Supporting information to

Synthesis, biological evaluation, acute toxicity and molecular docking studies of thiazolidine-2,4-diones derivatives as new class of α-glucosidase and α-amylase inhibitors.

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1.Spectral data

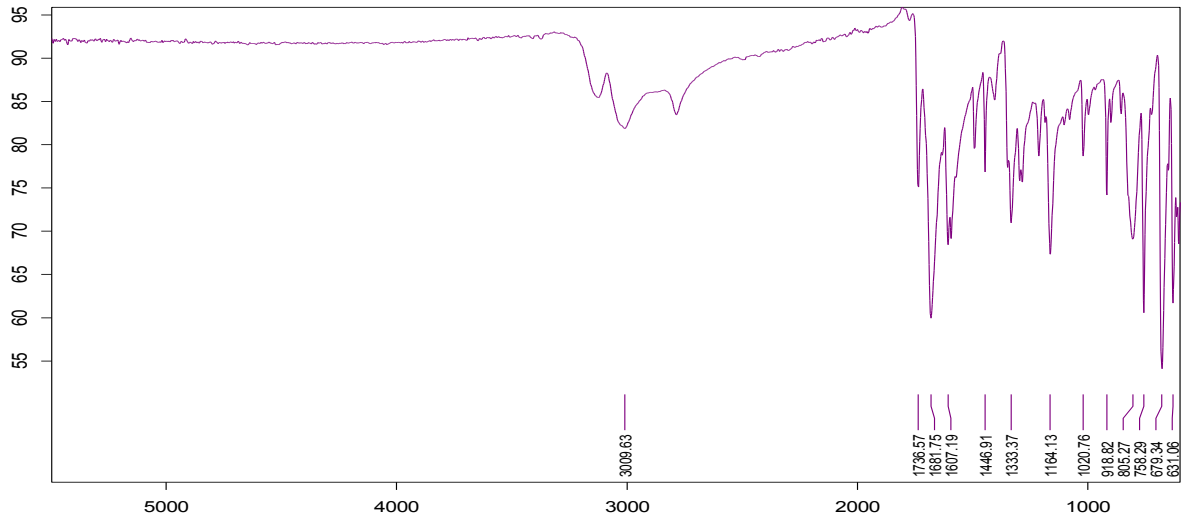

Figure S1. FT-IR spectrum of **(3a).**

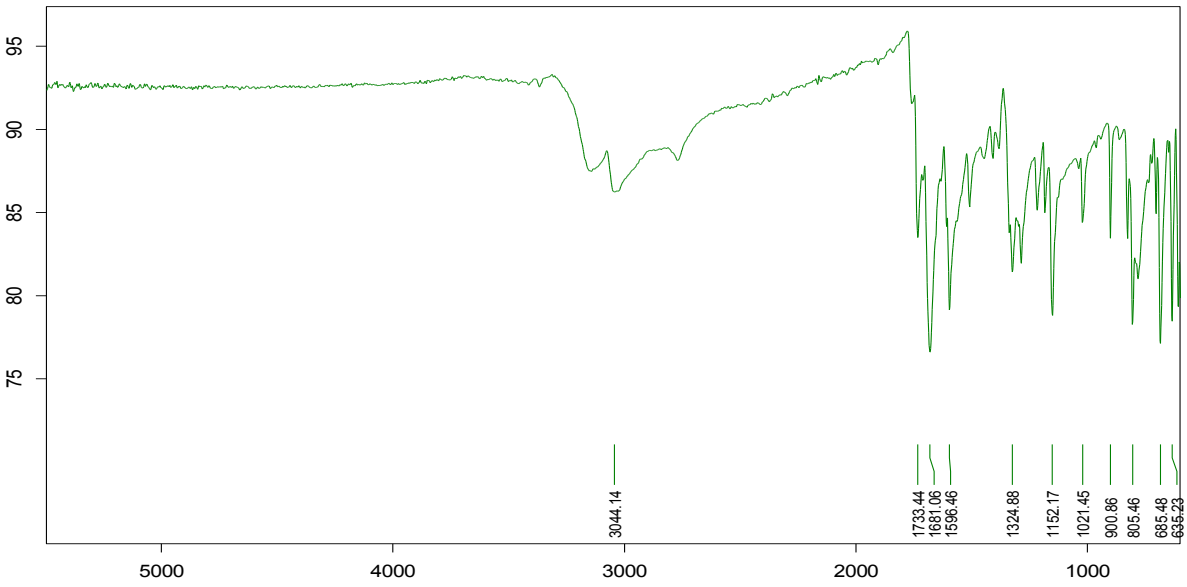

Figure S2. FT-IR spectrum of **(3b).**

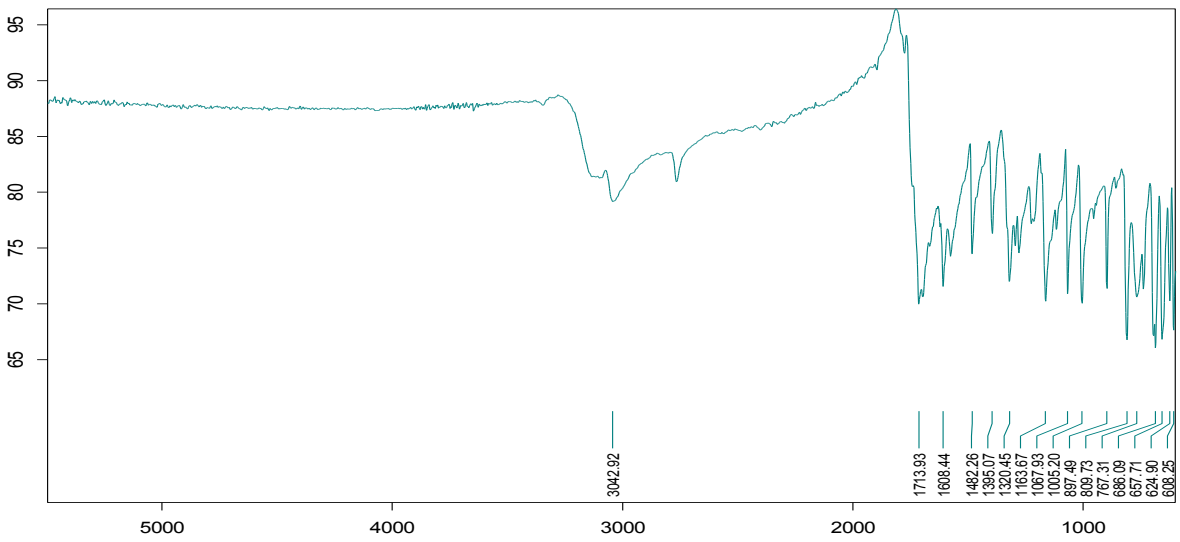

Figure S3. FT-IR spectrum of **(3d).**

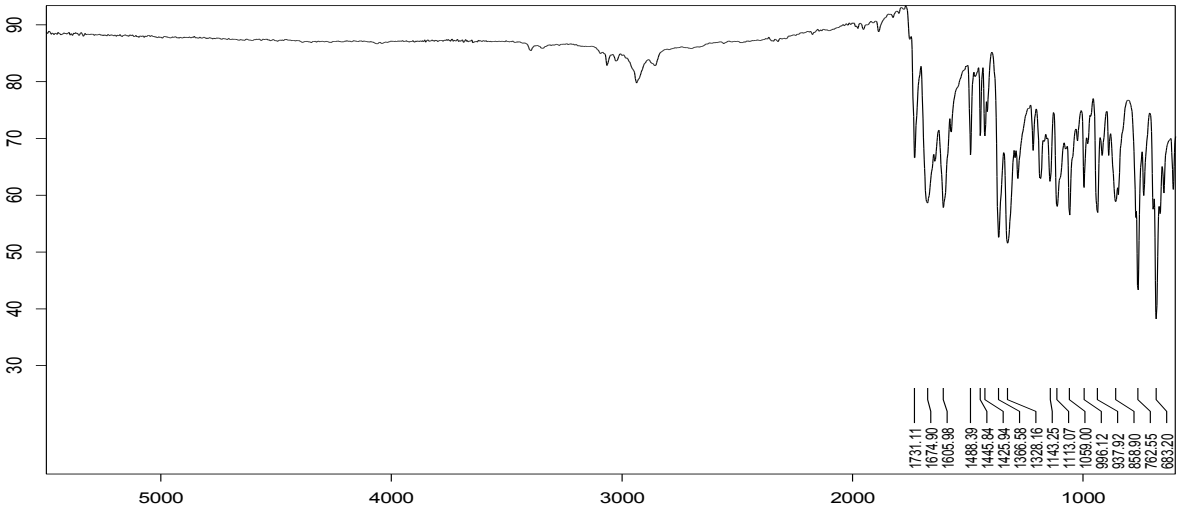

Figure S4. FT-IR spectrum of **(4a).**

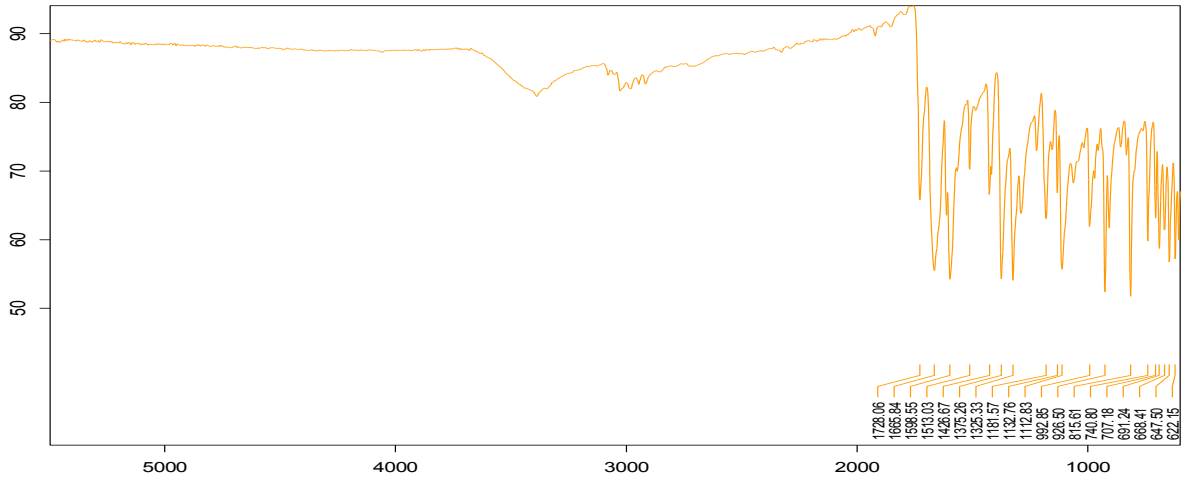

Figure S5. FT-IR spectrum of (**4b).**

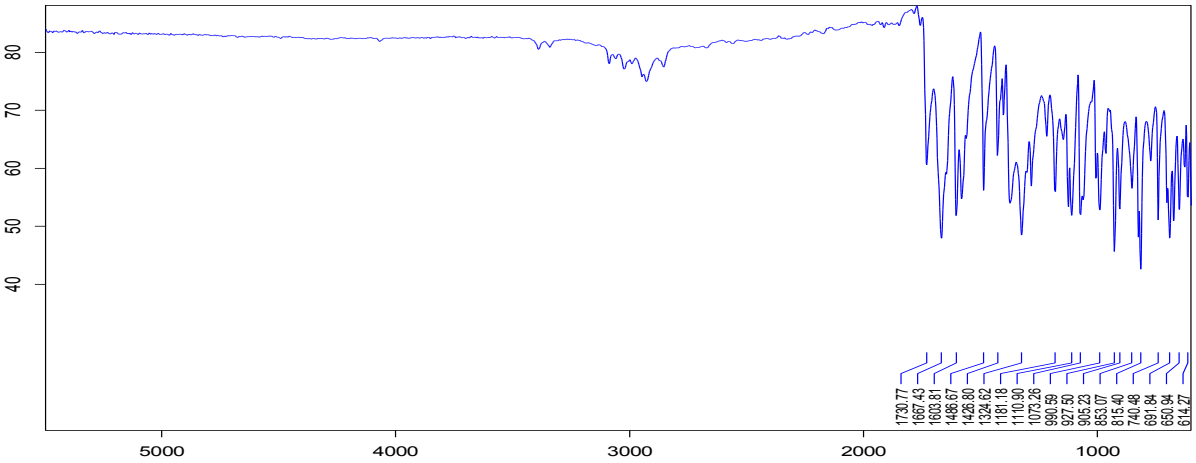

Figure S6. FT-IR spectrum of (**4d).**

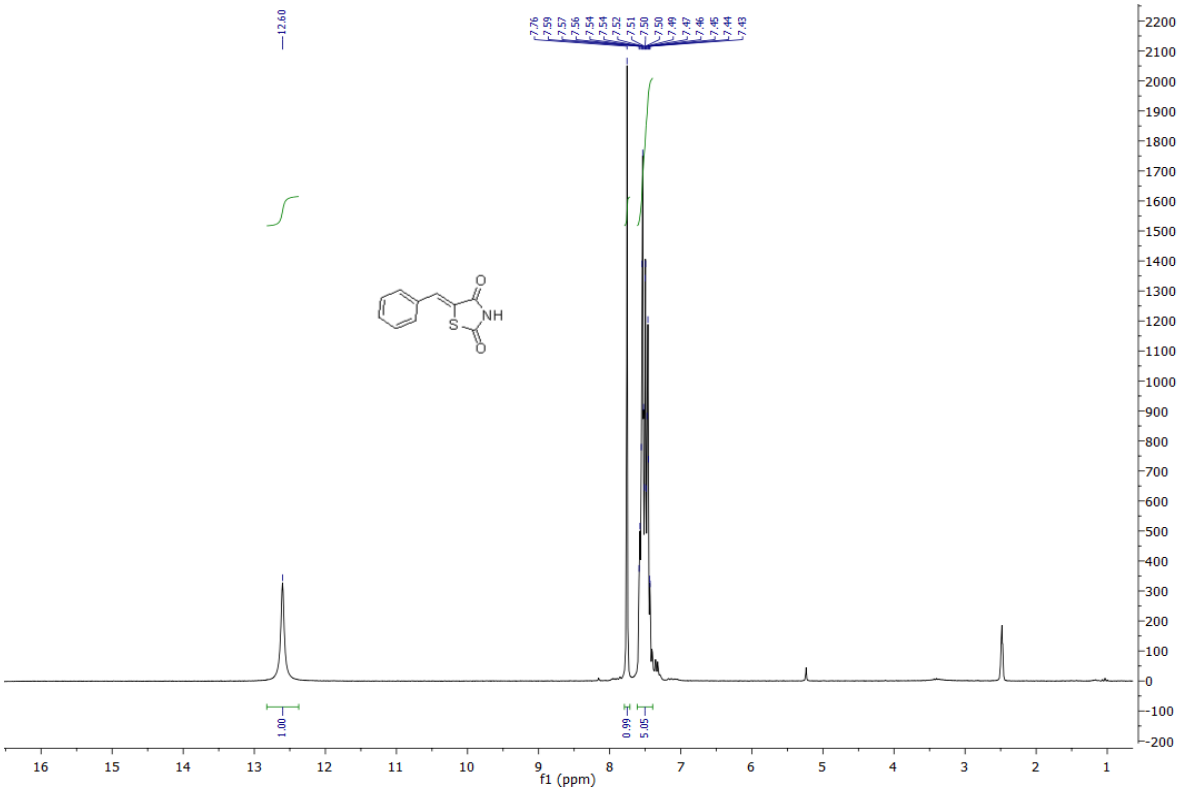

Figure S7. ^{1}H NMR spectrum of **(3a).**

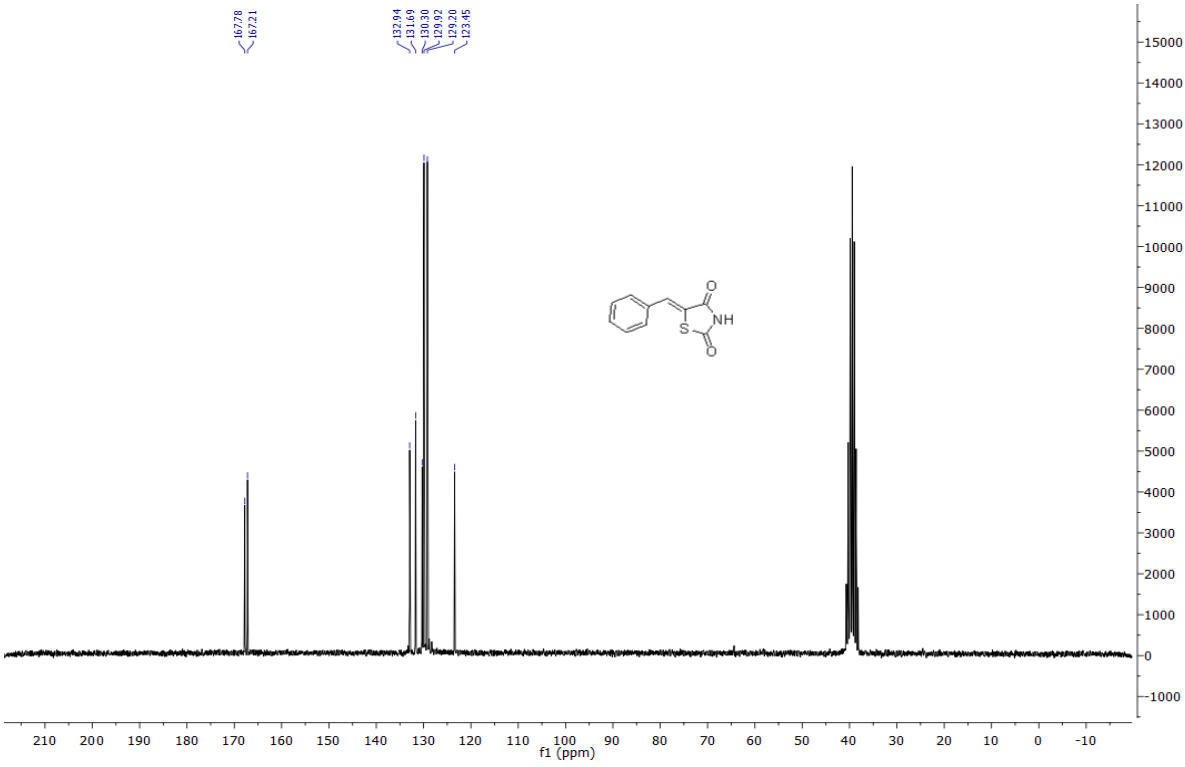

Figure S8. ^{13}C NMR Spectrum of **(3a)**.

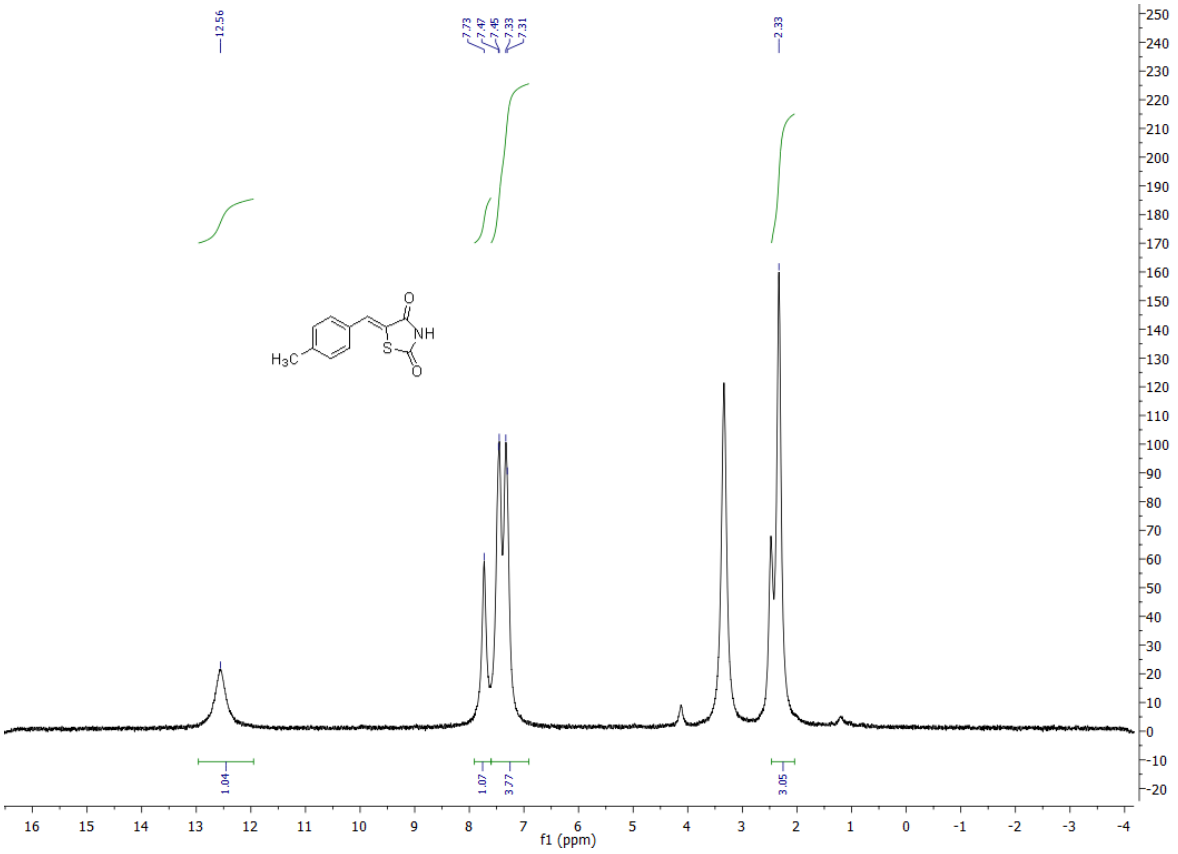

Figure S9. ^{1}H NMR spectrum of (**3b).**

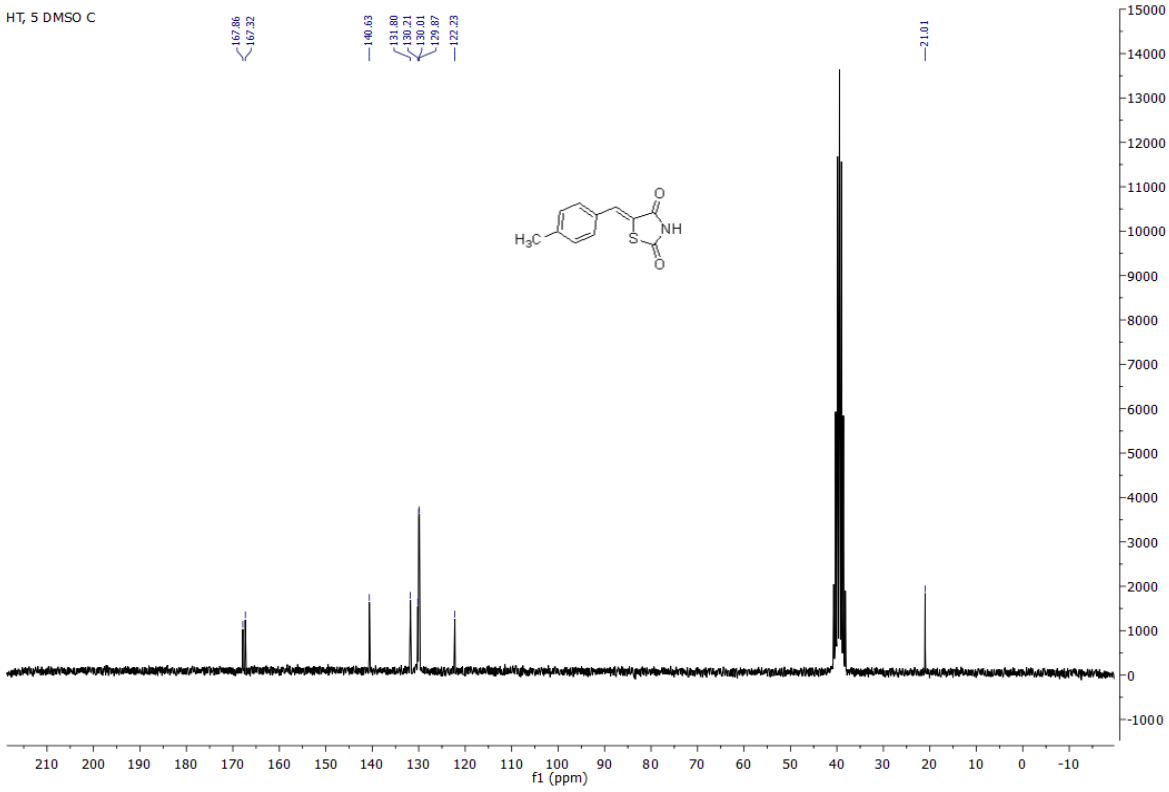

Figure S10. ^{13}C NMR Spectrum of **(3b).**

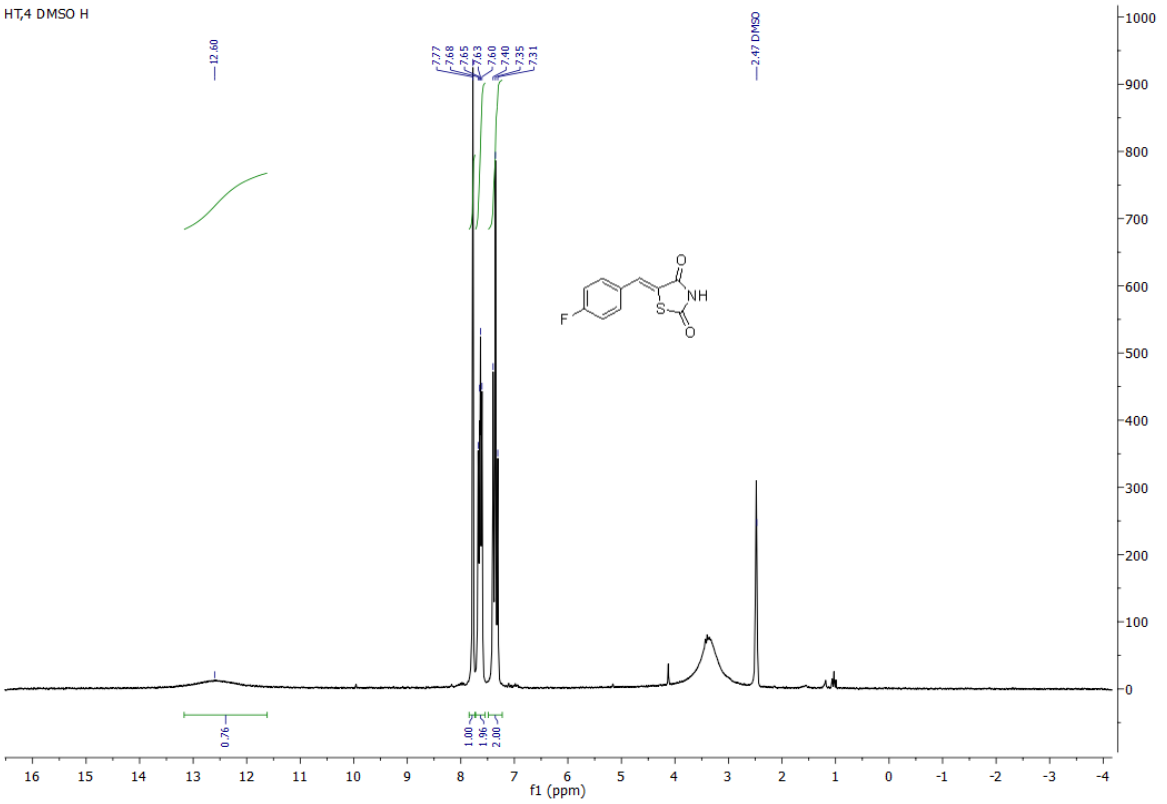

Figure S11. ^{1}H NMR Spectrum of **(3c)**.

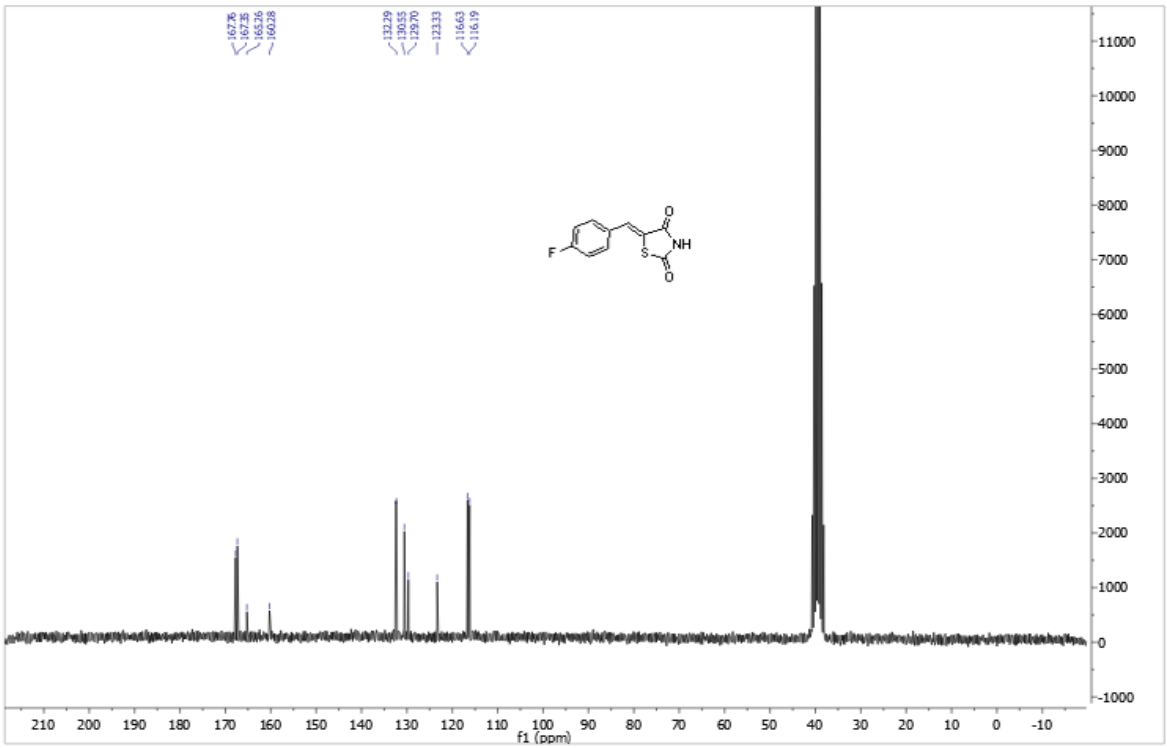

Figure S12. ^{13}C NMR Spectrum of **(3c)**.

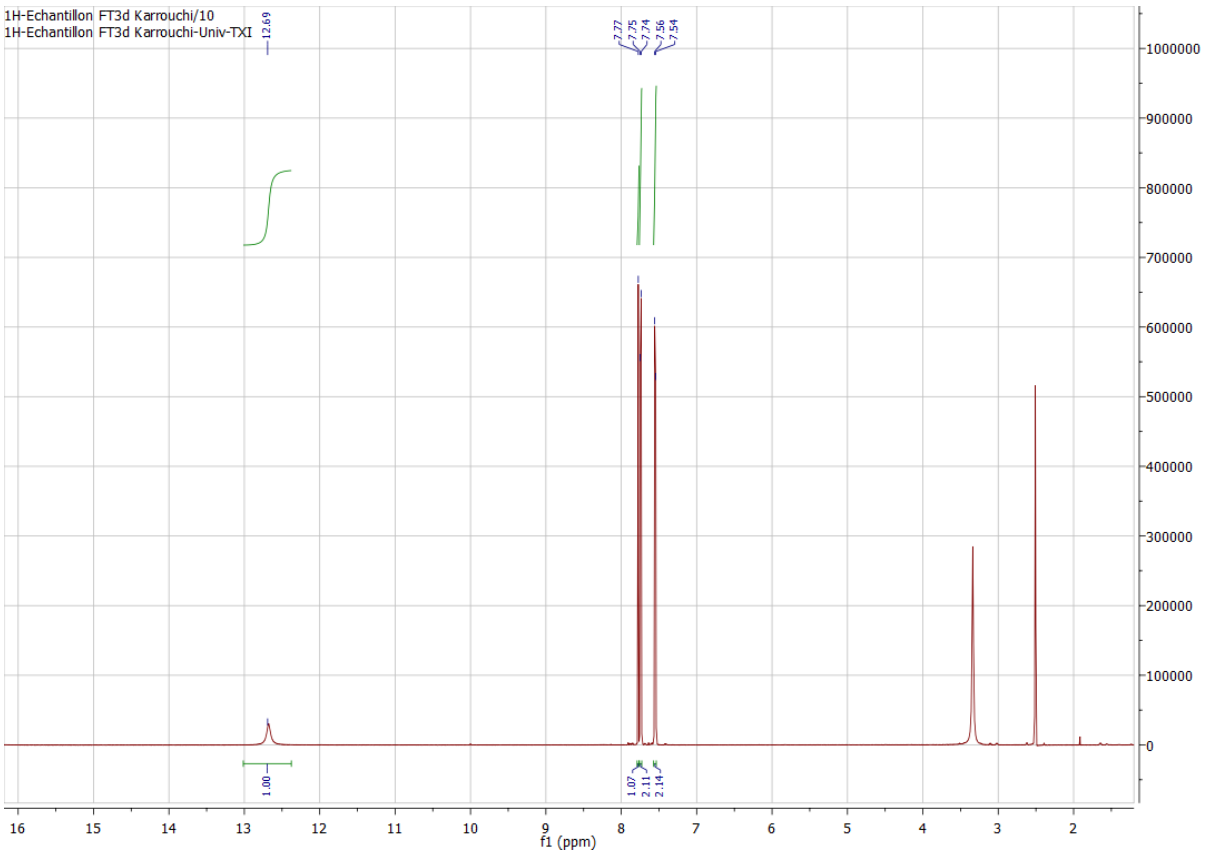

Figure S13. ^{1}H NMR Spectrum of **(3d)**.

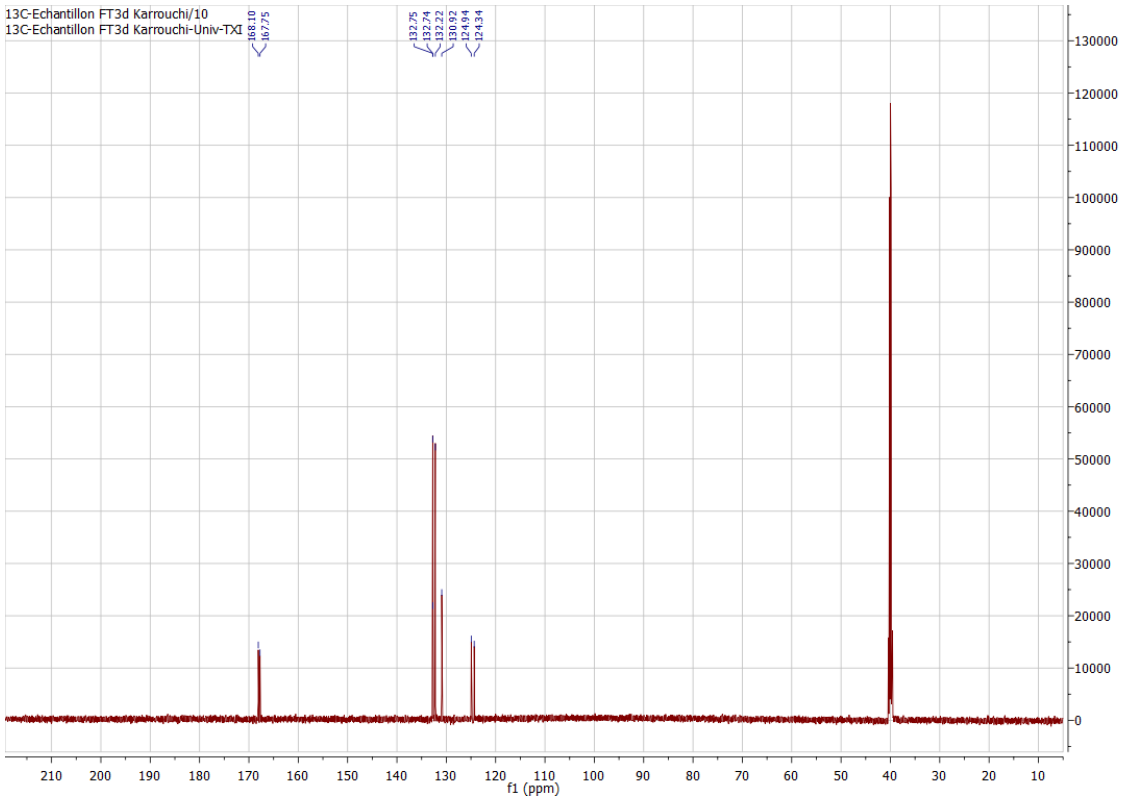

Figure S14. ^{13}C NMR Spectrum of **(3d)**.

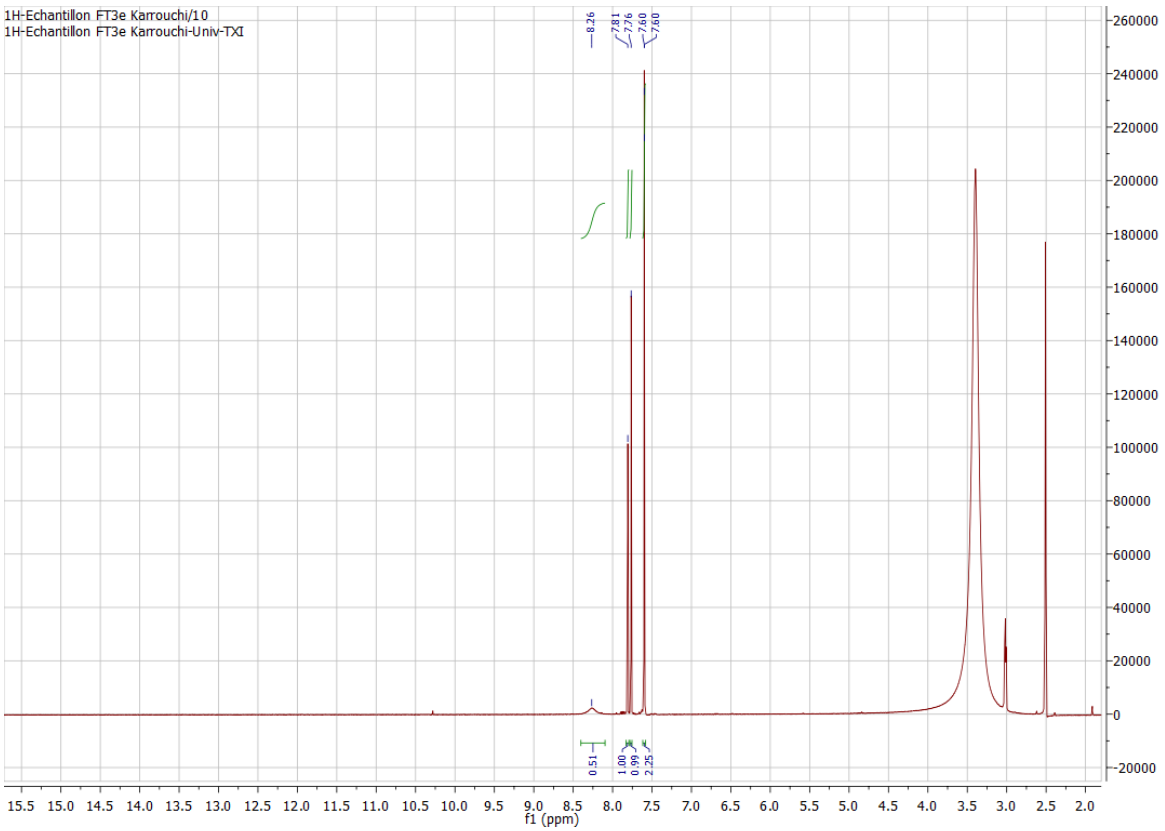

Figure S15. ^{1}H NMR Spectrum of **(3e)**.

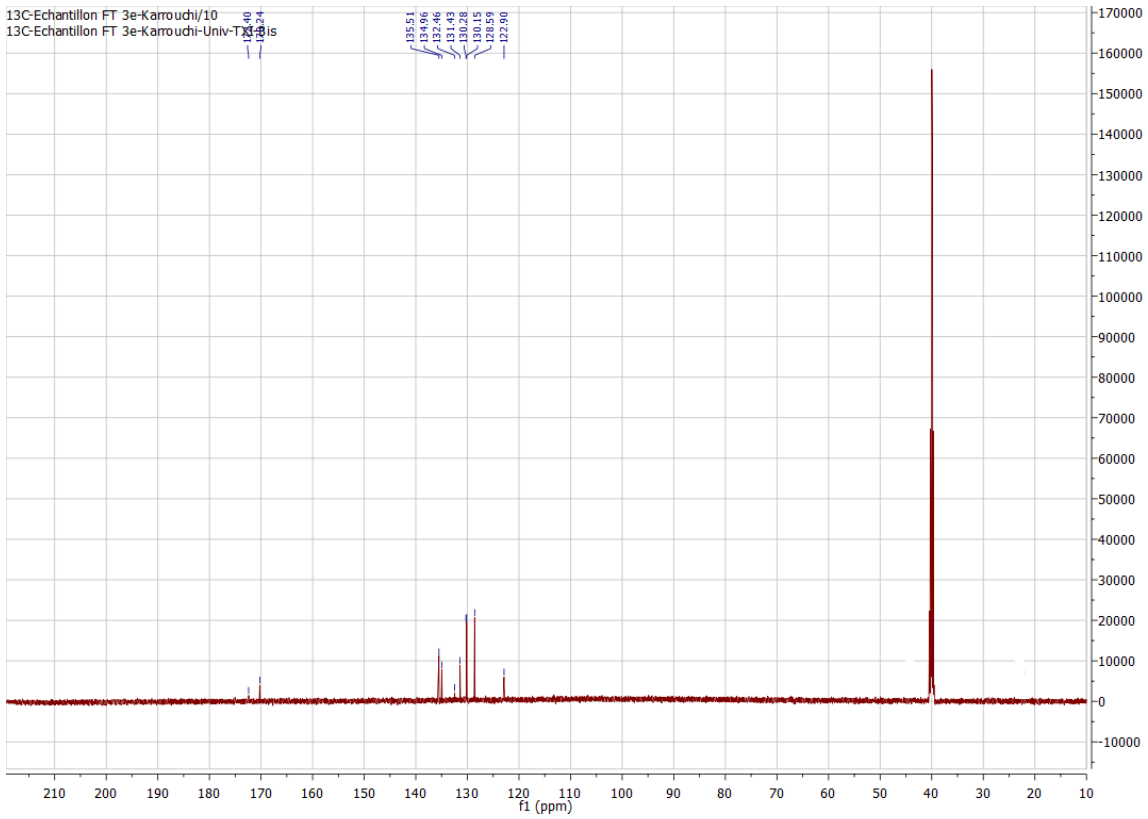

Figure S16. ^{13}C NMR Spectrum of **(3e)**.

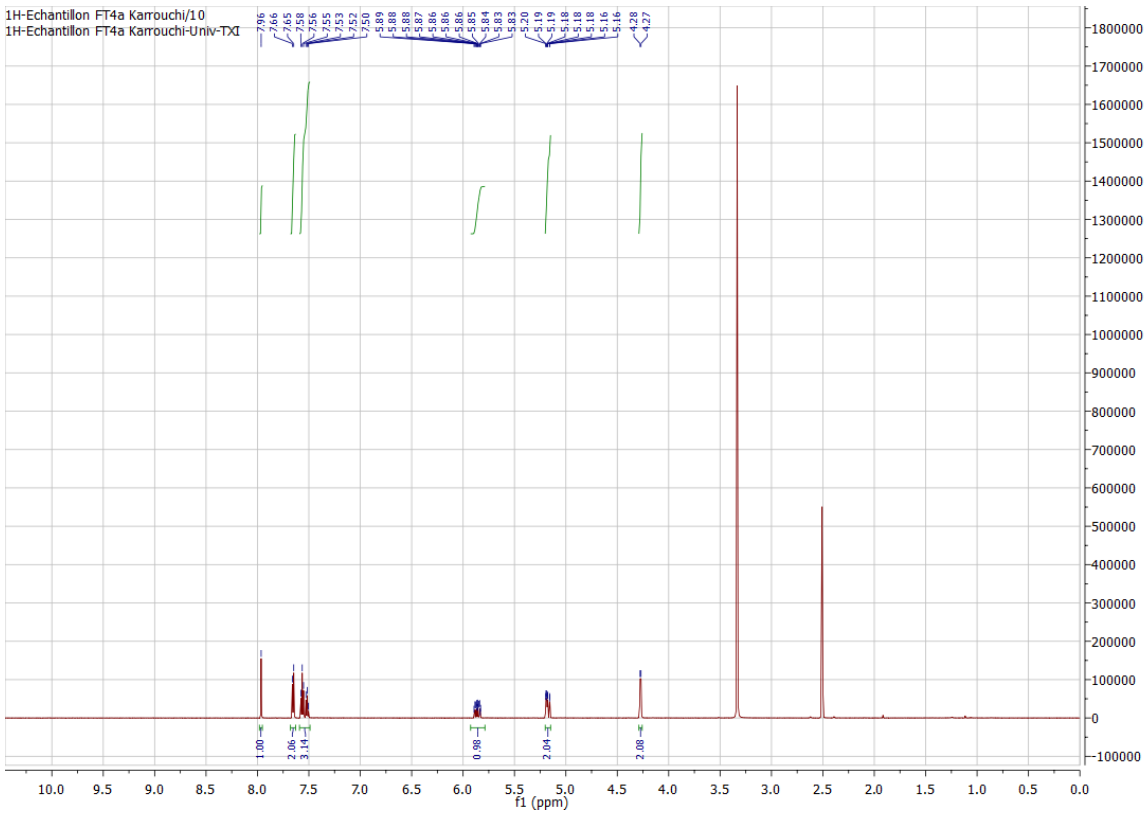

Figure S17. ^{1}H NMR Spectrum of **(4a)**.

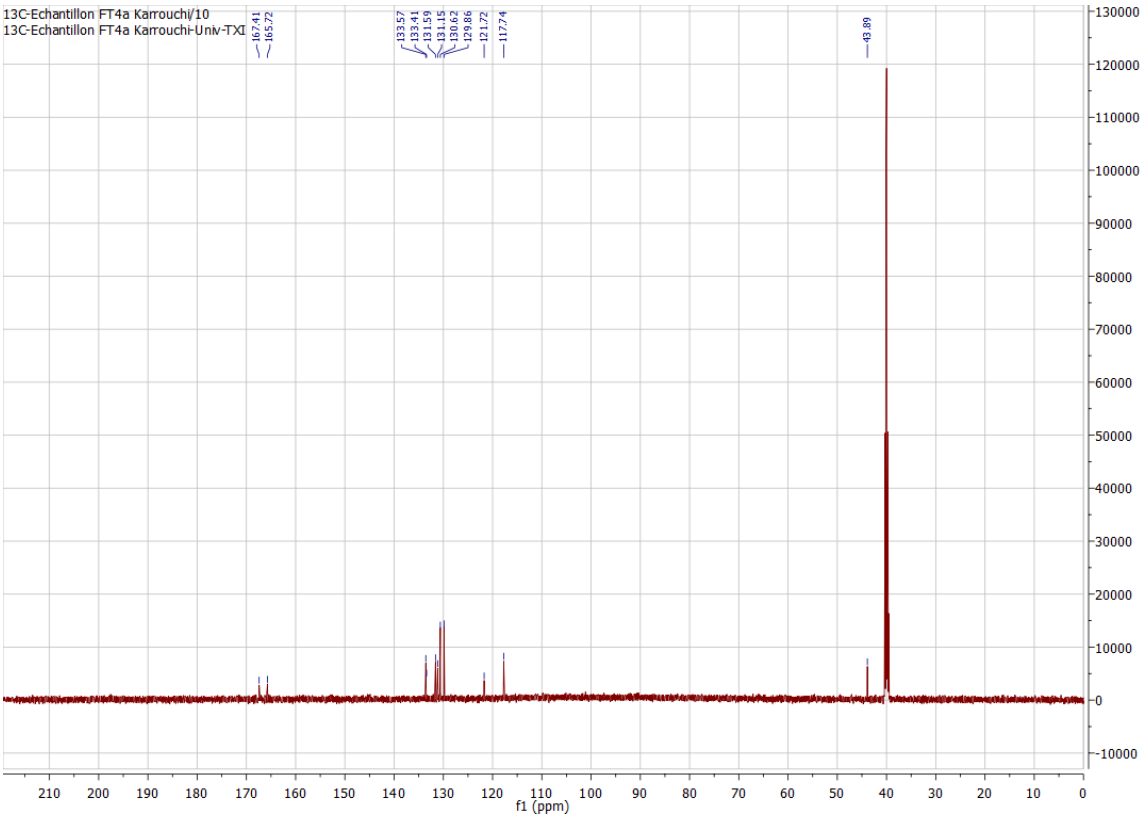

Figure S18. ^{13}C NMR Spectrum of **(4a)**.

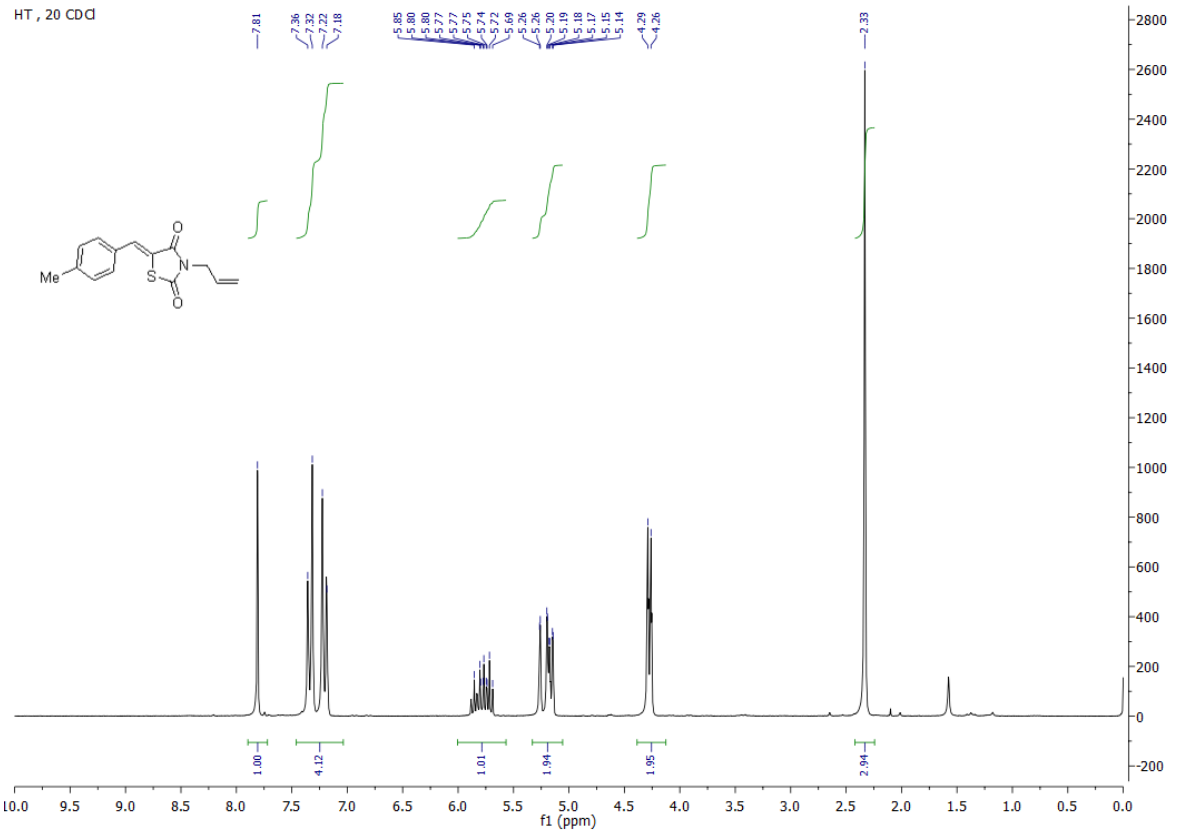

Figure S19. ^{1}H NMR spectrum of (**4b**).

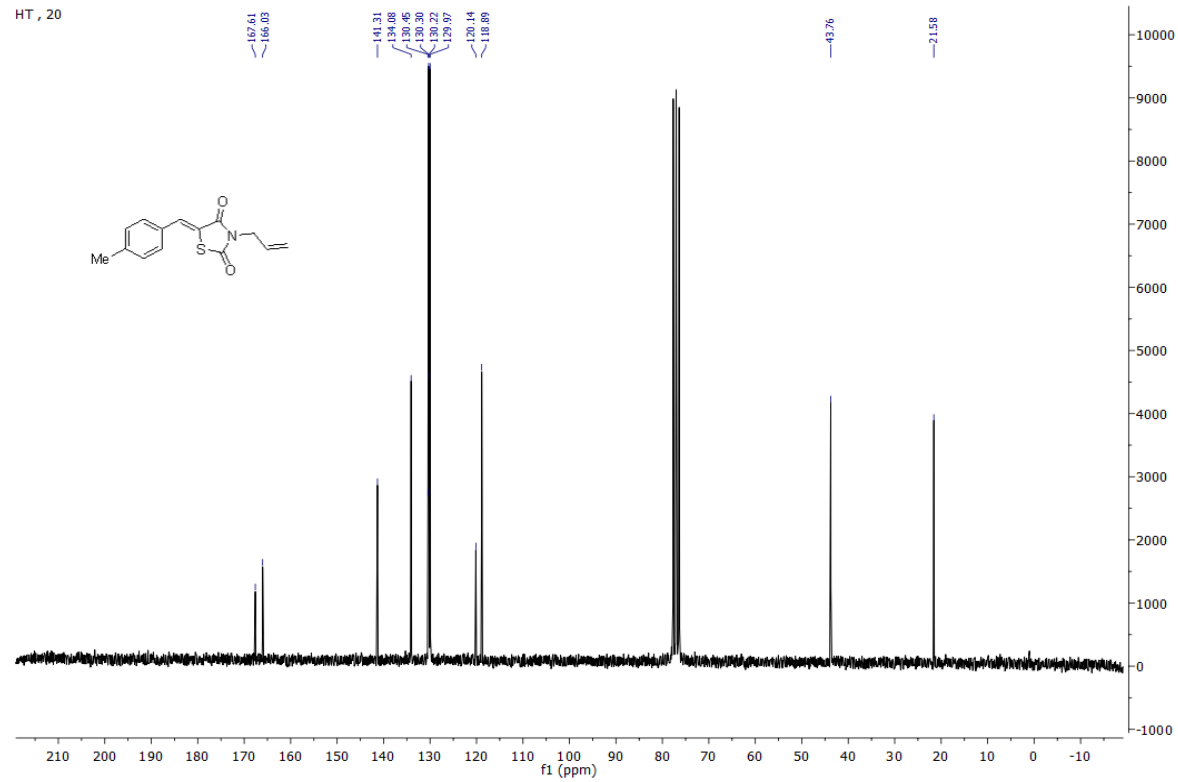

Figure S20. ^{13}C NMR spectrum of (**4b**).

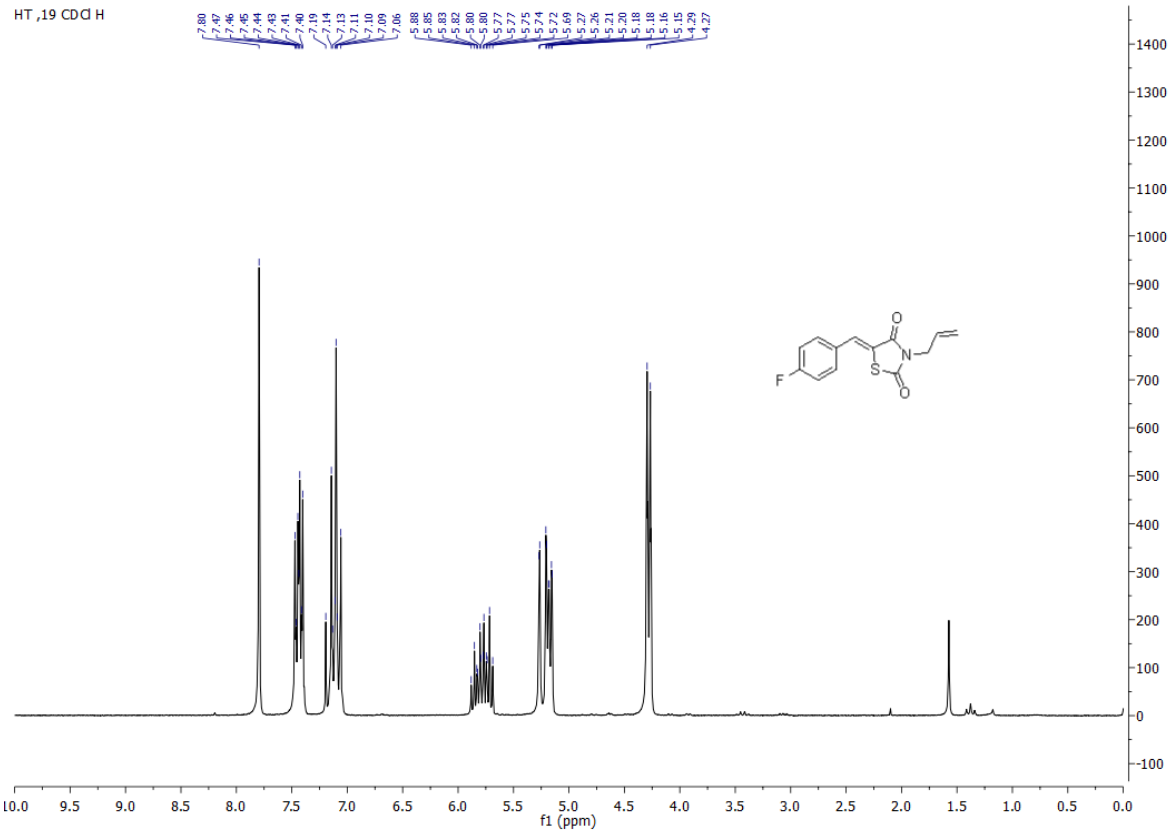

Figure S21. ^{1}H NMR spectrum of (**4c**).

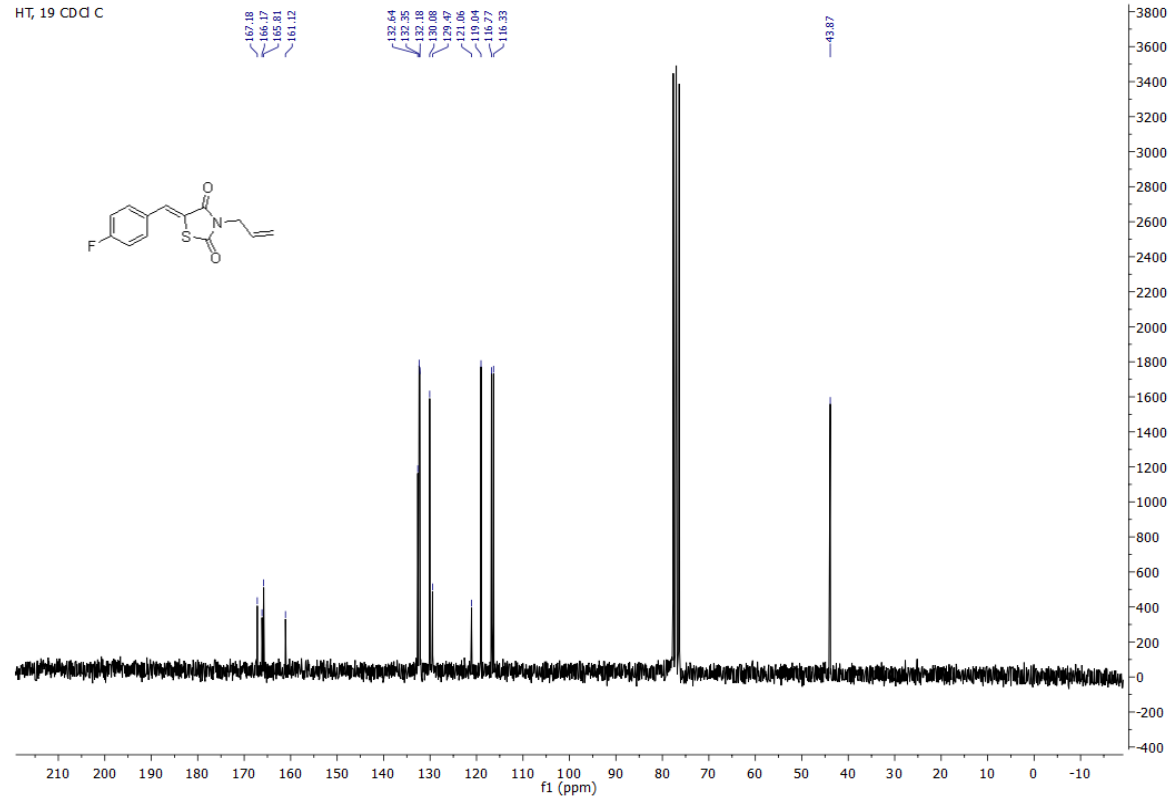

Figure S22. ^{13}C NMR spectrum of (**4c**).

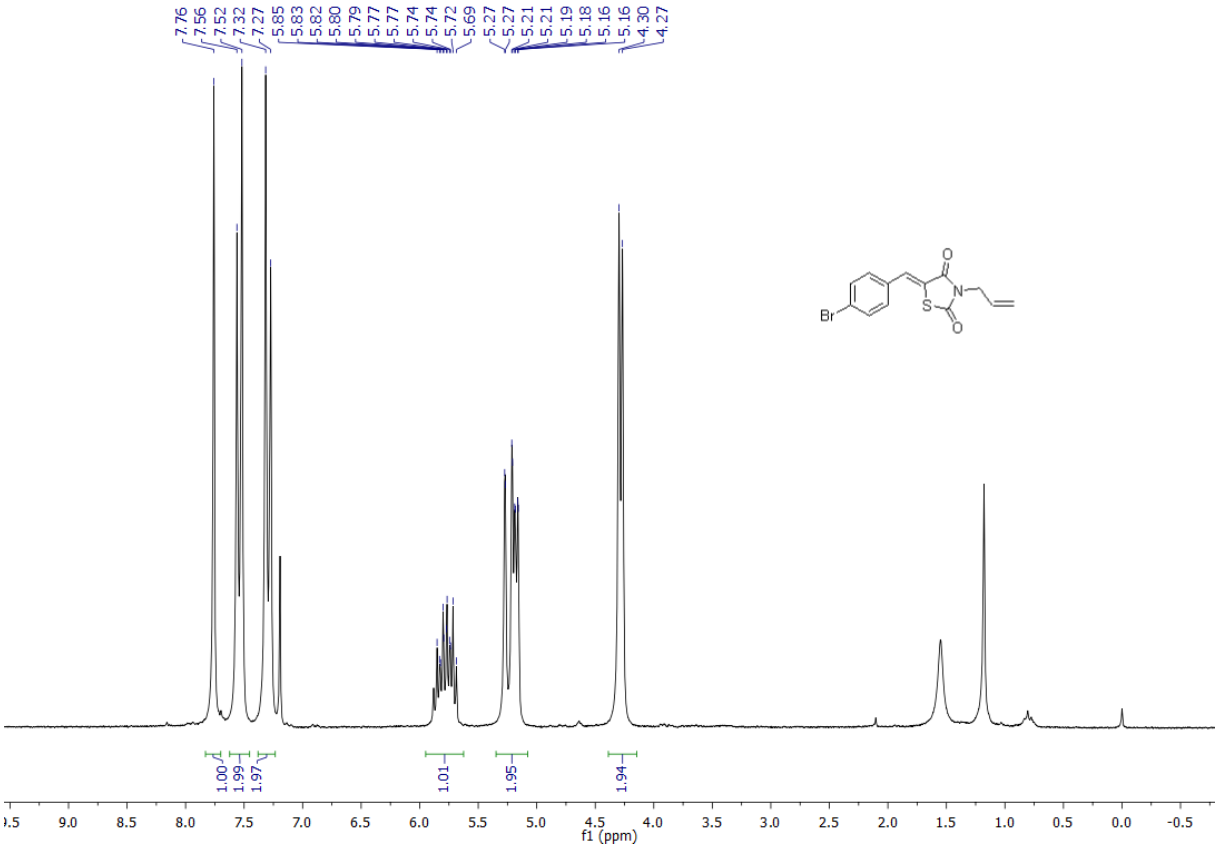

Figure S23. ^{1}H NMR spectrum of (**4d).**

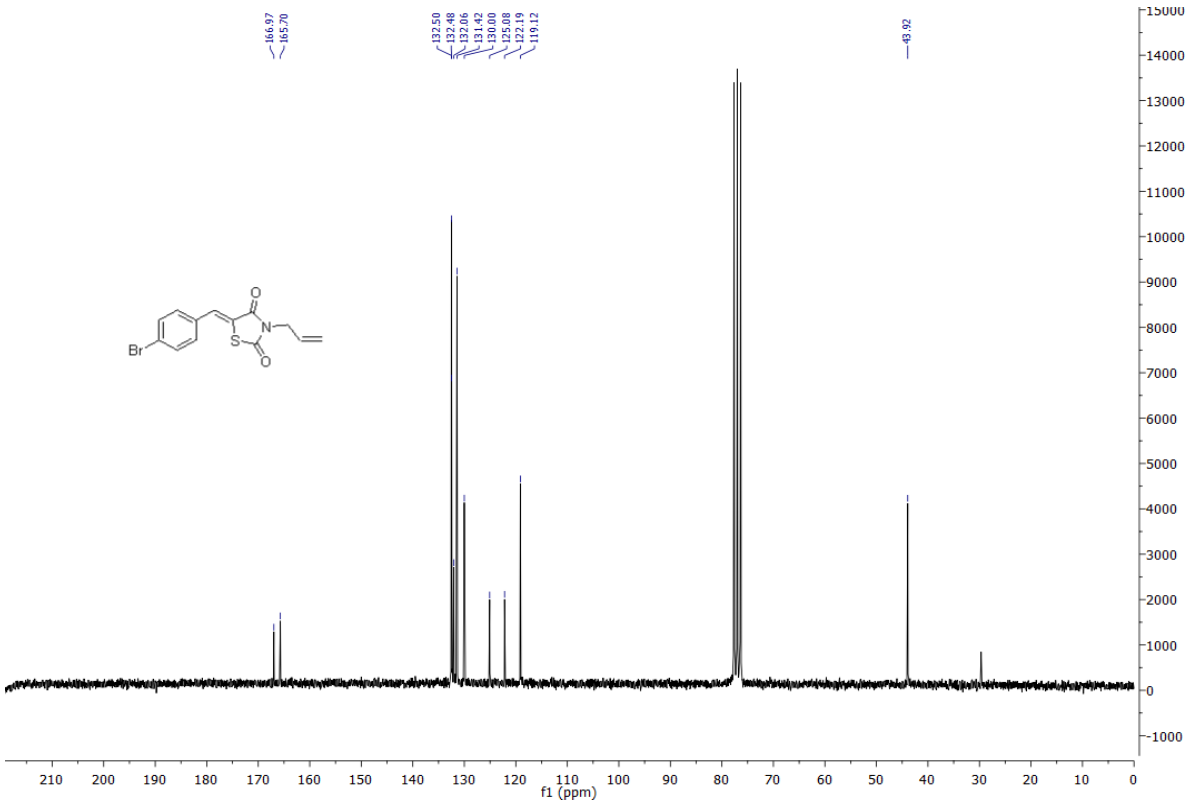

Figure S24. ^{13}C NMR spectrum of (**4d).**

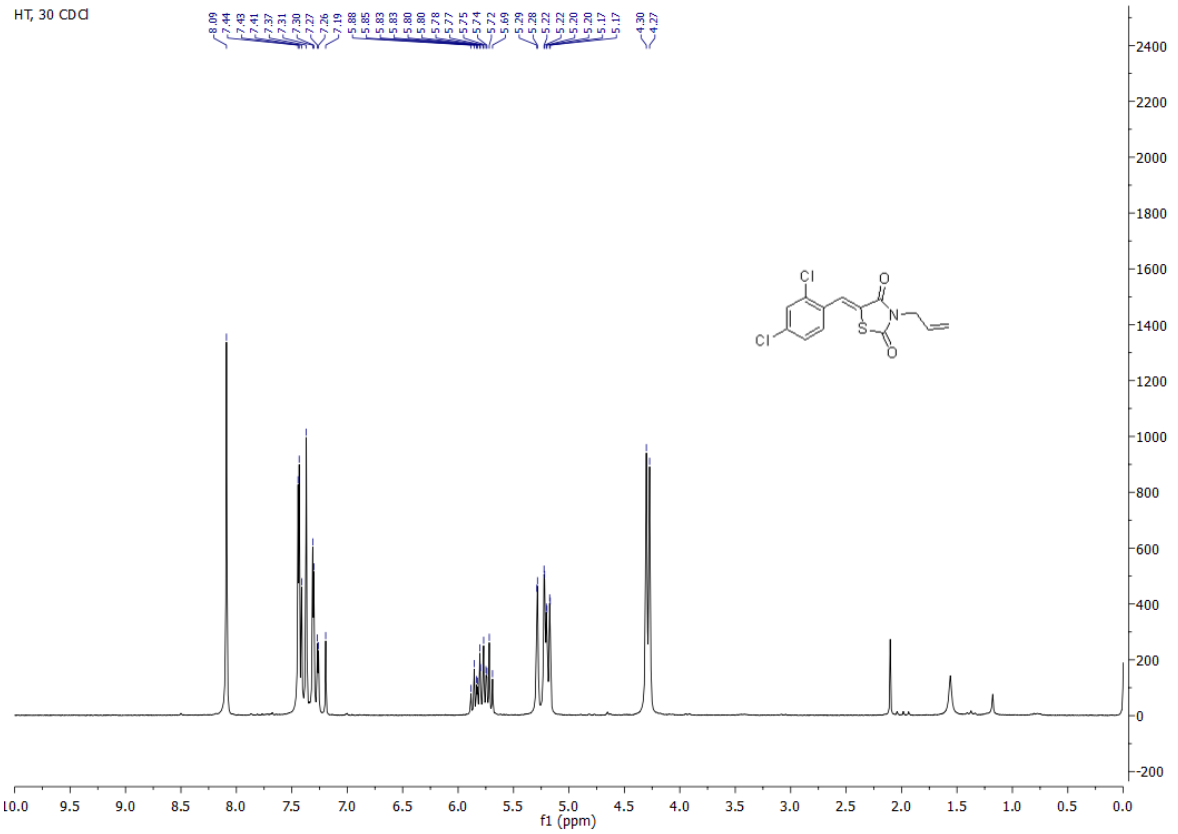

Figure S25. ^{1}H NMR spectrum of (**4e**).

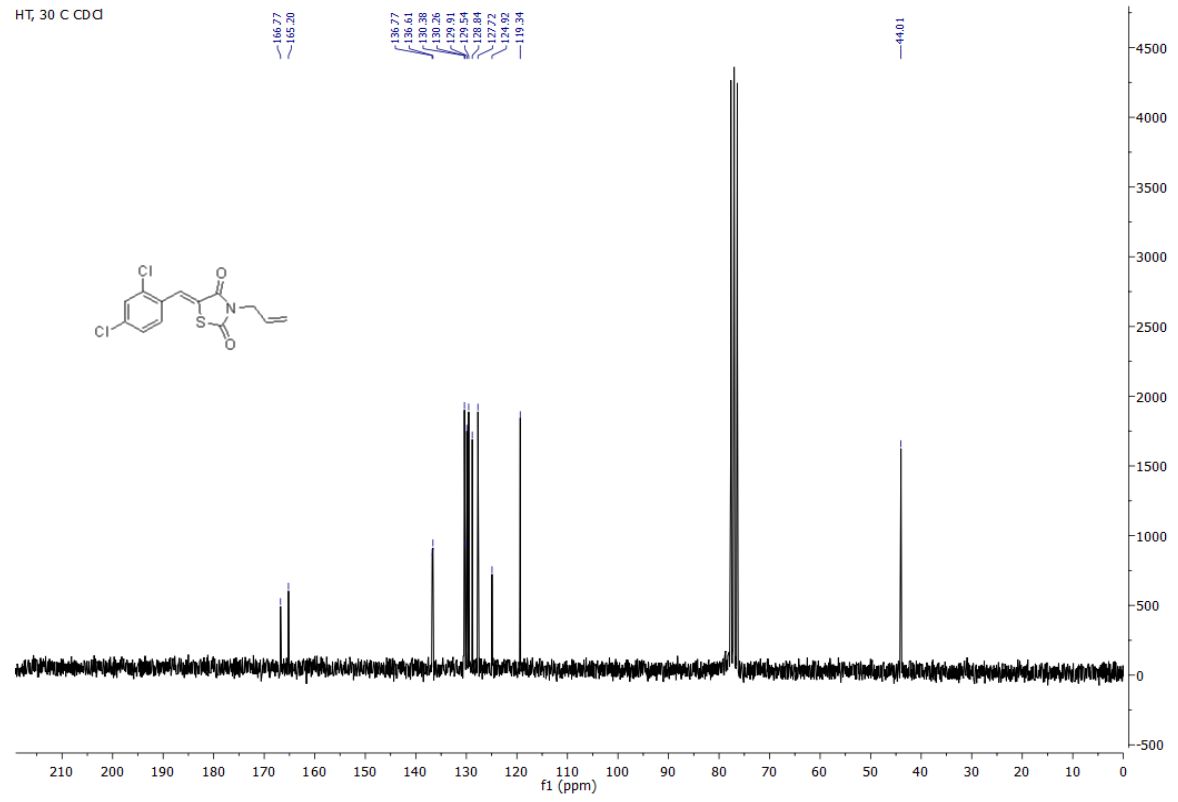

Figure S26. ^{13}C NMR spectrum of (**4e**).

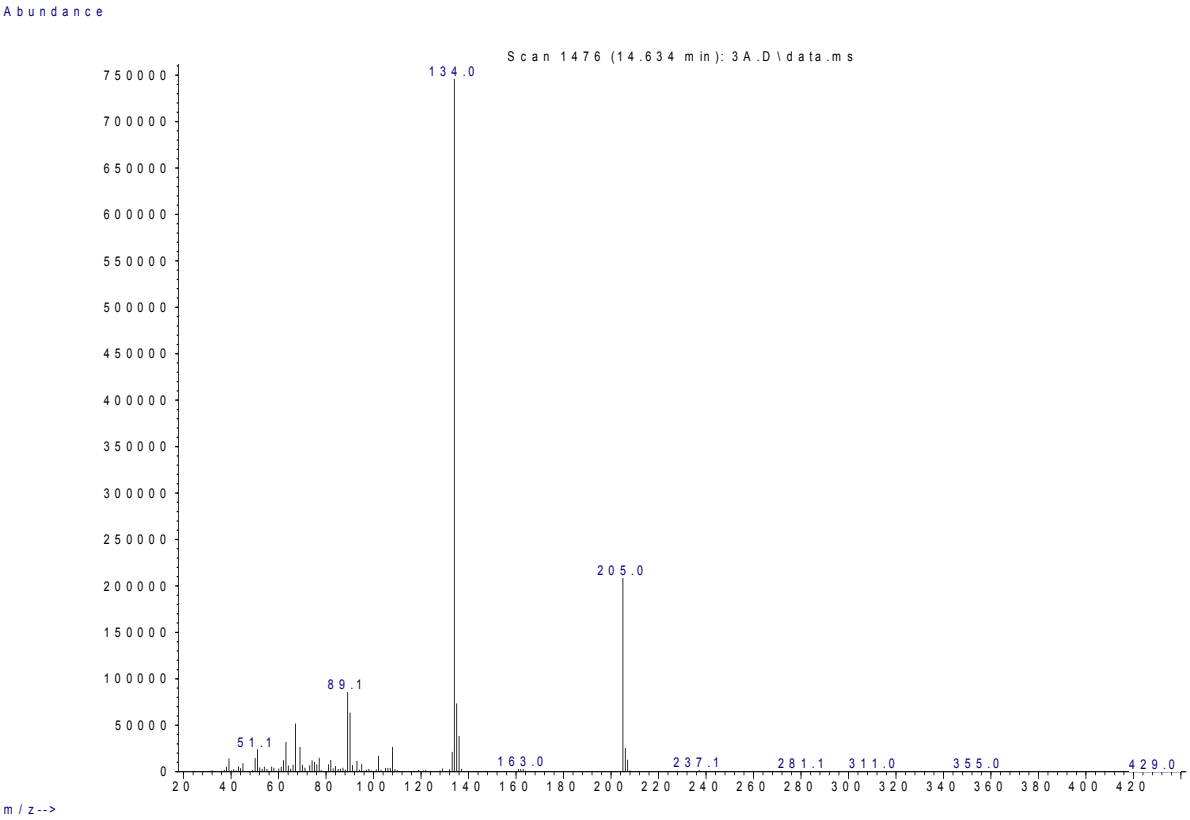

Figure S27. ESI$^+$-MS spectrum of (**3a**).

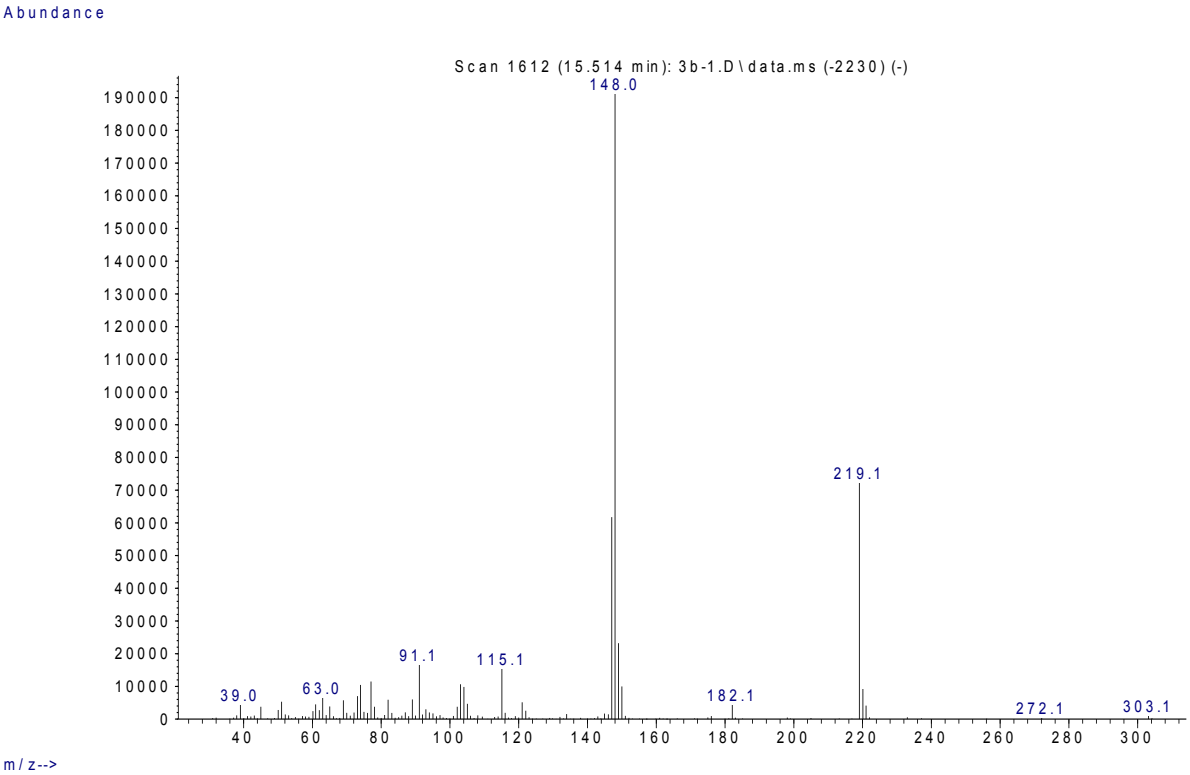

Figure S28. ESI$^+$-MS spectrum of (**3b**).

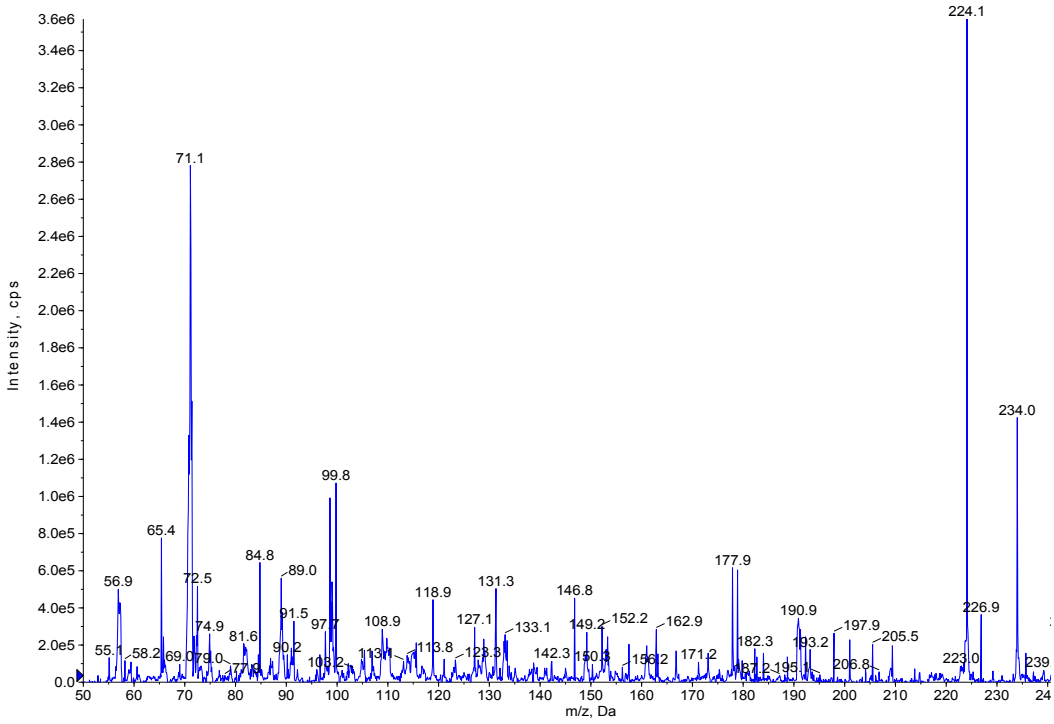

Figure S29. ESI$^+$-MS spectrum of (**3c**).

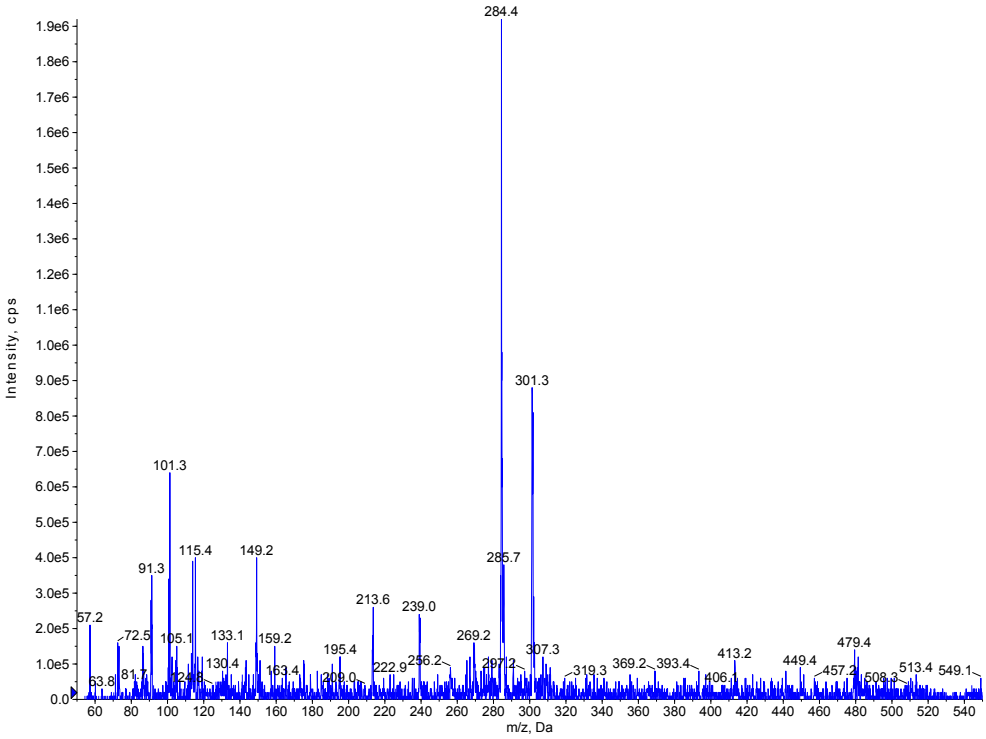

Figure S30. ESI$^+$-MS spectrum of (**3d**).

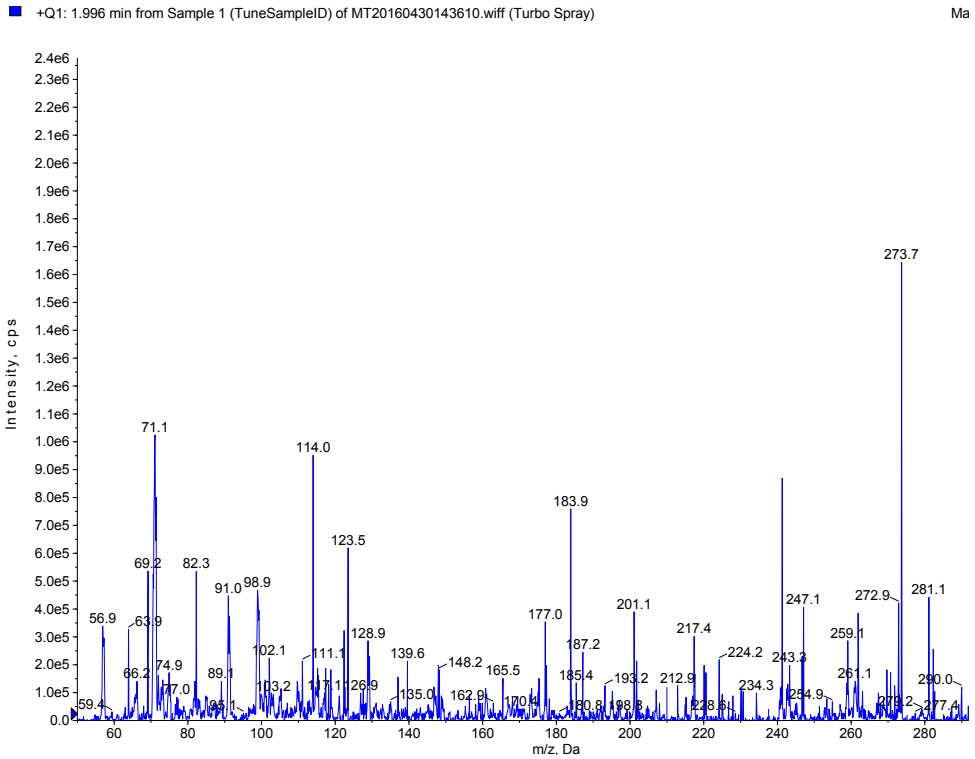

Figure S31. ESI$^+$-MS spectrum of (**3e**).

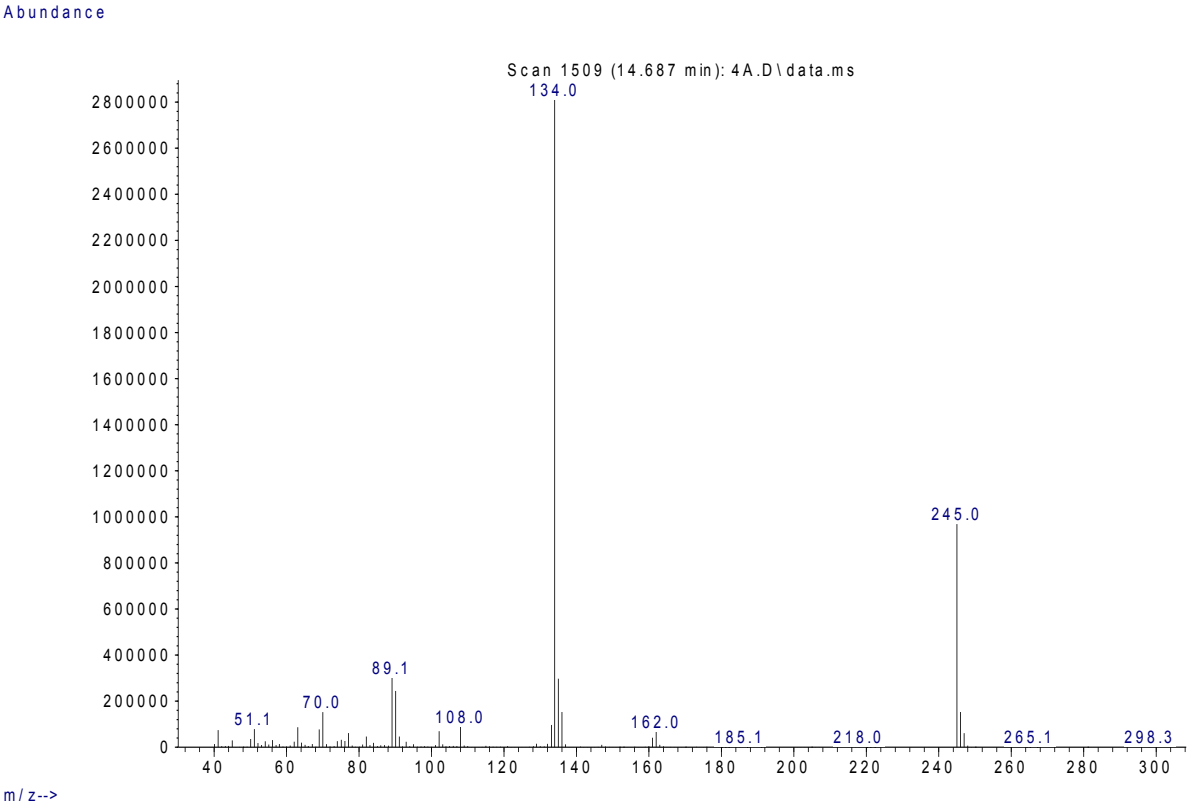

Figure S32. ESI$^+$-MS spectrum of (**4a**).

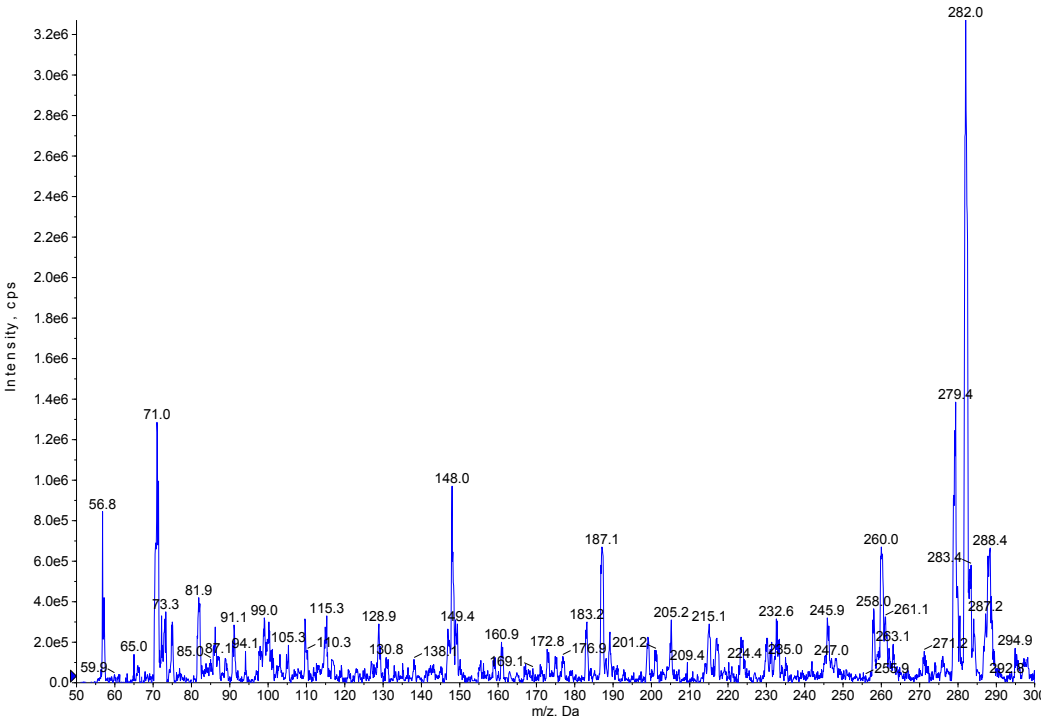

Figure S33. ESI$^+$-MS spectrum of (**4b**).

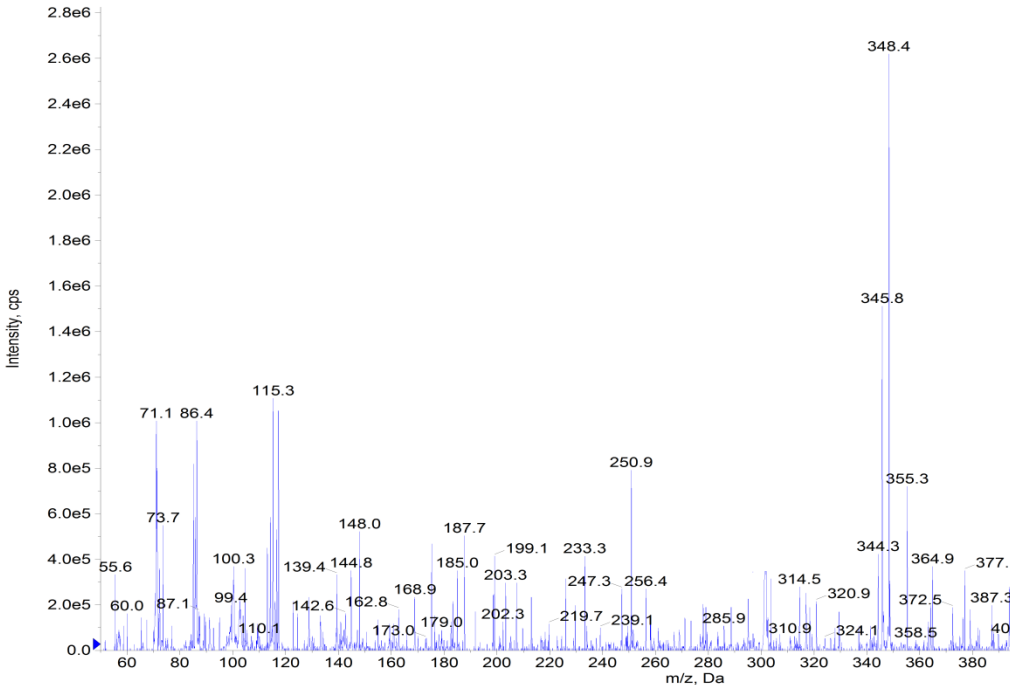

Figure S34. ESI$^+$-MS spectrum of (**4c**).

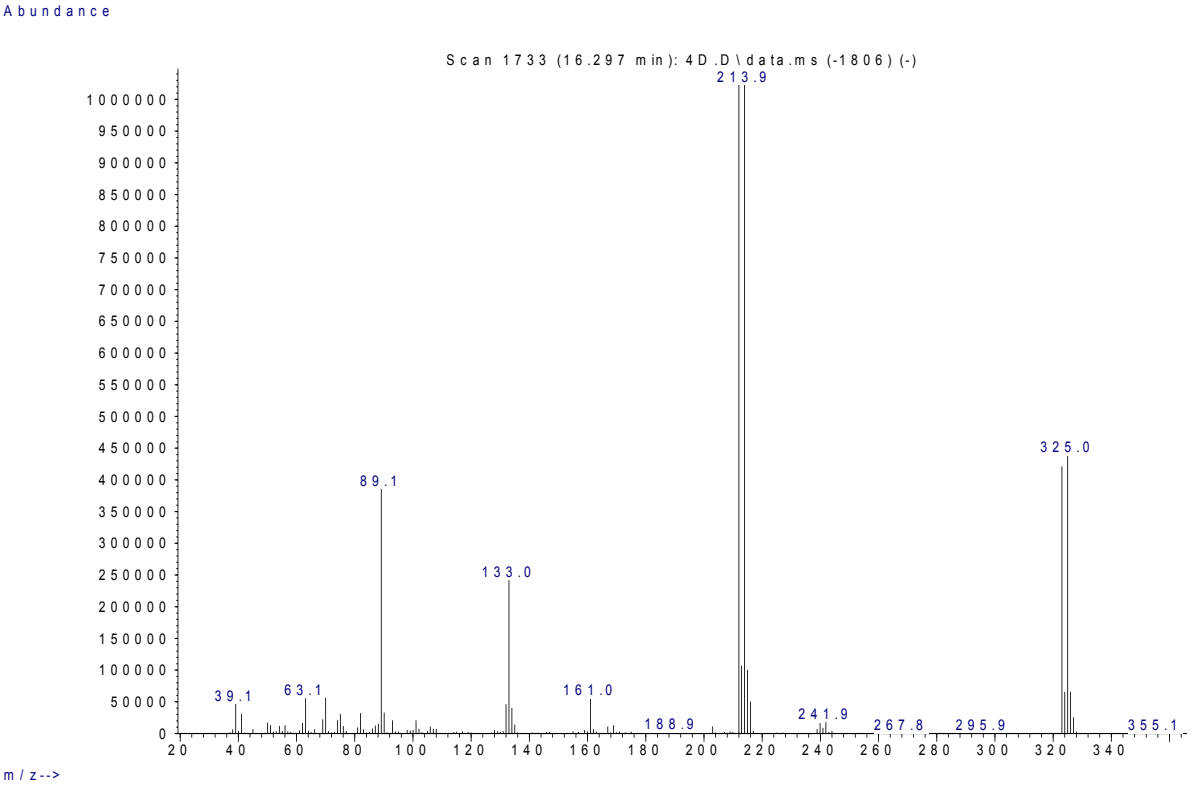

Figure S35. ESI$^+$-MS spectrum of (**4d**).

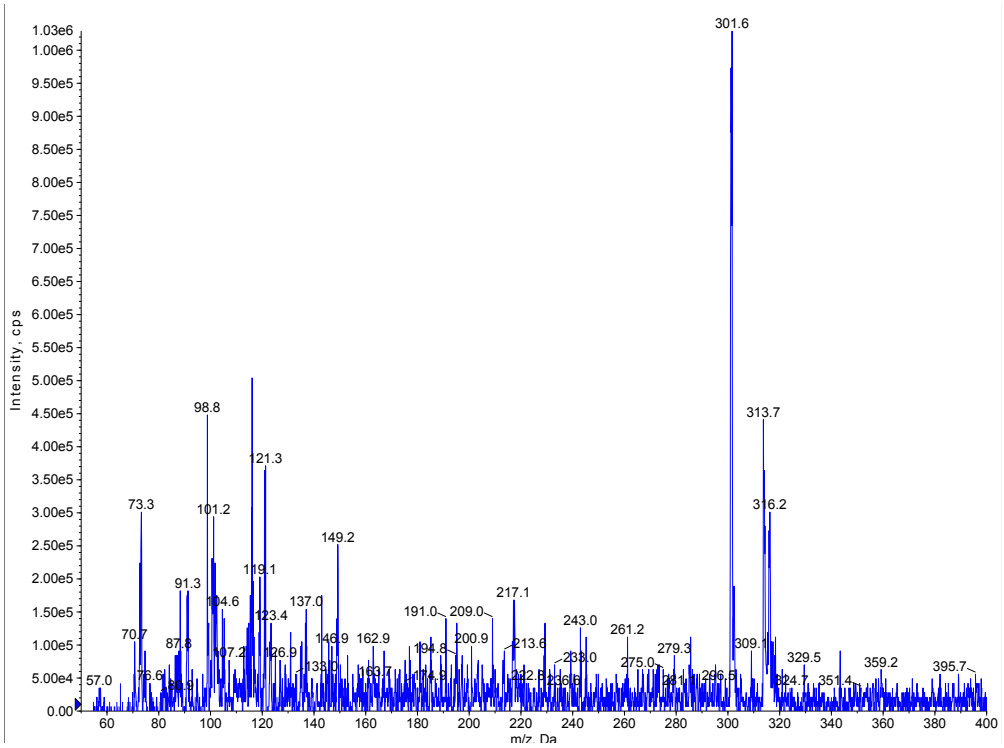

Figure S36. ESI$^+$-MS spectrum of (**4e**).

2. Ligand-receptor interactions of synthesized compounds with the target enzymes.

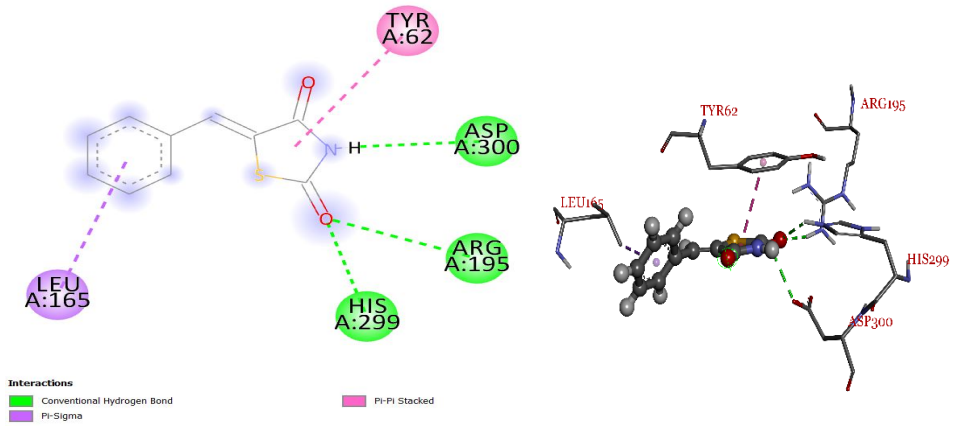

Figure S37. Ligand-receptor interaction of **3a** with the α-amylase target enzyme (PDB=1B2Y).

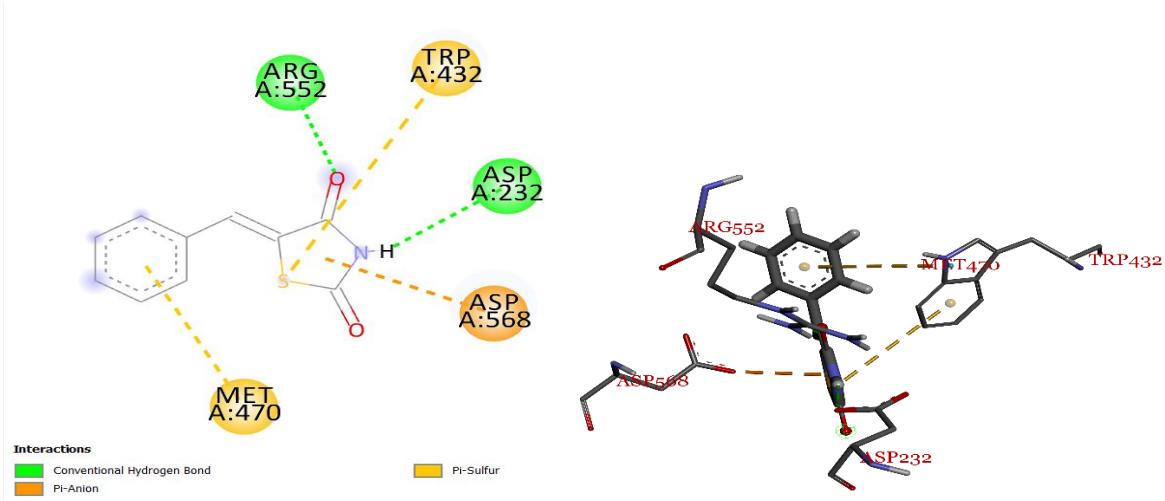

Figure S38. Ligand-receptor interaction of **3a** with α-glucosidase target enzyme (PDB=3W37).

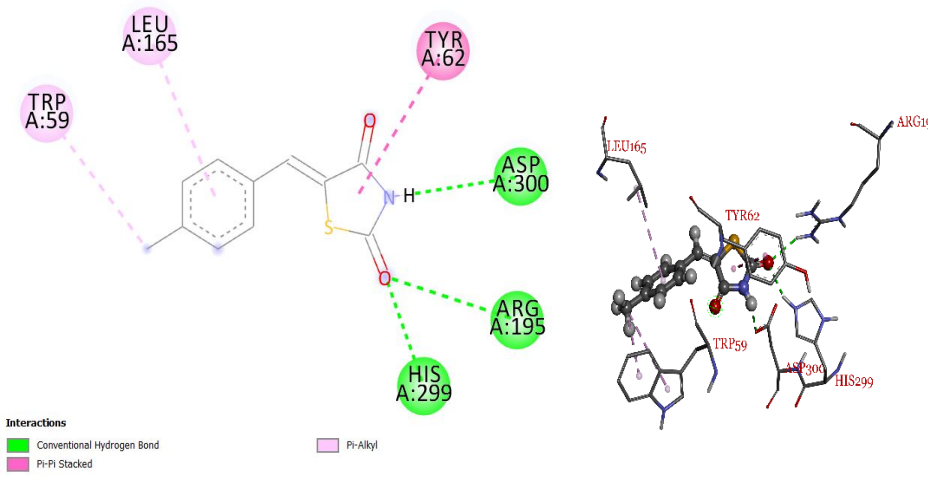

Figure S39. Ligand-receptor interaction of **3b** with the α-amylase target enzyme (PDB=1B2Y).

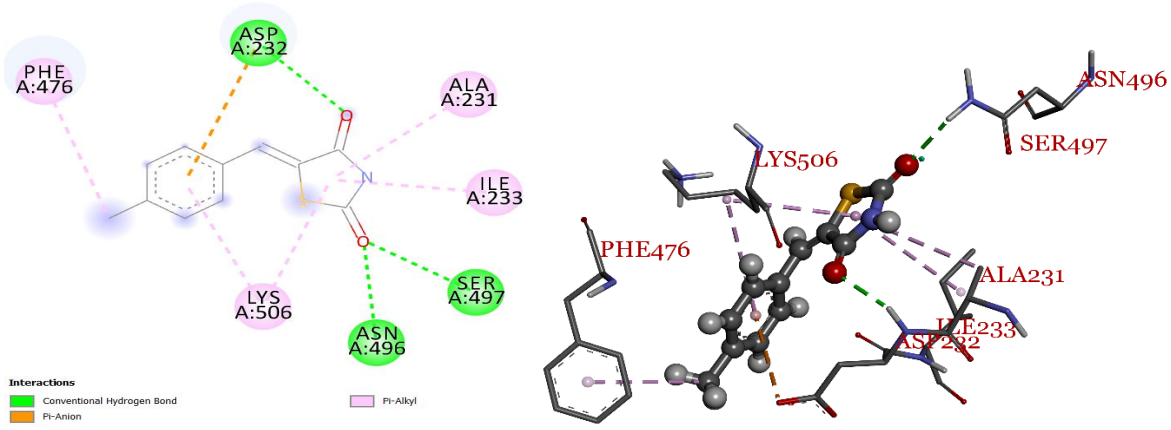

Figure S40. Ligand-receptor interaction of **3b** with α-glucosidase target enzyme (PDB=3W37).

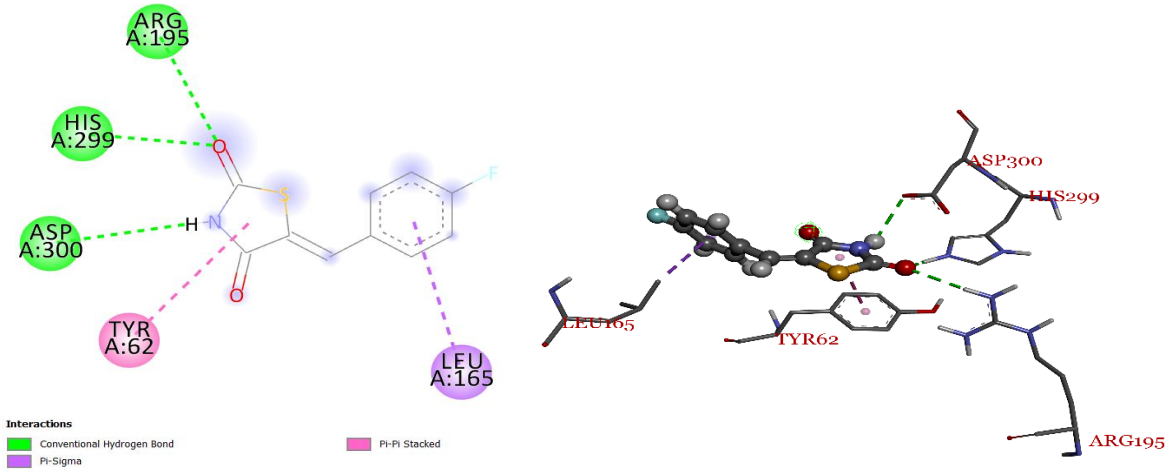

Figure S41. Ligand-receptor interaction of **3c** with the α-amylase target enzyme (PDB=1B2Y).

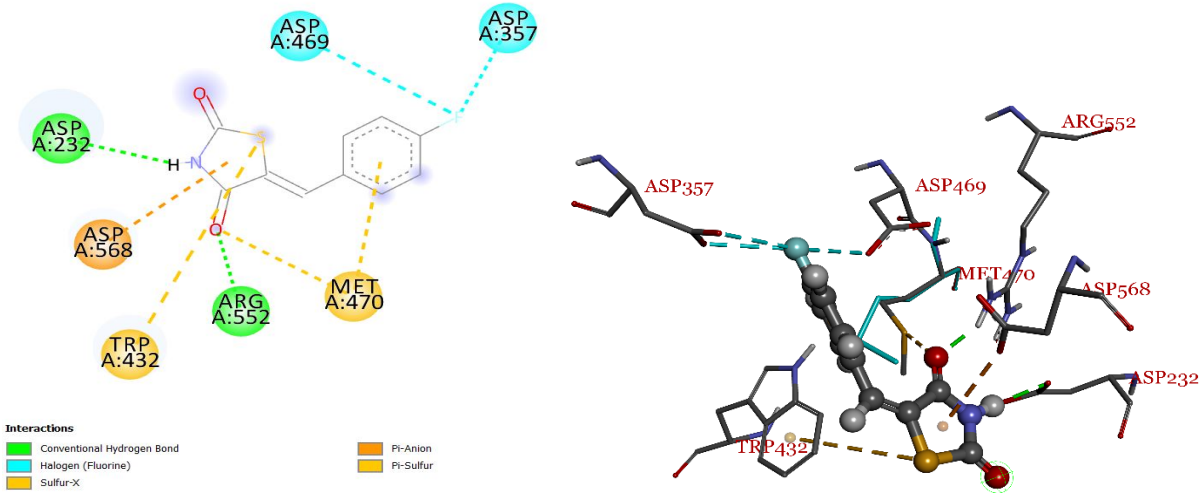

Figure S42. Ligand-receptor interaction of **3c** with α-glucosidase target enzyme (PDB=3W37).

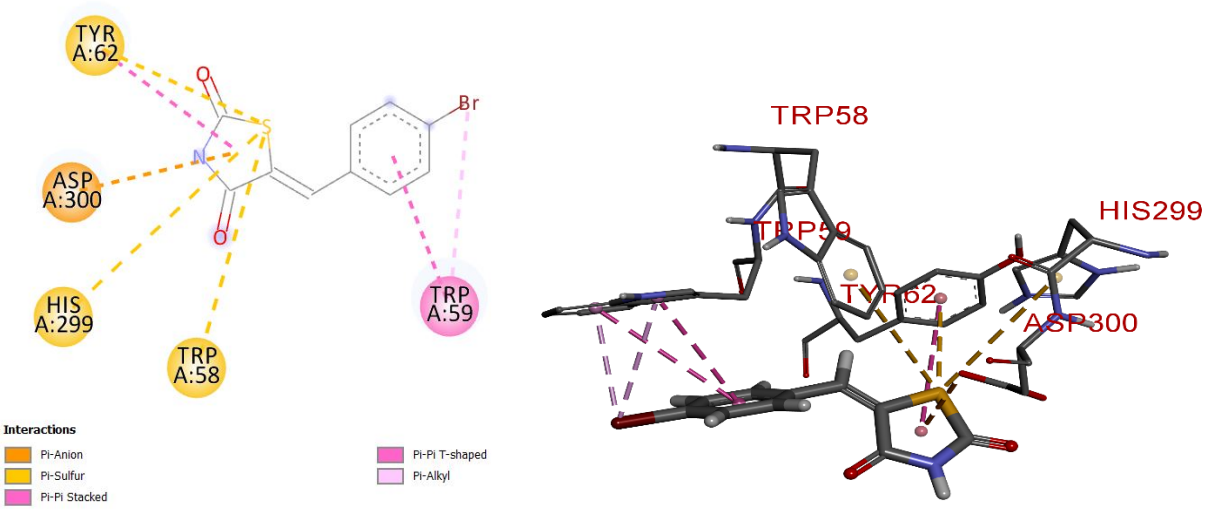

Figure S43. Ligand-receptor interaction of **3d** with the α-amylase target enzyme (PDB=1B2Y).

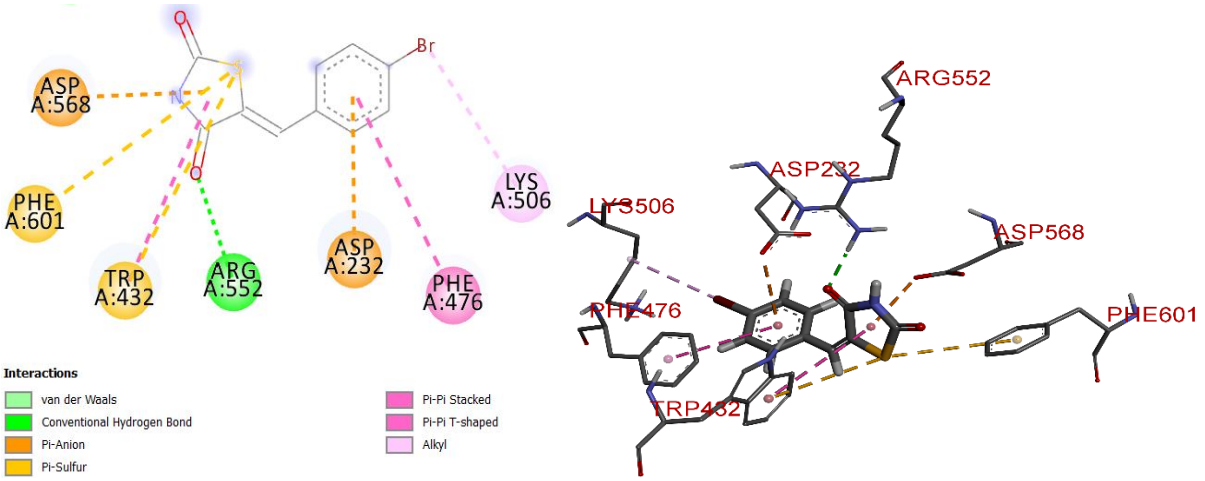

Figure S44. Ligand-receptor interaction of **3d** with the α-glucosidase target enzyme (PDB=3W37).

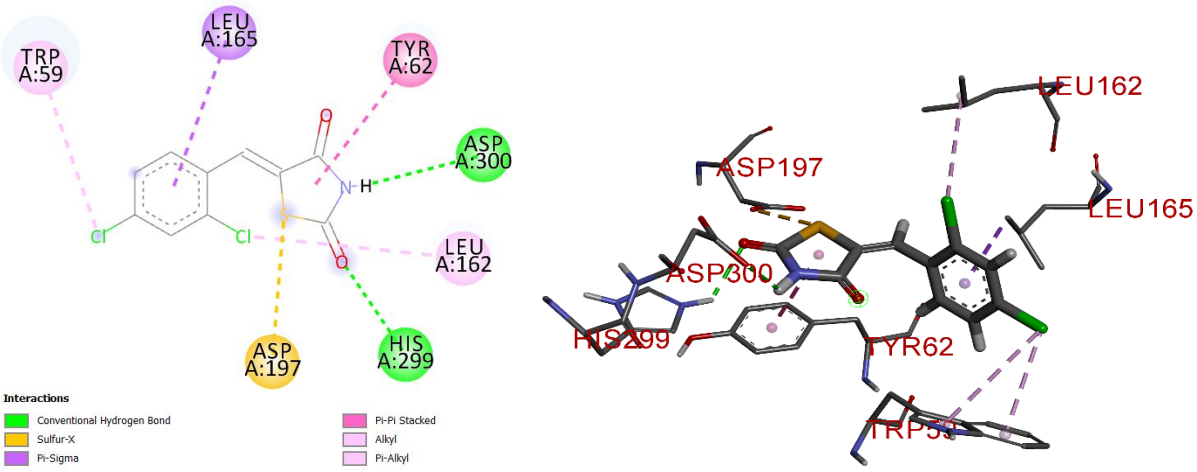

Figure S45. Ligand-receptor interaction of **3e** with the α-amylase target enzyme (PDB=1B2Y).

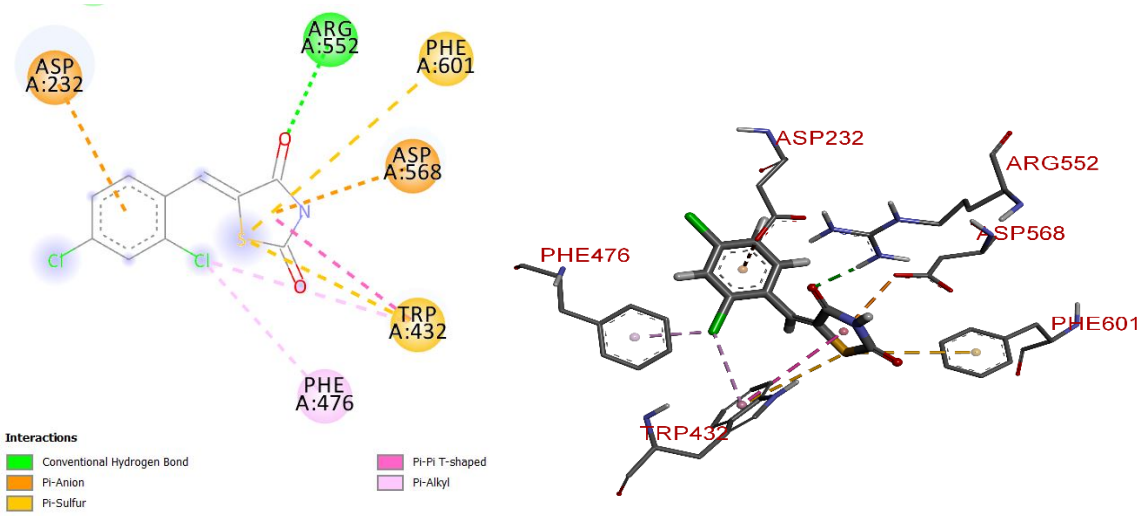

Figure S46. Ligand-receptor interaction of **3e** with the α-glucosidase target enzyme (PDB=3W37).

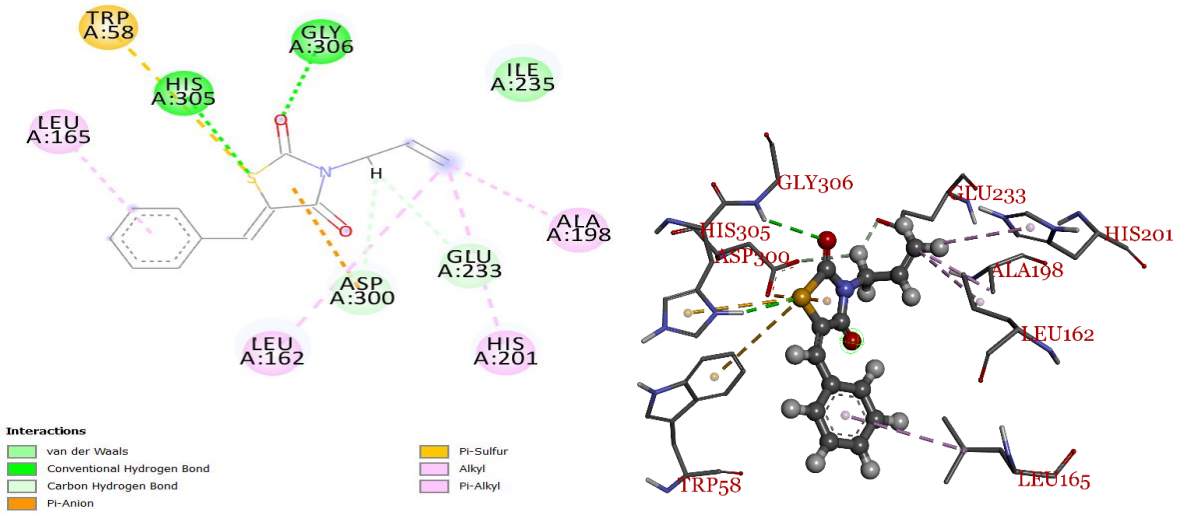

Figure S47. Ligand-receptor interaction of **4a** with the α-amylase target enzyme (PDB=1B2Y).

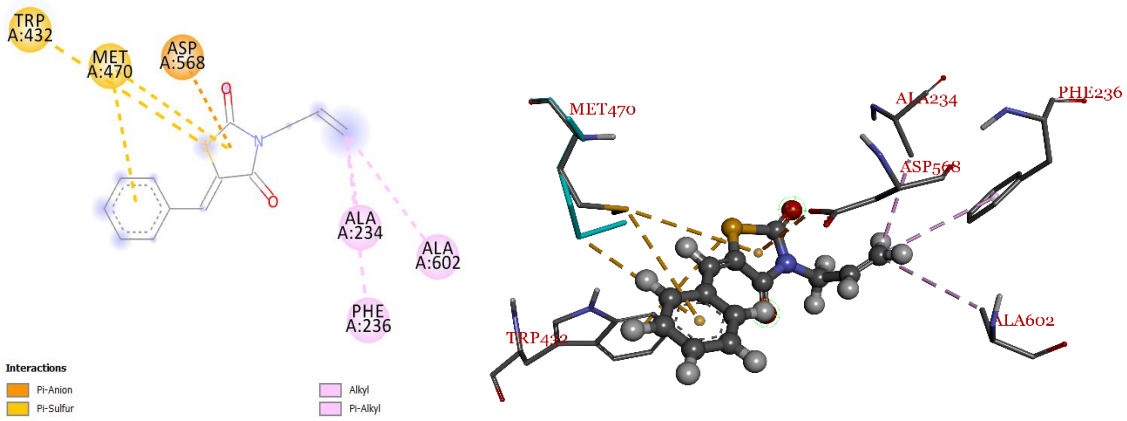

Figure S48. Ligand-receptor interaction of **4a** with the α-glucosidase target enzyme (PDB=3W37).

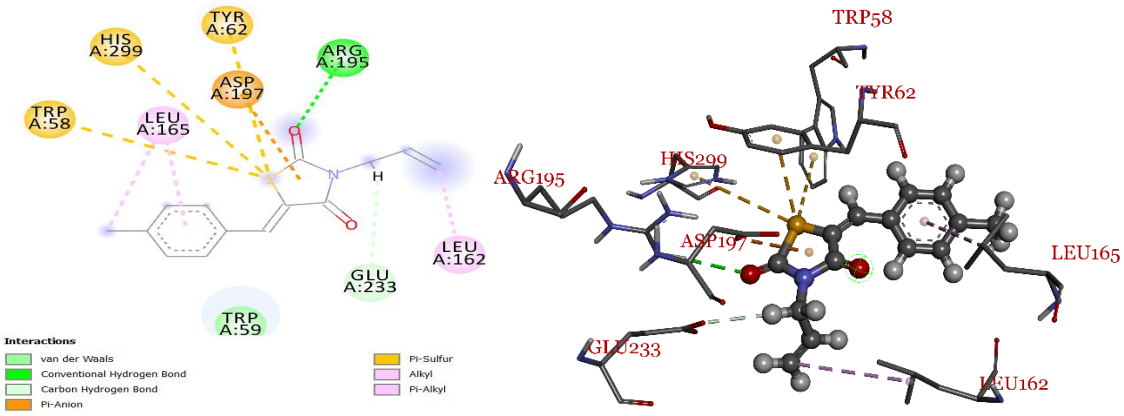

Figure S49. Ligand-receptor interaction of **4b** with the α-amylase target enzyme (PDB=1B2Y).

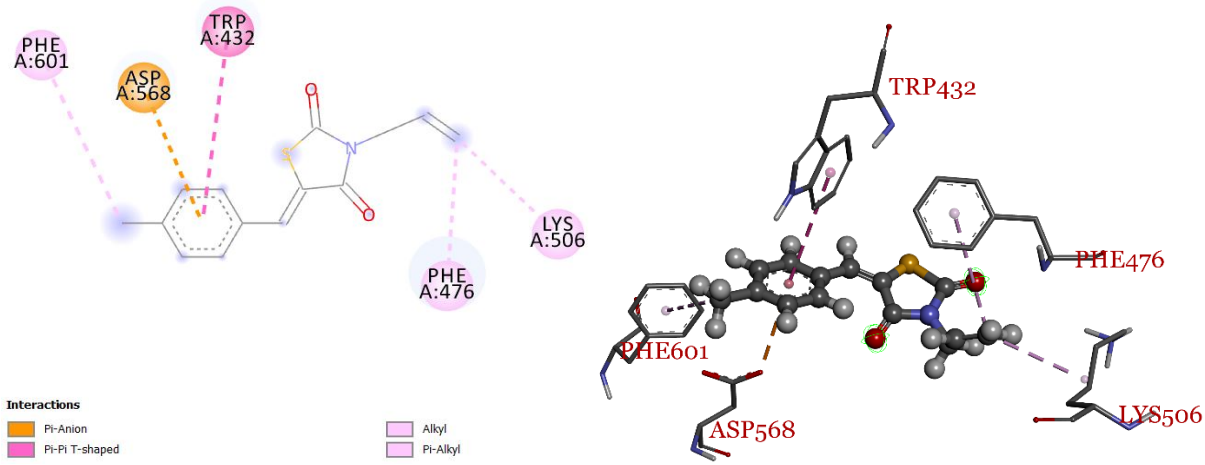

Figure S50. Ligand-receptor interaction of **4b** with the α-glucosidase target enzyme (PDB=3W37).

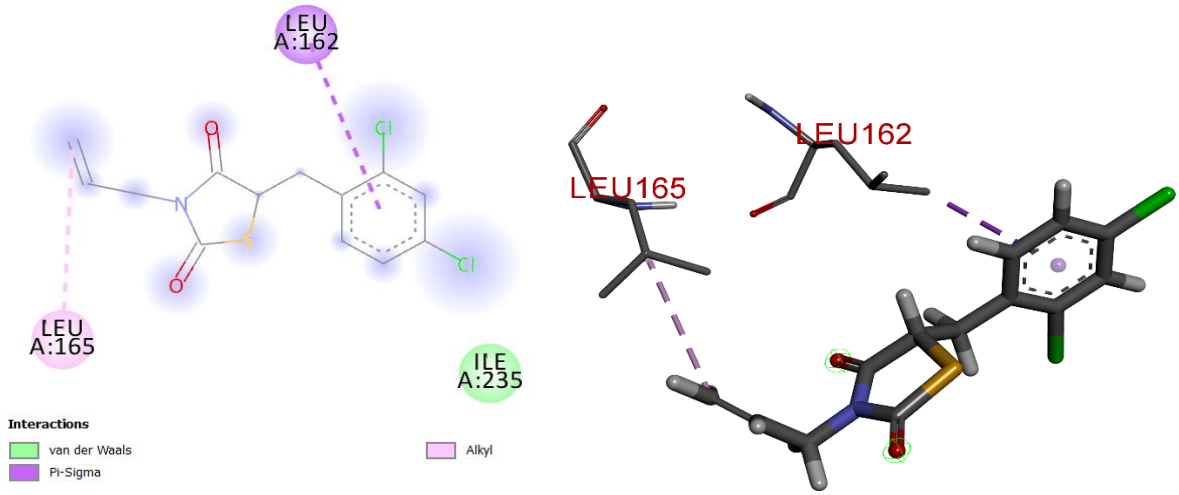

Figure S51. Ligand-receptor interaction of **4e** with the α-amylase target enzyme (PDB=1B2Y).

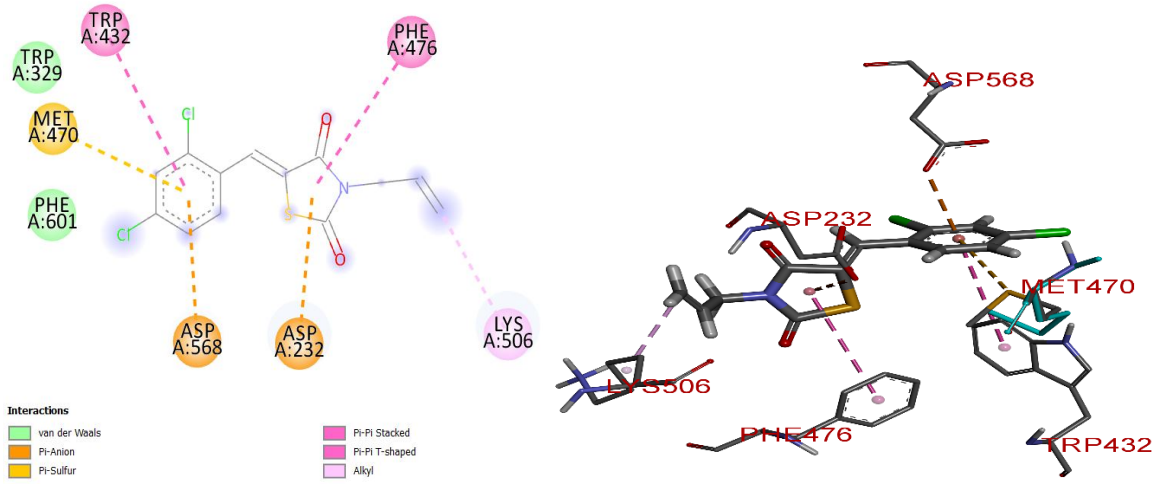

Figure S52. Ligand-receptor interaction of **4e** with the α-glucosidase target enzyme (PDB=3W37).

3.Tables section

Table S1. Results of the interaction details and docking score in (kJ/mol) of the synthesized ligands for series 1 against target enzyme α-amylase (PDB=1B2Y).

Compounds	Docking Score	Ligand	Receptor pocket	Interactions Category	Distance(Å)
3a	-7.1	O(C=O)	ARG195	Hydrogen Bond	2.83541
		O(C=O)	HIS299	Hydrogen Bond	2.48143
		H(NH)	ASP300	Hydrogen Bond	2.52493
		Ring(C6)	LEU165	Hydrophobic	3.96459
		Ring(C5)	TYR62	Hydrophobic	3.96765
3b	-7.5	O(C=O)	ARG195	Hydrogen Bond	2.85611
		O(C=O)	HIS299	Hydrogen Bond	2.45409
		H(NH)	ASP300	Hydrogen Bond	2.56529
		Ring(C5)	TYR62	Hydrophobic	3.95238
		C(CH3)	TRP59	Hydrophobic	5.04666
		C(CH3)	TRP59	Hydrophobic	4.18717
		Ring(C6)	LEU165	Hydrophobic	4.95242
3c	-7.3	O(C=O)	ARG195	Hydrogen Bond	2.79224
		O(C=O)	HIS299	Hydrogen Bond	2.49571
		H(NH)	ASP300	Hydrogen Bond	2.63554
		Ring(C6)	LEU165	Hydrophobic	3.92915
		Ring(C5)	TYR62	Hydrophobic	3.98189
3d	-7.2	Ring(C5)	ASP300	Electrostatic	3.70496
		S	TRP58	Pi-Sulfur	5.74905
		S	TYR62	Pi-Sulfur	3.81625
		S	HIS299	Pi-Sulfur	5.3007
		Ring(C6)	TRP59	Hydrophobic	4.30007
		Ring(C6)	TRP59	Hydrophobic	4.88728
		Ring(C5)	TYR62	Hydrophobic	5.23954
		Br	TRP59	Hydrophobic	4.21931
		Br	TRP59	Hydrophobic	3.74643
3e	-8	O(C=O)	HIS299	Hydrogen Bond	2.38003
		H(NH)	ASP300	Hydrogen Bond	2.49795
		S	ASP197	Sulfur-X	3.2659
		Ring(C6)	LEU165	Hydrophobic	3.91364
		Ring(C5)	TYR62	Hydrophobic	3.96918
		Cl	LEU162	Hydrophobic	4.71739
		Cl	TRP59	Hydrophobic	4.94162
		Cl	TRP59	Hydrophobic	4.03657

Table S2. Results of the interaction details and docking score in (kJ/mol) of the synthesized ligands for series 2 against target enzyme α-amylase (PDB=1B2Y).

Compounds	Docking Score	Ligand	Receptor pocket	Interactions Category	Distance(Å)
4a	- 8	S	HIS305	Hydrogen Bond	2.68965
		O(C=O)	GLY306	Hydrogen Bond	3.01297
		H(CH2)	GLU233	Hydrogen Bond	2.68907
		H(CH2)	ASP300	Hydrogen Bond	3.08527
		Ring(C5)	ASP300	Electrostatic	3.50217
		S	TRP58	Pi-Sulfur	5.86397
		O(C=O)	HIS305	Pi-Sulfur	4.71381
		C(C=C)	ALA198	Hydrophobic	4.11088
		C(C=C)	LEU162	Hydrophobic	5.25624
		C(C=C)	HIS201	Hydrophobic	5.34449
		Ring(C6)	LEU165	Hydrophobic	5.17414
4b	-7.5	O(Carbonyl)	ARG195	Hydrogen Bond	2.76616
		H(CH2)	GLU233	Hydrogen Bond	2.66252
		Ring(C5)	ASP197	Electrostatic	3.9687
		S	TRP58	Pi-Sulfur	5.5271
		S	TYR62	Pi-Sulfur	3.77689
		S	HIS299	Pi-Sulfur	5.22861
		C(C=C)	LEU162	Hydrophobic	5.2245
		C(CH3)	LEU165	Hydrophobic	4.83264
		Ring(C5)	LEU165	Hydrophobic	5.17052
4c	-8	O(C=O)	ARG195	Hydrogen Bond	2.66447
		H(CH2)	GLU233	Hydrogen Bond	2.60439
		Ring(C5)	ASP197	Electrostatic	3.96059
		S	TRP58	Pi-Sulfur	5.44318
		S	TYR62	Pi-Sulfur	3.74206
		S	HIS299	Pi-Sulfur	5.20353
		Ring(C5)	TYR62	Hydrophobic	4.61768
		C(C=C)	LEU162	Hydrophobic	5.37164
		Ring(C6)	LEU165	Hydrophobic	5.22392
4d	-7.3	Ring(C6)	TRP59	Hydrophobic	4.13376
		Ring(C6)	TRP59	Hydrophobic	3.82265
		C(C=C)	ALA198	Hydrophobic	3.74543
		C(C=C)	LEU162	Hydrophobic	5.27224
		Br	TRP59	Hydrophobic	4.18253
4e	-6.8	Ring(C6)	LEU162	Hydrophobic	3.95739
		C(C=C)	LEU165	Hydrophobic	4.27445

Table S3. Results of the interaction details and docking score in (kJ/mol) of the synthesized ligands for series 1 against target enzyme α-glucosidase (PDB=3W37).

Ligands	Docking Score	Ligand	Receptor pocket	Interactions Category	Distance(Å)
3a	-6.3	O(C=O)	ARG552	Hydrogen Bond	1.97409
		H(NH)	ASP232	Hydrogen Bond	2.18003
		Ring(C6)	ASP568	Electrostatic	3.36955
		S	MET470	Pi-Sulfur	5.94495
		Ring(C6)	TRP432	Pi-Sulfur	5.64193
3b	-6.3	O(C=O)	ASP232	Hydrogen Bond	2.48477
		O(C=O)	ASN496	Hydrogen Bond	2.49696
		O(C=O)	SER497	Hydrogen Bond	2.6634
		Ring(C6)	ASP232	Electrostatic	4.08235
		$C(CH_3)$	PHE476	Hydrophobic	4.60532
		Ring(C6)	LYS506	Hydrophobic	4.75824
		Ring(C5)	ALA231	Hydrophobic	4.84317
		Ring(C5)	ILE233	Hydrophobic	5.1237
		Ring(C5)	LYS506	Hydrophobic	4.38306
3c	-6.3	O(C=O)	ARG552	Hydrogen Bond	1.88342
		H(NH)	ASP232	Hydrogen Bond	2.2003
		F	ASP357	Halogen	2.98576
		F	ASP357	Halogen	2.89295
		F	ASP469	Halogen	3.36572
		O(C=O)	MET470	Sulfur-X	3.30596
		Ring(C5)	ASP568	Electrostatic	3.66551
		Ring(C6)	MET470	Pi-Sulfur	5.77304
		S	TRP432	Pi-Sulfur	5.54841
3d	-6.2	O(C=O)	ARG552	Hydrogen Bond	2.13676
		Ring(C6)	ASP232	Electrostatic	3.85389
		Ring(C5)	ASP568	Electrostatic	3.38999
		S	TRP432	Pi-Sulfur	5.1095
		S	PHE601	Pi-Sulfur	5.09116
		Ring(C6)	PHE476	Hydrophobic	5.25809
		Ring(C5)	TRP432	Hydrophobic	5.28489
		Br	LYS506	Hydrophobic	4.32975
3e	-6.1	O(C=O)	ARG552	Hydrogen Bond	2.29523
		Ring(C6)	ASP232	Electrostatic	3.70874
		Ring(C5)	ASP568	Electrostatic	3.3898
		S	TRP432	Pi-Sulfur	5.29858
		S	PHE601	Pi-Sulfur	5.10977
		Ring(C5)	TRP432	Hydrophobic	5.2463
		Cl	TRP432	Hydrophobic	4.28825
		Cl	PHE476	Hydrophobic	3.97954

Table S4. Results of the interaction details and docking score in (kJ/mol) of the synthesized ligands for series 2 against target enzyme α-glucosidase (PDB=3W37).

Ligands	Docking Score	Ligand	Receptor pocket	Interactions Category	Distance(Å)
4a	-7.5	Ring(C5)	ASP568	Electrostatic	3.30089
		Ring(C6)	MET470	Pi-Sulfur	5.15779
		Ring(C6)	MET470	Pi-Sulfur	5.30669
		Ring(C5)	MET470	Pi-Sulfur	5.6995
		S	TRP432	Pi-Sulfur	5.65507
		C(C=C)	ALA234	Hydrophobic	4.06981
		C(C=C)	ALA602	Hydrophobic	4.4746
		C(C=C)	PHE236	Hydrophobic	4.88736
4b	-6.8	Ring(C6)	ASP568	Electrostatic	3.69295
		Ring(C6)	TRP432	Hydrophobic	4.96559
		C(C=C)	LYS506	Hydrophobic	3.90011
		C(C=C)	PHE476	Hydrophobic	4.89158
		C(CH3)	PHE601	Hydrophobic	5.10302
4c	-7.7	O(C=O)	ARG552	Hydrogen Bond	2.74136
		H(CH2)	ASP232	Hydrogen Bond	2.74263
		H(CH2)	ASP232	Hydrogen Bond	2.70926
		F	ASP357	Halogen	2.70359
		F	ASP469	Halogen	3.15327
		Ring(C5)	ASP568	Electrostatic	3.72285
		Ring(C6)	MET470	Pi-Sulfur	5.62496
		S	PHE601	Pi-Sulfur	5.3454
		Ring(C5)	TRP432	Hydrophobic	5.7127
		C=C	PHE476	Hydrophobic	4.15225
4d	-6.6	Ring(C6)	ASP568	Electrostatic	3.7256
		Ring(C5)	PHE476	Hydrophobic	5.16251
		Ring(C6)	TRP432	Hydrophobic	4.9641
		Ring(C6)	PHE601	Hydrophobic	5.73706
		C=C	LYS506	Hydrophobic	3.61135
		Br	TRP329	Hydrophobic	4.42954
		Br	TRP329	Hydrophobic	4.08377
		Br	TRP432	Hydrophobic	5.3273
		Br	PHE601	Hydrophobic	5.34674
4e	-6.8	Ring(C5)	ASP232	Electrostatic	3.86579
		Ring(C6)	ASP568	Electrostatic	3.52354
		Ring(C6)	MET470	Pi-Sulfur	5.09173
		Ring(C5)	PHE476	Hydrophobic	5.23761
		Ring(C5)	TRP432	Hydrophobic	5.18127
		C=C	LYS506	Hydrophobic	3.82812