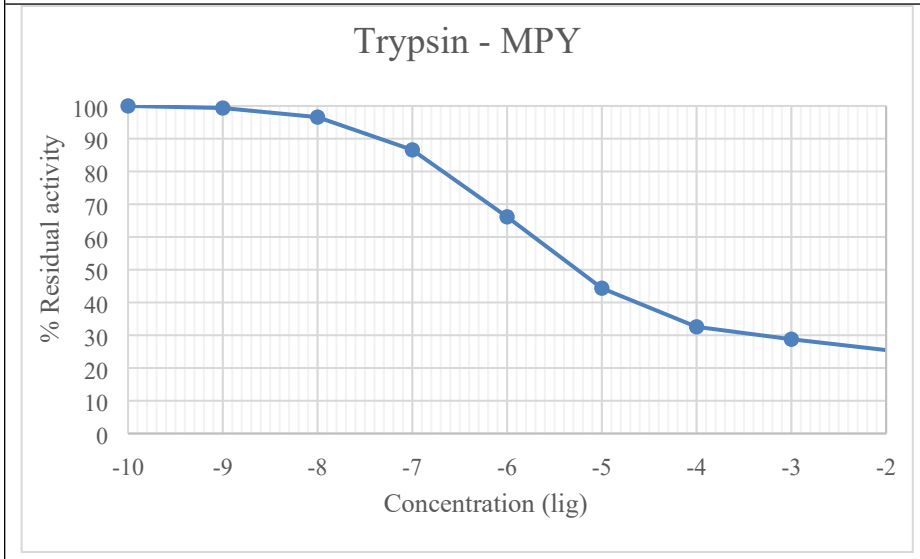

Trypsin- Ru 1 complex
% Residual Activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)

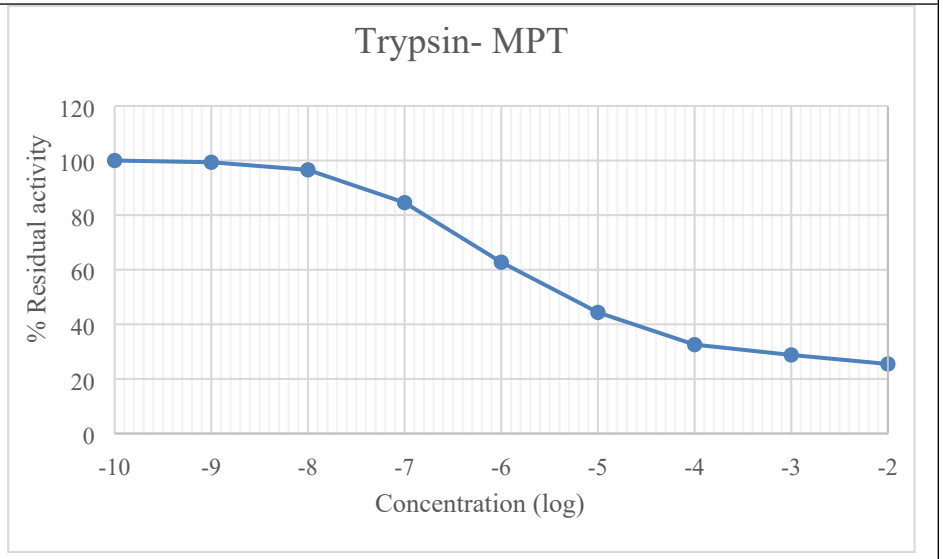

Trypsin-Ru 2 complex
% Residual Activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)

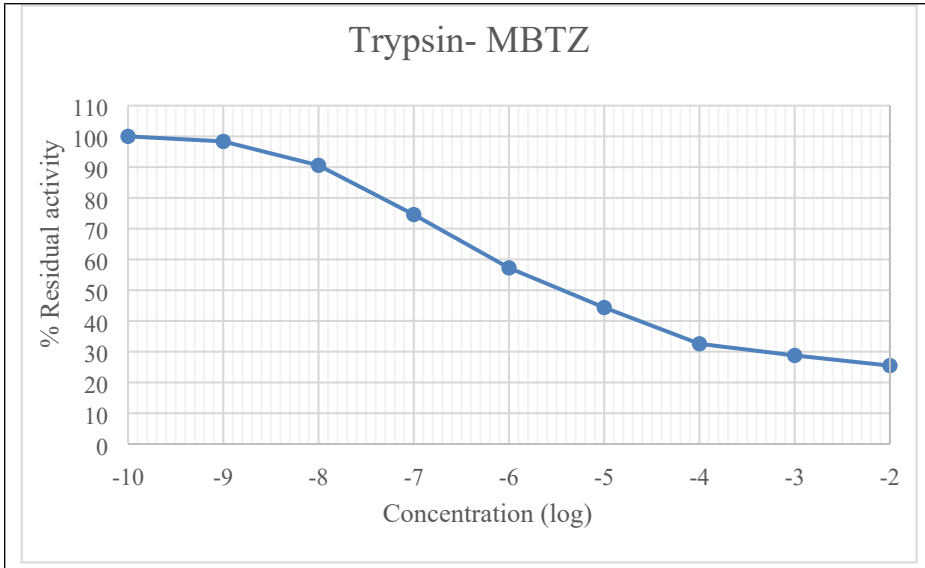

Trypsin- Ru 3 complex
% Residual Activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
Concentration (log)

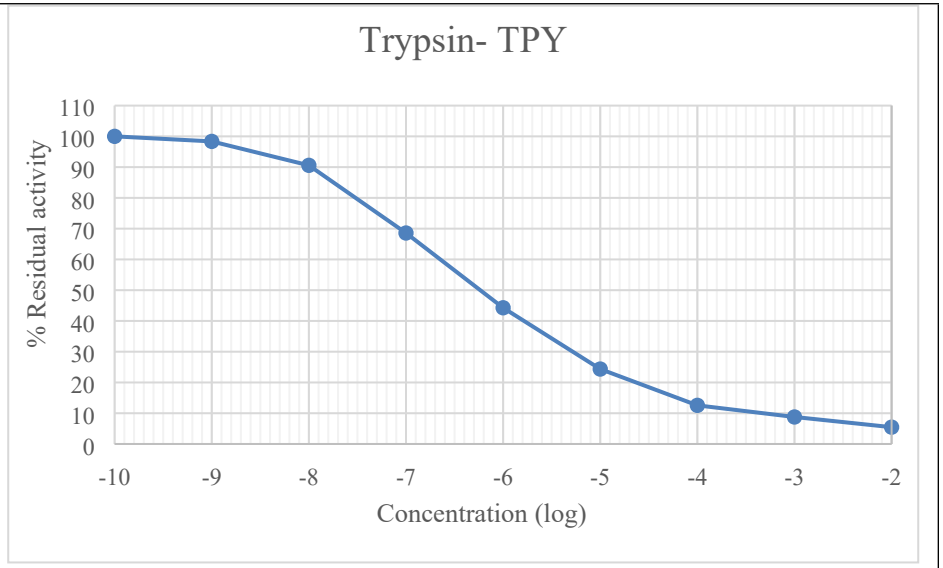

Trypsin- Ru 4 complex
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4

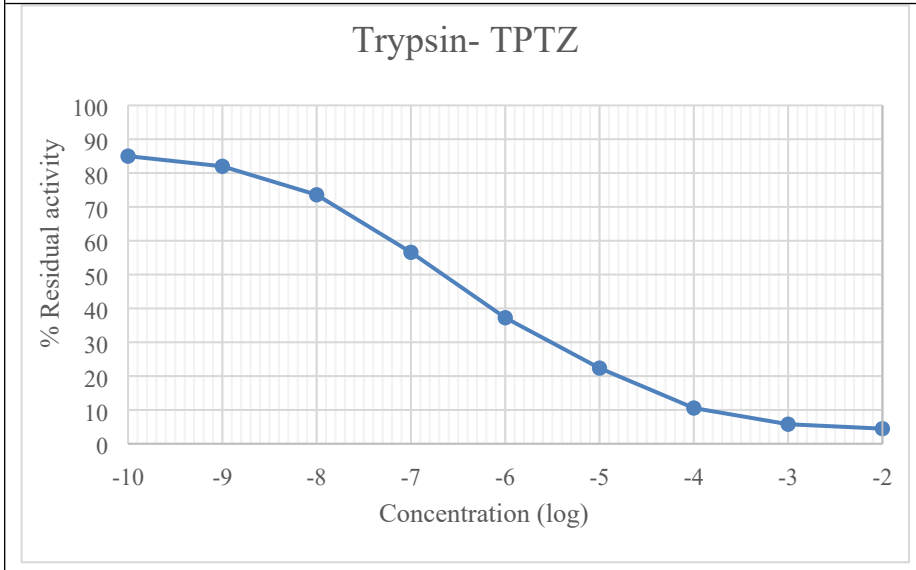

Trypsin- Ru 5 complex
% Residual Activtiy
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
Concnetration (log)


Trypsin - MPY
% Residual activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (lig)

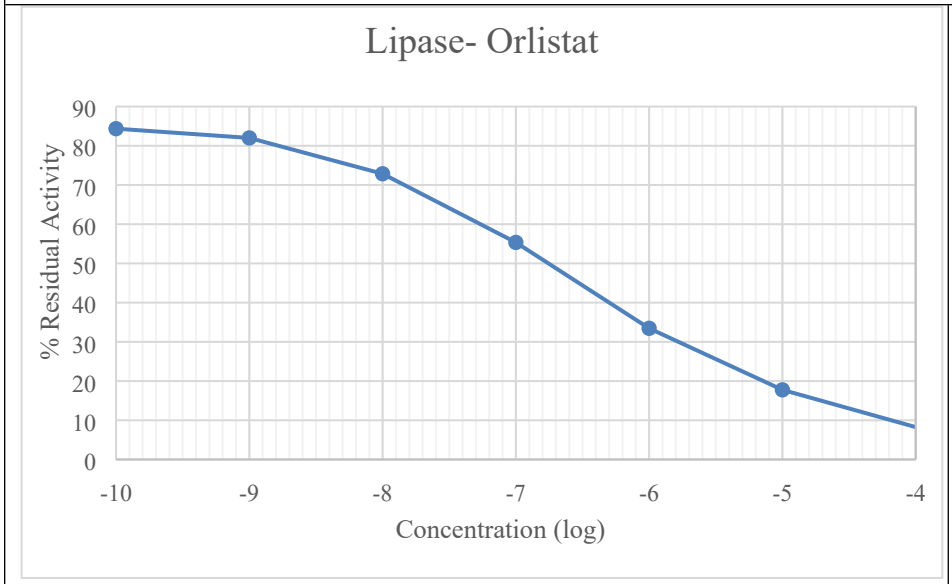

Trypsin- MPT
% Residual activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

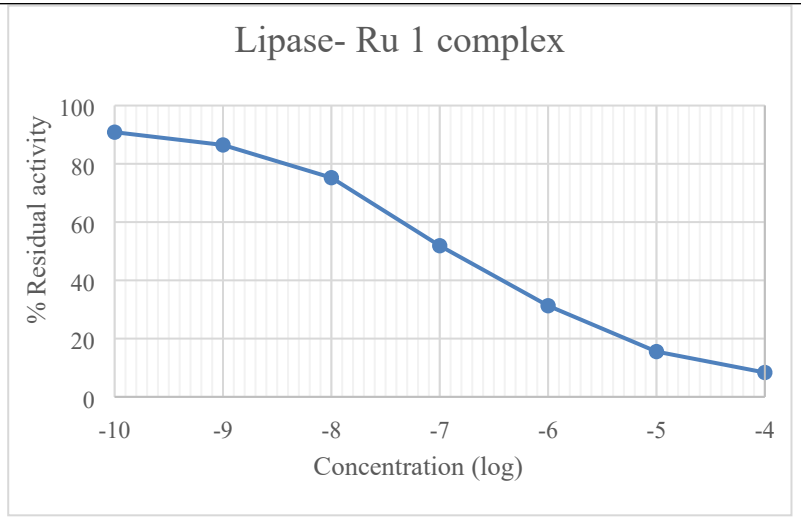

Trypsin- MBTZ
% Residual activity
110
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

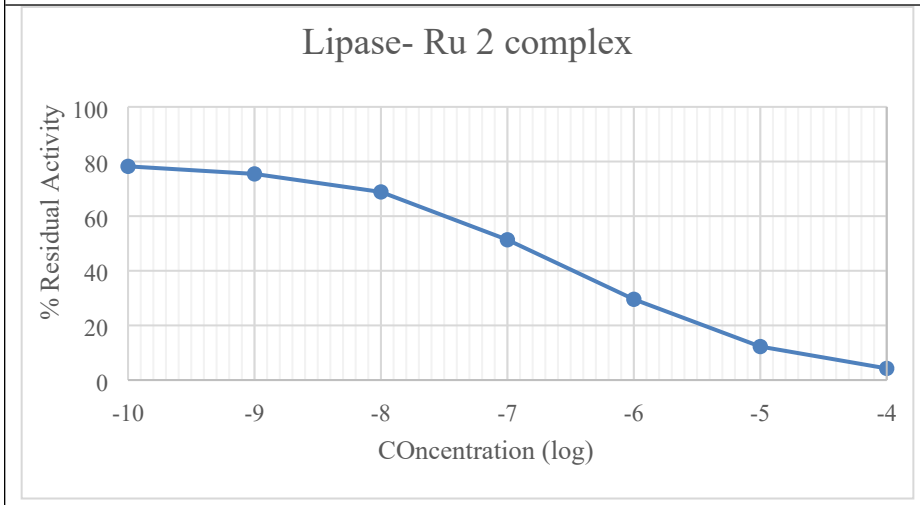

Trypsin- TPY
% Residual activity
110
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

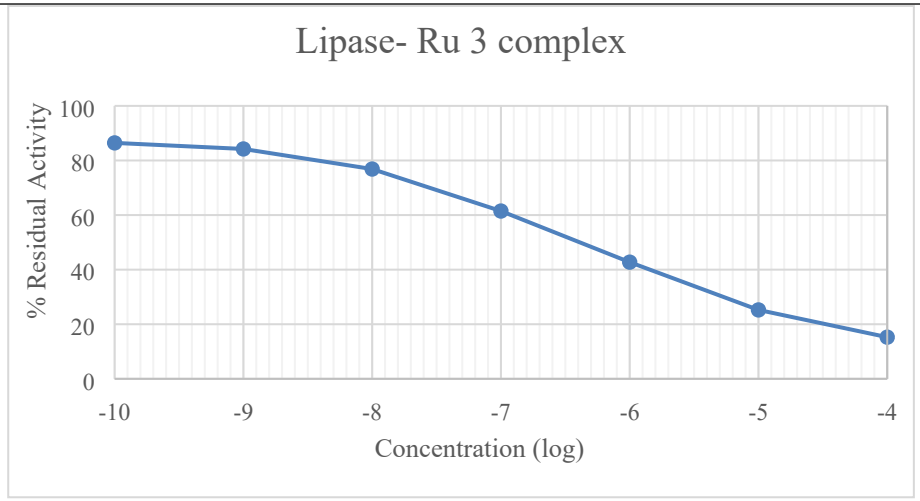

Trypsin- TPTZ
% Residual activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

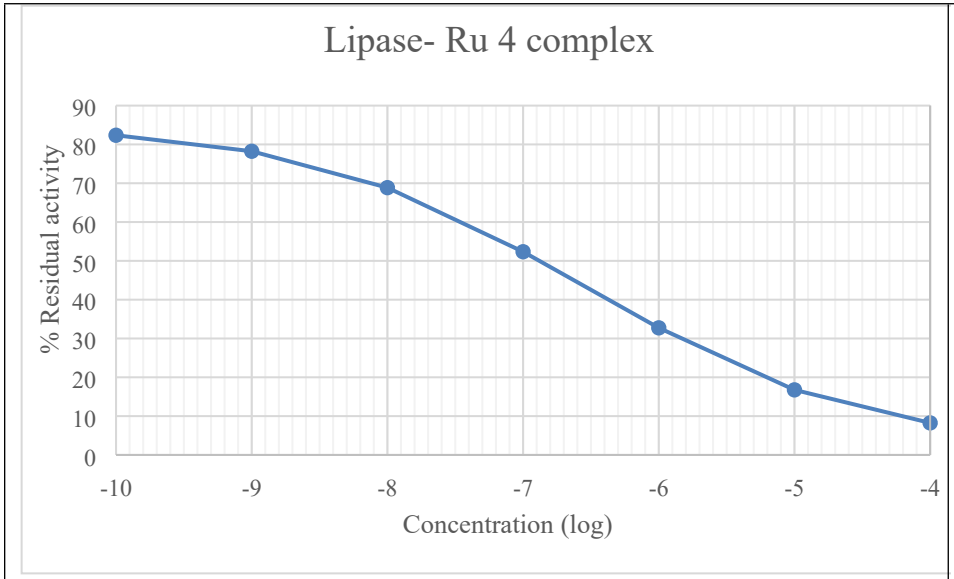
Lipase

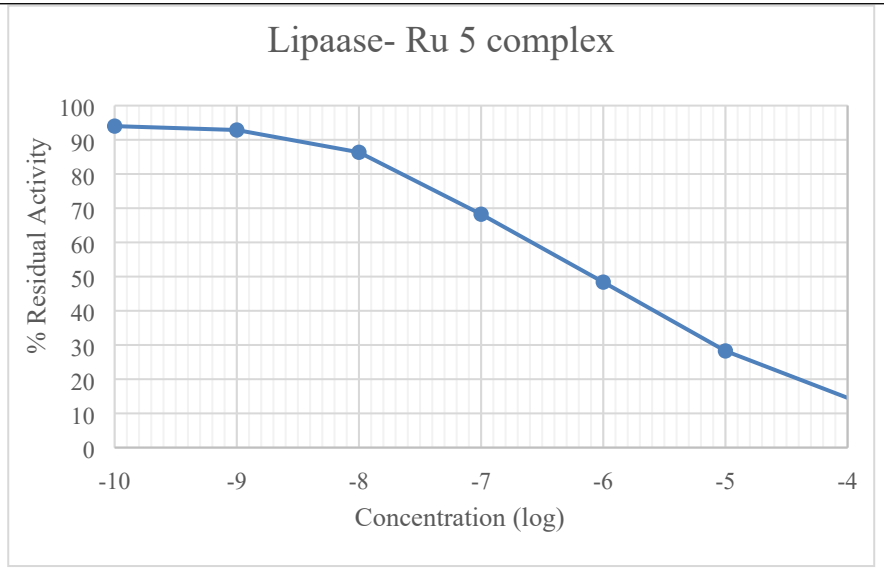

Lipase- Orlistat
% Residual Activity
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)

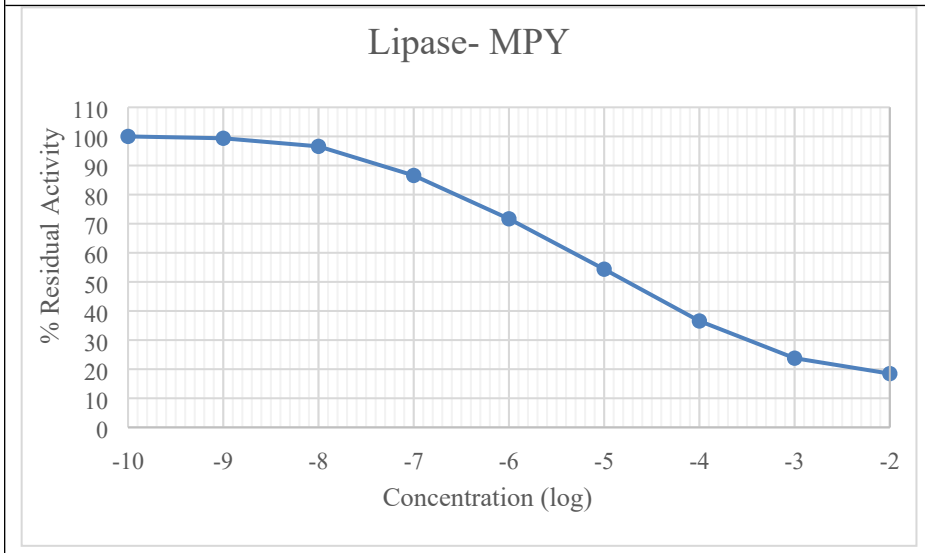

Lipase- Ru 1 complex
% Residual activity
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)

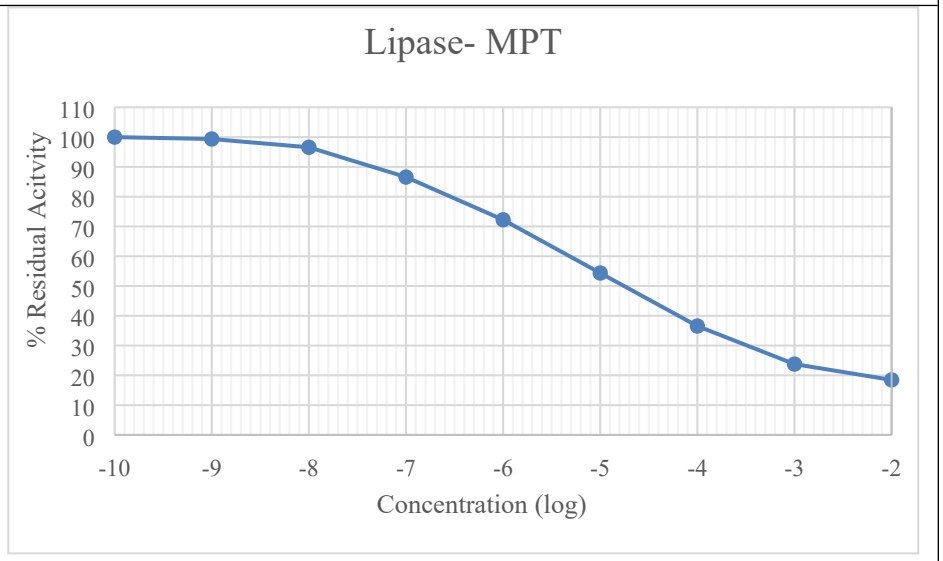

Lipase- Ru 2 complex
% Residual Activity
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
COncentration (log)

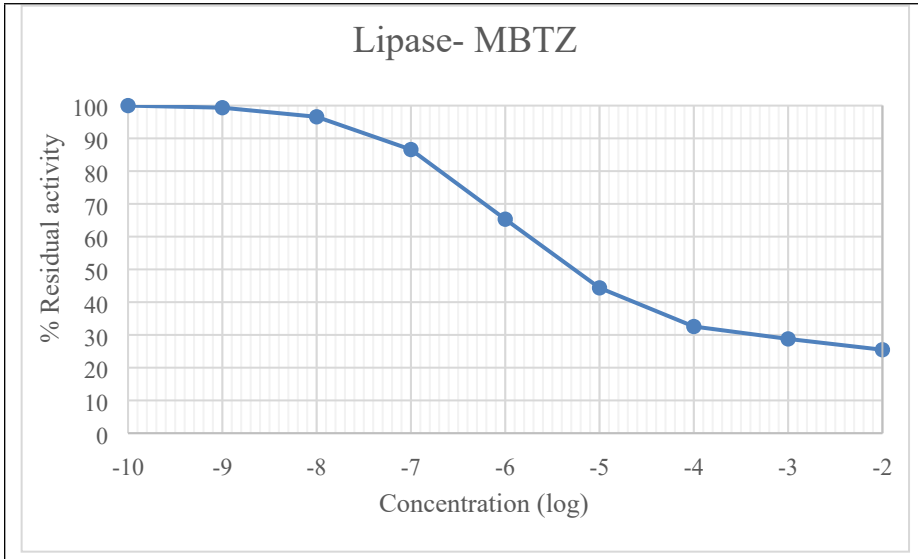

Lipase- Ru 3 complex
% Residual Activity
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)

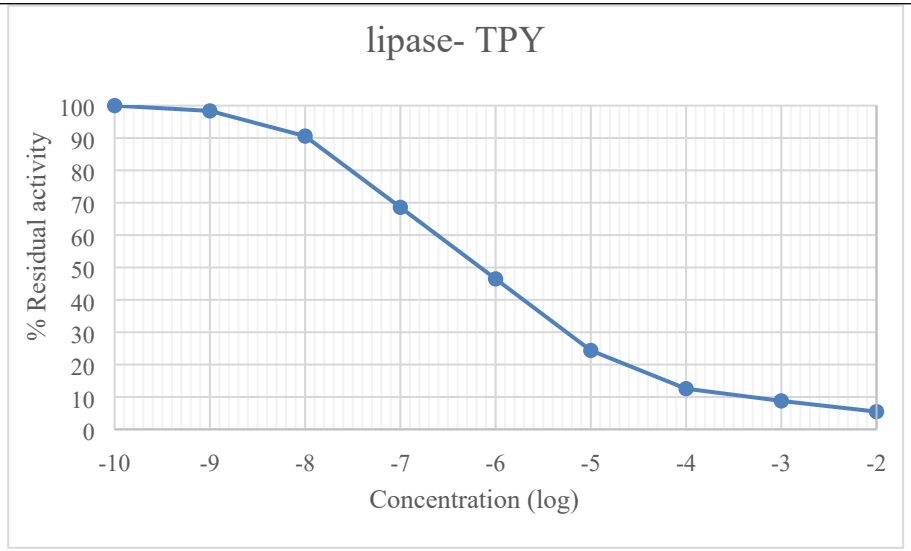

Lipase- Ru 4 complex
% Residual activity
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)


Lipaase- Ru 5 complex
% Residual Activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Concentration (log)


Lipase- MPY
% Residual Activity
110
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)


Lipase- MPT
% Residual Acitvity
110
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)


Lipase- MBTZ
% Residual activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)


lipase- TPY
% Residual activity
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

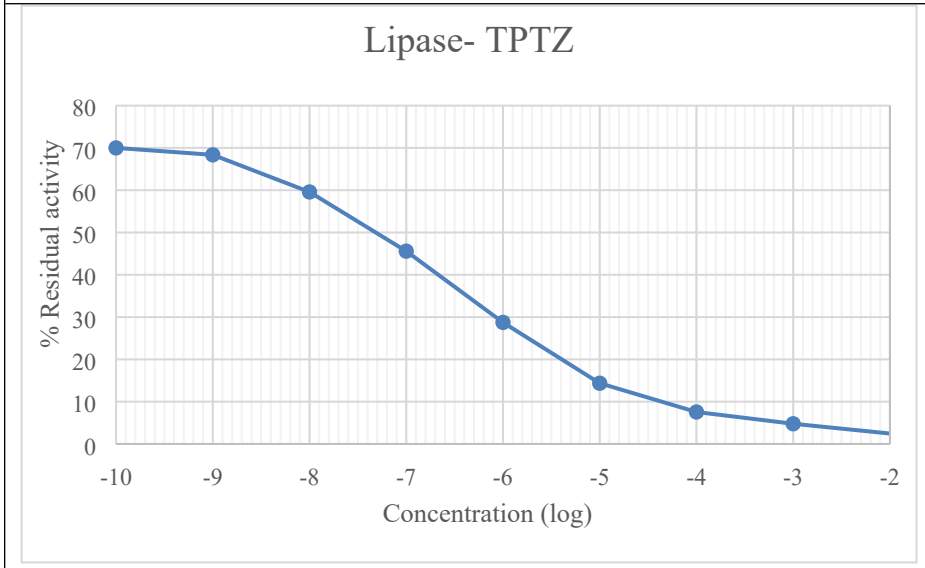

Lipase- TPTZ
% Residual activity
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
-3
-2
Concentration (log)

Table S3. Crystallographic data for the complex **Ru1**.

Empirical formula	$C_{28}\ H_{20}\ N_8\ Ru\ S_2$	
Formula weight	633.71	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 17.4346(3) Å	a= 90°.
	b = 8.91820(10) Å	b= 105.318(2)°.
	c = 17.5800(2) Å	g = 90°.
Volume	2636.32(7) $Å^3$	
Z	4	
Density (calculated)	1.597 Mg/m^3	
Absorption coefficient	0.788 mm^{-1}	
F(000)	1280	
Crystal size	0.3 x 0.15 x 0.1 mm^3	
Theta range for data collection	1.918 to 25.500°.	
Index ranges	-21<=h<=21, -10<=k<=10, -21<=l<=21	
Reflections collected	38260	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9033	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4903 / 0 / 352	

Goodness-of-fit on F^2	1.085
Final R indices [I>2sigma(I)]	R1 = 0.0261, wR2 = 0.0687
R indices (all data)	R1 = 0.0309, wR2 = 0.0711
Largest diff. peak and hole	0.710 and -0.354 e.$Å^{-3}$

Table S4. Stability of complexes.

Sample	Sample Code	%Pepsin Inhibition at $1x10^{-6}$ M			
		0 week	**1st week**	**2nd week**	**3rd week**
Control	**Curcumin**	60.40±1.2	59.40±1.9	60.40±1.6	61.40±2.2
	Orlistat	-	-	-	-
	MPY	25.66±0.8	24.56±1.4	26.75±0.9	25.12±1.8
	MPT	29.24±1.4	27.24±1.1	29.74±1.4	28.14±1.6
	MBTZ	35.62±2.1	33.62±2.0	34.12±1.5	35.74±2.4
	TPY	49.62±1.6	47.62±1.4	47.22±0.9	49.62±1.4
	TPTZ	62.21±2.4	60.21±2.1	61.41±1.6	62.21±2.6
	Ru1	69.46±2.0	67.46±2.4	68.56±1.4	68.46±2.1
	Ru2	64.28±1.8	62.28±1.7	63.22±1.2	65.78±1.8
	Ru3	58.64±0.6	57.64±1.5	56.28±2.4	59.74±0.4
	Ru4	55.26±1.1	54.86±1.4	53.24±1.2	55.26±1.4
	Ru5	53.26±2.0	53.18±2.2	51.44±1.4	53.26±2.2

Sample	Sample Code	% Trypsin Inhibition at $1x10^{-6}$ M			
		0 week	**1st week**	**2nd week**	**3rd week**
Control	**Curcumin**	49.11±2.0	48.74±2.2	47.24±2.1	50.64±2.1
	Orlistat	-	-	-	-
	MPY	32.86±1.4	32.56±1.1	31.86±1.9	30.24±1.5
	MPT	36.24±1.1	37.14±1.4	35.24±1.4	34.84±1.5
	MBTZ	43.56±1.8	41.56±1.6	42.76±1.9	44.76±1.7
	TPY	53.42±1.6	54.52±1.7	52.72±1.5	51.52±1.5
	TPTZ	60.15±2.1	61.45±2.4	61.75±2.4	59.75±2.2
	Ru1	63.38±0.6	63.28±0.8	62.38±1.8	61.37±1.8
	Ru2	68.20±1.4	67.16±1.6	66.46±1.6	69.88±1.4
	Ru3	57.48±2.0	57.38±2.4	56.68±2.4	58.68±2.2
	Ru4	57.28±1.8	58.17±2.0	56.47±1.4	59.47±1.2
	Ru5	51.46±0.6	51.28±1.6	50.78±1.8	52.47±1.4

Sample	Sample Code	%Lipase inhibition at $1x10^{-6}$ M			
		0 week	1st week	2nd week	3rd week
Control	Curcumin			-	
	Orlistat	66.45±1.0	65.14±1.7	64.15±2.0	64.11±1.1
	MPY	28.32±1.2	27.13±1.1	26.22±1.9	28.34±1.4
	MPT	27.76±0.5	26.17±0.8	25.16±0.8	27.70±1.5
	MBTZ	34.68±1.8	33.18±1.6	32.61±1.7	34.80±2.8
	TPY	53.52±1.4	52.12±1.2	51.55±1.6	53.05±1.6
	TPTZ	71.26±0.8	70.16±0.9	70.27±0.5	71.20±1.8
	Ru1	68.72±1.6	67.12±1.1	66.44±1.4	68.64±1.7
	Ru2	70.36±0.7	69.16±0.4	68.55±0.9	70.16±1.6
	Ru3	57.26±1.5	56.16±1.6	55.27±1.3	57.18±1.2
	Ru4	67.26±2.1	66.16±2.8	65.15±2.2	67.45±2.0
	Ru5	51.62±1.8	50.12±1.5	49.16±1.1	51.50±1.1

Sample	Sample Code	%α-amylase activation at $1x10^{-5}$ M

		0 week	1st week	2nd week	3rd week
Control	**Curcumin**	24.25±1.2	23.05±1.4	22.25±1.8	26.23±1.1
	Orlistat	-	-	-	-
	MPY	16.76±2.6	15.26±2.0	17.44±2.4	18.36±2.2
	MPT	19.42±1.9	20.82±1.4	18.25±1.0	20.17±1.3
	MBTZ	28.42±2.6	29.32±2.4	27.28±2.0	30.12±2.4
	TPY	34.76±1.7	35.26±1.6	33.16±1.6	36.18±1.5
	TPTZ	42.86±2.3	41.66±2.1	40.22±2.2	44.69±2.6
	Ru1	64.75±1.1	65.35±1.8	62.25±1.6	66.50±1.7
	Ru2	58.26±1.8	59.46±1.7	56.16±1.4	60.12±1.8
	Ru3	57.84±2.7	58.22±2.1	56.47±2.6	60.47±2.0
	Ru4	55.78±1.5	54.36±1.2	53.18±1.4	57.45±1.4
	Ru5	48.64±1.2	47.24±1.0	46.28±1.1	49.44±1.1

Compounds	Solubility (g/L)
Omeprazole	56
Pantoprazole	30
Curcumin	74
Orlistat	19
Ru1	333
Ru2	142
Ru3	249
Ru4	198
Ru5	166.6
Tpy	55.55
Mpt	45.4
Mbtz	98
Tbtz	62.5
mpy	97