De novo drug Designing and biological evaluation of Coumarin-Pyrimidine co-drug derivatives as diabetic inhibitors: Expending multi-algorithm approach with integration of machine learning in Pharmaceutical research

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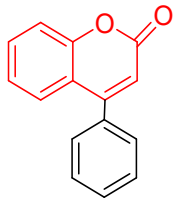
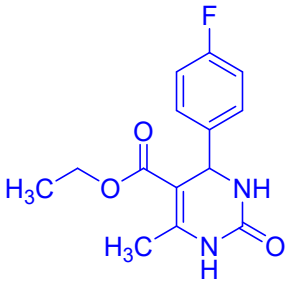
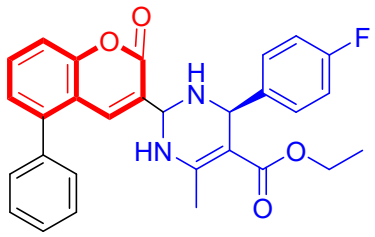
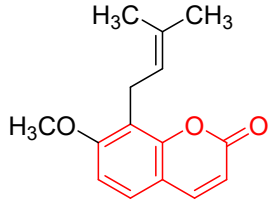
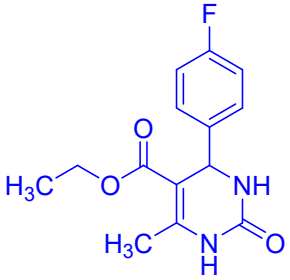
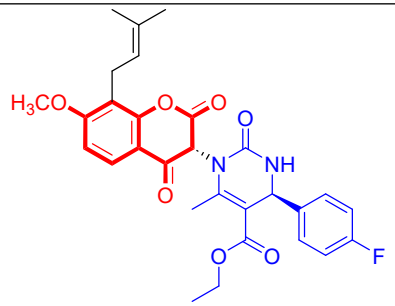
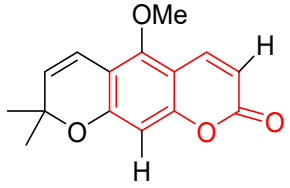
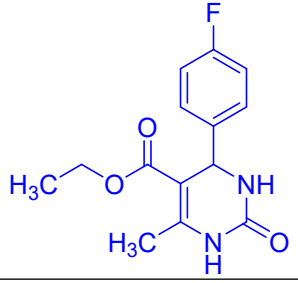
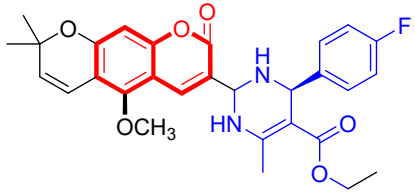
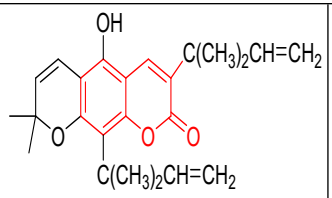
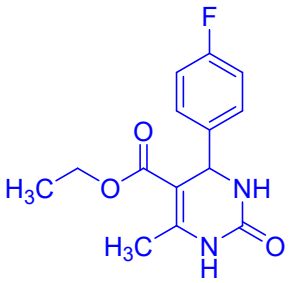
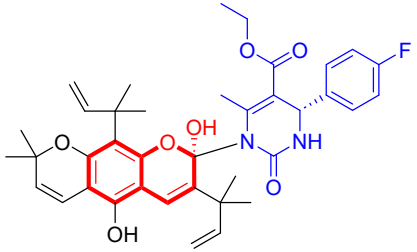
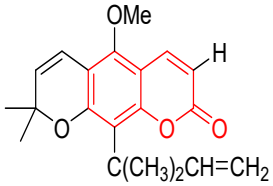
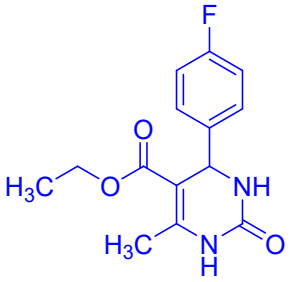
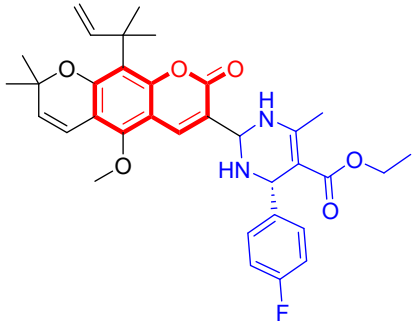
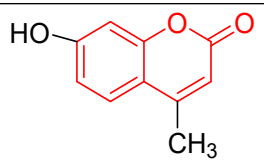
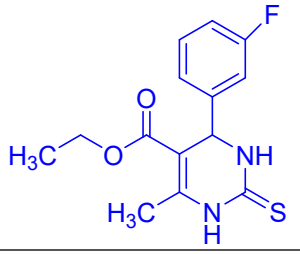
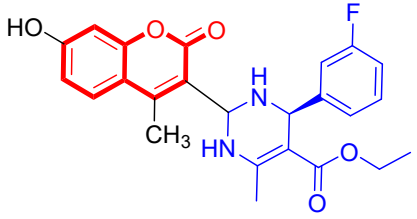
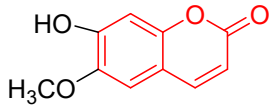
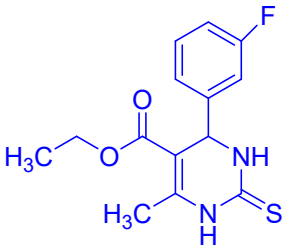
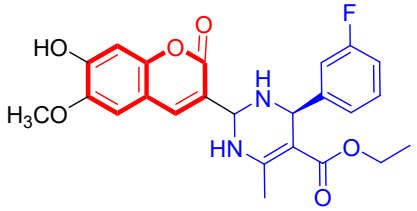
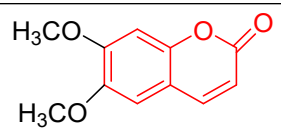
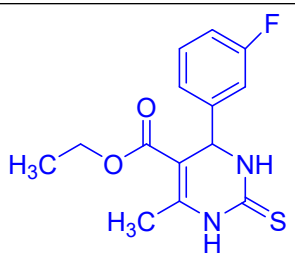
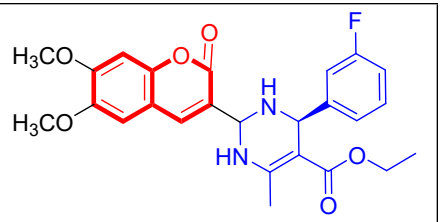
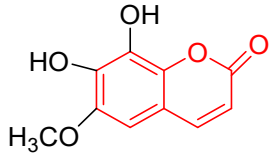
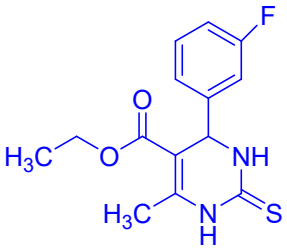
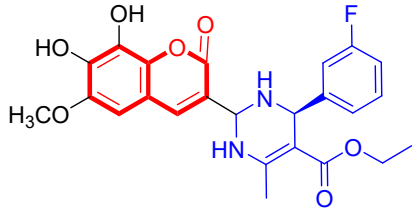
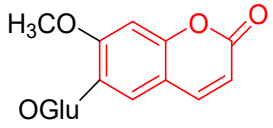
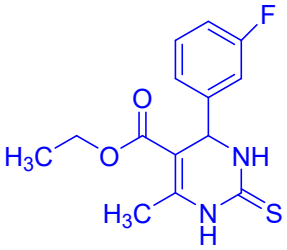
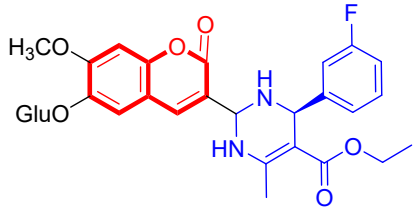
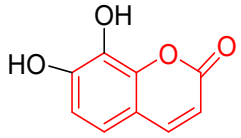
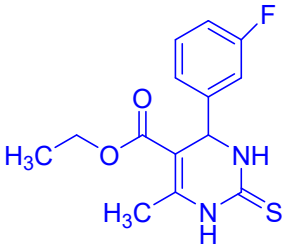
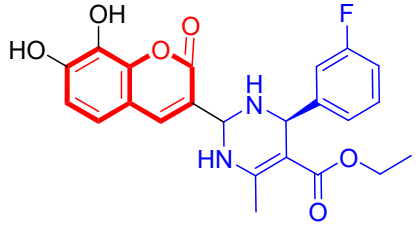
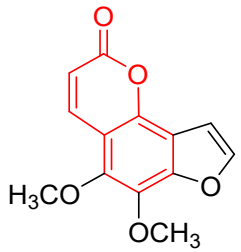
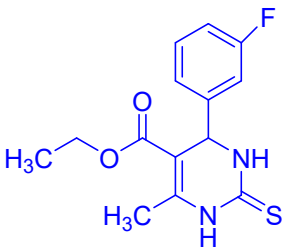
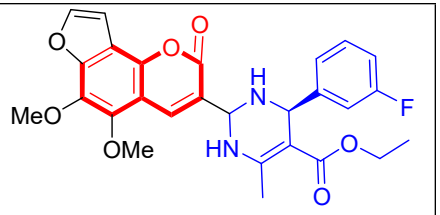
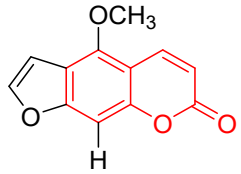
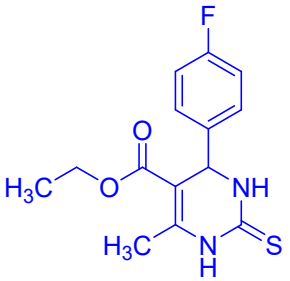
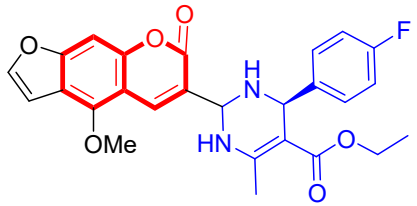
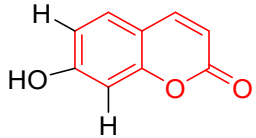
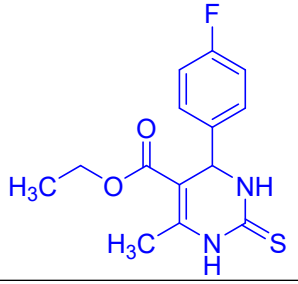
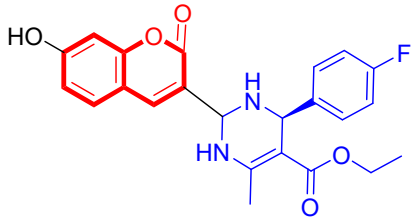
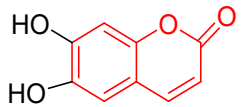
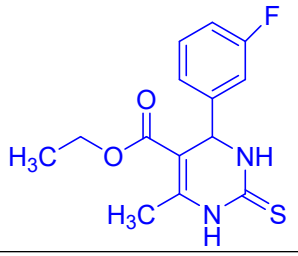
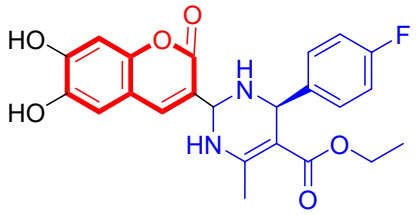
Supplementary material

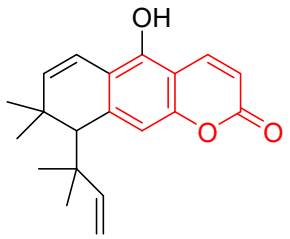
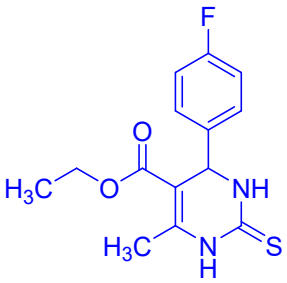
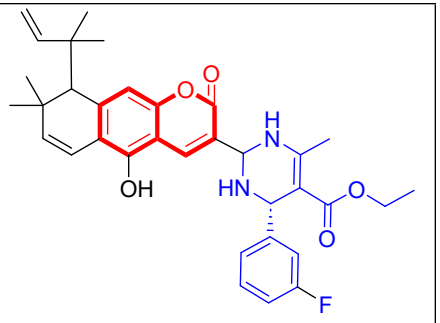
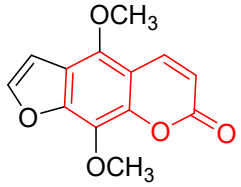
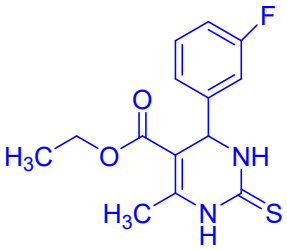
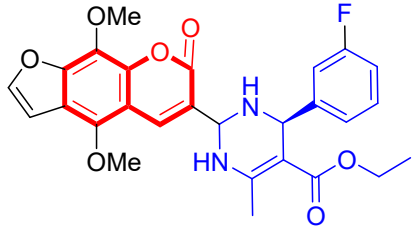
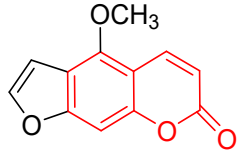
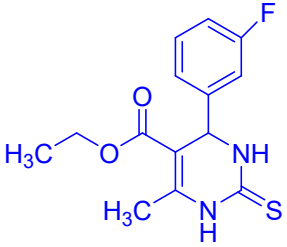
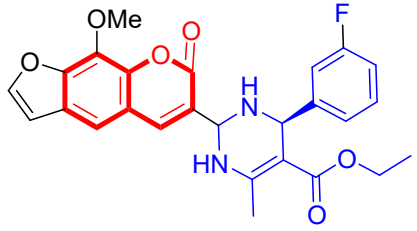
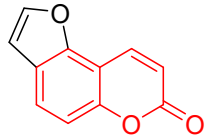
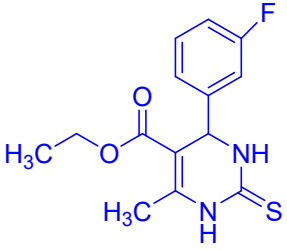
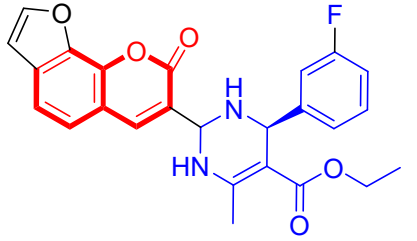
Table S1.Classification of coumarin derivatives according to linkages (oxime and amide) [22]

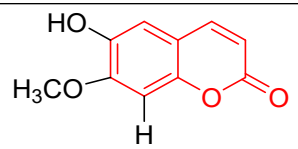
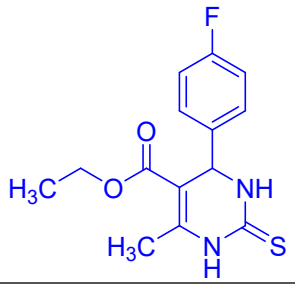
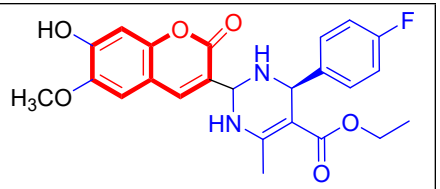
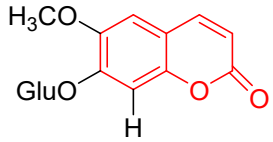
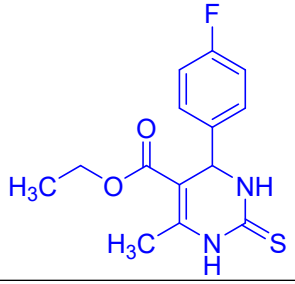
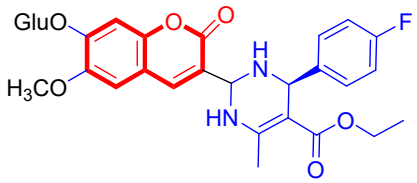
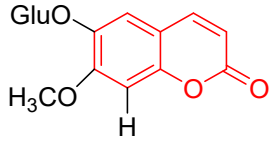
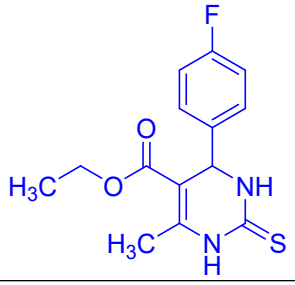
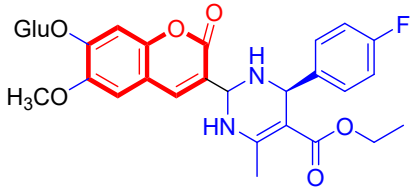
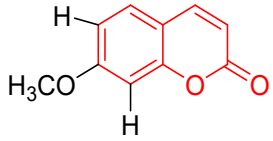
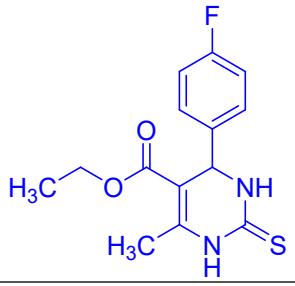
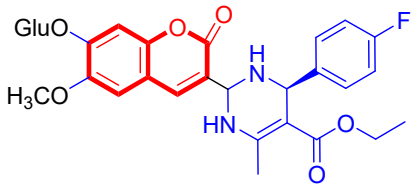
Sr no	**Coumarin Derivatives**	**Pub Chem ID**	**Previous Literature**	**IC_{50} Value for Coumrin** (Anti-cancer activity)	**Pyrimidine derivatives**	**Pyrimidine derivatives IC_{50} (anti-diabetic activity)**	**Structure**
1	 4 Phenyl coumarin	613729	Synthesis [23]	2.6 μM		7.681 μM	 **W1**
2	 Osthol	10659145	[24]	77.94μM		7.681 μM	 **W2**
3	 Xanthoxyletin	66548	Anticancer activity [25]	35.54$\mu g \cdot m L^{-1}$		7.681 μM	 **W3**

4	 Clausenidin	5315947	[26]	15.92*μg·mL-1*		7.681 *μ*M	 **W4**
5	 Dentatin	342801	Antioxidant activity [27]	*8.63μg·mL-1*		7.681 *μ*M	 **W5**
6	 4-methyl Umbelliferon	477470	[28]	0.218*μ*M		9.764 *μ*M	 **W6**
7	 Scopoletin	5280460	[29]	0.560*μ*M		9.764 *μ*M	 **W7**

8	 Scoparone	8417	Anti-inflammatory activity [30]	0.192μM,		9.764 μM	 **W8**
9	 Fraxetin	5273569	[31]	0.239μM		9.764 μM	 **W9**
10	 Esculin	5281471	[32]	0.141μM		9.764 μM	 **W10**
11	 Daphnetin	5280569	[33]	0.280μM		9.764 μM	 **W11**

12	 Pimpinellin	4285		17.16μg/mol		9.764 μM	 **W12**
13	 5-methoxy Psoralen	125303077	[34]			13.02 μM	 **W13**
14	 Umbelliferones	5281426	[35]	2.95±0.02μM		13.02 μM	 **W14**
15	 Esculetin	5281416	[36]	20 µM		9.764 μM	 **W15**

16	 Nordentatin	5320206	[37]	5.45μM		13.02 μM	 **W16**
17	 Isopimpinellin		[38]	11.83μg/mol		9.764 μM	 **W17**
18	 Bergapten	2355	[39]	38.39μg/mol		9.764 μM	 **W18**
19	 Bakuchicin	3083848	[40]	44.03μg/mol		9.764 μM	 **W19**

20	 Isoscopoletin	69894	[41]	18.78±0.50 μM		13.02 μM	 **W20**
21	 Scopolin	439514	[42]	60.10±0.11 μM		13.02 μM	 **W21**
22	 Isoscopolin		[43]	41.04±2.71 μM		13.02 μM	 **W22**
23	 7-methoxy Coumarin	18355513	[44]	490.20±9.32μM		13.02 μM	 **W23**

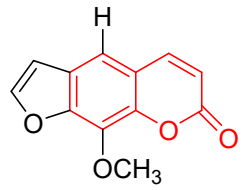
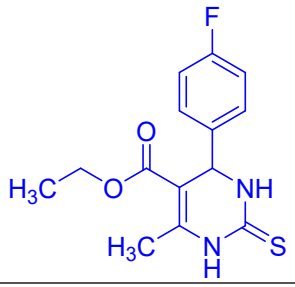
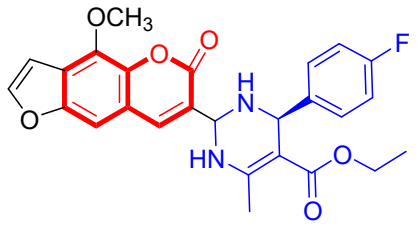
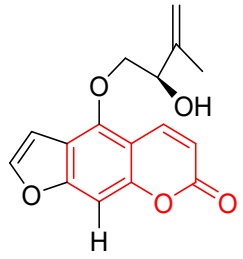
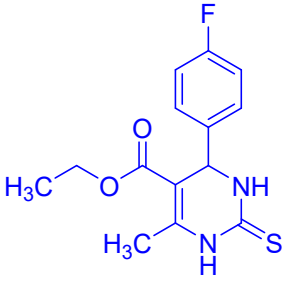
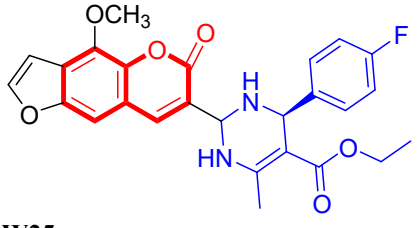
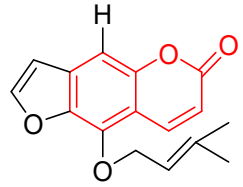
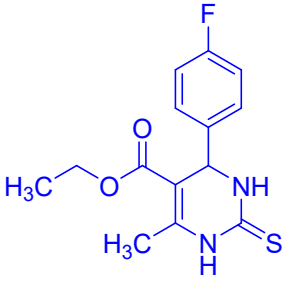
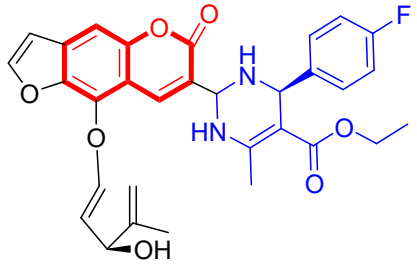
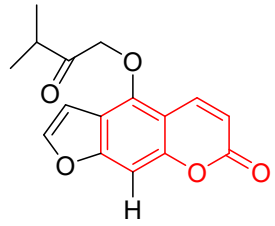
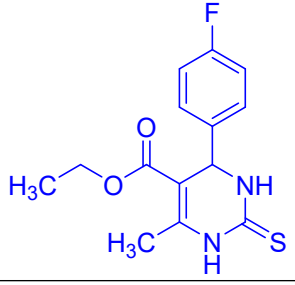
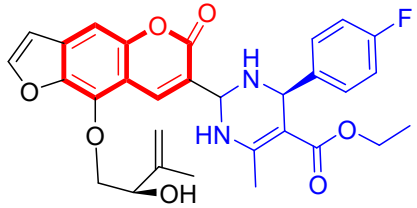
24	 8 methoxy Psoralen	125303077				13.02 μM	 **W24**
25	 Pabulenol	3009225	[45]			13.02 μM	 **W25**
26	 Imperatorin	10212	[46]	78 µM		13.02 μM	 **W26**
27	 Isooxypeucedanin	625383	[47]			13.02 μM	 **W27**

Table S2. Classification of protein with PDB-ID

Activity	**PDB-ID**	**Resolution**	**Classification**	**Inhibitor**
Antidiabetic	3BAJ	2.10	Hydrolase	Alpha –amylase
Antidiabetic	4J3J	3.20	Hydrolase	DPP-1V
Antidiabetic	3RX2	1.90	Oxidoredutase	Aldose Reductase
Antidiabetic	1GPY	2.40	Glycogen Phosphorylase	Glycogen Phosphorylase

Table S3: Classification of different compound showed different interaction for antidiabetic activity (3BAJ)

Compound	Binding Energy Kcal/mol	Protein ligand interaction by H-bonding					Protein ligand interaction by Van der Waals forces			
		No. of H-bonds	Amino acid residues	Category	Type of interaction	Distance (Å)	Amino acid residues	Category	Types of interaction	Distance (Å)
PDB ID: 3BAJ (α-amylase)										
W6	-9.7	7	GLN63 HIS201 HIS305 HIS305 TRP 59 GLU233	H-bonding H-bonding H-bonding H-bonding H-bonding H-bonding	Conventional Conventional Conventional Conventional Conventional C-H bond	2.6015 2.20973 2.38042 1.93783 2.56822 3.42336	ASP 300 ASP 300 ASP 197 ASP 300 HIS 305 LYS 200 ILE 235 HIS 201	Electrostatic Halogen Electrostatic Electrostatic Other Hydrophobic Hydrophobic Hydrophobic	Attractive Charge Halogen (F) Pi-Anion Pi-Anion Pi-Sulfur Alkyl Alkyl Pi-Alkyl	4.33811 3.6383 4.92837 3.49397 4.36015 4.52096 4.30297 4.8665
W23	-9.6	7	ASP300 HIS101 ILE235 HIS305 HIS305 GLU 233 HIS201	H-bonding H-bonding H-bonding H-bonding H-bonding H-bonding H-bonding	Salt bridge Conventional Conventional Conventional C-H bond C-H bond Pi-Cation	2.13696 3.00767 2.45371 2.79587 3.6018 3.24215 2.70916	ASP197 GLU233 HIS201 LEU162 ILE235 TYR62 HIS305 TPR59 HIS201	Electrostatic Electrostatic Electrostatic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Attractive Attractive Pi-Cation Pi-Sigma Pi-Sigma Pi-Sigma Pi-Pi Stacked Pi-Pi Stacked	5.58373 5.50542 4.36458 3.79269 3.89142 3.89197 5.13774 5.05748
W24	-9.6	2	HIS305 HIS201	H-bonding H-bonding	Conventional Pi-Cation	2.71284 2.42888	ASP300 HIS201 HIS201 LEU162 ILE235 TYR62 HIS305 HIS305 TRP59 HIS201	Electrostatic Electrostatic Electrostatic Hydrophobic Hydrophobic Hydrophobic Other Hydrophobic Hydrophobic Hydrophobic	Attractive Pi-Cation Pi-Cation Pi-Sigma Pi-Sigma Pi-Sigma Pi-Sulfur Pi-Pi Stacked Pi-Pi T-shaped Pi-Pi T-shaped Pi-Pi T-shaped Alkyl Pi-Alkyl	3.4249 4.25454 3.95061 3.66325 3.83121 3.85638 5.87048 5.00074 4.72142 4.51018

							HIS201	Hydrophobic	Pi-Alkyl	4.80925
									Pi-Alkyl	
							ILE235	Hydrophobic	Pi-Alkyl	3.68448
							LEU162	Hydrophobic	Pi-Alkyl	5.46998
							ALA198	Hydrophobic		5.30199
							LYS200	Hydrophobic		5.46484
							ILE235	Hydrophobic		4.90718
							LYS200	Hydrophobic		4.02549
W19	-9.5	5	ASP300	H-bonding	Salt bridge	2.90184	HIS201	Electrostatic	Pi-Cation	3.65489
			HIS305	H-bonding	Conventional	3.00667	LEU162	Hydrophobic	Pi-Sigma	3.81855
			ALA198	H-bonding	C-H bond	3.64251	LEU162	Hydrophobic	Pi-Sigma	3.42946
			GLU233	H-bonding	C-H bond	3.72485	ILE235	Hydrophobic	Pi-Sigma	3.79065
			HIS 201	H-bonding	Pi-Cation	2.43756	TRR59	Hydrophobic	Pi-Sigma	3.90168
							TRP59	Hydrophobic	Pi-Pi T Shaped	5.11293
							HIS201		Pi-Pi T Shaped	
							HIS201	Hydrophobic	Pi-Pi T Shaped	4.59222
							ALA198		Pi-Alkyl	
							LEU 162	Hydrophobic	Pi-Alkyl	4.61484
							ILE235		Pi-Alkyl	
							ALA198	Hydrophobic	Pi-Alkyl	5.3981
							LYS200	Hydrophobic	Pi-Alkyl	5.18346
								Hydrophobic		5.1784
								Hydrophobic		5.06342
								Hydrophobic		4.55796
W3	9.3		ARG195	H-bonding	Conventional	2.72813	GLU233	Electrostatic	Pi-Anion	4.53193
			HIS201	H-bonding	Conventional	1.99778	ILE235	Hydrophobic	Pi-Sigma	3.67908
			ASP300	H-bonding	Conventional	2.56721	LEU162	Hydrophobic	Pi-Alkyl	4.99773
			GLY306	H-bonding	C-H bond	3.70602				
Acarbose	-6.9		HIS305	H-bonding	Conventional	2.52565				
			HIS305	H-bonding	Conventional	2.38951				
			HIS305	H-bonding	Conventional	2.52418				
			HIS305	H-bonding	Conventional	2.2535				
			HIS305	H-bonding	Conventional	1.74703				
			GLU233	H-bonding	Conventional	2.86147				
			ASP300	H-bonding	C-H Bond	2.97326				
			HIS305	H-bonding	Pi-Donor	2.41595				
PDB-ID: 4J3J *(DPP-IV inhibitor*)										

W24	-9.5	2	HIS305 HIS201	H-Bonding H-Bonding	Conventional Pi-Cation	2.70957 2.3994	ASP300 HIS201 HIS201 LEU162 ILE235 TYR62 HIS305 HIS305 TYR59 HIS201 HIS201 ILE235 LEU162 ALA198 ILE235 LYS200	Electrostatic Electrostatic Electrostatic Hydrophobic Hydrophobic Hydrophobic Other Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Attractive Pi-Cation Pi-Cation Pi-Sigma Pi-Sigma Pi-Sigma Pi-Sulfur Pi-Pi Stacked Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl	3.46504 4.28596 3.88473 3.61903 3.83502 3.89424 5.82084 5.00121 4.6848 4.49368 4.75457 3.80224 5.40531 5.32485 4.96267 4.03379
W19	-9.1	5	ASP300 HIS305 ALA198 GLU233 HIS201	H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding	Salt bridge Conventional C-H C-H Pi-Cation	2.89461 3.00288 3.64921 3.7268 2.43418	HIS201 LEU162 LEU162 ILE235 TRP59 TRP59 HIS201 HIS201 ALA198 LEU162 ILE235 ALA198 LYS200	Electrostatic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Cation Pi-Sigma Pi-Sigma Pi-Sigma Pi-Sigma Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S Pi-Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl	3.65636 3.82111 3.43283 3.78791 3.91845 5.10972 4.58884 4.61633 5.39871 5.18238 5.17934 5.06849 4.55536
W3	-9.2	4	HIS201 GLU233 ASP233 GLY306	H-Bonding H-Bonding H-Bonding H-Bonding	Conventional Conventional Conventional Conventional	1.97795 2.65933 2.56377 3.62827	GLU233 ILE233 LEU162	Electrostatic Hydrophobic Hydrophobic	C-H Pi-Sigma Pi-Alkyl	4.5773 3.66176 4.95881

W18	-9.1	4	ASP300 HIS305 ALA198 HIS201	H-Bonding H-Bonding H-Bonding H-Bonding	Salt bridge Conventional C-H Pi-Cation	2.69611 2.78394 3.54086 3.82336	HIS201 HIS201 GLU233 LEU162 ILE235 HIS305 TRP59 HIS201 HIS201 ILE235 LEU162 ALA198 ILE235 ALA198 LYS200	Electrostatic Electrostatic Electrostatic Hydrophobic Hydrophobic Other Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Cation Pi-Cation Pi-Anion Pi-Sigma Pi-Sigma Pi-Sulfur Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl Pi-Alkyl	4.34417 3.82336 4.16065 3.5139 3.83357 5.69304 4.70953 4.48603 4.71534 3.85985 5.26391 5.30084 5.10445 5.15513 4.22881
W1	-9.1	2	ARG125 GLU205	H-Bonding H-Bonding	Conventional Conventional	2.47452 2.7107	PHE357	Hydrophobic	Pi-Pi Stacked	4.1925
aldose Reductase (PDB-ID: 3RX2)										
W1	-10.1	3	GLN49 HIS201 TRP111	H-Bonding H-Bonding H-Bonding	Conventional Conventional Conventional	1.89386 2.99307 2.32768	VAL47 VAL47 LEU300 PHE122 TRP219 TRP219 PHE121 PHE122 CYS298	Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Sigma Pi-Sigma Pi-Sigma Pi-Pi Stacked Pi-Pi Stacked Pi-Pi Stacked Pi-Alkyl Pi-Alkyl Pi-Alkyl 	3.74691 3.92342 3.96218 3.77271 5.96886 4.42708 5.23972 5.32597 4.91791
W3	-9.8	2	HIS201 VAL47	H-Bonding H-Bonding	Conventional Conventional	2.02681 2.88608	CYS298 TRP20 TRP20	Other Hydrophobic Hydrophobic	Pi-Sulfur Pi-Pi Stacked Pi-Pi Stacked 	4.98245 4.44707 4.22271

W23	-9.5	6	TRP20 TRP111 GLN183 TYR48 HIS110 CYS298	H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding	Conventional Conventional C-H C-H Pi-Cation Pi-Donor	2.94991 2.28525 3.69605 3.47001 3.07576 4.15191	HIS110 TYR209 TRP219 HIS110 HIS110 PHE122 TYR209	Electrostatic Other Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Cation Pi-sulfur Pi-Sigma Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S	4.20045 3.96558 4.63375 5.06463 5.18651 4.80163 5.16568
W27	-9.0	1	TRP20	H-Bonding	Conventional	2.71665	TYR209 CYS298 TPR20 TPR20 TPR20 TPR20 TRP20 TRP111 VAL47 CYS298 LEU300	Hydrophobic Other Hydrophobic Other Other Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Sigma Pi-Sulfur Pi-Sulfur Pi-Pi Stacked Pi-Pi Stacked Pi-Pi Stacked Pi-Pi Stacked Pi-Pi Stacked Pi-Pi T-S Pi-Alkyl Pi-Alkyl Pi-Alkyl	3.8608 5.80356 4.55364 4.79532 5.41824 5.4756 5.13994 5.7253 5.41148 4.72791 4.40051 5.2388
Epalrestat	-8.1	1	HIS110	H-Bonding	Pi-Cation Pi-Donor Hydrogen Bond	2.89213	CYS298 TRP20 HIS110	Other Hydrophobic Hydrophobic	Pi-Sulfur Pi-Pi T-shaped Pi-Pi T-shaped	4.3683 5.05102 5.04106
Glycogen Phosphorylase (*PDB-ID: 1GPY)*										
W19	-9.5	4	ARG309 ARG310 GLN72 GLN72	H-Bonding H-Bonding H-Bonding H-Bonding	Conventional Conventional Conventional Conventional	2.19655 2.14712 3.78503 2.24876	ARG193 ARG193 TYR75 TRP67 TRP67 TRP67 TRP67 ILE68	Electrostatic Electrostatic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Cation Pi-Cation Pi-Pi Stacked Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S Pi-Pi T-S Pi-Alkyl Pi-Alkyl	3.73479 3.36219 4.31857 4.85976 5.11973 5.16939 4.98225 5.3573

							ILE68	Hydrophobic		4.43571
W1	-9.0	3	ARG242 GLN71 ASP227	H-Bonding H-Boning H-Bonding	Conventional Conventional Carbon H	2.5075 2.29945 3.13905	TRP67 TYR75 TYP75 PHE196 ARG310	Hydrophobic Hydrophobic Hydrophobic Hydrophobic Hydrophobic	Pi-Sigma Pi-Pi Stacked Pi-Pi T-S Pi-Pi T-S Pi-Alkyl	3.84262 4.17575 5.65775 4.94675 4.86395
W14	-8.8	11	ARG242 ARG242 ARG242 ARG309 ARG309 ARG310 THR240 ASP227 ARG310 ILE68 SER313	H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding H-Bonding	Conventional Conventional Conventional Conventional Conventional Conventional Conventional Conventional Conventional Carbon-H Carbon -H	2.90312 2.78665 2.41498 2.21038 2.32075 2.67763 3.77673 2.76423 2.79955 3.63428 3.78979	GLU195 ARG81 TRP67 TRP67 TYR155 PHE196 ARG310	Halogen Electrostatic Hydrophobic Hydrophobic Other Hydrophobic Hydrophobic	Halogen (F) Pi-Cation Pi-Sigma Pi-Sigma Pi-Sulfur Pi-Pi T-S Pi-Alkyl	2.9638 4.67446 3.5958 3.94833 5.70625 5.07087 4.72502
Metformin	-5.7	2	ARG310 GLN71	H-B H-B	Conventional Conventional	2.33757 2.34374				

Table S4: Eigenvalue for docked coplexes

Docked complex names	Eigenvalue
1GPY-W6	1.30× 10−4
3BAJ-W6	2.22× 10−4
3RX2-W6	4.55× 10−4
4J3J-W6	2.50× 10−5

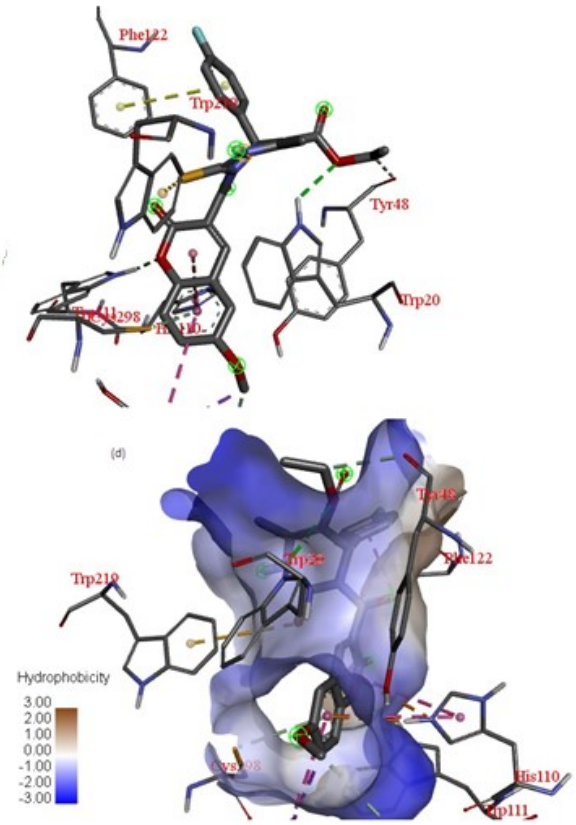


Figure S1: Interaction of W1 with 3BAJ, 3D-protein-ligand interaction, hydrophobic interaction

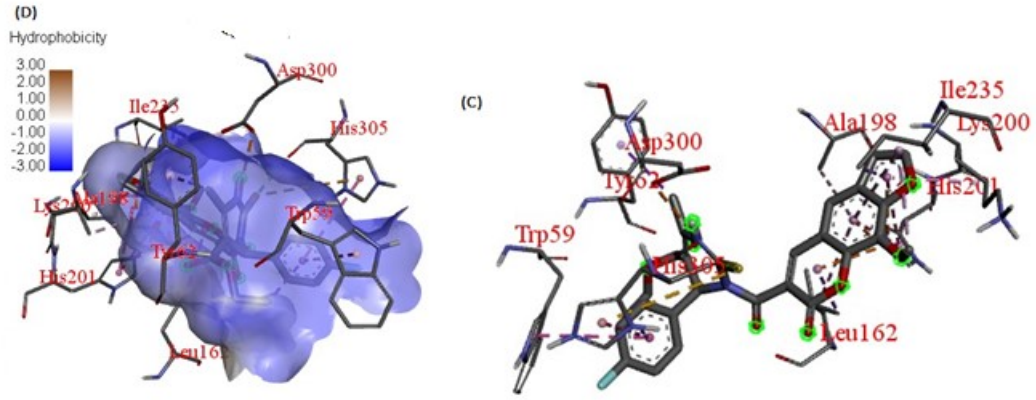


Figure S2: c)-compound W24 within protein pocket; b)-3D-interaction of 8-methoxy Psoralen-Pyrimidine complex (**W24**) *with 4J3J, , and d-hydrophobic interaction*

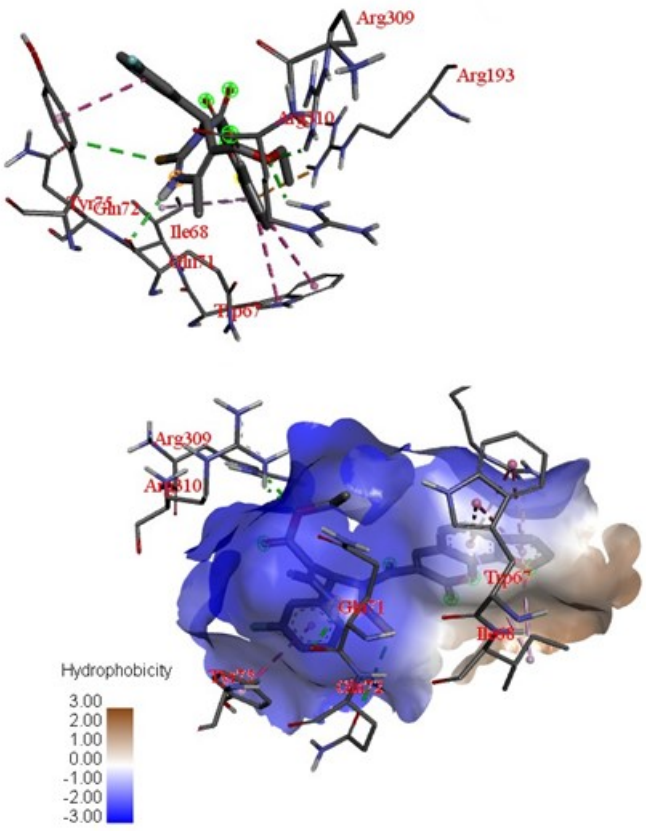


Figure S3: Interaction of W19 *with* 1GPY *Protein in complex with Ligand, 3D-protein-ligand interaction & hydrophobic interaction*

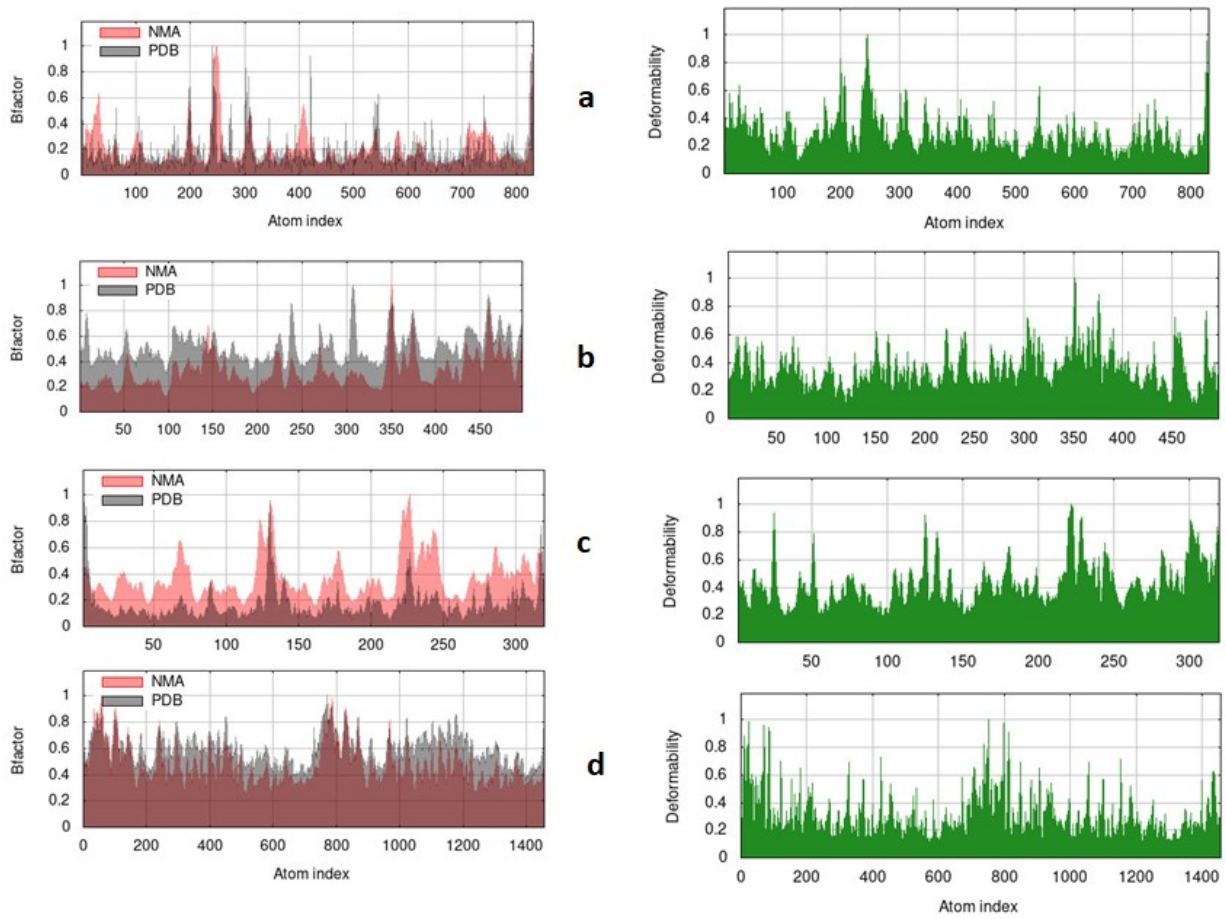


*Figure **S4**: Deformability and B-factor graphs of complex a) complex 1GPY-W6 b) complex 3BAJ-W6 c) complex 3RX2-W6 d) complex 4J3J-W6.*

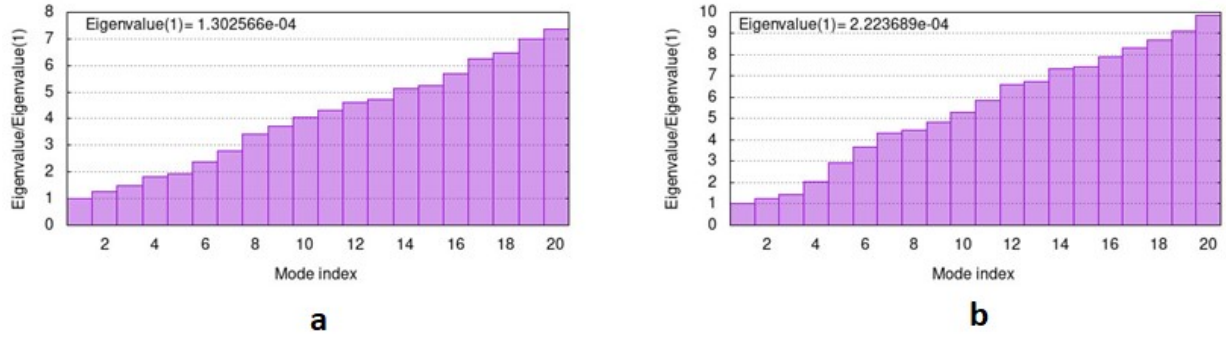


Figure S5: Eigenvalue of the complexes a) complex 1GPY-W6 b) complex 3BAJ-W6

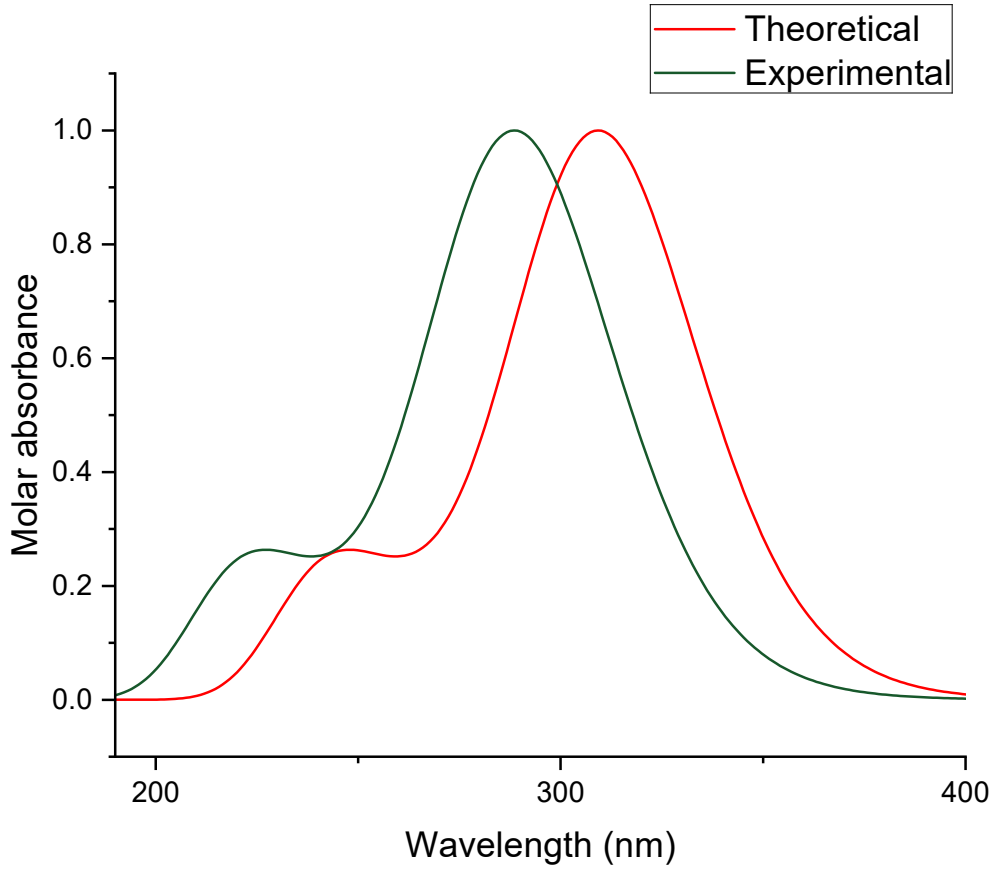


*Figure S6a: Plot of λ_{max} (nm) and molar absorbance of compound **A***

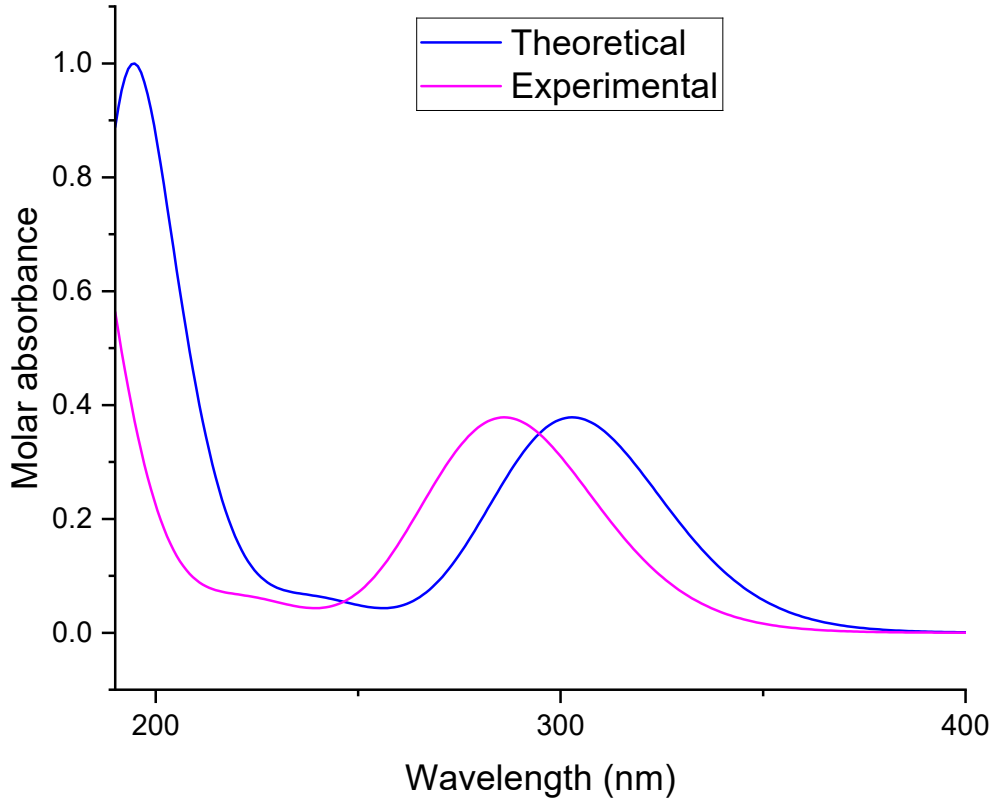


Figure S6b: Plot of λ_{max} (nm) and molar absorbance of compound ***B***

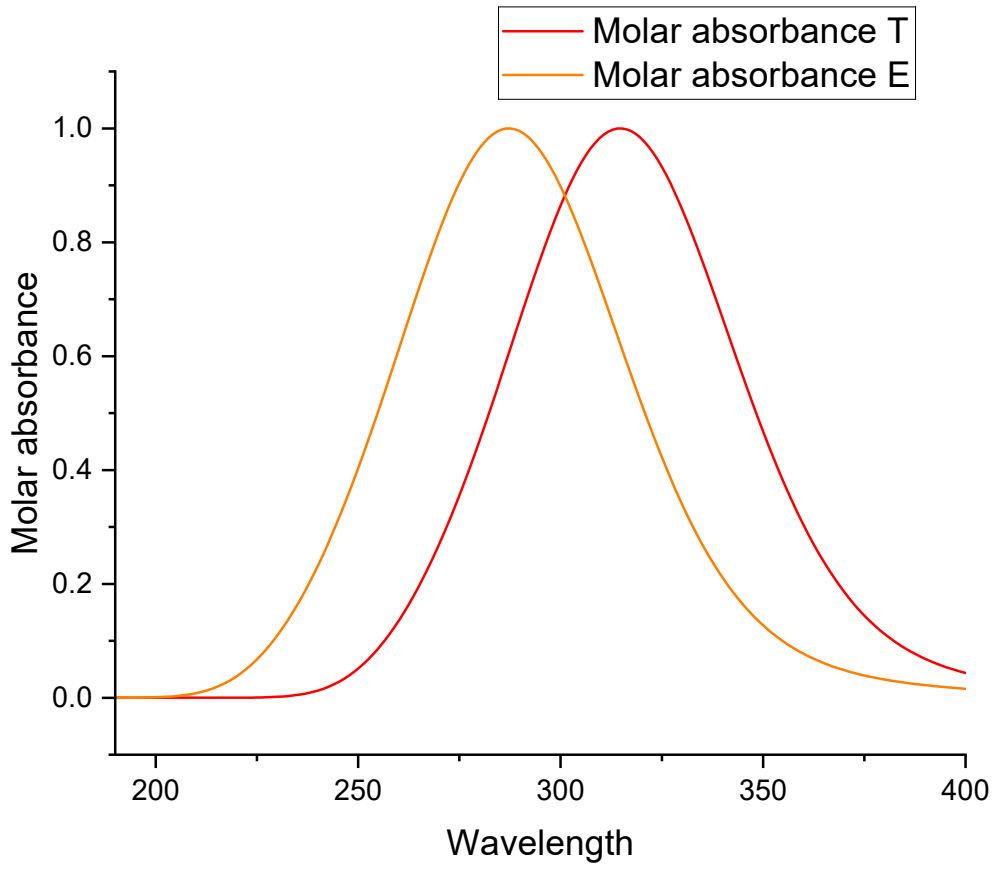


Figure S6c: Plot of λ_{max} (nm) and molar absorbance of compound ***C***

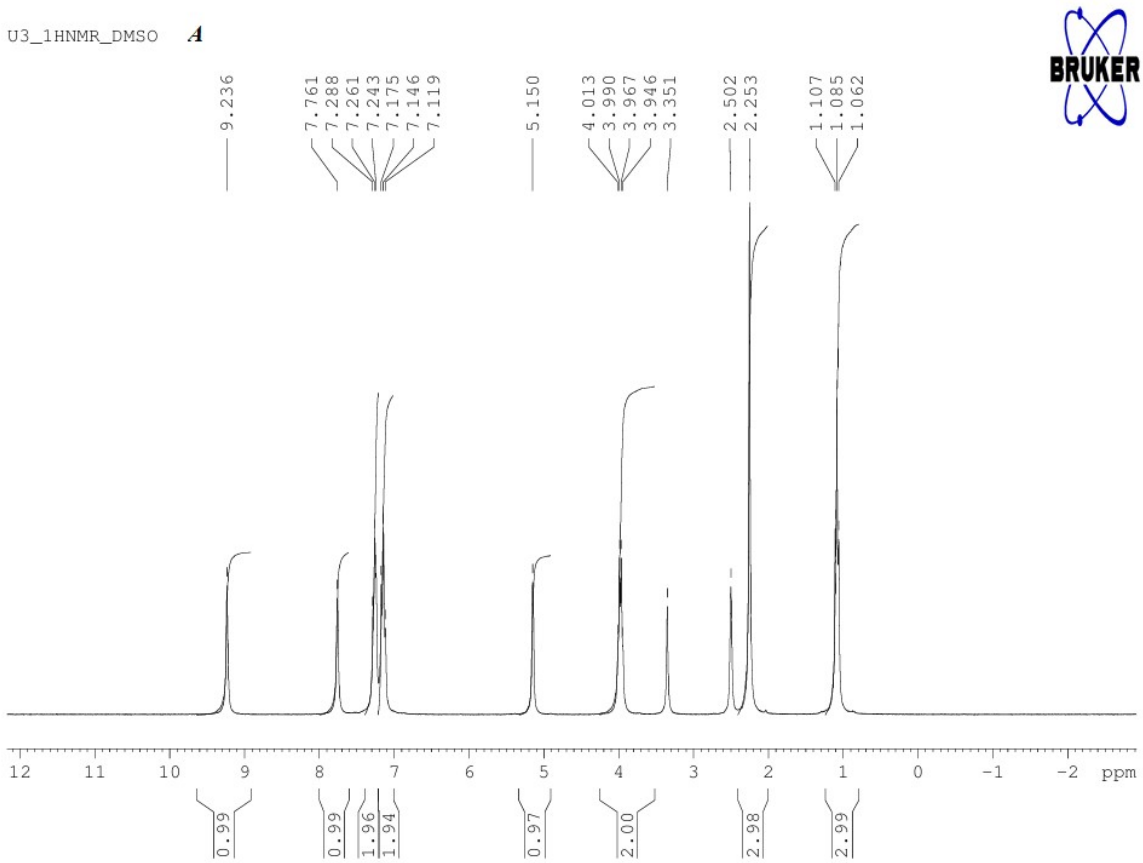


Figure S7: [1]H-NMR of compound A (precursor)

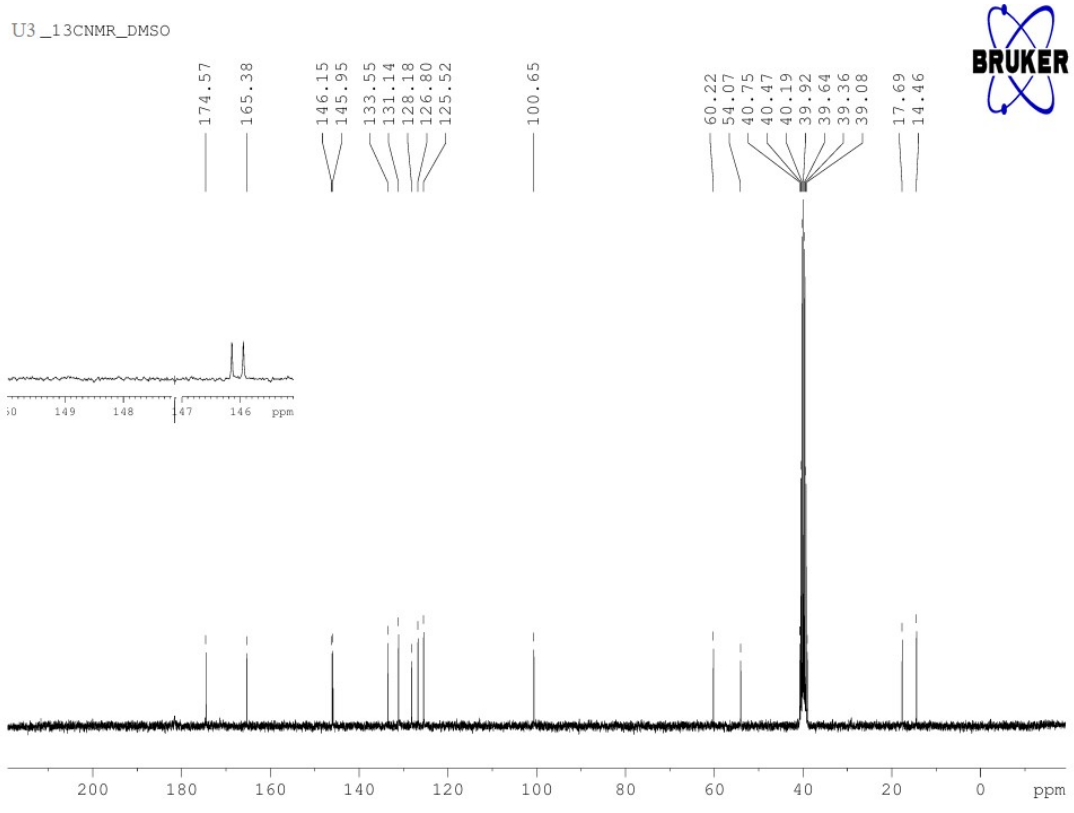


Figure S8: Experimental [13]C-NMR of compound A (precursor)

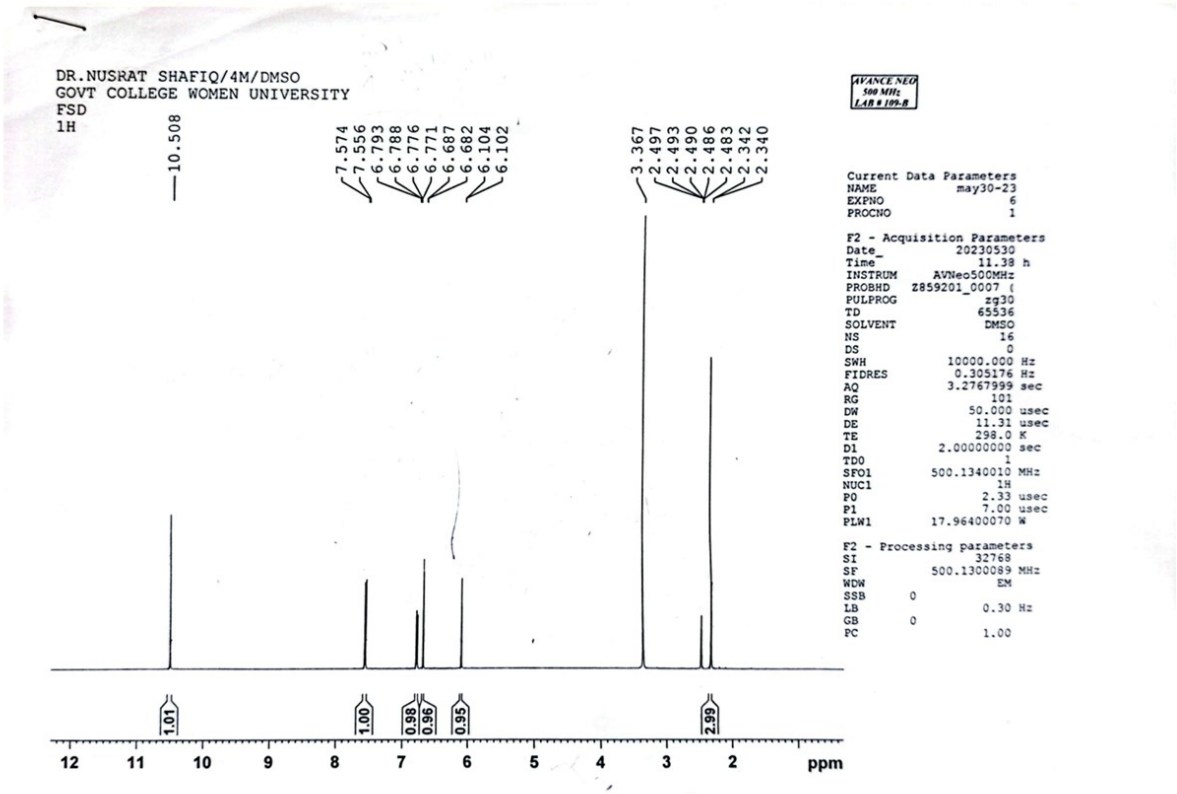


Figure S9: Experimental ^{1}H-NMR of compound B (precursor)

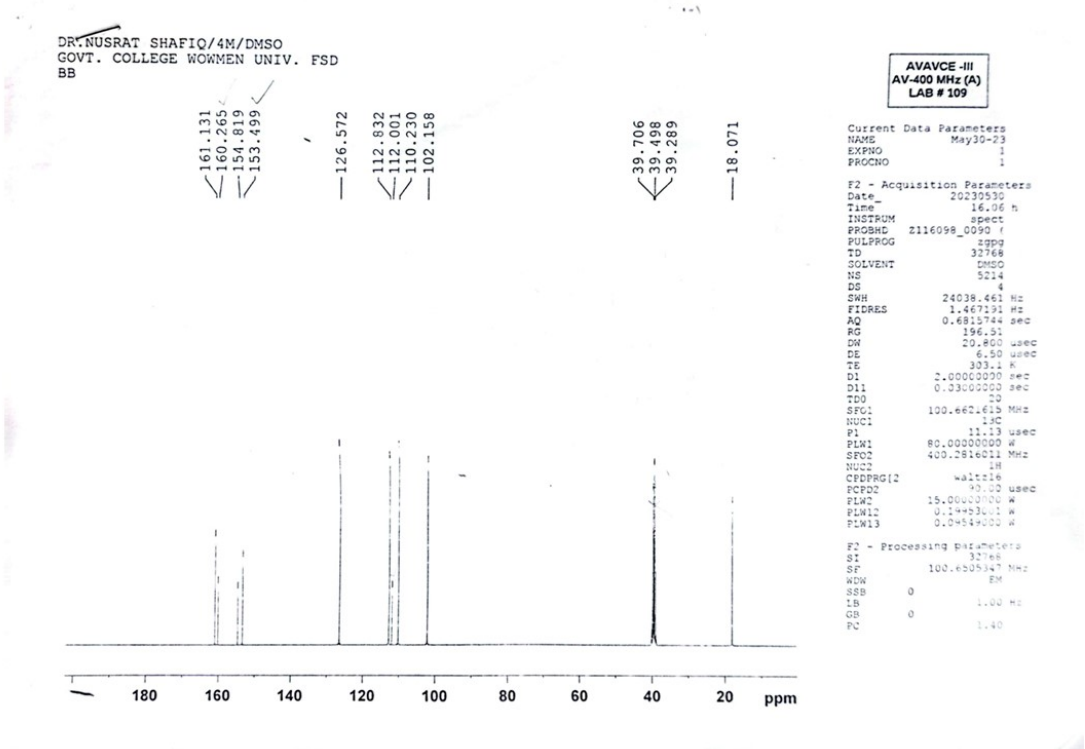


Figure S10: Experimental ^{13}C-NMR of compound B (precursor)

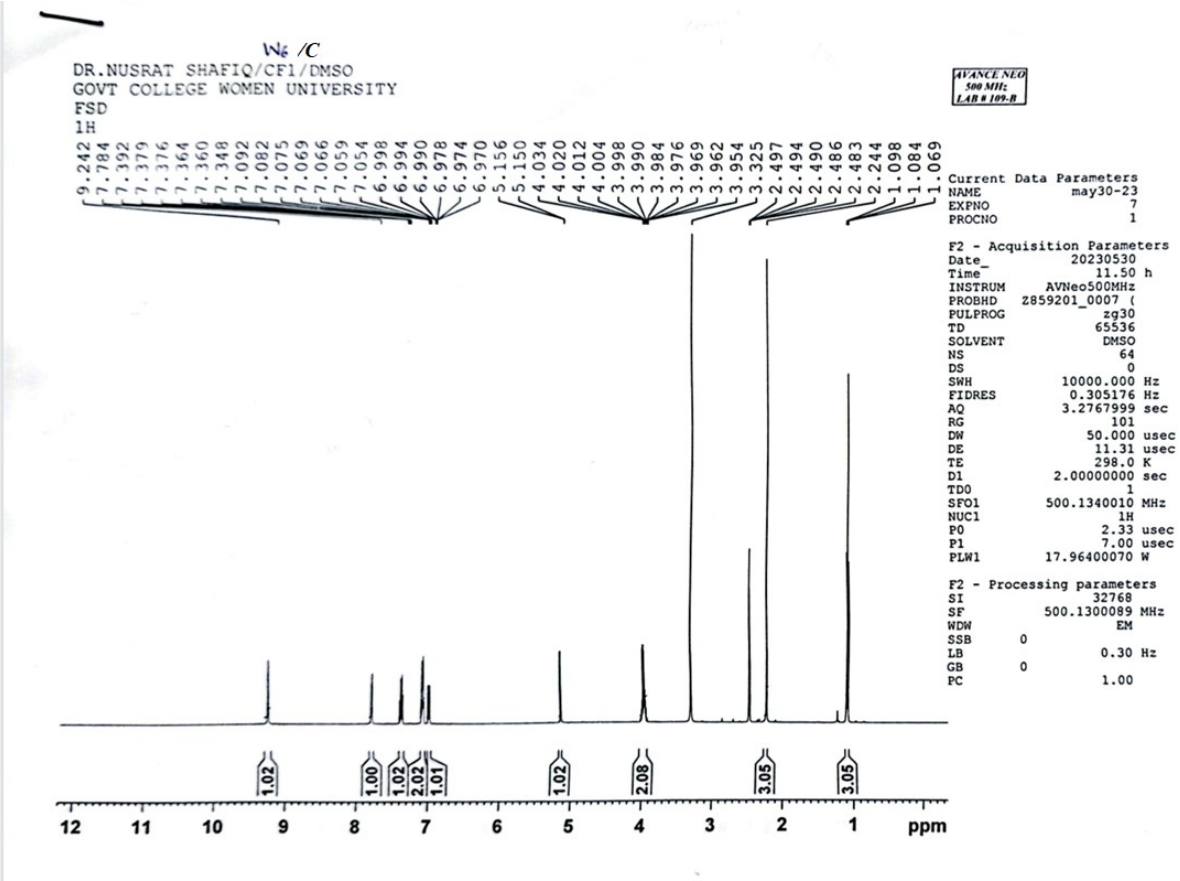


Figure S11: Experimental ^{1}H-NMR of compound C (**W6**)

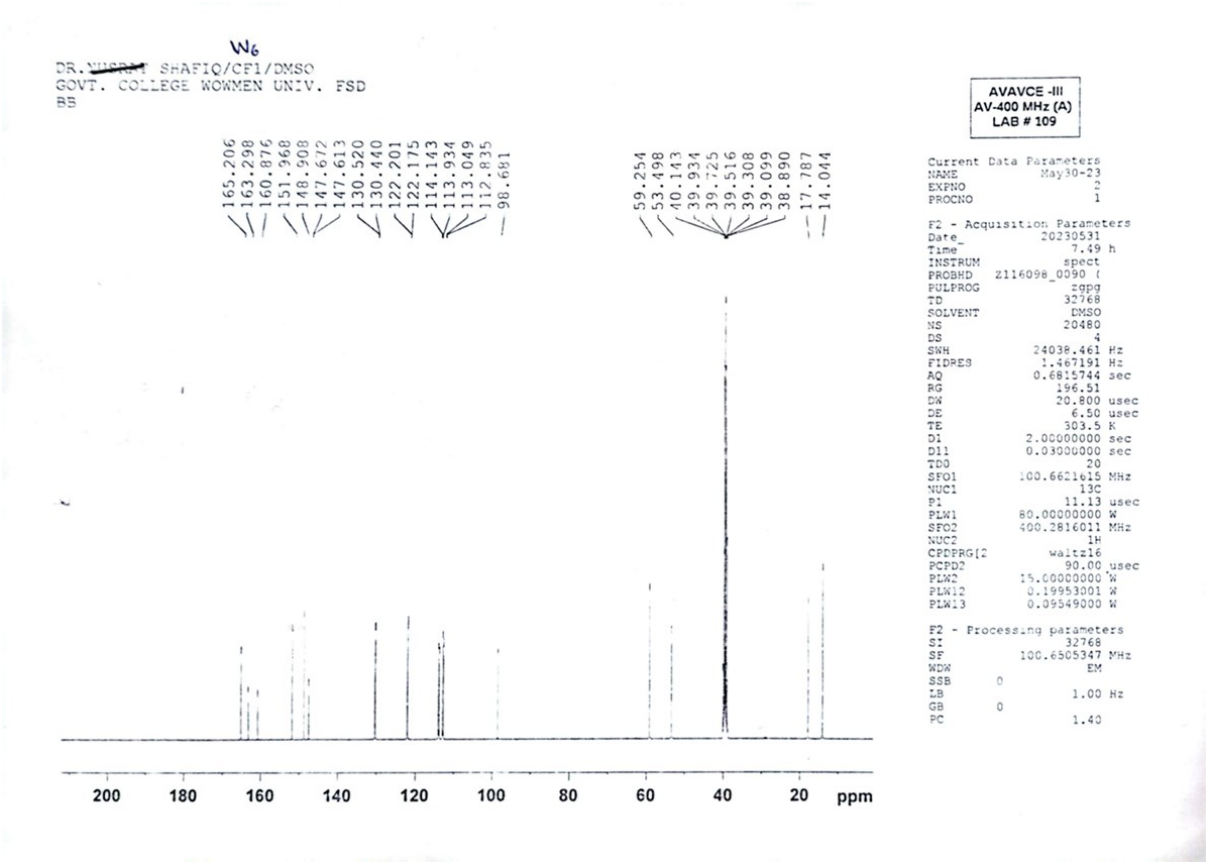


Figure S12: Experimental ^{13}C-NMR of compound C (**W6**)

1.1. Spectroscopic characterization

Synthesized target lead was analyzed for structure confirmation by ^{1}H- and ^{13}C-NMR spectroscopy.

Characterization of A*:* White shiny crystalline solid; soluble in DMSO; M.P = 202–206 ◦C; UV: λ_{max}. 218, 325; FT-IR: 3163, 2811, 1893, 1879, 1852, 1802, 1672, 1614, 1451, 1391, 1370, 1336, 1328, 1312, 1275, 1240, 1227, 1216, 1160, 1135, 1069, 1018, 983, 898, 878, 865, 845, 806,763, 755, 748, 694, 643, 584, 530 cm^{-1}; *^{1}H-NMR* (DMSO-d_6,300 MHz): δ 10.43 (1H, *s*, NH-6), 9.75 (1H, *s*, NH-2), 7.44 (1H, *dd*, H-12), 7.08 (1H, *d*, H-11), 7.15 (1H, *d*, H-13), 6.97 (1H, *s*, H-9), 5.21 (1H, *s*, H-3), 4.05 (1H, *q*, *J* = 6.3 Hz, CH_2-2′), 2.50 (1H, *s*, CH_3-6), 1.12 (1H, *t*, CH_3-3′); *^{13}C-NMR* (DMSO-d_6, 25 MHz) (see supplementary material): δ 165.43 (C-1′), 174.61 (C-1), 160.97 (C-5), 146.51 (C-8), 164.21 (C-10), 131.27 (C-12), 113.73 (C-11), 113.44 (C-9), 122.87 (C-13), 100.74 (C-4), 60.18 (2′-CH_2), 53.99 (C-3), 17.67 (CH_3), 14.46 (3′-CH_3); EIMS: m/z 294.02 (calcd. For $C_{14}H_{15}FN_2O_2S$) [14].

Characterization of B*: C*olorless crystalline material; UV: λ_{max}. 285.58; FT-IR: 332, 3010, 154, 1482, 1234, 1095, 550 cm^{-1}; *^{1}H-NMR* (DMSO-d_6, 500 MHz): δ 6.10 (1H, s, H-3), 7.57

(1H, d, J=9.0Hz, H-5), 6.68 (1H, d, J=2.5Hz, H-8), 10.5 (1H, s, 7-OH), 6.79 (1H, dd, J= 9.0, 2.5 Hz, H-6), 2.99 (3H, s, 11-CH_3); *^{13}C-NMR* (DMSO- d_6, 400MHz): δ 160.2 (C-2), 112.8 (C-2), 153.4 (C-4), 126.5 (C-5), 110.2 (C-6), 161.1 (C-7), 102.1 (C-8), 154.8 (C-9), 112.0 (C-10), 18.0 (CH_3-11), EIMS: m/z 176.02 (cacld. For $C_{10}H_8O_3$).

Characterization of C**: C*olorless shiny crystalline material, Soluble in DMSO; ***UV**: λ_{max}*. 218, 284; ***FT-IR: 3327, 3163, 3010, 2811, 1893, 1879, 1852, 1802, 1672, 1614, 1451, 1391, 1370, 1336, 1328, 1312, 1275, 1240, 1227, 1216, 1160, 1135, 1069, 1018, 983, 898, 878, 865, 845, 806,763, 755, 748, 694, 643, 584, 530, 154, 1482, 1234, 1095, 550 cm^{-1}**; *^{1}H-NMR*** (DMSO-d_6, 500 MHz): δ 9.24 (-NH), 7.39 (1H, dd, J=8, 2Hz, H-5), 6.99 (1H, dd, J=8, 2Hz, H-6), 9.24 (1H, s, 7-OH), 7.09 (1H, d, J= 2.0 Hz, H-8), 2.25 (3H, s, CH_3-11), 5.15 (1H, s, H-6′), 2.24 (3H, s, 4′-CH_3), 7.36 (1H, dd, J=2.0Hz, H-8′), 7.05 (1H, dd, J=6, 2Hz, H-10′), 7.37 (1H, m, H-11′), 6.99 (1H, dd, J=6,2Hz, H-12′), 4.03 (2H, d, CH_2-2″), 1.09 (3H, dd, J=7.4Hz, CH_3-3″); ***^{13}C-NMR*** (DMSO-d_6, 400MHz): δ 122.1 (C-3), 147.6 (C-4), 126.5 (C-5), 113.0 (C-6), 160.8 (C-7), 98.6 (C-8), 113.1 (C-9), 151.9 (C-10), 14.0 (CH_3-11), 69.6 (C-2′), 148.9 (C-4′), 104.1 (C-5′), 53.9 (C-6′), 17.7 (CH_3-4′), 147.6 (C-7′), 114.1 (C-8′), 163.2 (C-9′), 113.9 (C-10′), 130.5 (C-11′), 122.2 (C-12′), 165.2 (C-1″), 59.2 (C-3″), 14.0 (C-4″); EIMS: m/z 470.12 (calcd. For $C_{24}H_{23}FN_2O_5S$).