Ultrasonic-assisted synthesis of heterocyclic curcumin analogs as Antidiabetic, Antibacterial and Antioxidant Agents combined with *in vitro* and *in silico* studies

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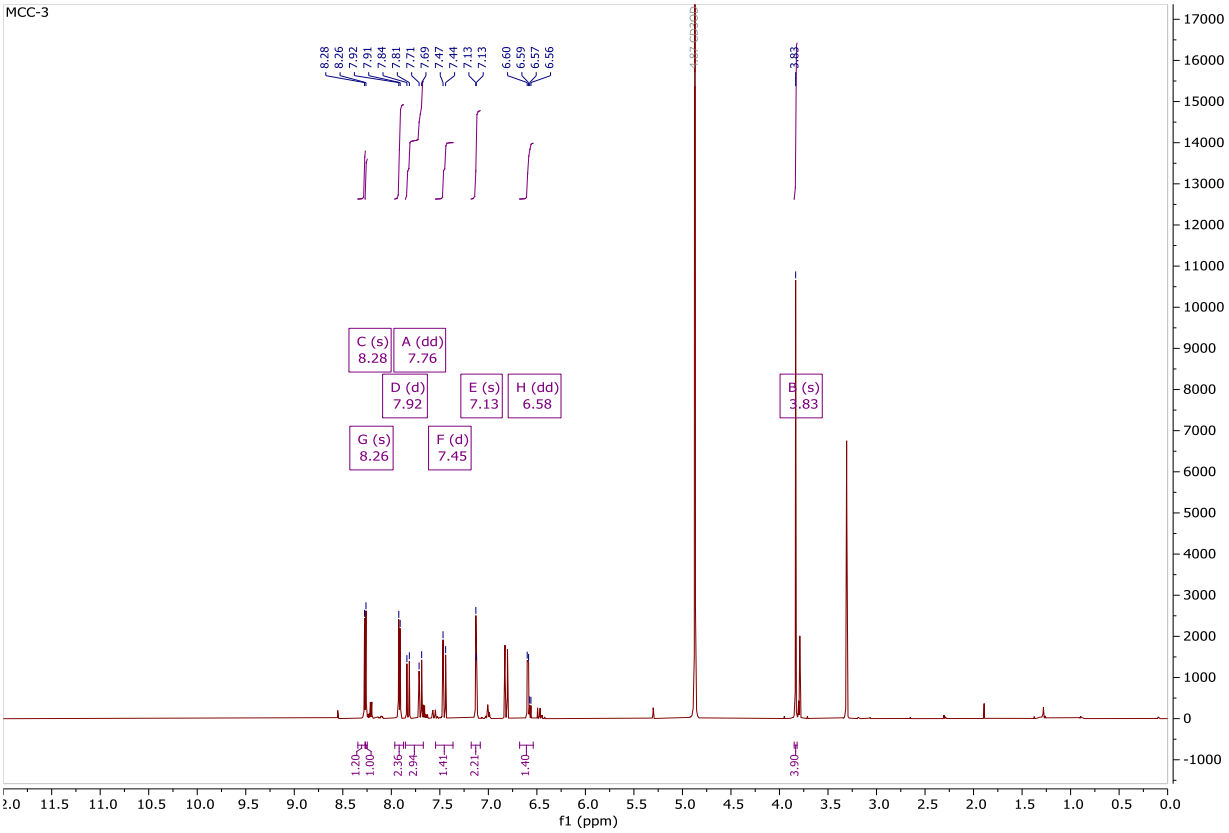
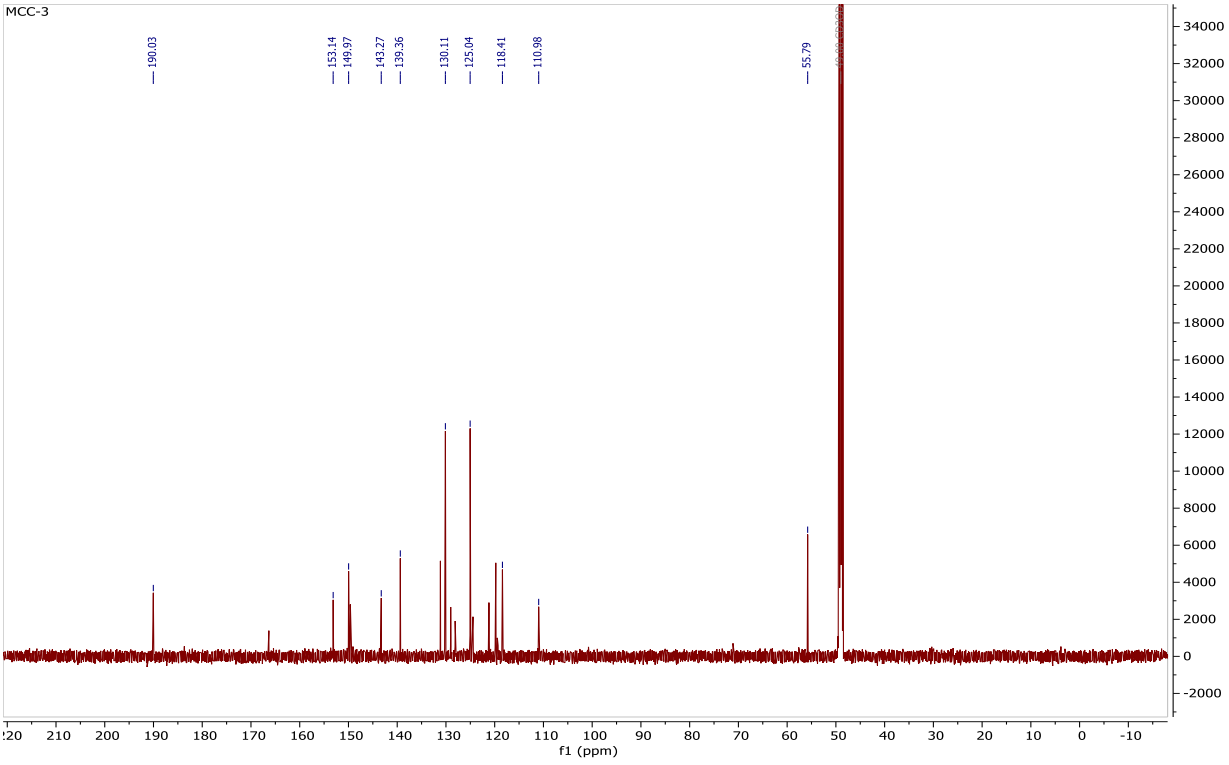
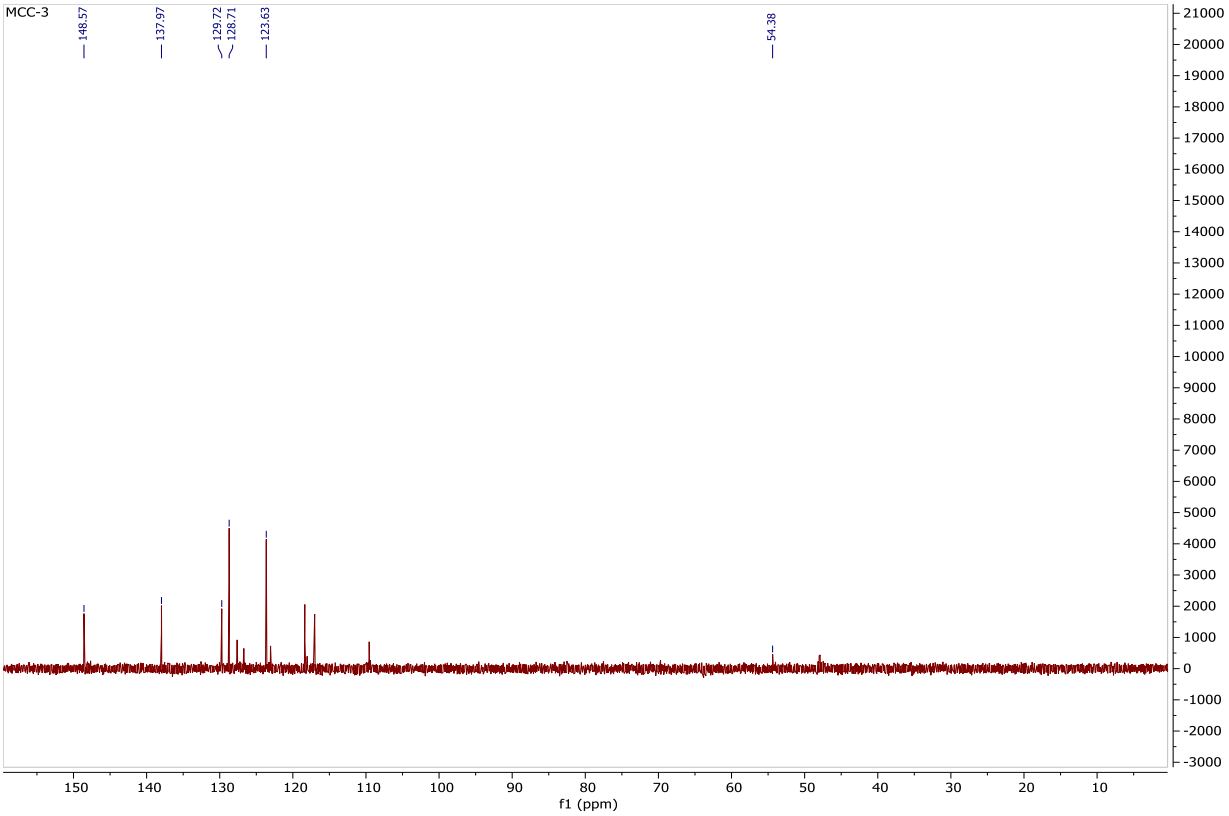
Appendix Ia. ^{1}H-NMR spectrum (400 MHz, MeOD-*d*$_4$) of compound **3**



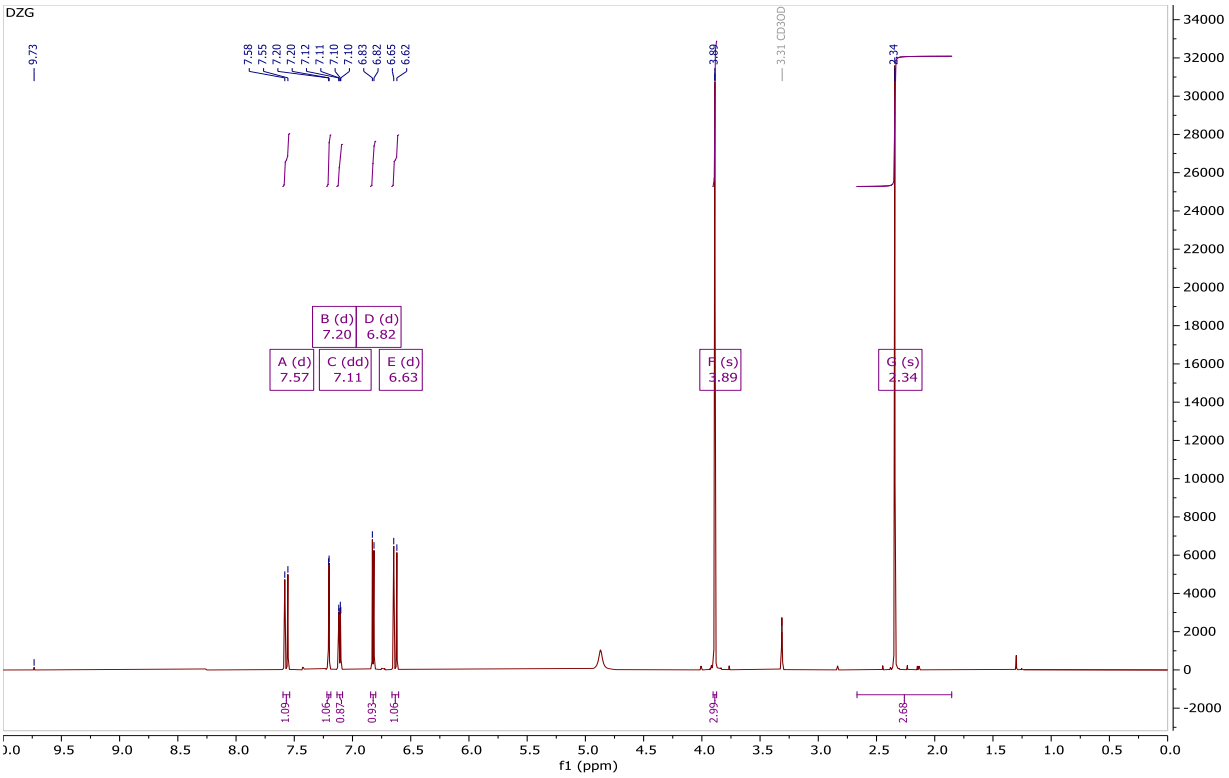
Appendix Ib. ^{13}C -NMR spectrum (100 MHz, MeOD-*d*$_4$) of compound **3**



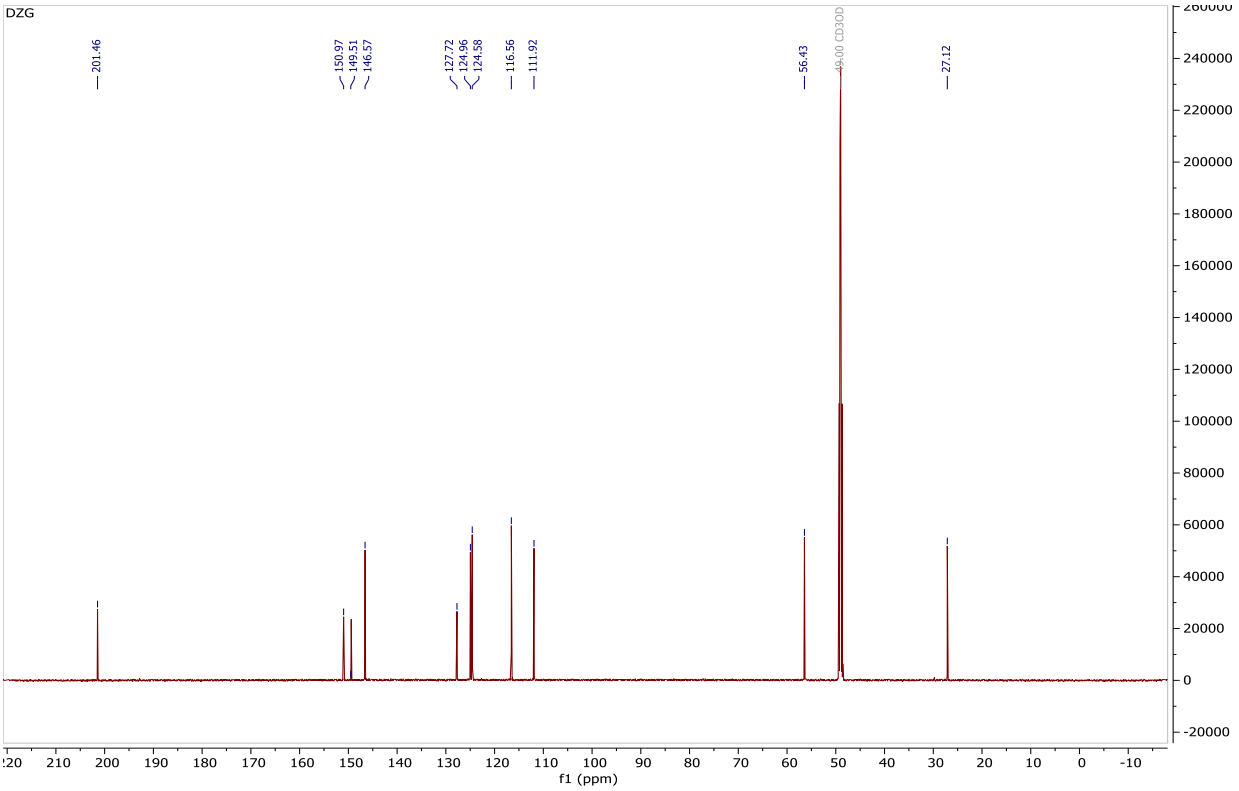
Appendix Ic. ^{13}C –DEPT-135 NMR spectrum (100 MHz, MeOD-d_4) of compound **3**



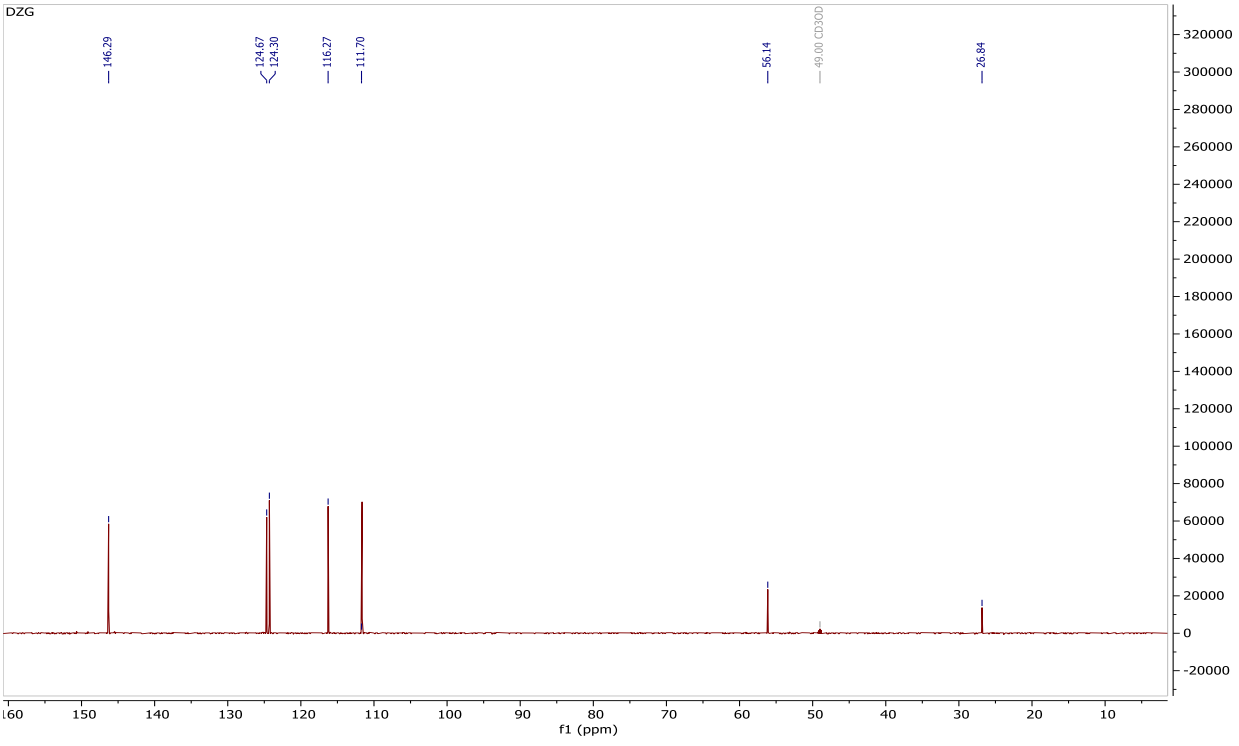
Appendix IIa. ^{1}H-NMR spectrum (400 MHz, MeOD-d_4) of compound **4**



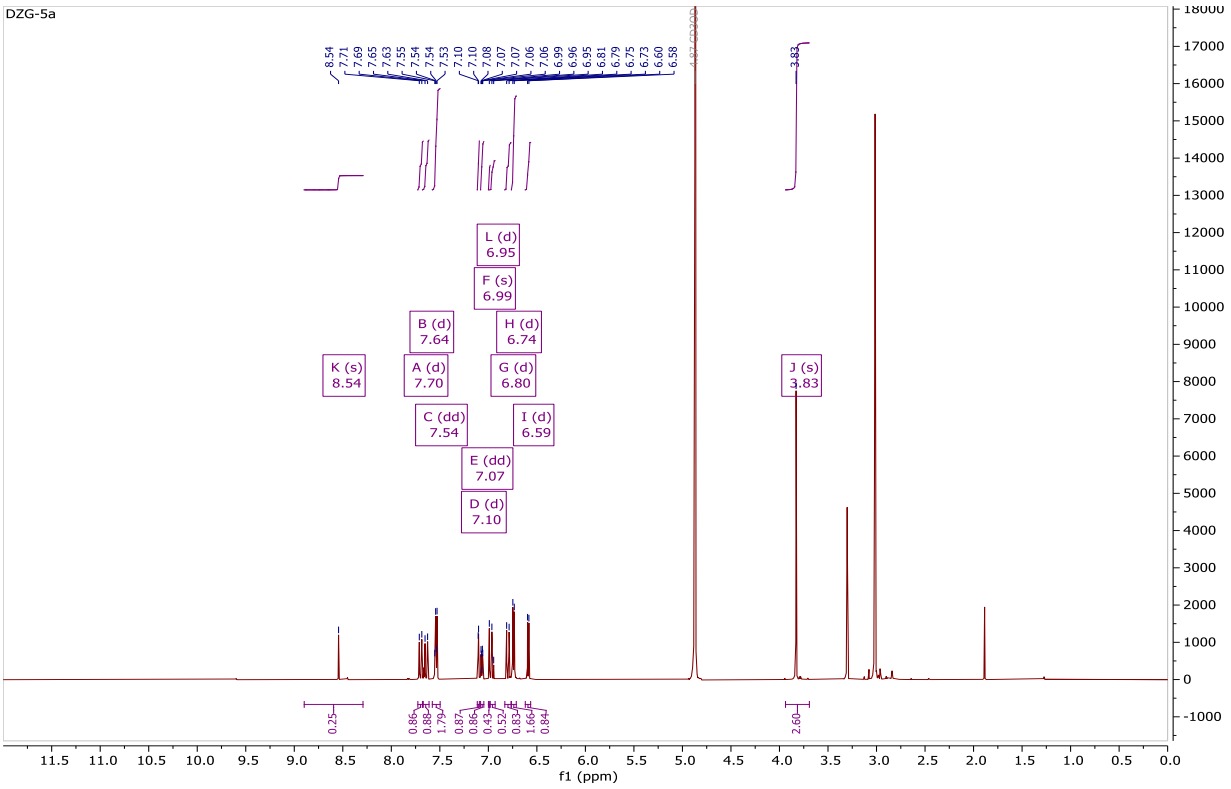
Appendix IIb. ^{13}C -NMR spectrum (100 MHz, MeOD-d_4) of compound **4**



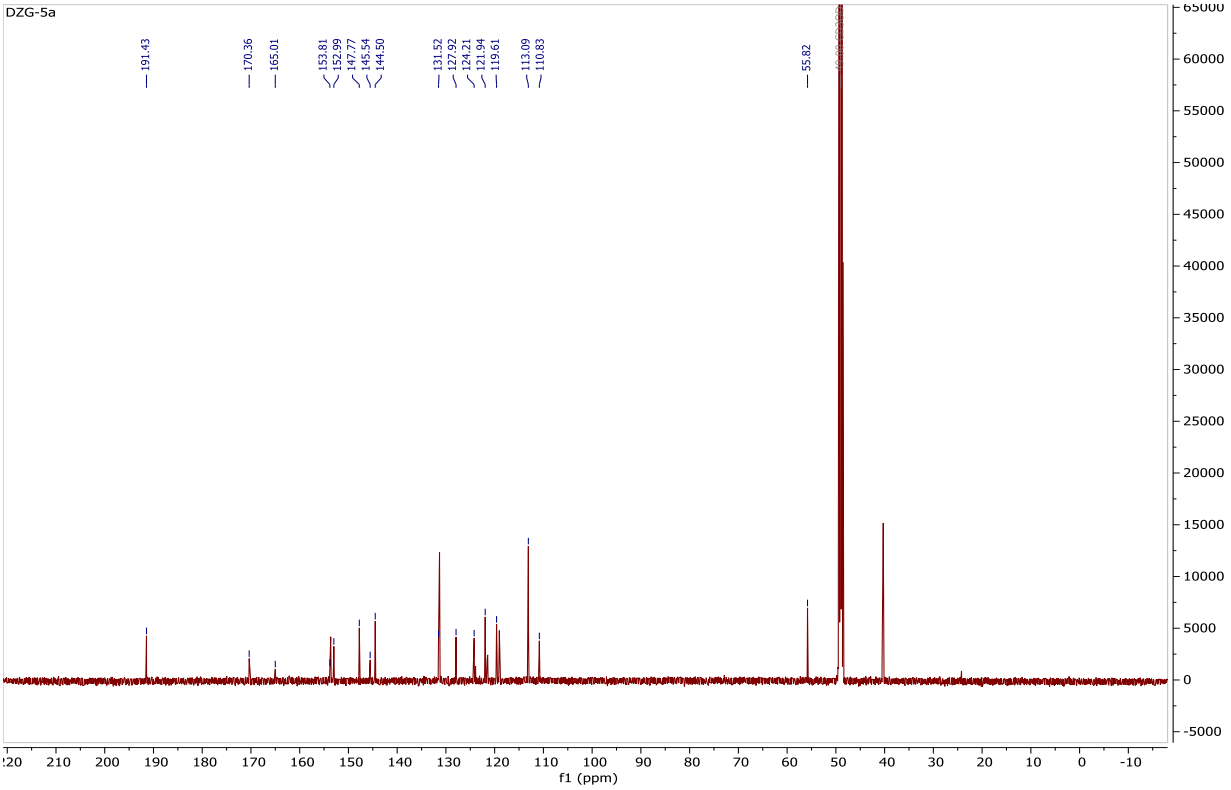
Appendix IIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, MeOD-d_4) of compound **4**



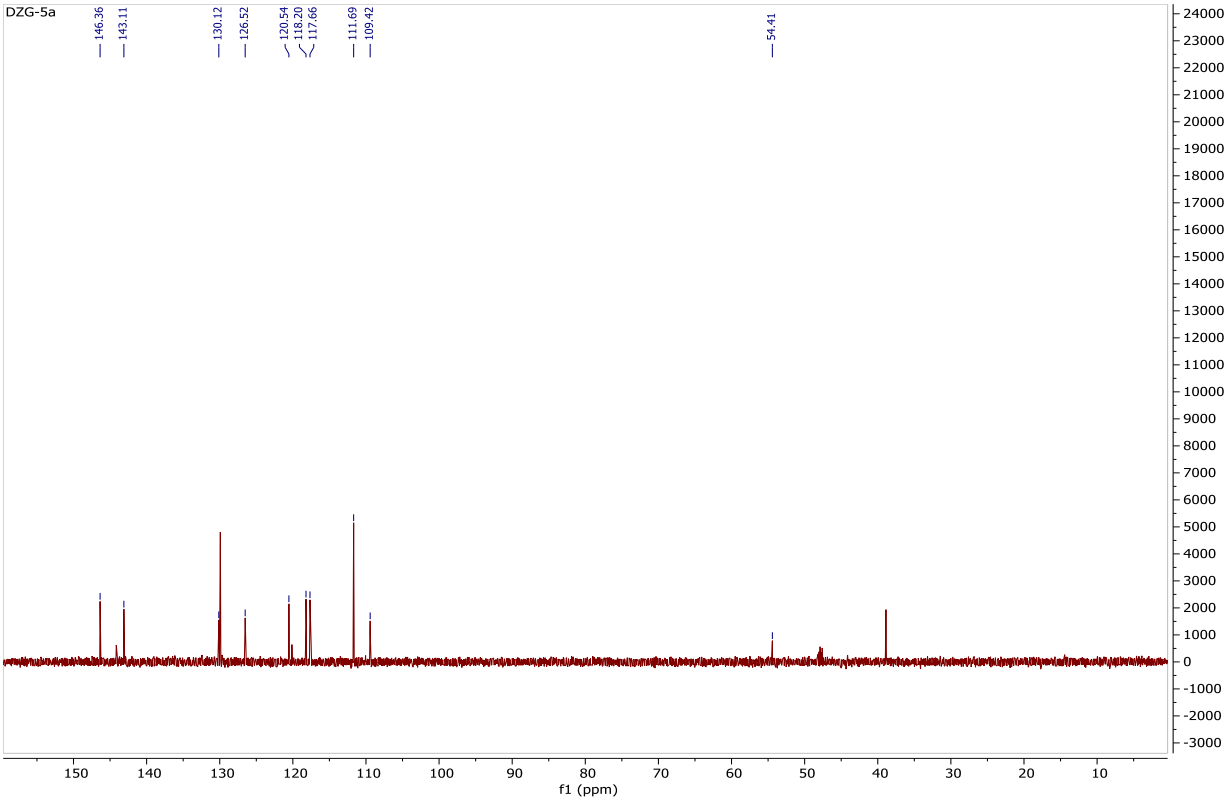
Appendix IIIa. ^{1}H-NMR spectrum (400 MHz, MeOD-*d*$_4$) of compound **5**



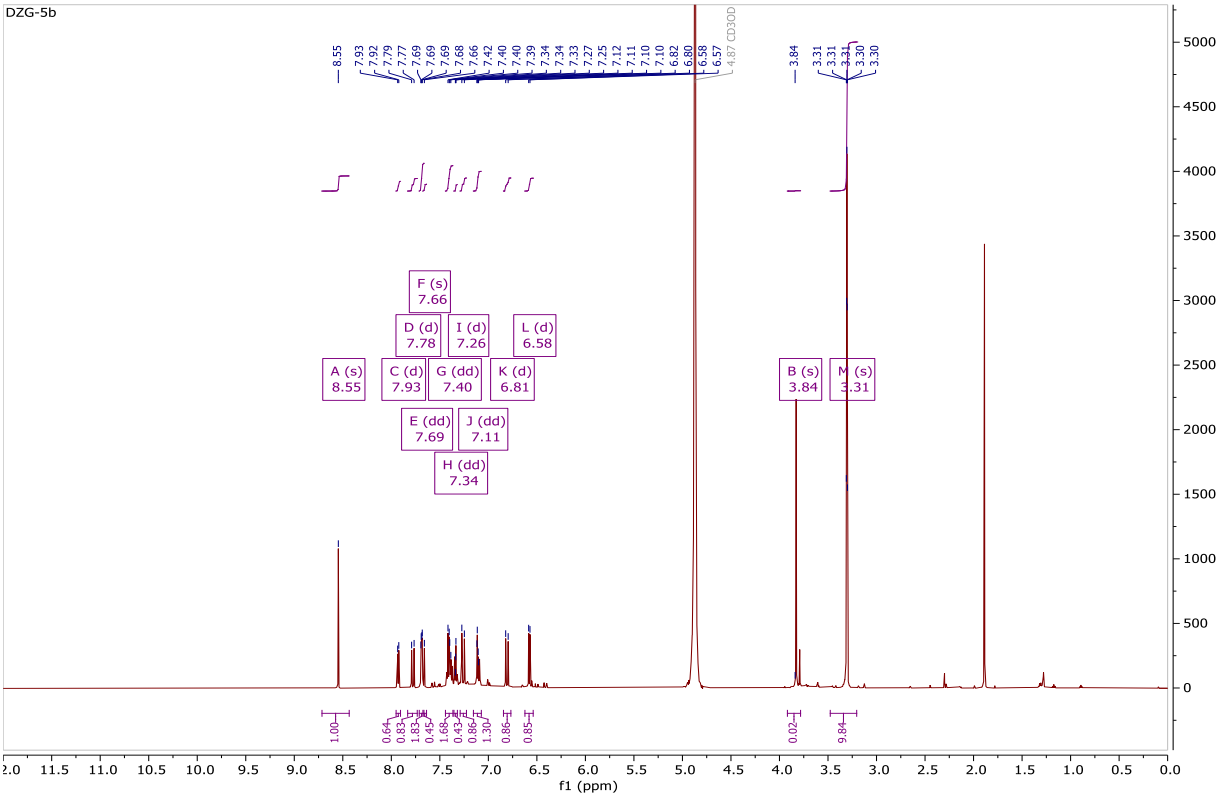
Appendix IIIb. ^{13}C -NMR spectrum (100 MHz, MeOD-*d*$_4$) of compound **5**



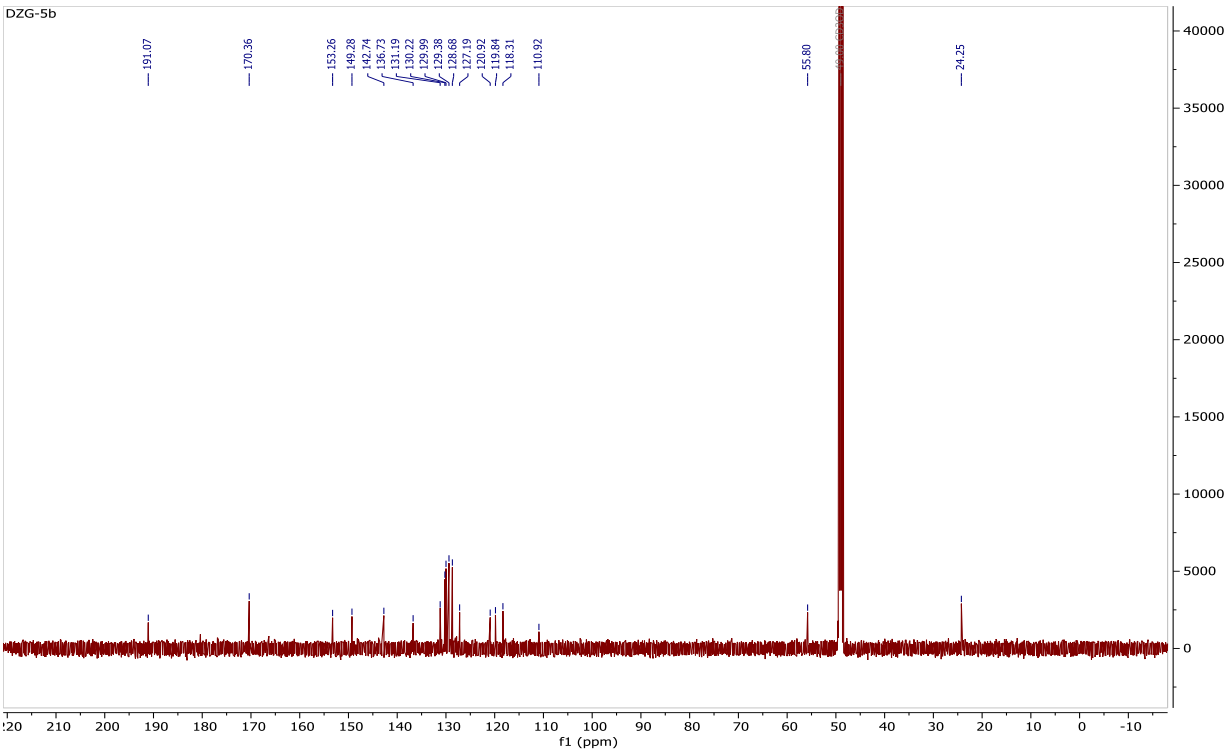
Appendix IIIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, MeOD-d_4) of compound **5**



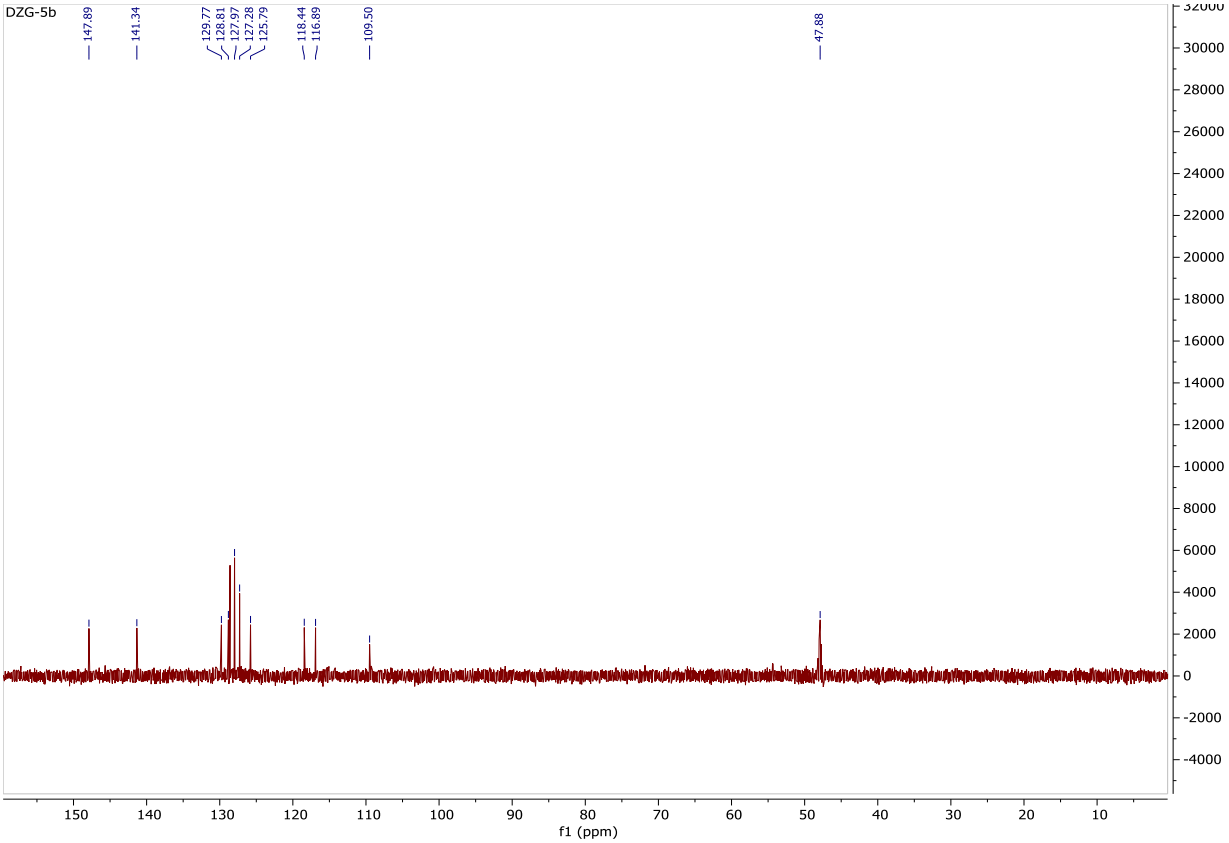
Appendix IVa. ^{1}H-NMR spectrum (400 MHz, MeOD-d_4) of compound **6**



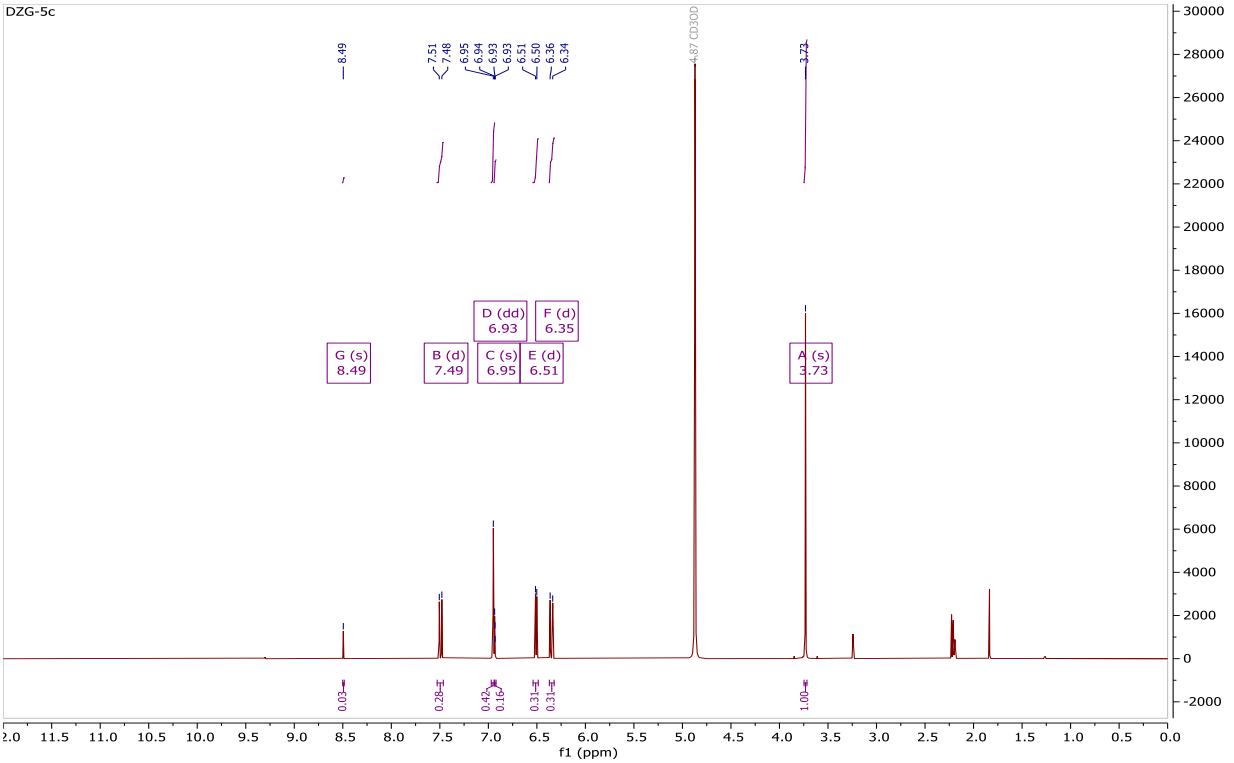
Appendix IVb. ^{13}C -NMR spectrum (100 MHz, MeOD-d_4) of compound **6**



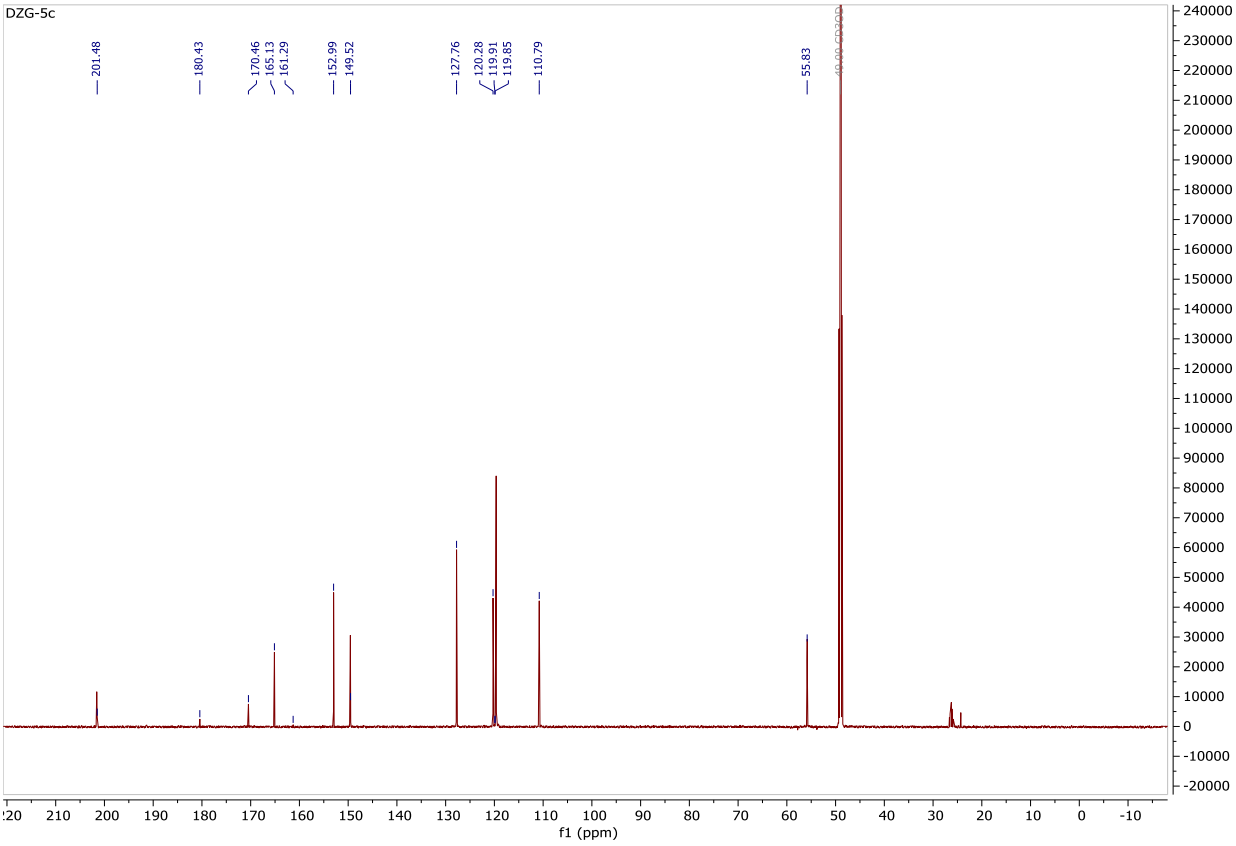
Appendix IVc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, MeOD-d_4) of compound **6**



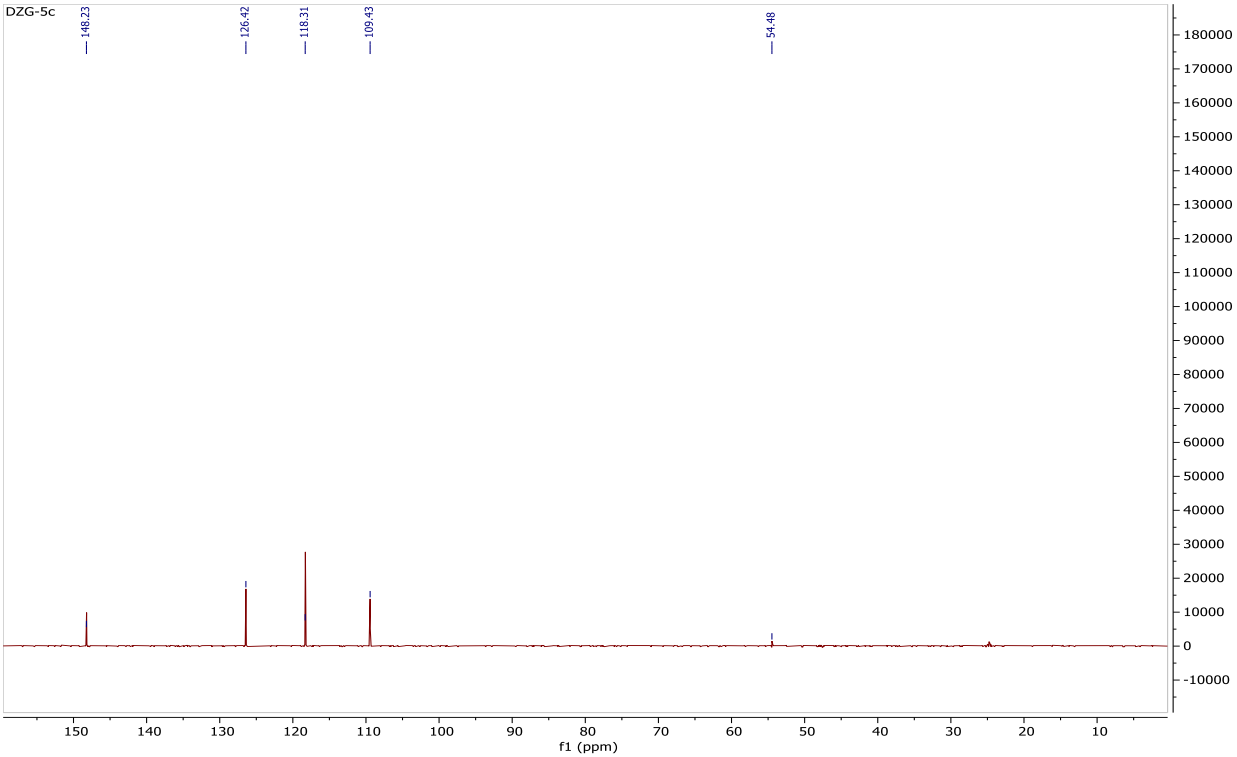
Appendix Va. ^{1}H-NMR spectrum (400 MHz, MeOD-*d*$_4$) of compound **7**



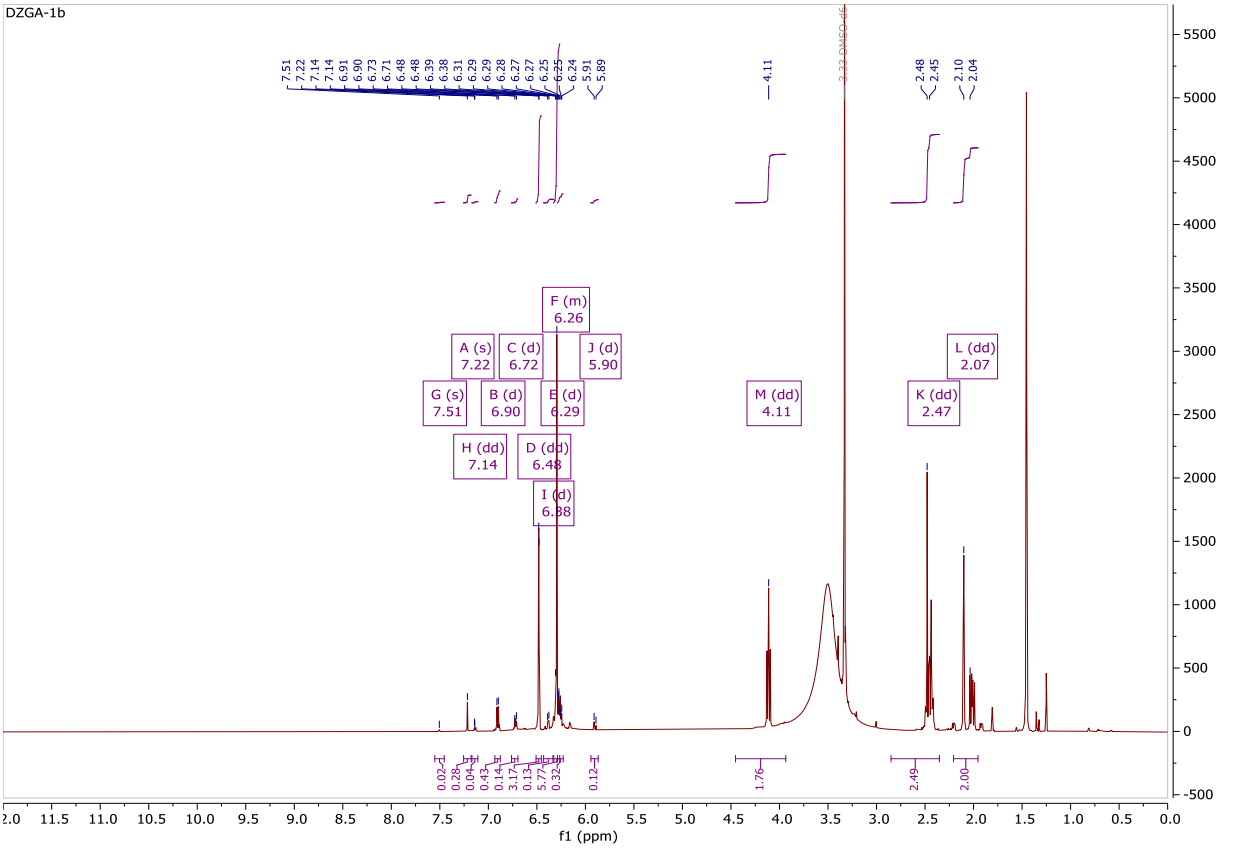
Appendix Vb. ^{13}C -NMR spectrum (100 MHz, MeOD-*d*$_4$) of compound **7**



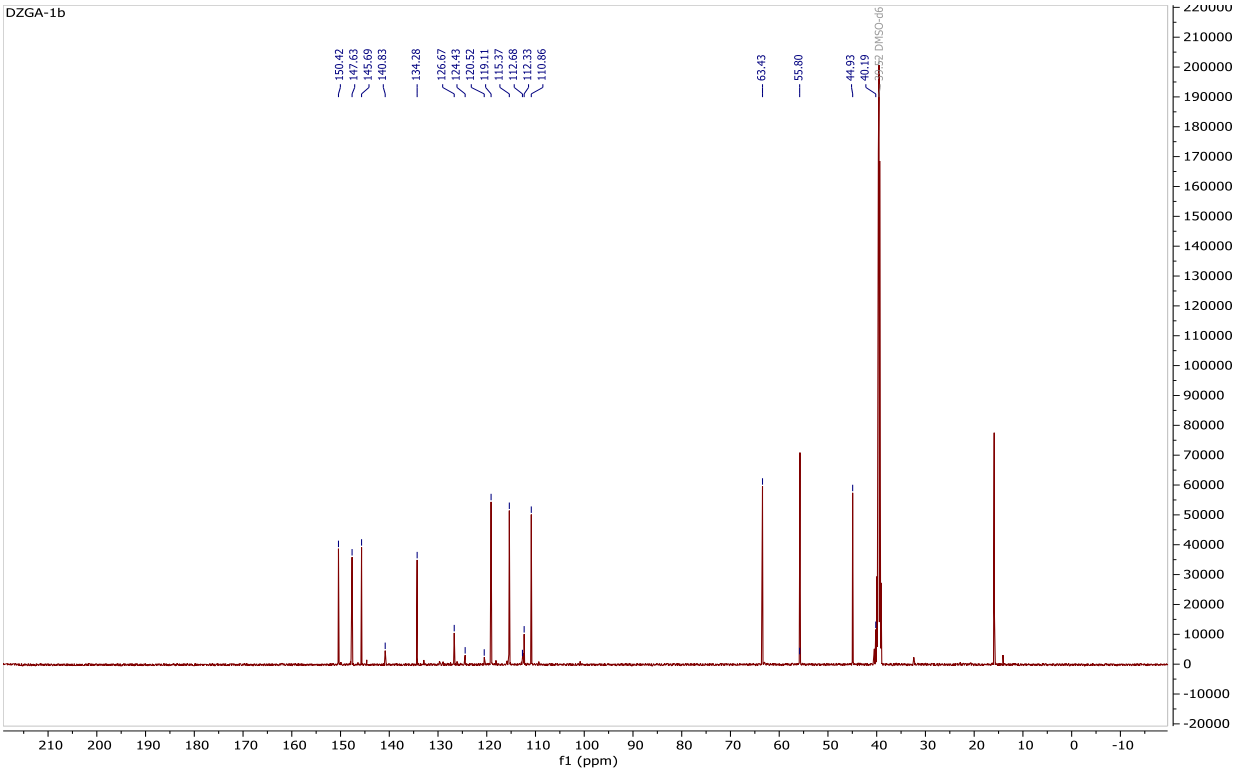
Appendix Vc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, MeOD-d_4) of compound **7**



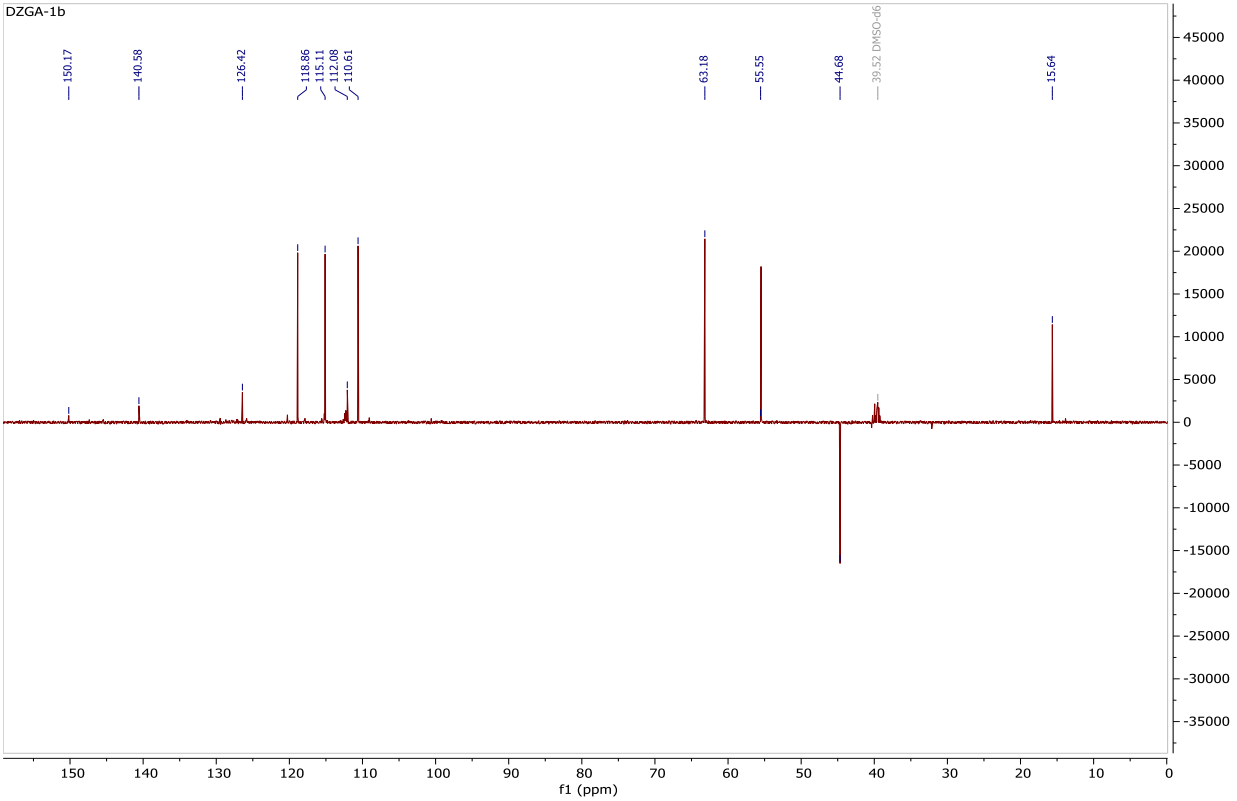
Appendix VIa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **8**



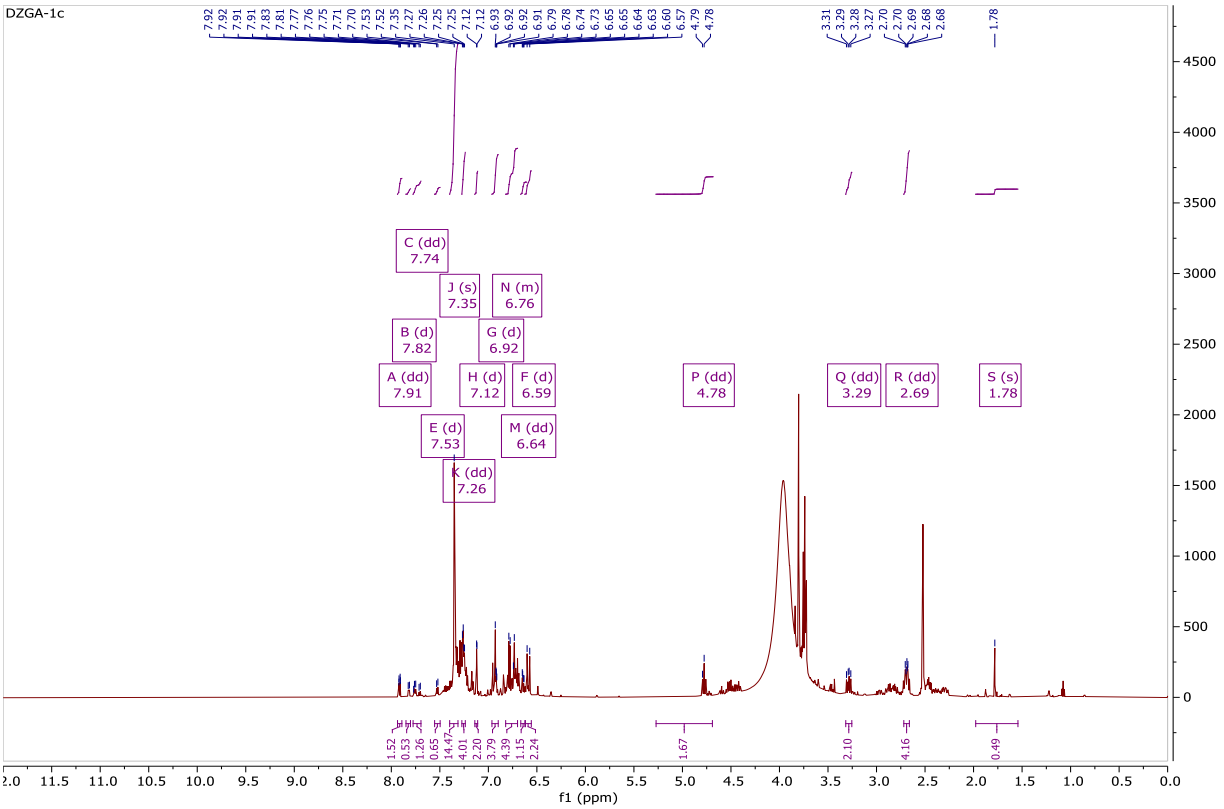
Appendix VIb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **8**



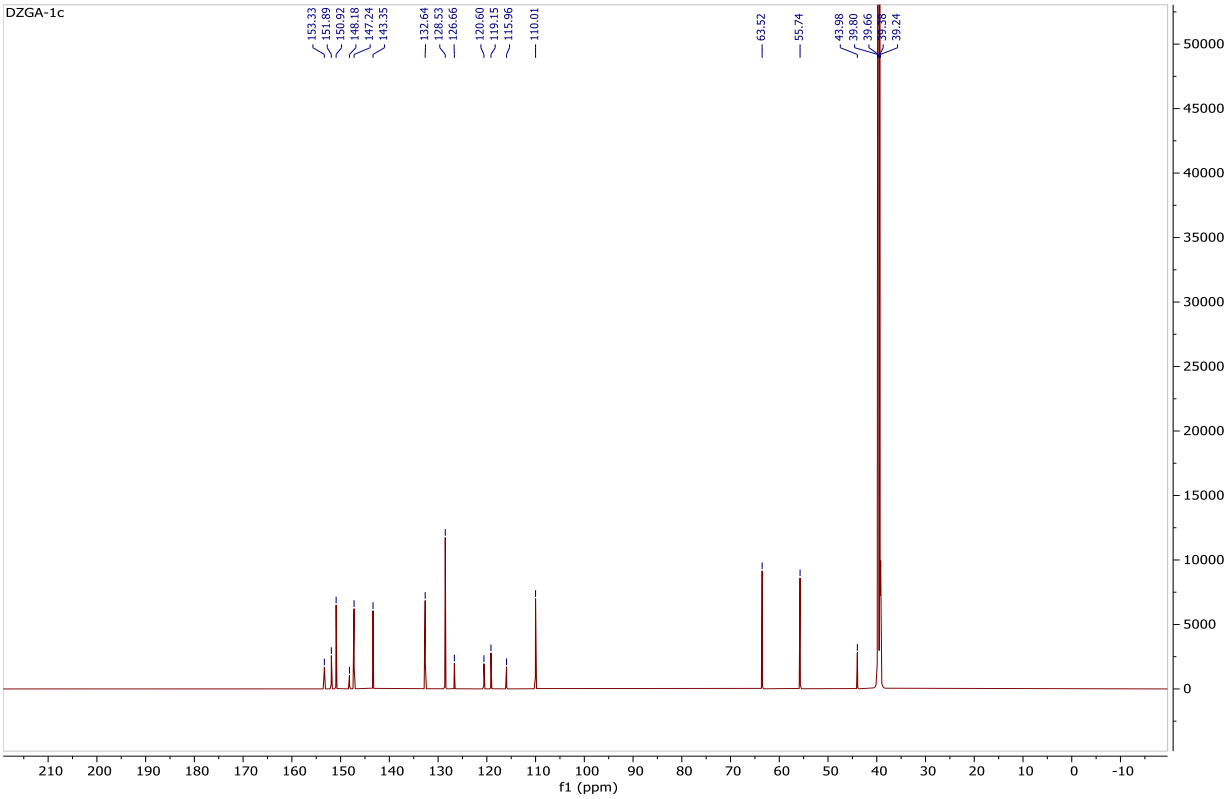
Appendix VIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **8**



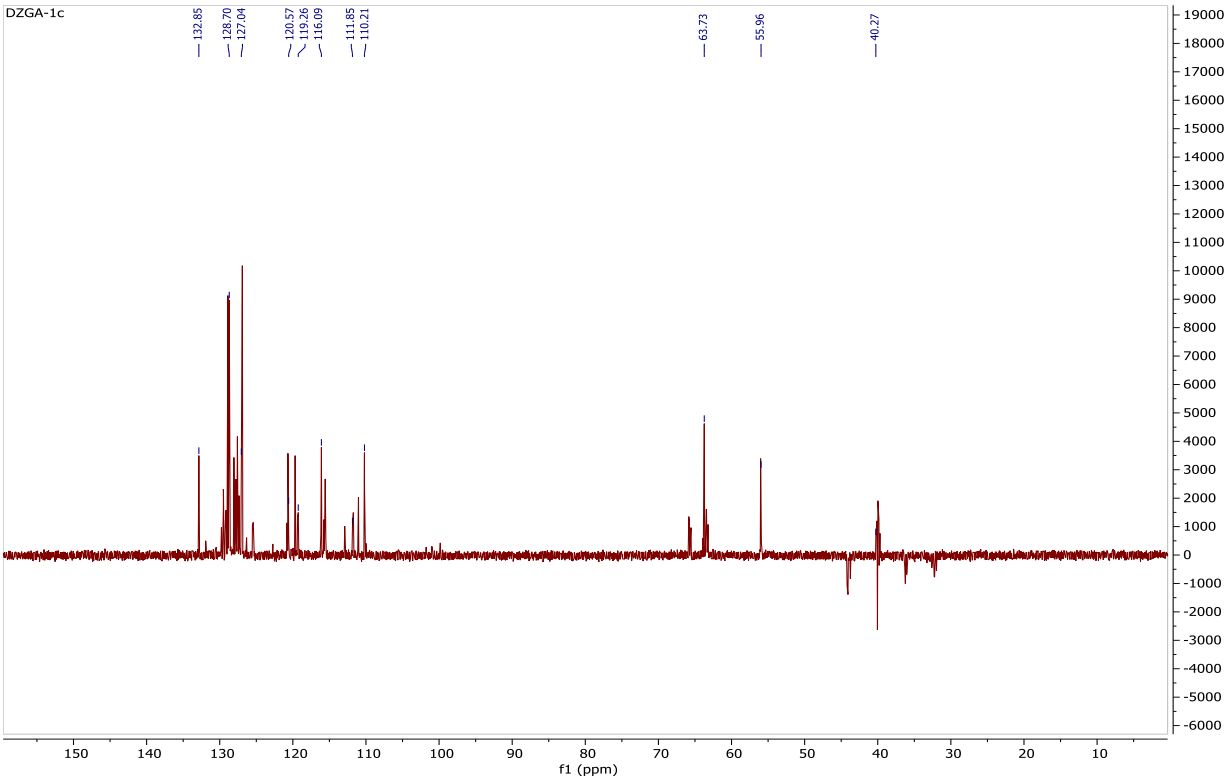
Appendix VIIa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **9**



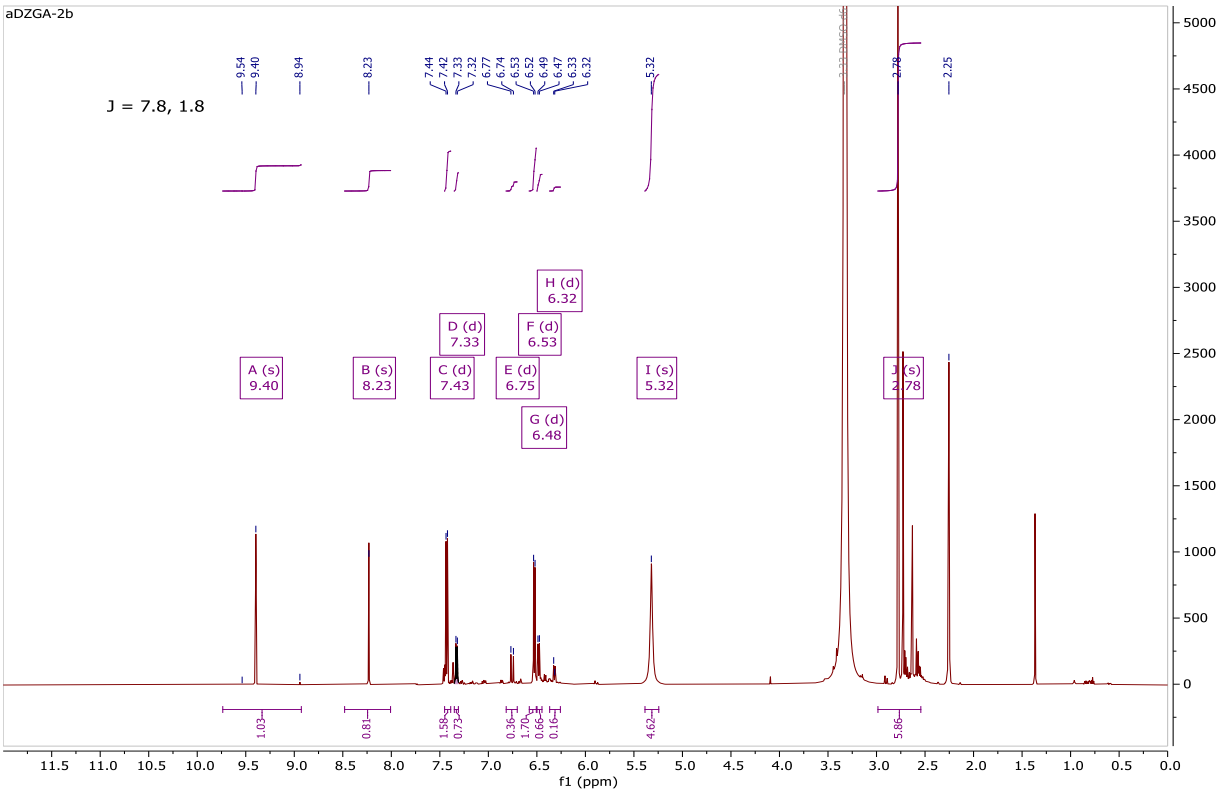
Appendix VIIb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **9**



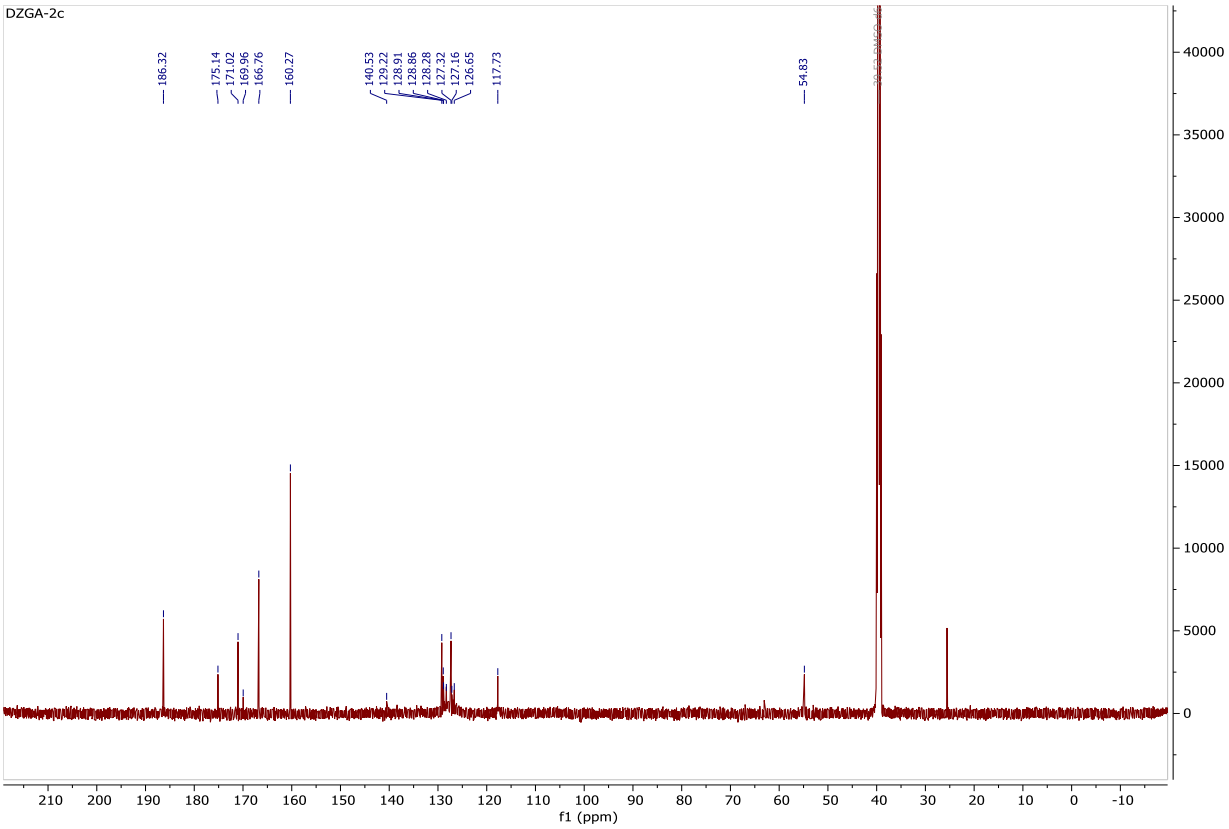
Appendix VIIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **9**



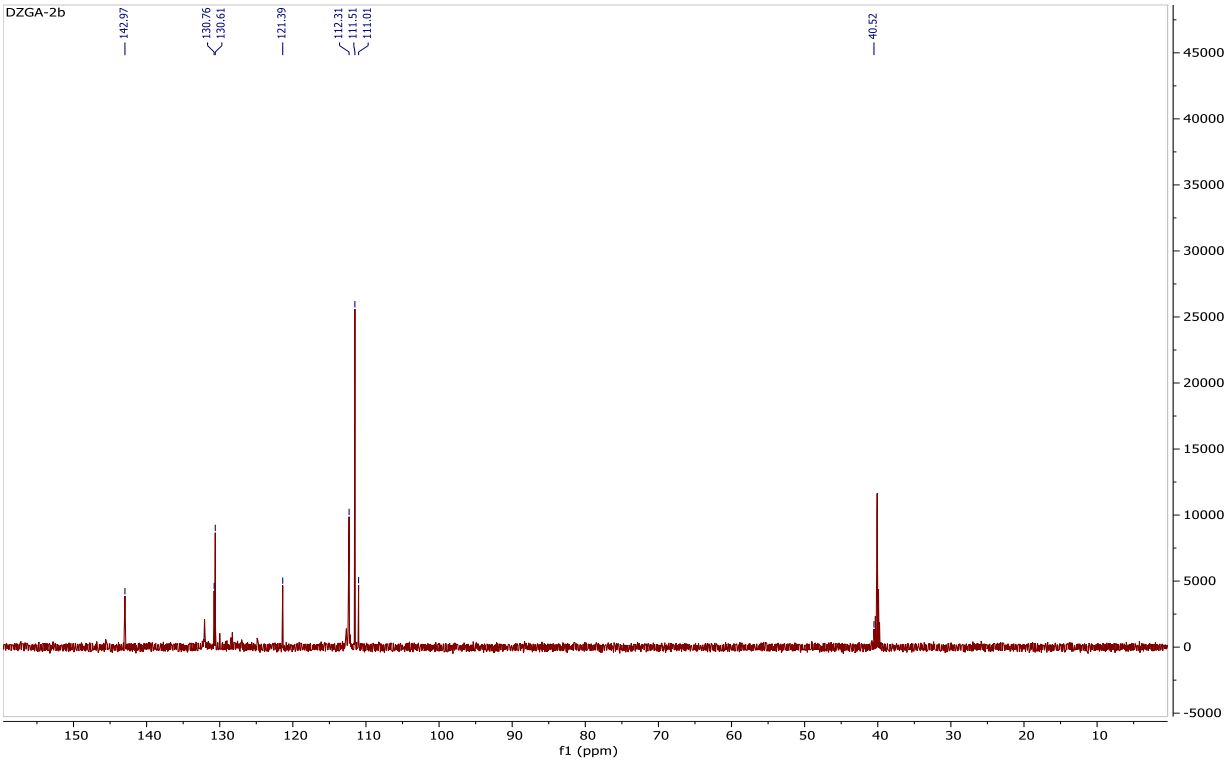
Appendix VIIIa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **10**



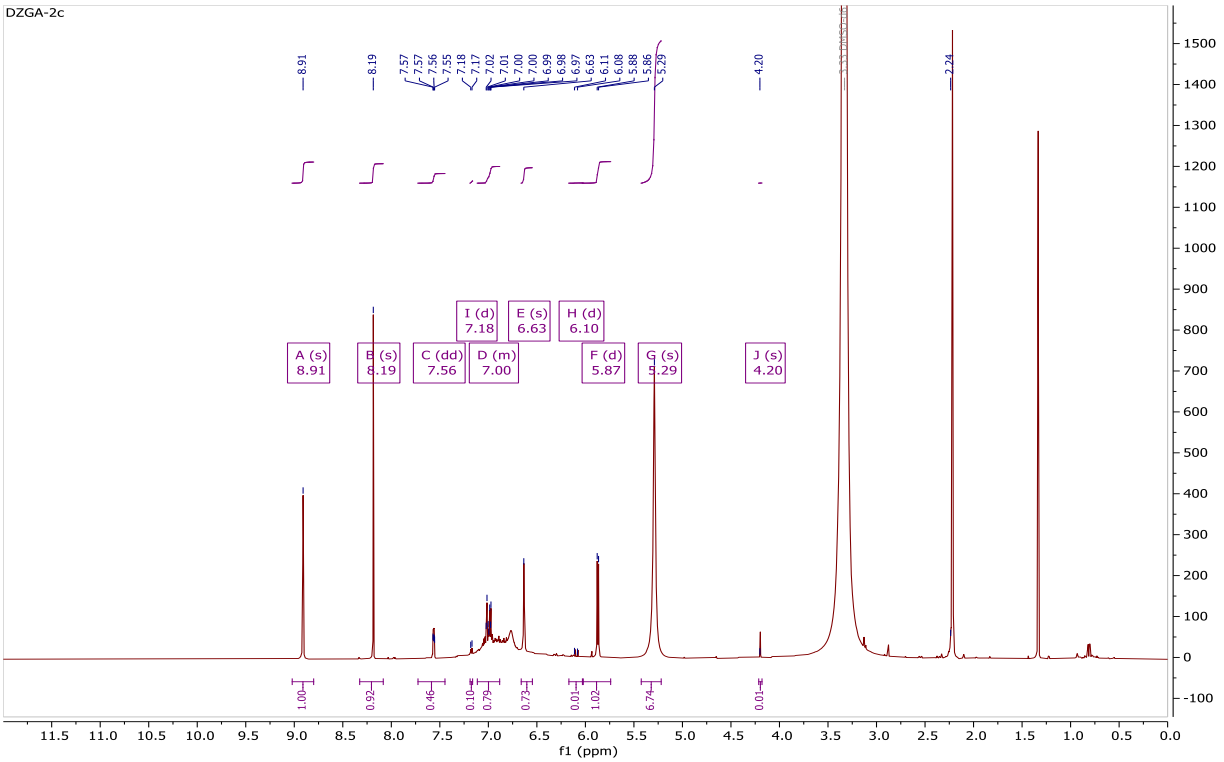
Appendix VIIIb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **10**



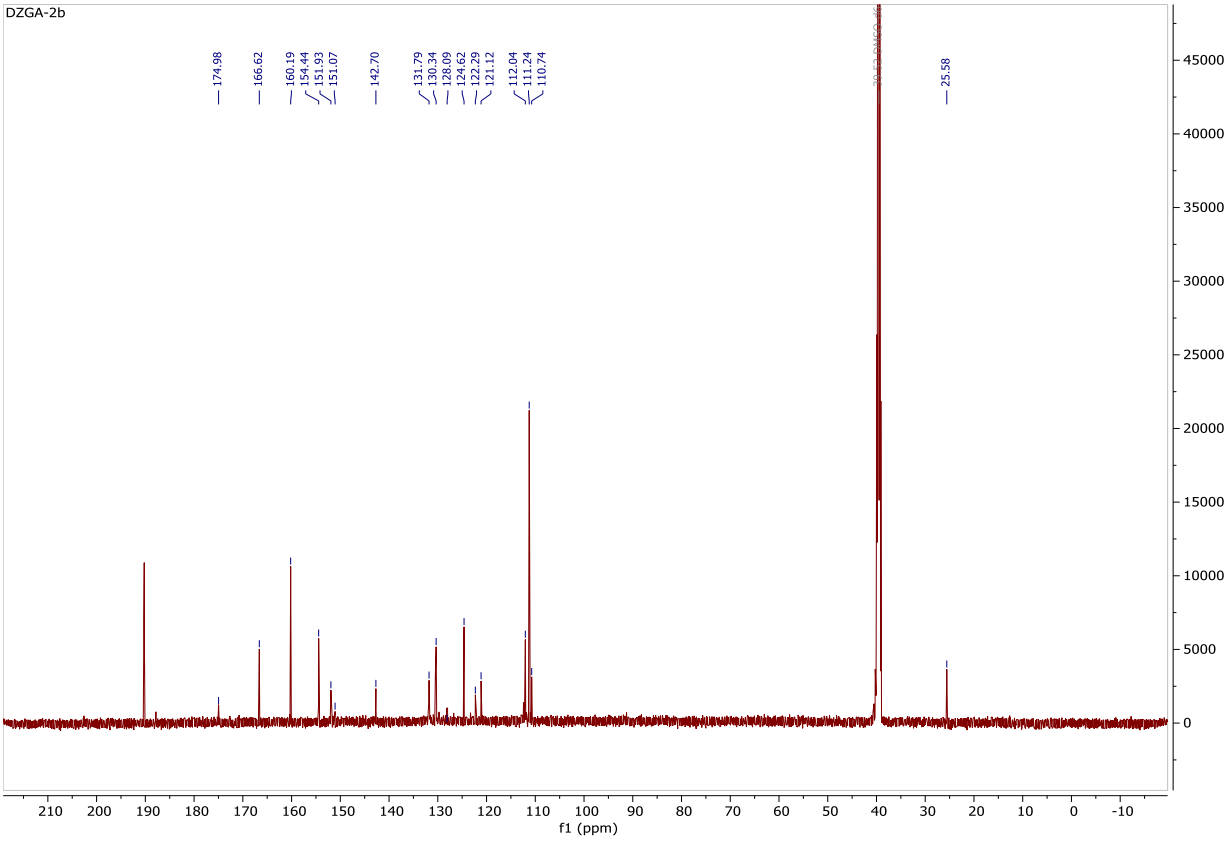
Appendix VIIIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **10**



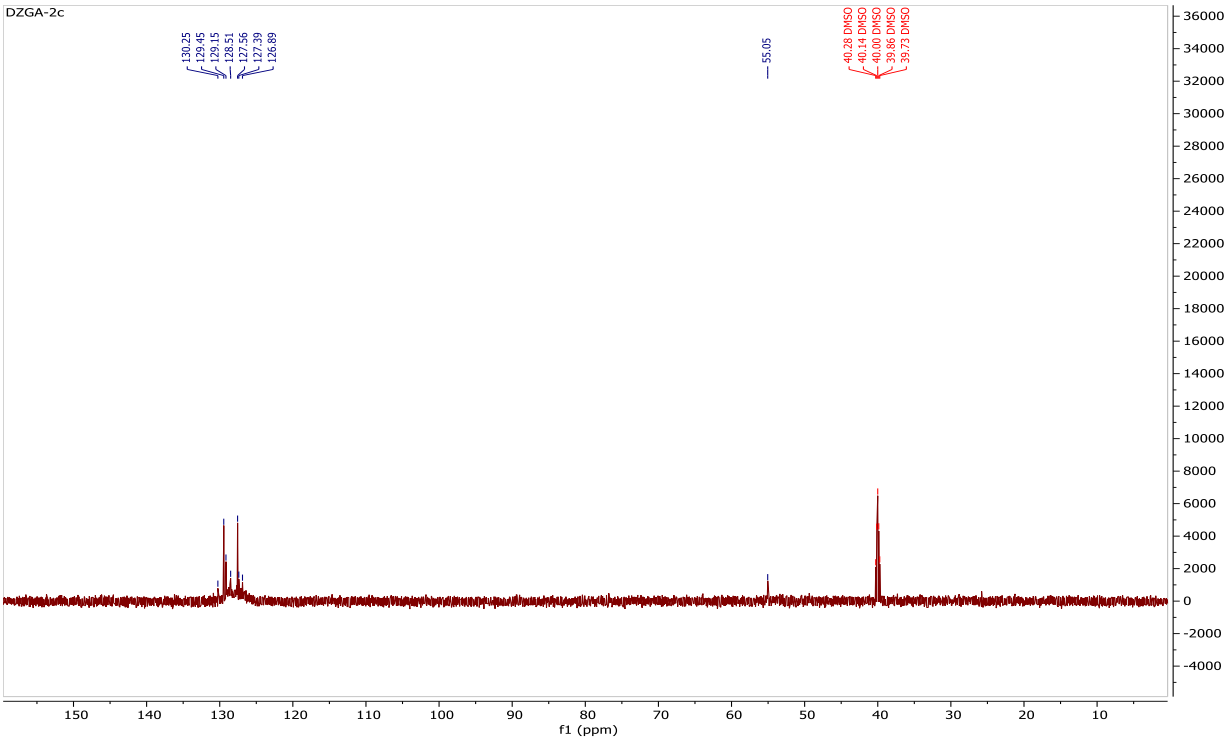
Appendix IXa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **11**



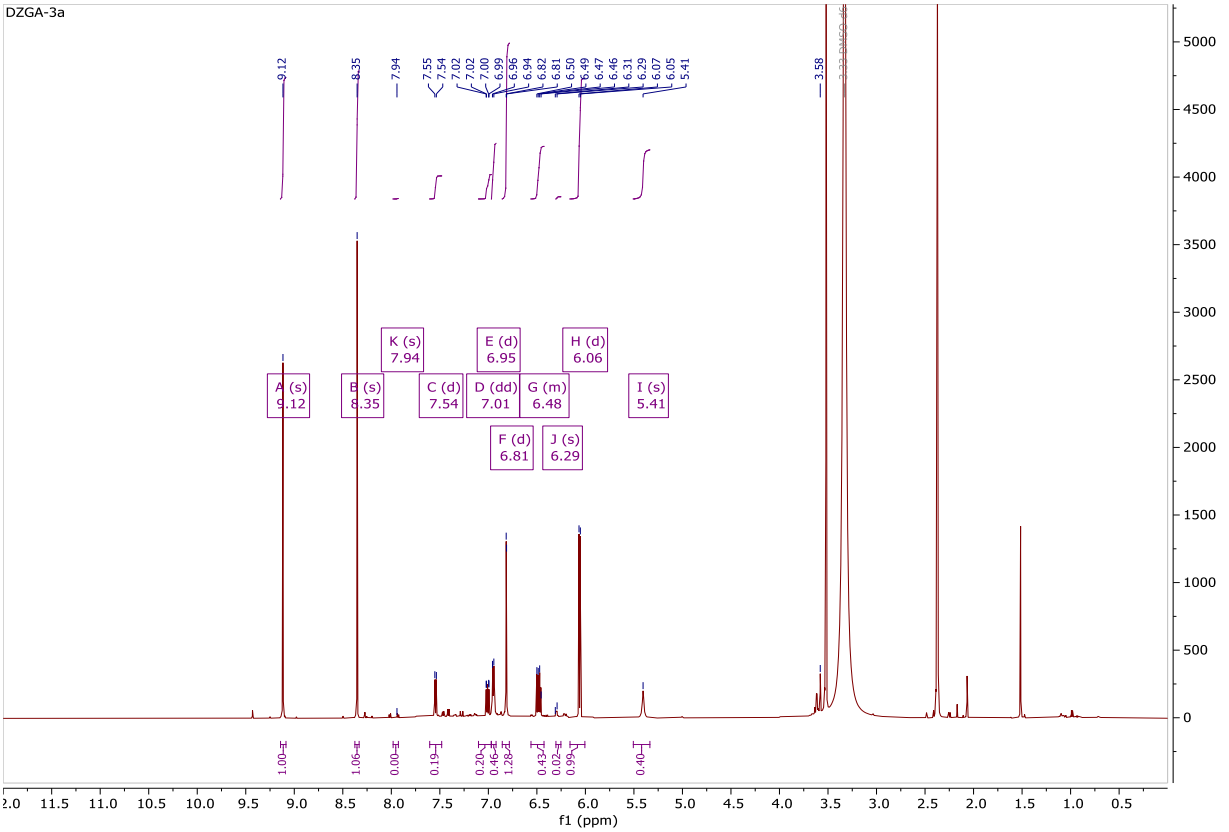
Appendix IXb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **11**



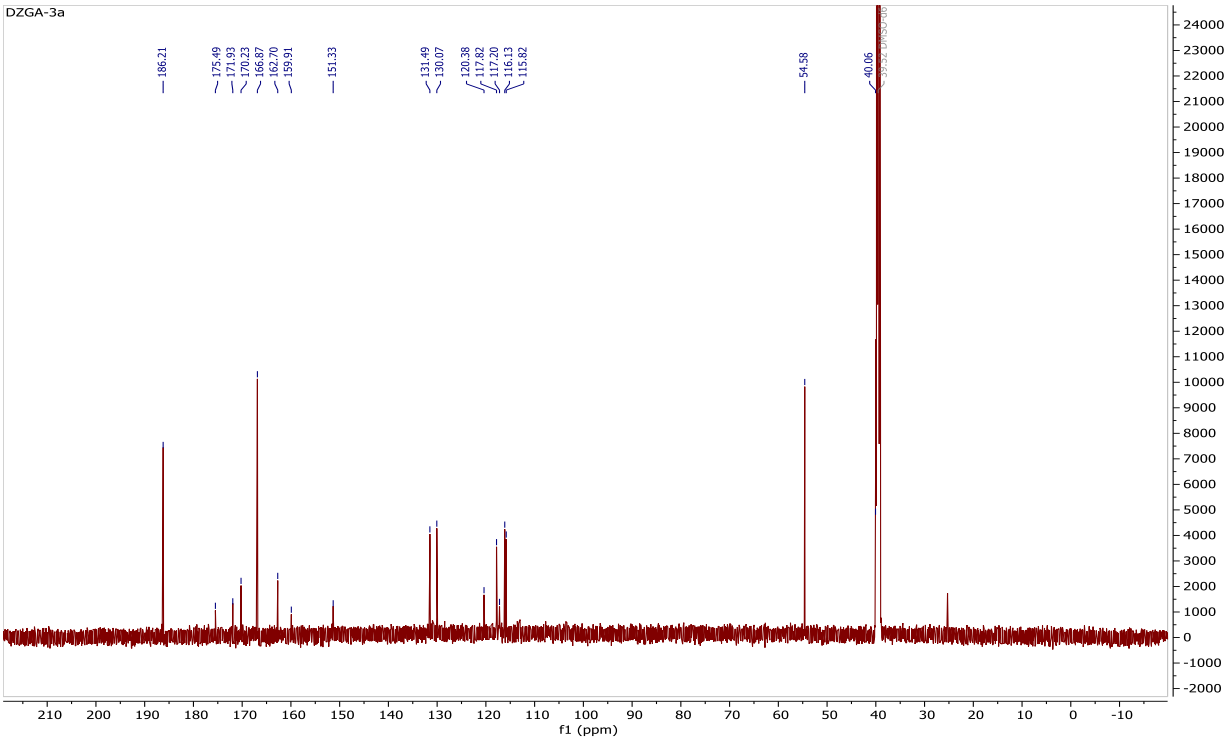
Appendix IXc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **11**



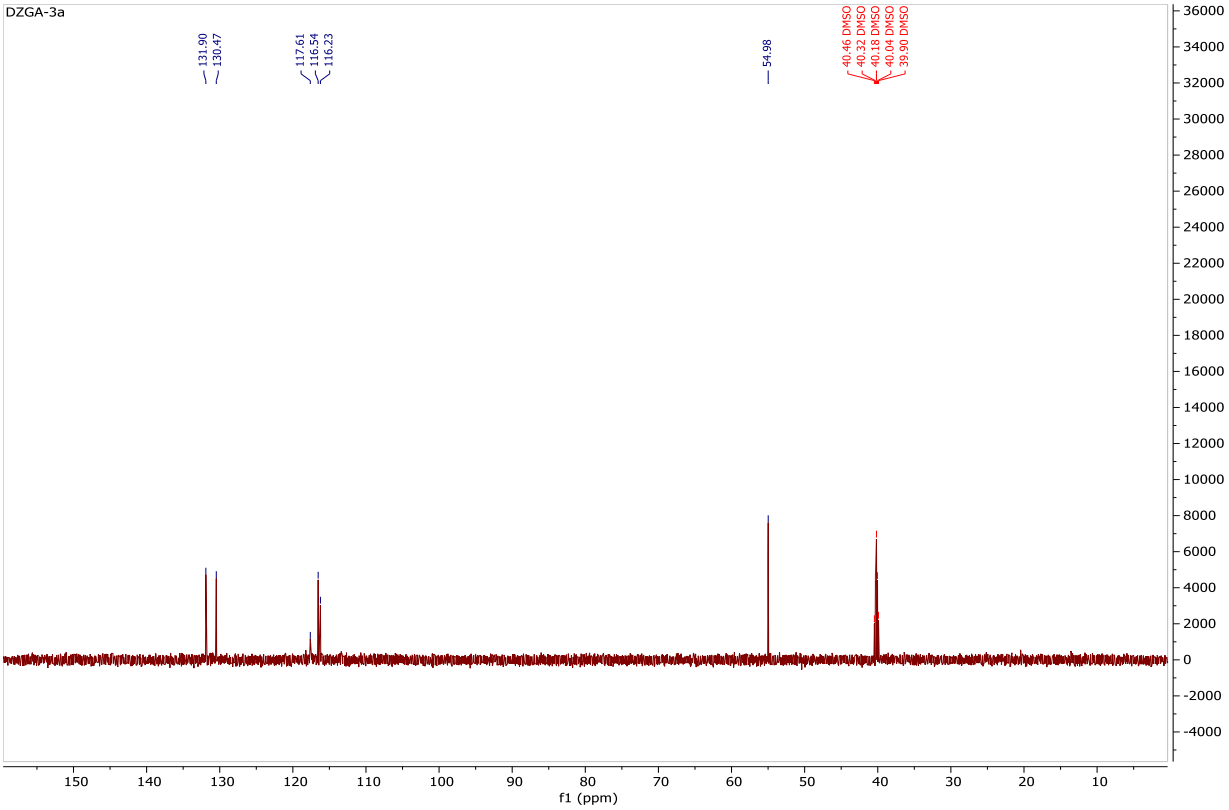
Appendix Xa.^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **12**



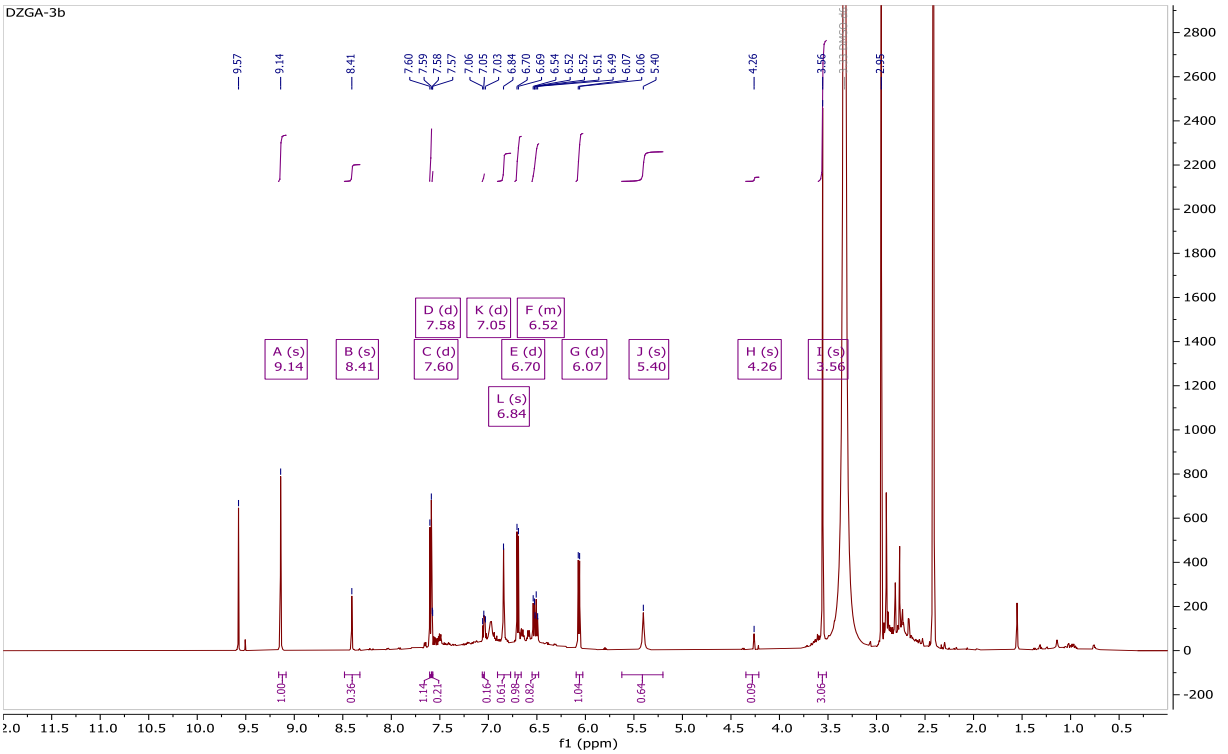
Appendix Xb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **12**



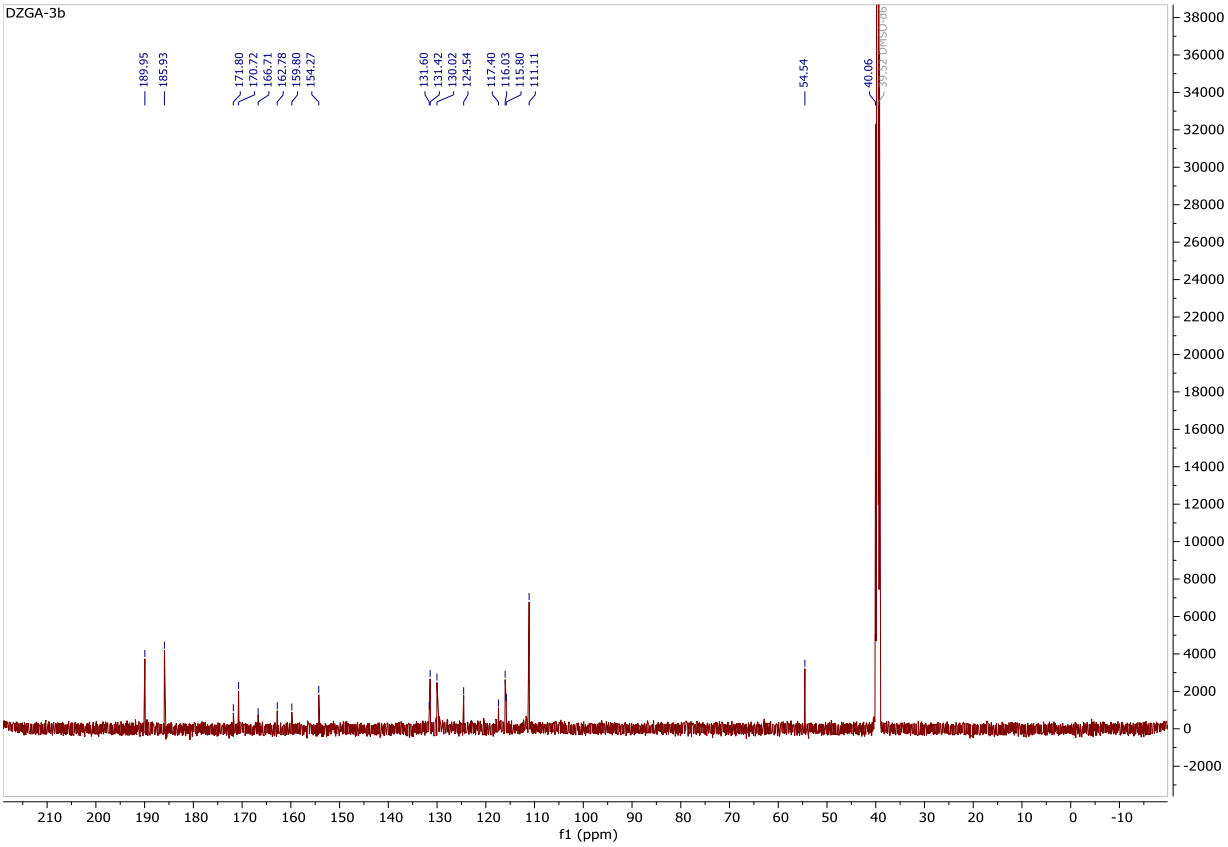
Appendix Xc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **12**



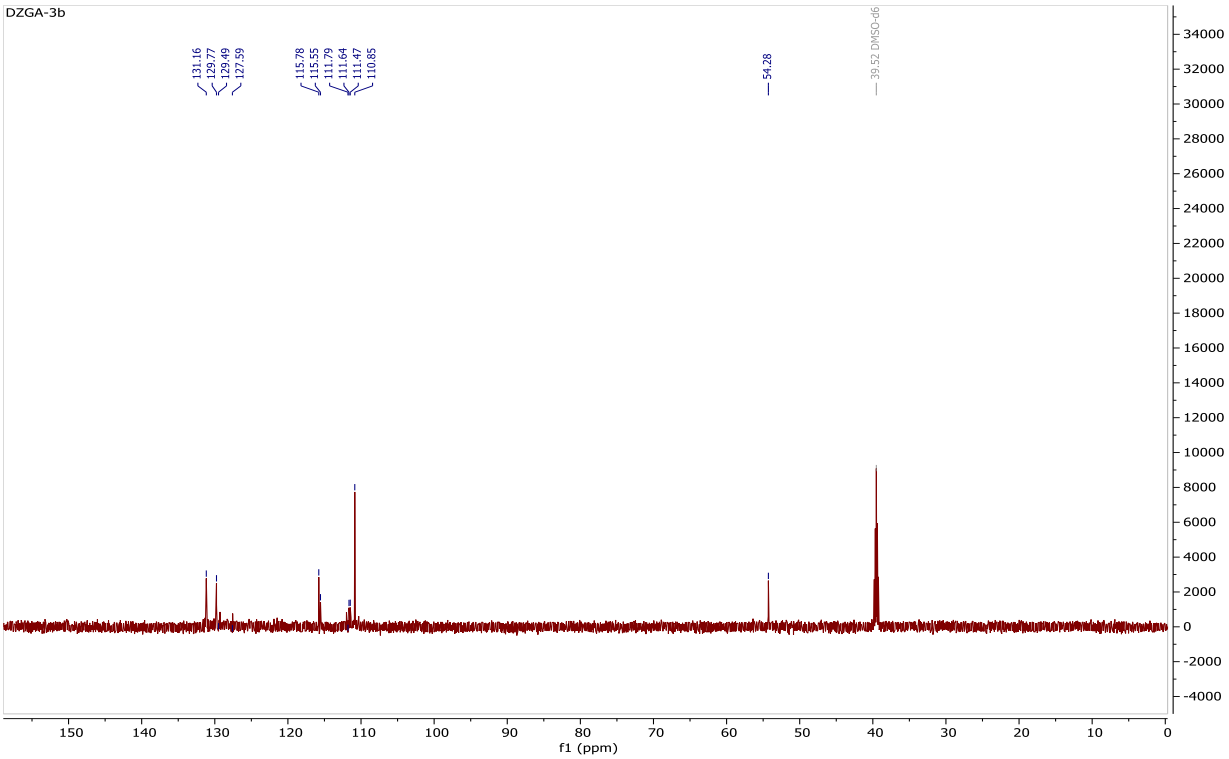
Appendix XIa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **13**



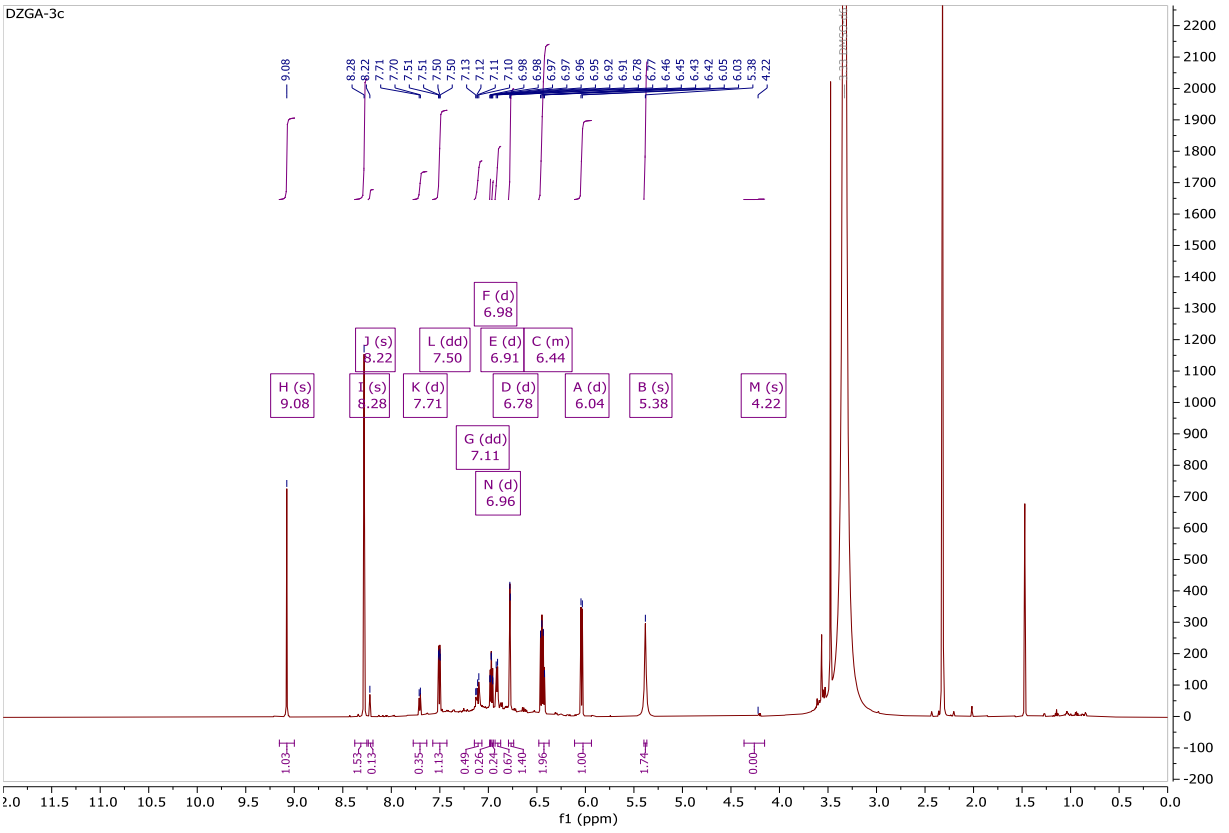
Appendix XIb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **13**



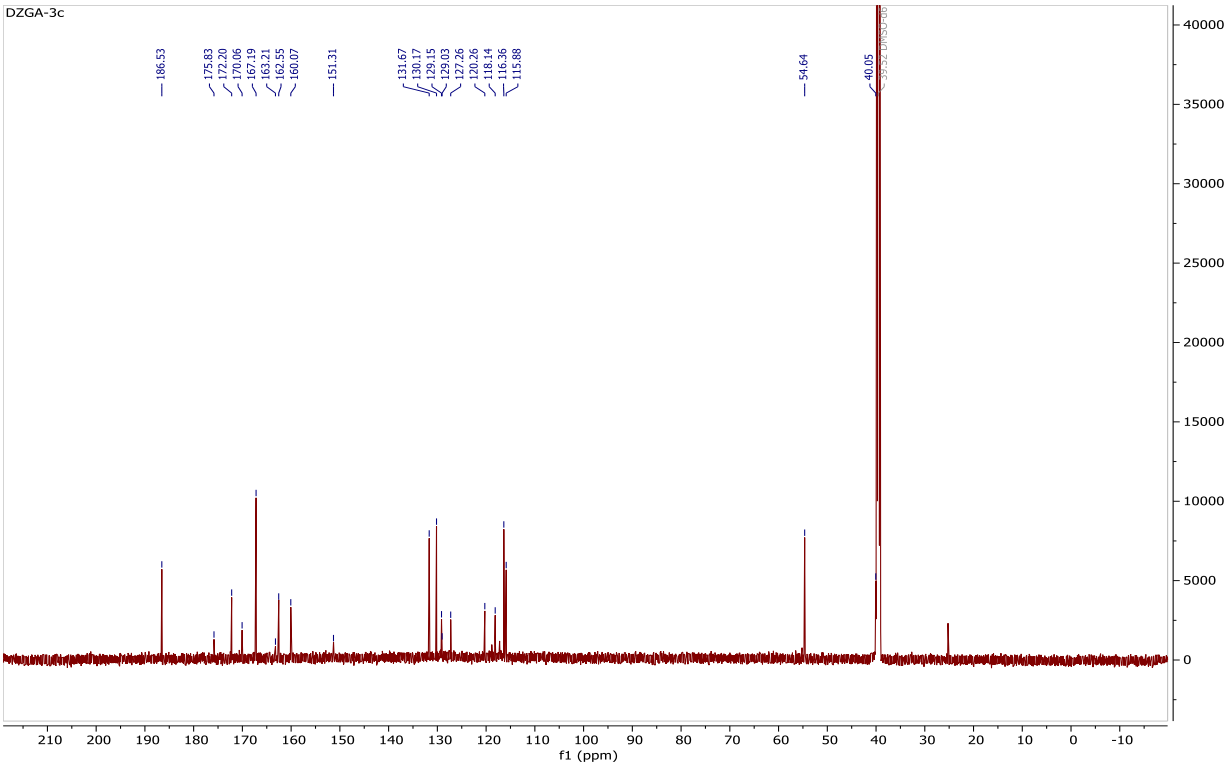
Appendix XIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **13**



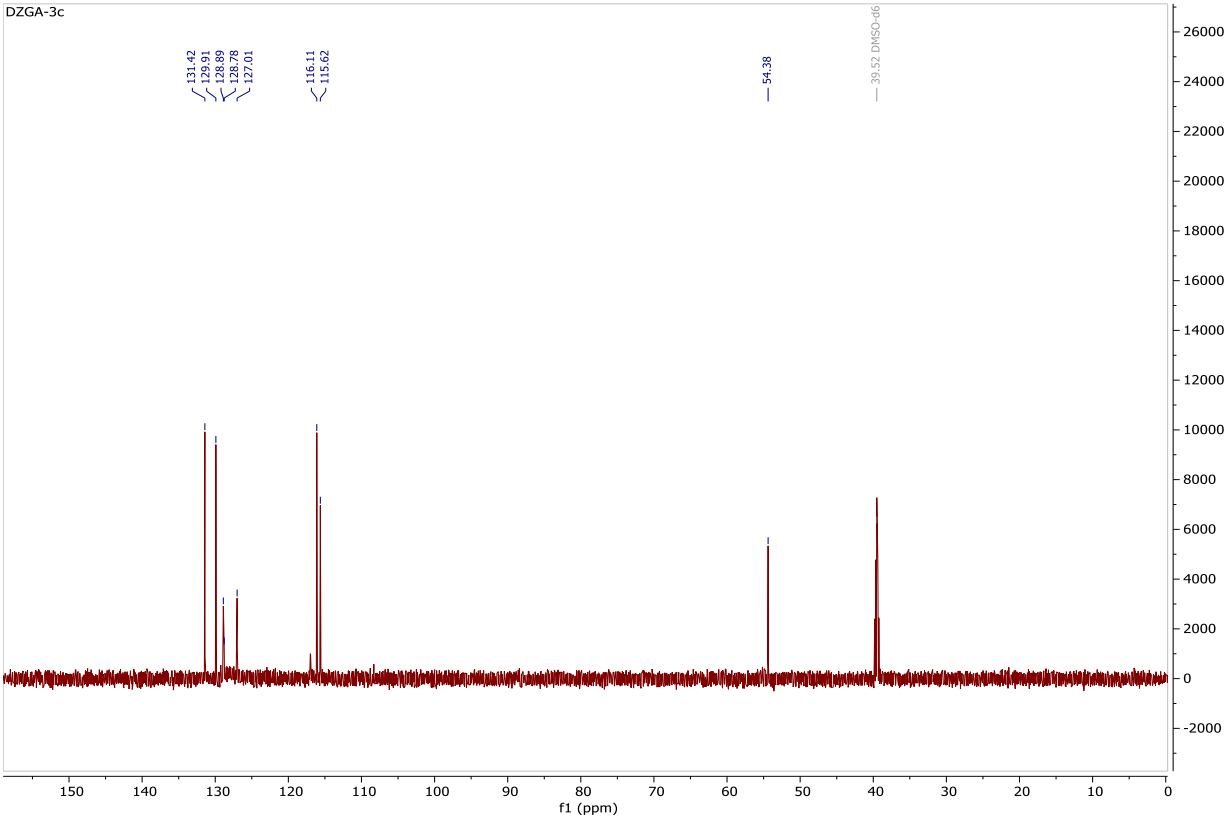
Appendix XIIa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **14**



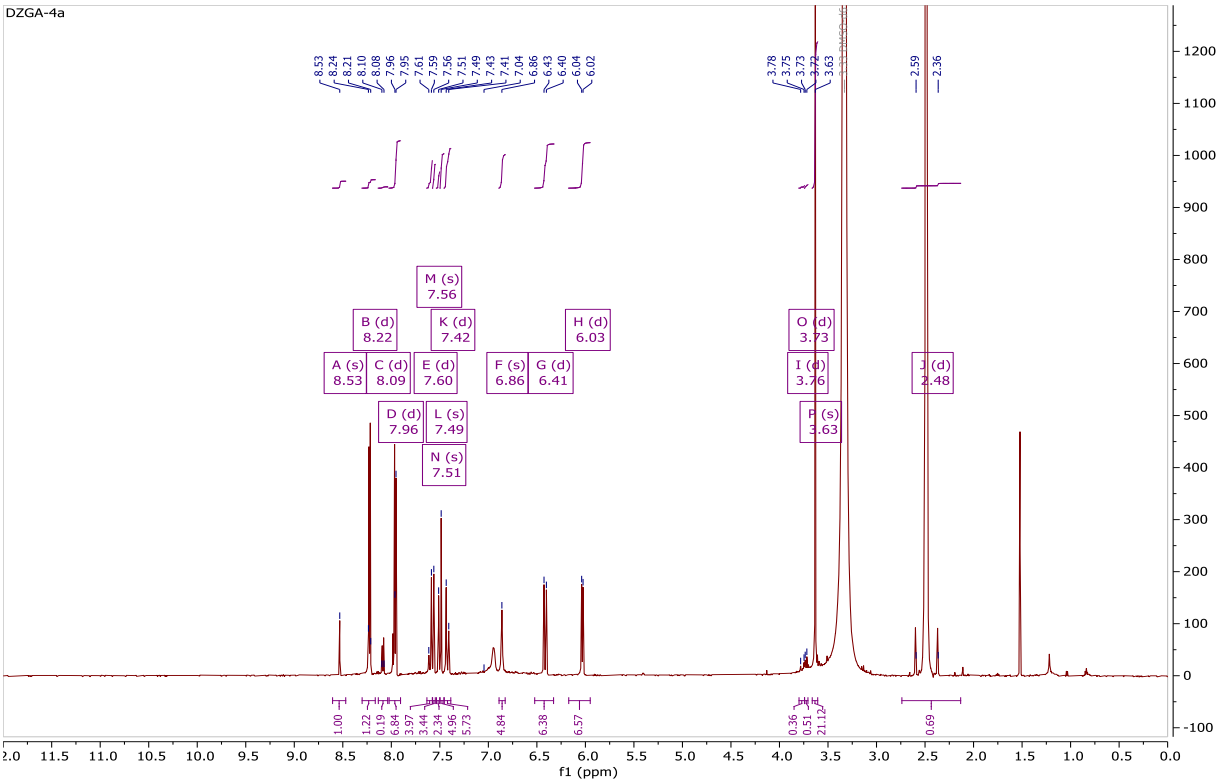
Appendix XIIb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **14**



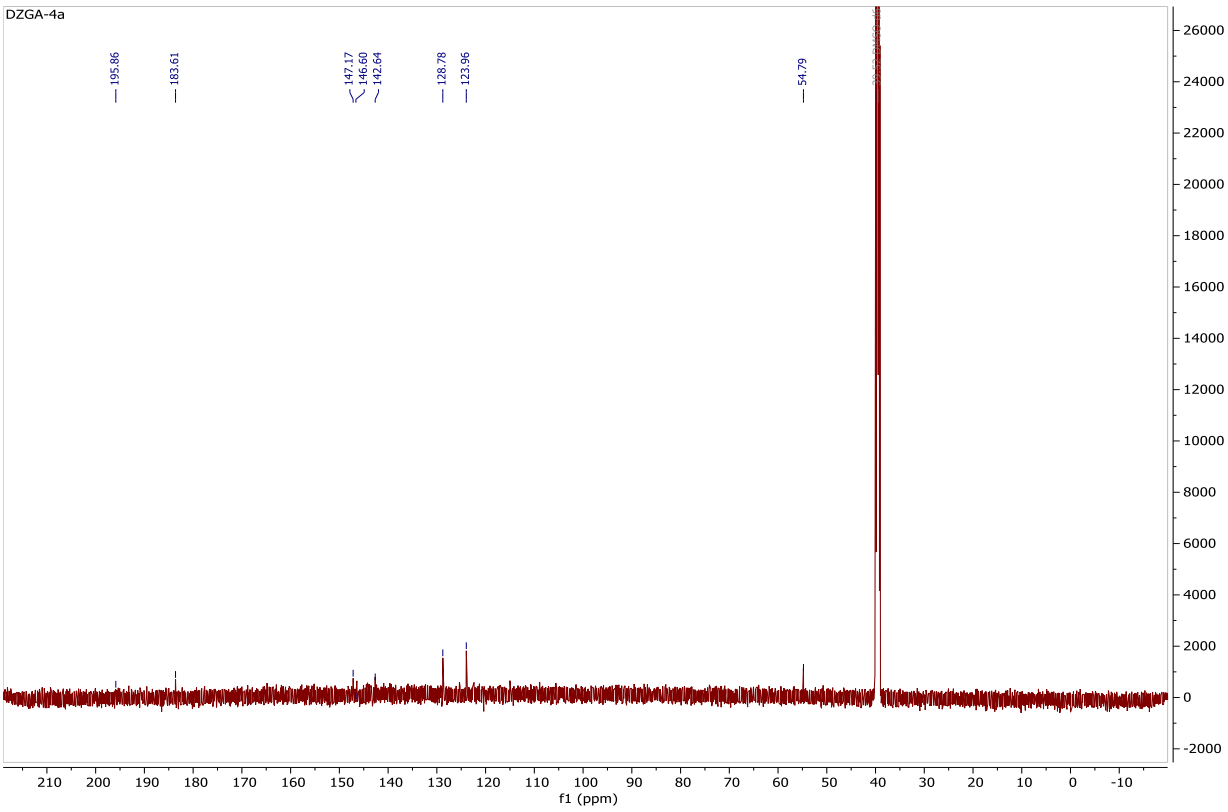
Appendix XIIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **14**



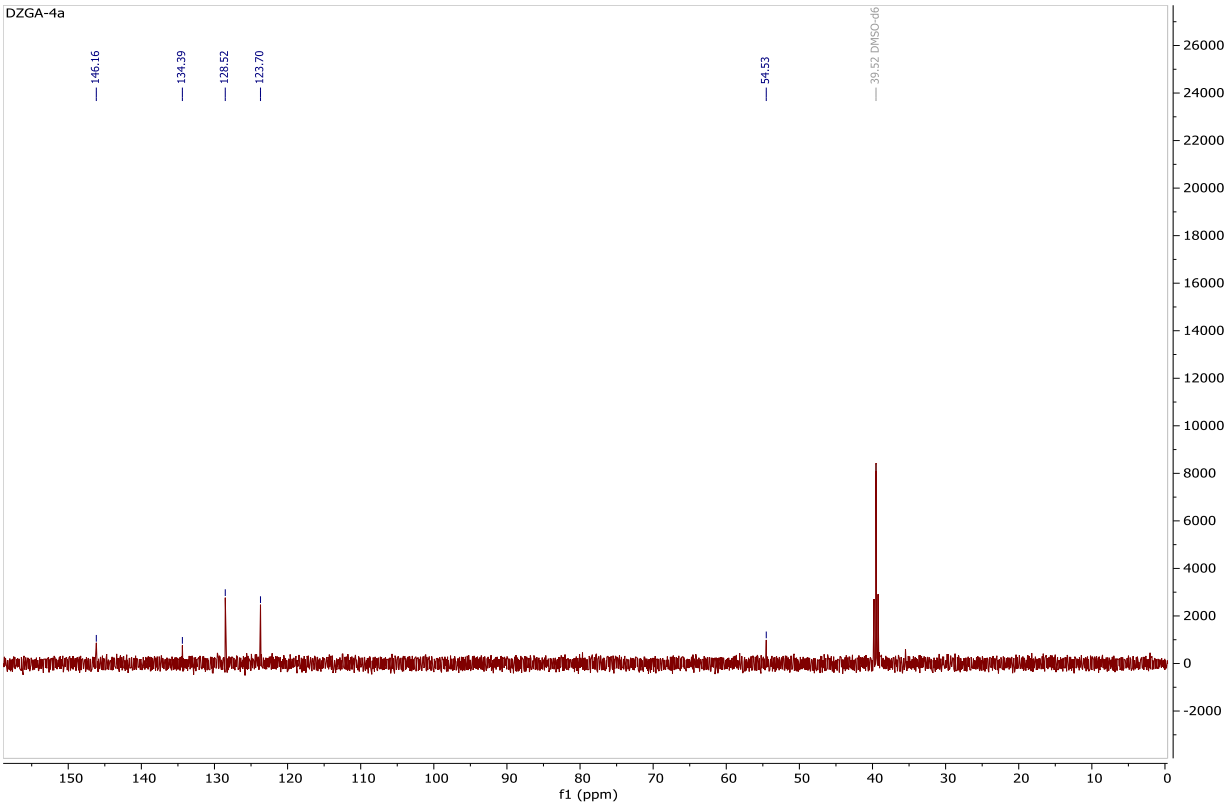
Appendix XIIIa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **15**



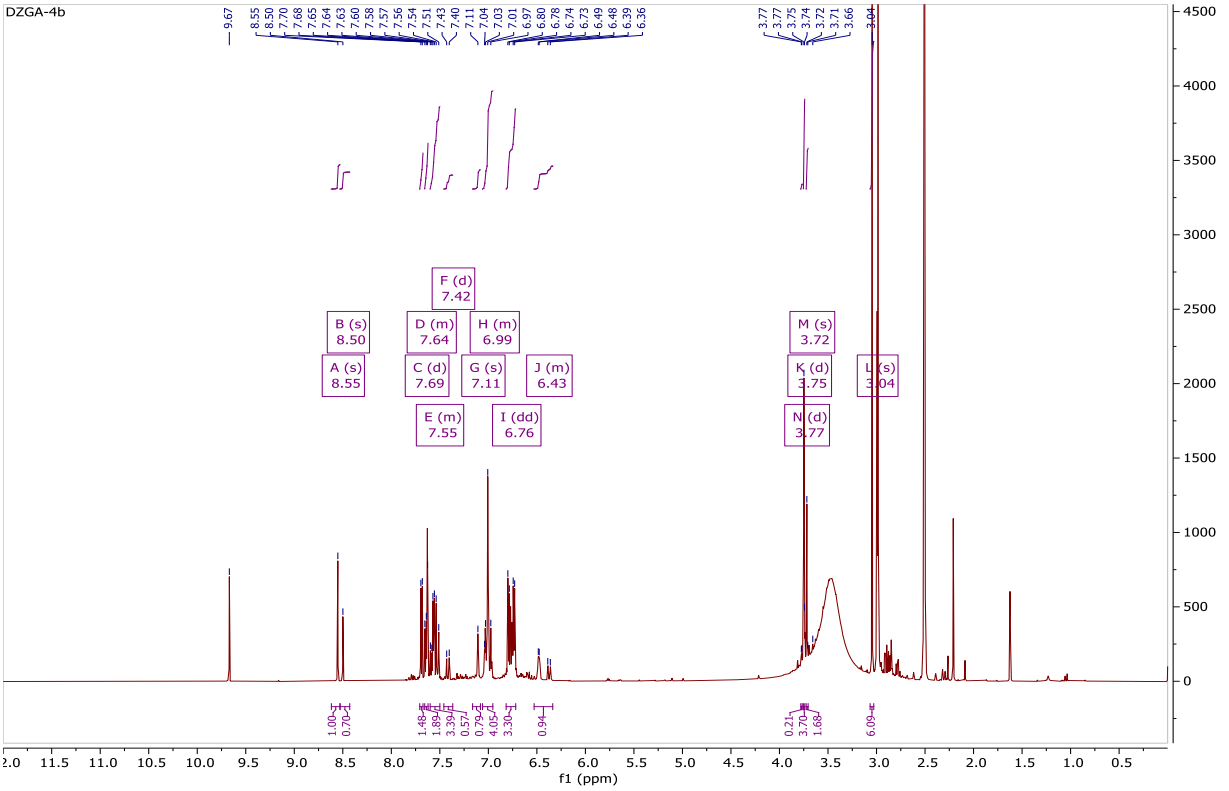
Appendix XIIIb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **15**



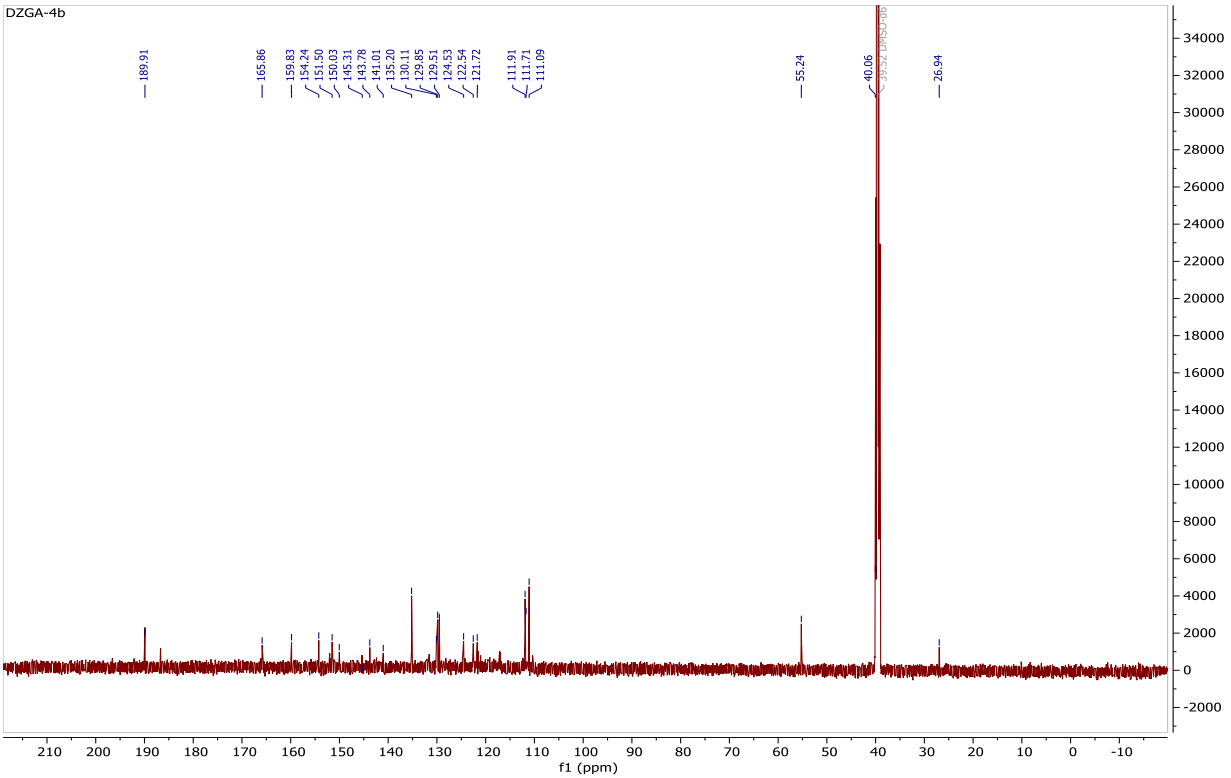
Appendix XIIIc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **15**



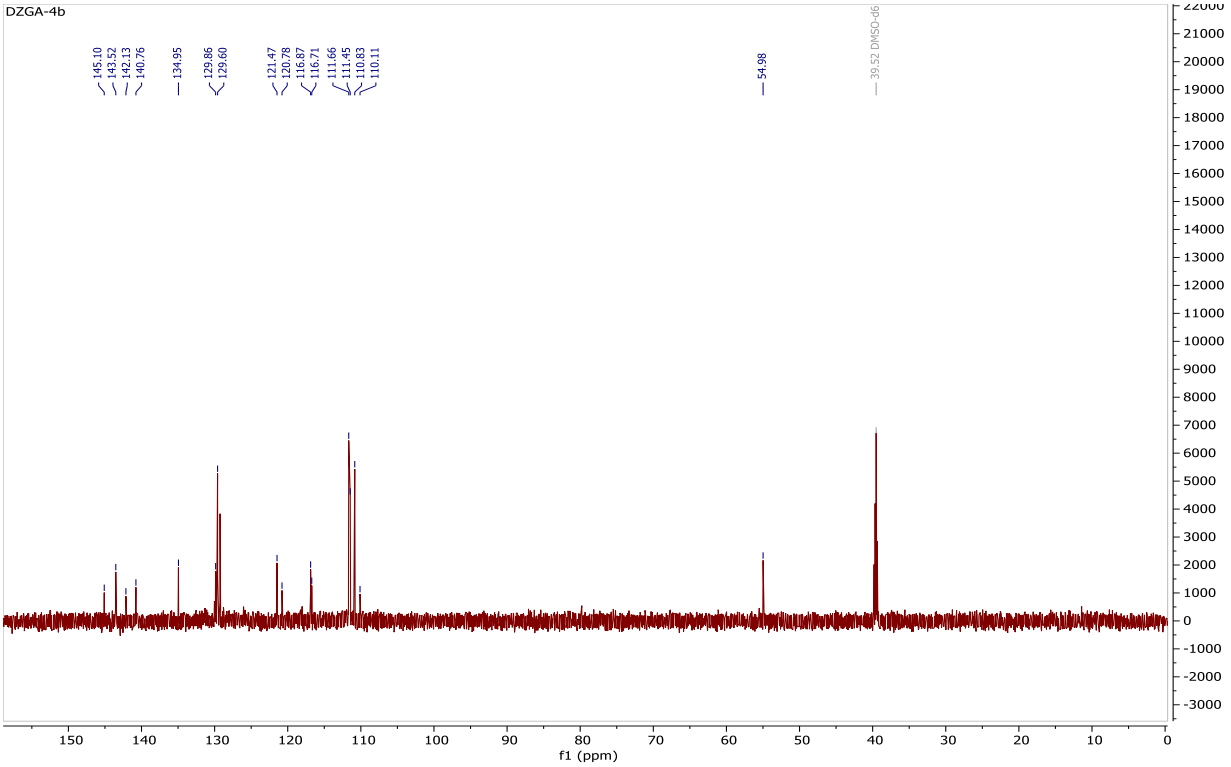
Appendix XIVa. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **16**



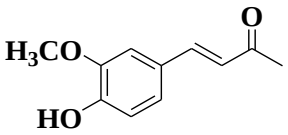
Appendix XIVb. ^{13}C -NMR spectrum (100 MHz, DMSO-d_6) of compound **16**



Appendix XIVc. ^{13}C –DEPT-135 NMR spectrum (100 MHz, DMSO-d_6) of compound **16**



Appendix XV. Synthesized monocarbonyl curcumin analogs derived from dehydrozingerone (**3-7**)



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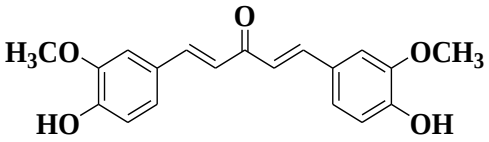
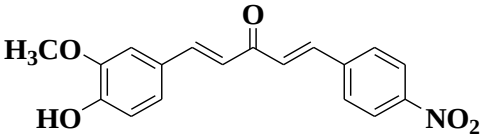


3



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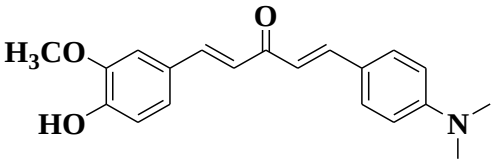

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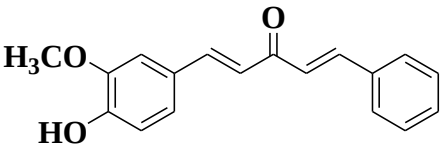
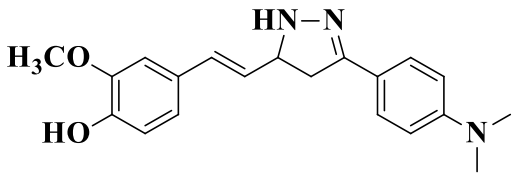
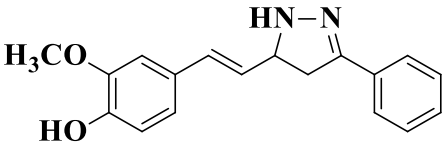


7

Appendix XVI. Synthesized of *N*-pyrazolines, **8** and **9**, 4-phenyl-6-styrylpyrimidine-2-ol, **11** and **12**, thiazolo[3,2-α] pyrimidines, **12-14**, and *β*-substituted imidazoles, **15** and **16**, derived from curcuminoid analogs using ultrasonic irradiation assisted condition



8



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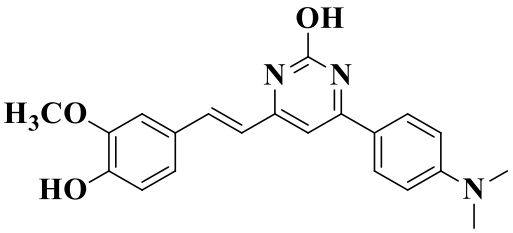

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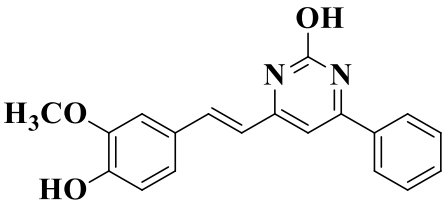

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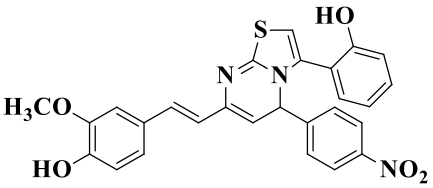
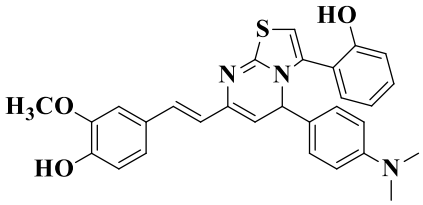
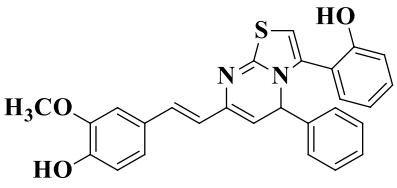

HO
S
N
N
H3CO
HO
NO2

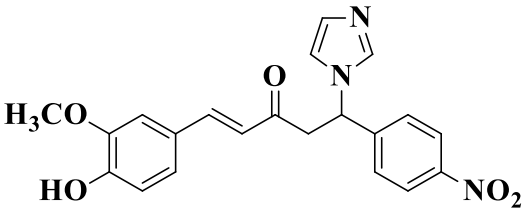
12


HO
S
N
N
H3CO
HO
N

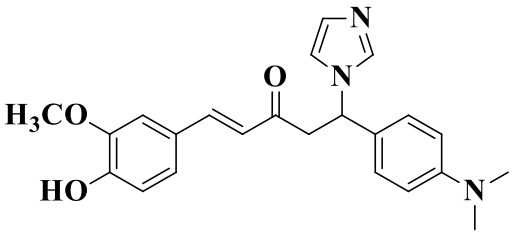
13


HO
S
N
N
H3CO
HO

14

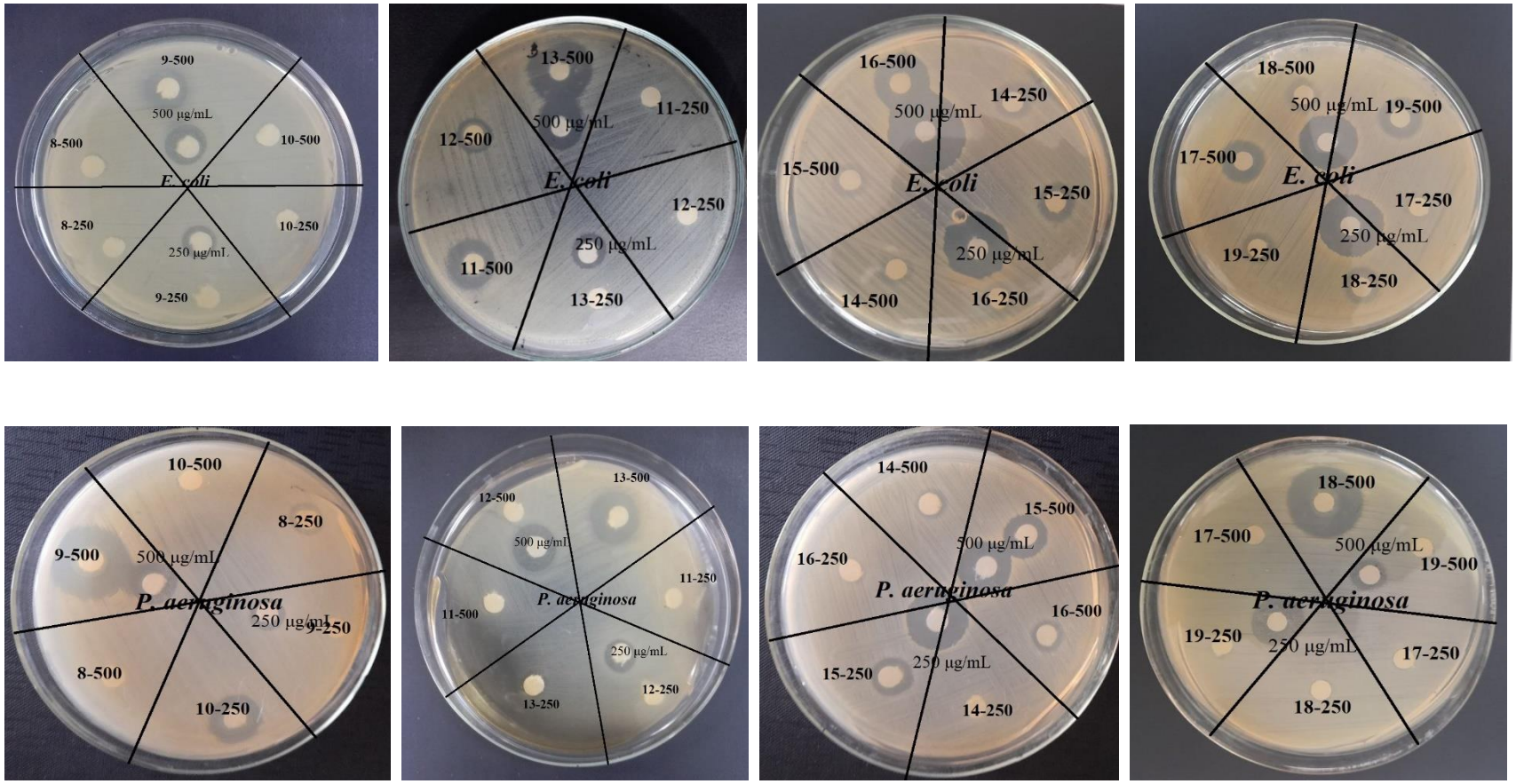

N
O
N
H3CO
HO
NO2

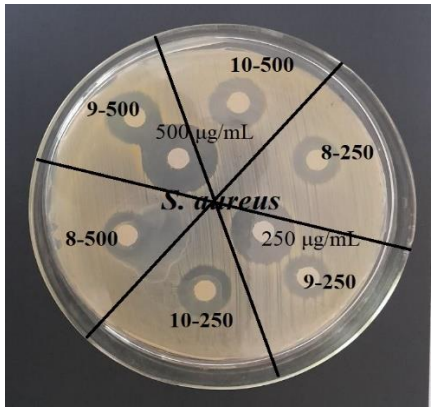
15

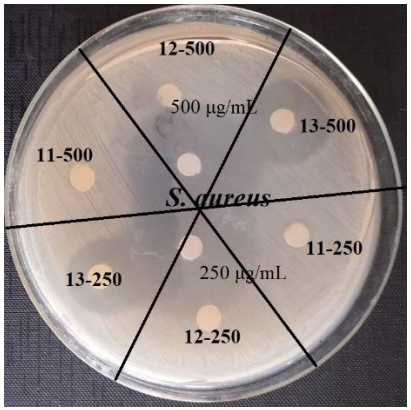

N
O
N
H3CO
HO
N

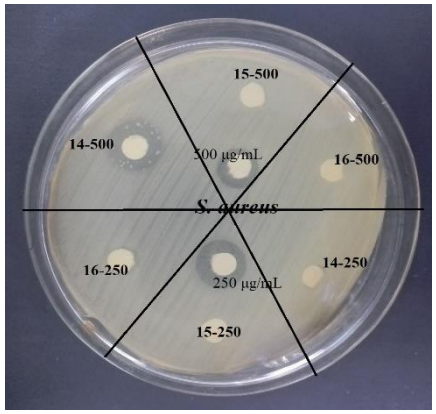
16

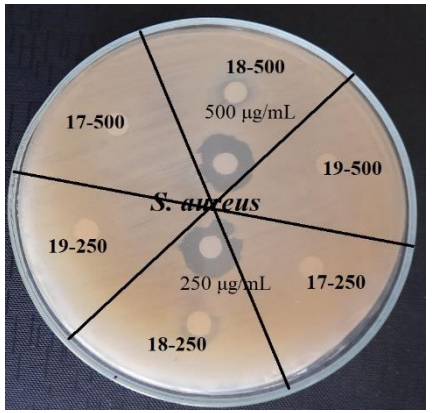
Appendix XVII. *In vitro* antibacterial activity of heterocyclics curcuminoid analogs (**8-16**) against pathological strains expressed as the diameter of inhibition zones in millimeters (unit, mm) based on agar well diffusion assay compared to a positive control (amoxicillin) and negative control (DMSO), results given in µg/mL sample

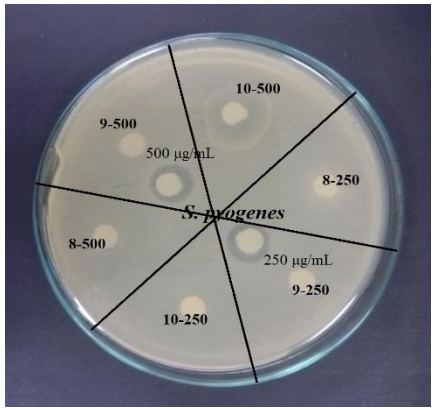


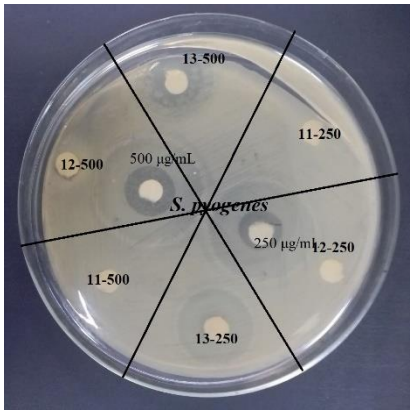

10-500
9-500
500 µg/mL
8-250
S. aureus
8-500
250 µg/mL
9-250
10-250

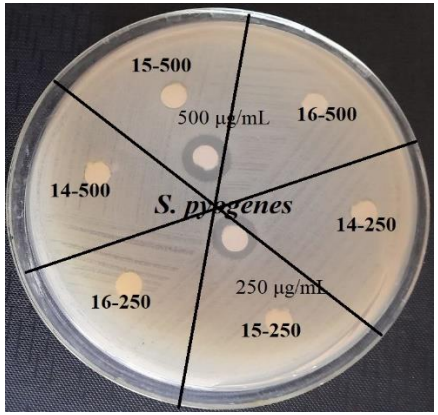

12-500
500 µg/mL
13-500
11-500
S. aureus
11-250
13-250
250 µg/mL
12-250

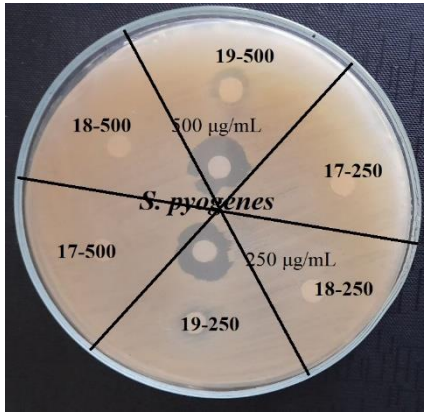

15-500
14-500
500 µg/mL
16-500
S. aureus
16-250
14-250
250 µg/mL
15-250

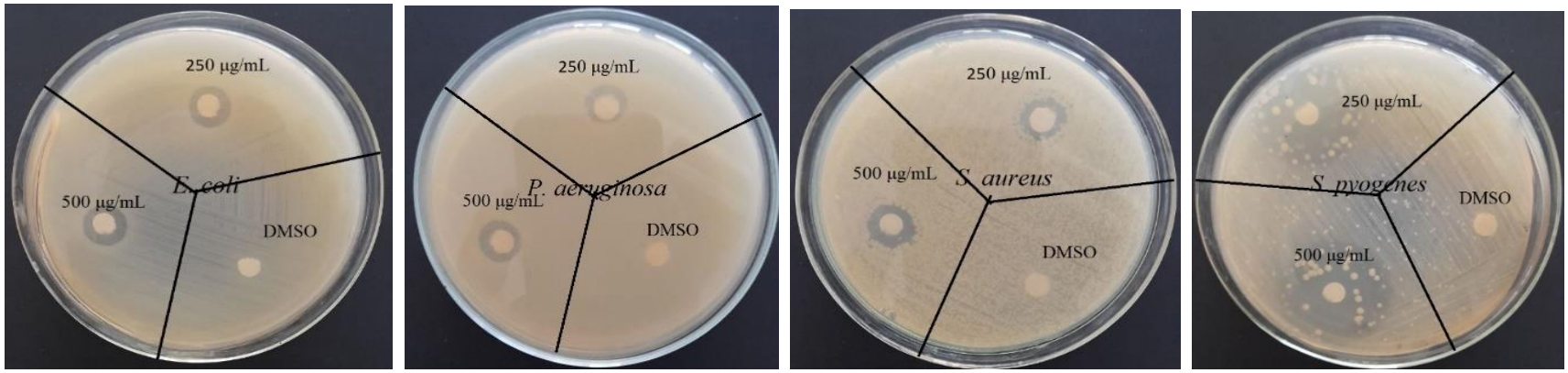

18-500
17-500
500 µg/mL
19-500
S. aureus
19-250
250 µg/mL
17-250
18-250


10-500
9-500
500 µg/mL
8-250
S. pyogenes
8-500
250 µg/mL
9-250
10-250


13-500
11-250
12-500
500 µg/mL
S. pyogenes
250 µg/mL
12-250
11-500
13-250


15-500
500 µg/mL
16-500
14-500
S. pyogenes
14-250
250 µg/mL
16-250
15-250

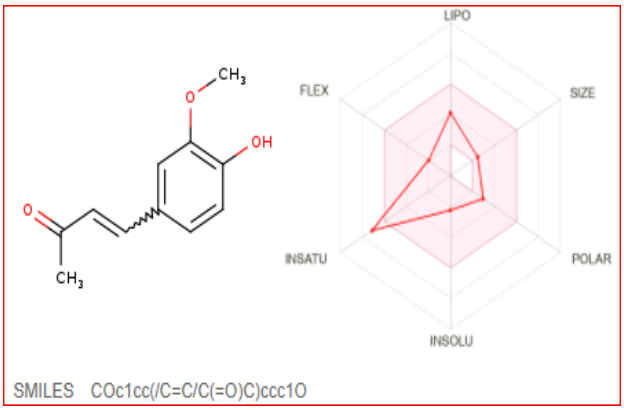

19-500
18-500
500 µg/mL
17-250
S. pyogenes
17-500
250 µg/mL
18-250
19-250

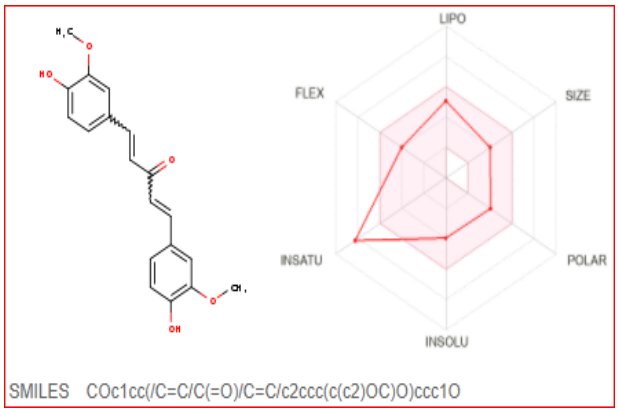


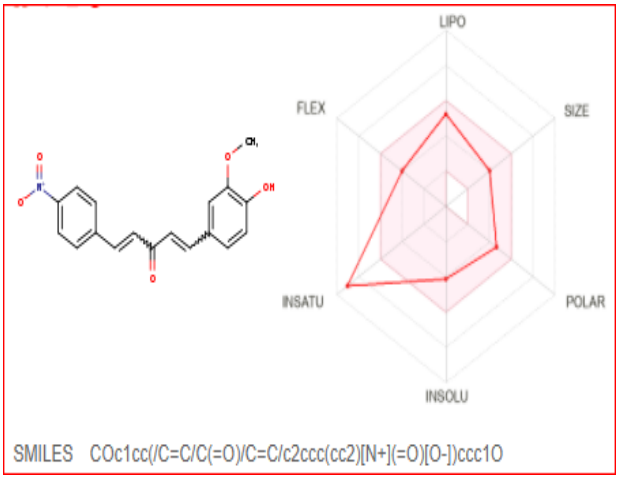
N.B. Gram-negative bacteria, *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853) and Gram-positive bacteria, *Staphylococcus aureus* (ATCC 25923) and *Streptococcus pyogenes* (ATCC 27853), respectively

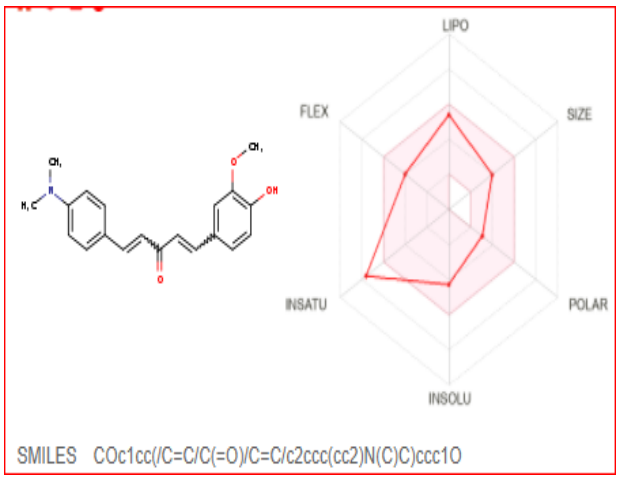
Appendix XVIII. Percent inhibition of the synthesized compounds (**8-16**) and the standard drug (ascorbic acid) at the different concentration ranges (namely 12.5, 25.0, 50.0, 100.0, and 200.0 µg/mL)

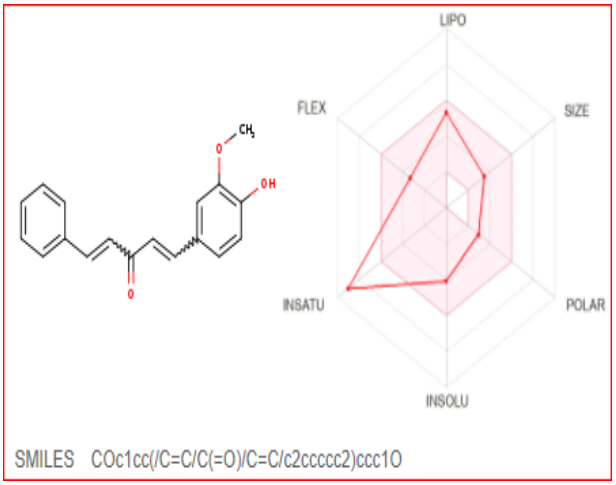
Appendix XIX. Bioavailability radar and Boiled- Egg model of the title, **8-16** by the drug-likeness criteria (Lipophilicity (− 0.7 < log P < 5.0), size (150 g/mol < MW < 500 g/mol), polarity (20˚A² < TPSA<140˚A²), insolubility (− 6<logS< 0), unsaturation (0.25< Fraction Csp^3<1) and flexibility (0 < Num. rotatable bonds < 9)



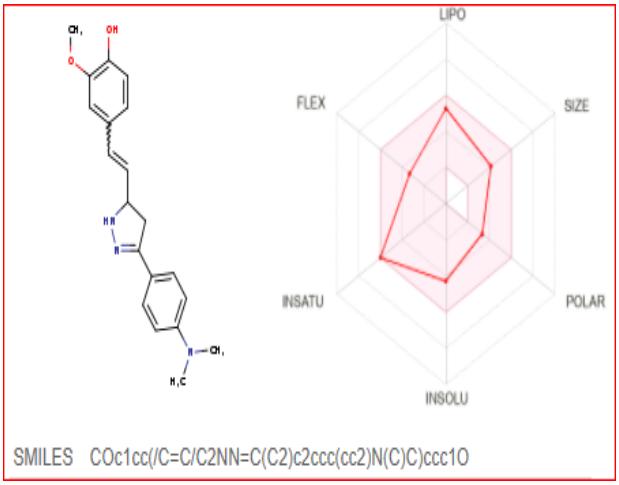




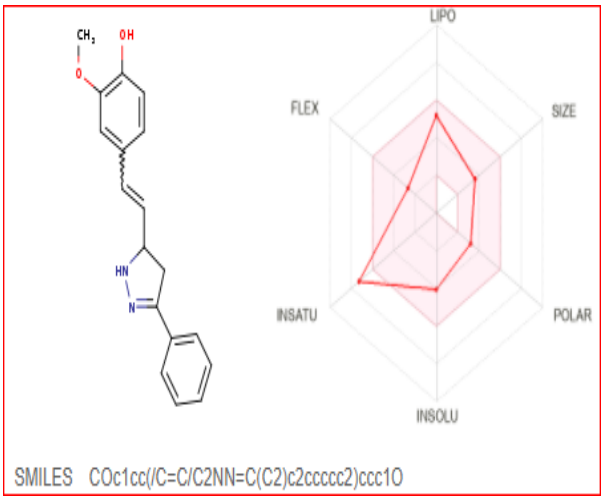




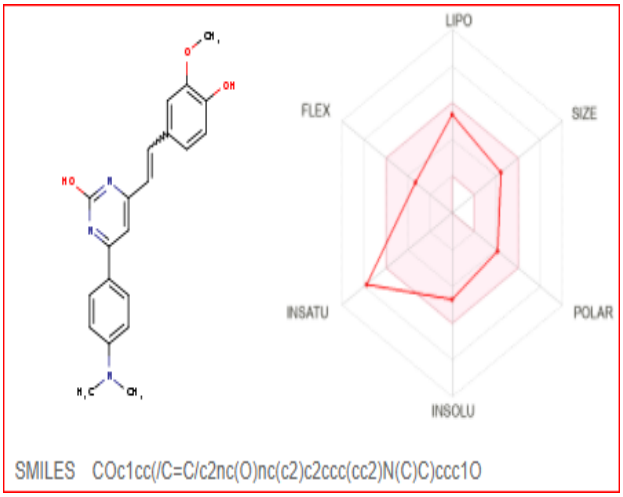
SMILES COc1cc(/C=C/C(=O)/C=C/c2ccccc2)ccc1O



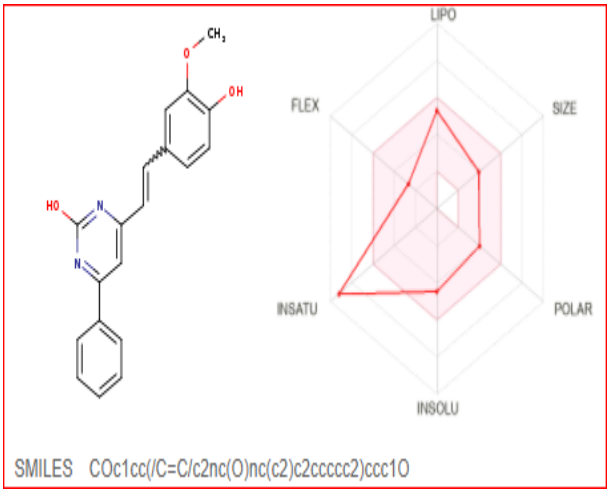
SMILES COc1cc(/C=C/C2NN=C(C2)c2ccc(cc2)N(C)C)ccc1O



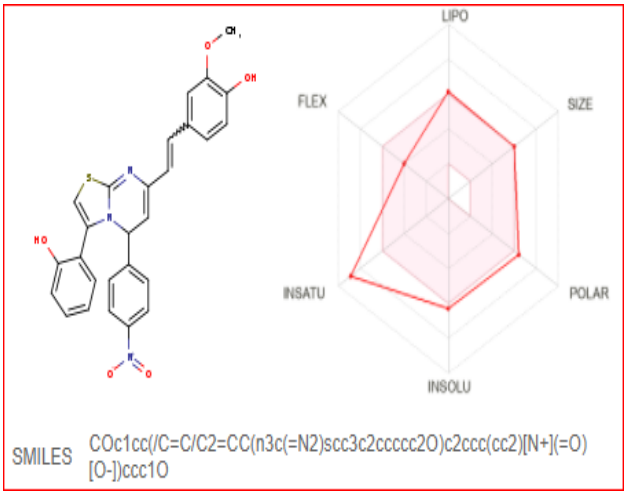
SMILES COc1cc(/C=C/C2NN=C(C2)c2ccccc2)ccc1O



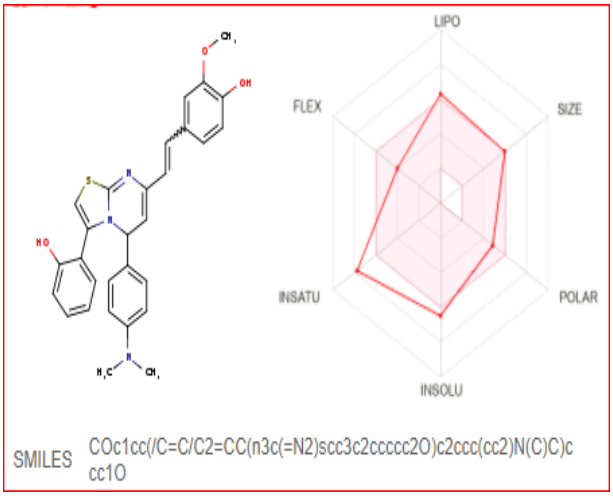
SMILES COc1cc(/C=C/c2nc(O)nc(c2)c2ccc(cc2)N(C)C)ccc1O



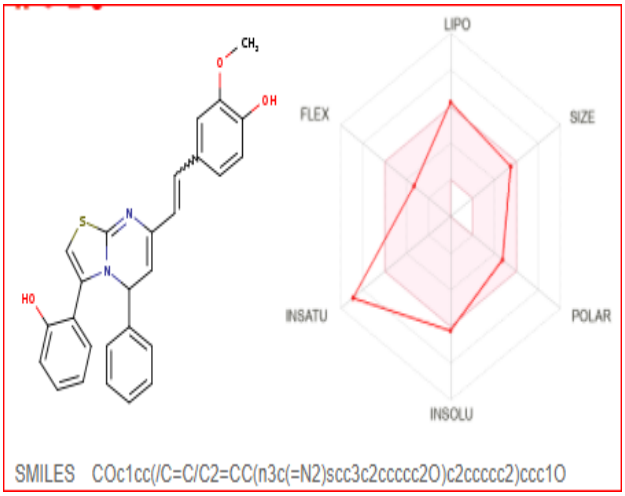
SMILES COc1cc(/C=C/c2nc(O)nc(c2)c2ccccc2)ccc1O



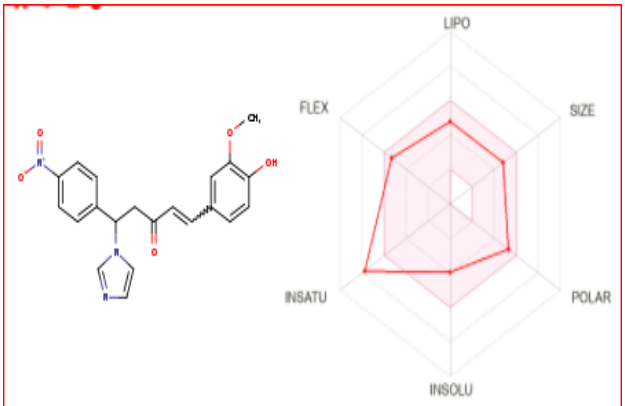
SMILES COc1cc(/C=C/C2=CC(n3c(=N2)scc3c2ccccc2O)c2ccc(cc2)[N+](=O)[O-])ccc1O



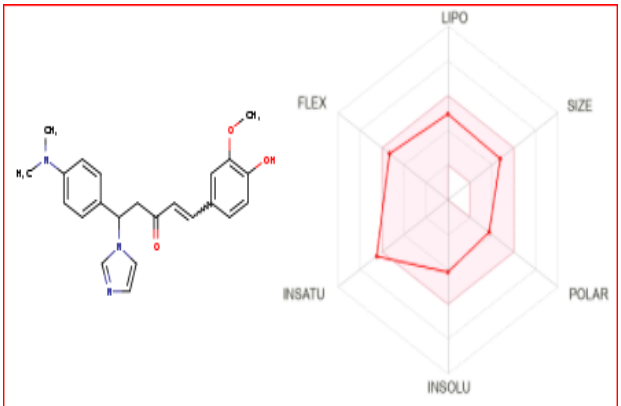
SMILES COc1cc(/C=C/C2=CC(n3c(=N2)scc3c2ccccc2O)c2ccc(cc2)N(C)C)ccc1O



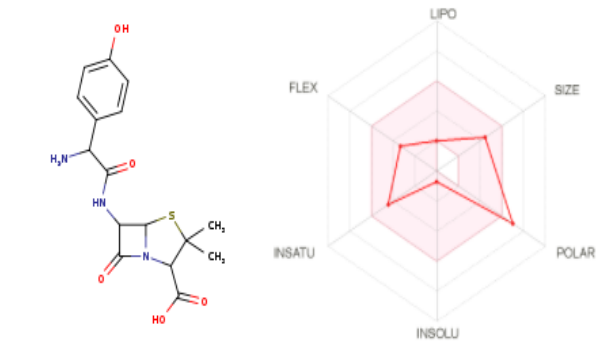
SMILES COc1cc(/C=C/C2=CC(n3c(=N2)scc3c2ccccc2O)c2ccccc2)ccc1O



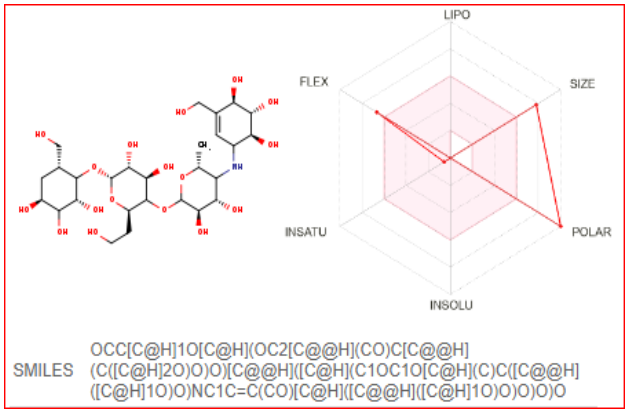
SMILES COc1cc(/C=C/C(=O)CC(n2cncc2)c2ccc(cc2)[N+](=O)[O-])ccc1O



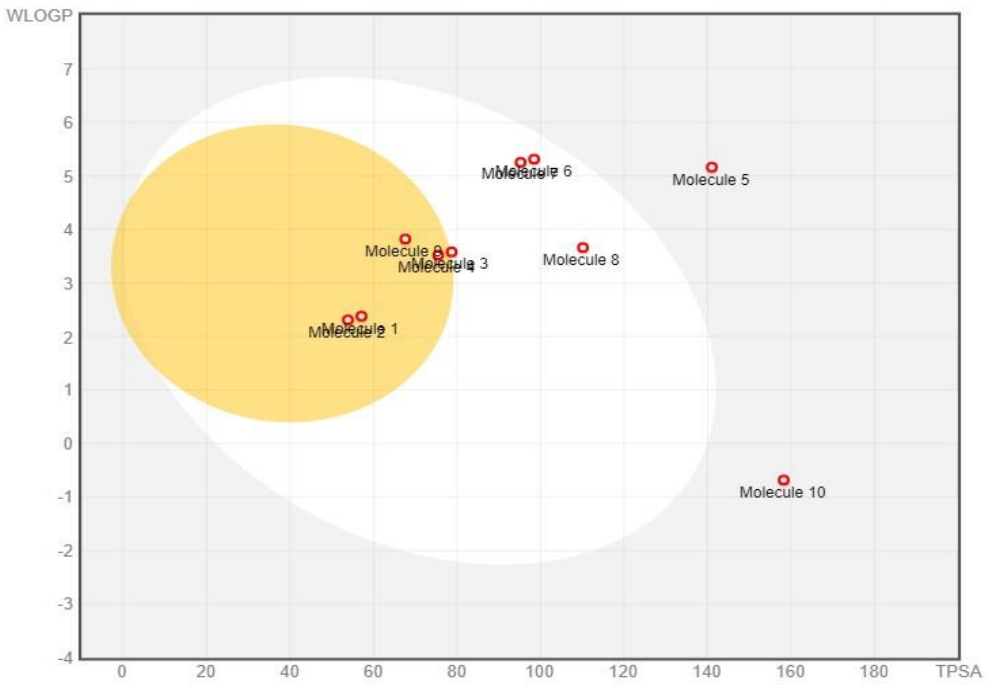
SMILES COc1cc(/C=C/C(=O)CC(n2cncc2)c2ccc(cc2)N(C)C)ccc1O



SMILES O=C(C(c1ccc(cc1)O)N)NC1C(=O)N2C1SC(C2C(=O)O)(C)C



SMILES OCC[C@H]1O[C@H](OC2[C@@H](CO)C[C@@H](C([C@H]2O)O)O)[C@@H]([C@H](C1OC1O[C@H](C)C([C@@H]([C@H]1O)O)NC1C=C(CO)[C@H]([C@@H]([C@H]1O)O)O)O)O


WLOGP
7
6
5
4
3
2
1
0
-1
-2
-3
-4
0
20
40
60
80
100
120
140
160
180
TPSA
Molecule 6
Molecule 5
Molecule 8
Molecule 10

Appendix XX. Molecular docking scores and residual amino acid interactions of synthesized compounds (**8-16**) against *E. coli* Gyrase B. (PDB ID: 6F86).

Synthesized compounds (Ligands)	Docking scores /Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-6.5	Pro-79, Arg-136, Arg-76, Ile-78, Gly-77, Asn-46, Ala-47, Asp-73		Glu-50, Thr-165
9	-7.6	Arg-76	Asn-46, Thr-165, Ala-47, Glu-50, Pro-79	Gly-77, Val-167, Val-43
10	-7.5	Arg-76, Arg-136	Glu-50, Pro-79, Ala-47, Asp-73, Asn-46, Ile-78	Asp-49, Val-167, Thr-165
11	-7.9	Gly-77, Arg-76	Thr-165, Ala-47, Ile-94, Pro-79, Ile-78, Asn-46	Asp-73, Gly-75, Glu-50
12	-6.4	Arg-76, Arg-136	Ala-47, Thr-165, Val-167, Ile-78, Val-120, Pro-79, Met-95	Asp-73, Val-43, Asn-46, Glu-50, Gly-77
13	-6.4	Asp-73, Thr-165	Ile-94, Ile-78, Ala-47, Pro-79	Arg-76, Asn-46, Gly-77
14	-7.6	Gly-77, Thr-165	Ile-78, Glu-50, Ile-94	Val-120, Ala-47, Asn-46, Asp-49
15	-7.2	Val-167	Arg-76, Asn-46, Ile-78, Ala-47, Thr-165, Pro-79	Met-166, Val-71, Val-43, Asp-73, Arg-136, Gly-77
16	-6.5		Pro-79, Thr-165, Ala-47, Ile-78, Ile-94	Arg-136, Asp-73
Amoxicillin	-6.1	Asp-73, Arg-76, Gly-77, Asn-46	Pro-79	Ile-94, Arg-136, Thr-165

Appendix XXI. Molecular docking scores and residual amino acid interactions of synthesized compounds (**8-16**) against the N-terminal domain of PqsA (PDB ID: 3T07_RE1).

Synthesized compounds (Ligands)	Docking scores \Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-5.2	Gly-462, Glu-460	Ile-359, Ala-358, Asn-465, Val-456	Ser-362, Thr-463, Thr-461, Gly-455
9	-5.8	Ser-383	Gly-270, Arg-386, Val-356	Thr-387, Leu-269, Lys-390, Asn-357, Glu-352, Ser-354
10	-5.6	Glu-460, Gly-462, Thr-463	Val-456, Leu-355, Ala-358, Met-467, Ile-359	Thr-461, Asn-465, Ser-362
11	-5.3	Thr-463, Gly-462, Glu-460	Leu-355, Ala-358, Ile-359, Val-456	Asn-465, Thr-461
12	-5.8	Asn-465, Val-456, Gly-462, Thr-463	Ile-359, Ala-358, Pro-457, Leu-355	
13	-5.6	Val-456, Asn-465	Ile-359, Ala-358, Thr-463, Glu-460	Pro-457, Gly-462, Leu-355
14	-5.5	Asn-465, Val-456	Ala-358, Ile-359, Pro-457	Gly-462, Thr-463, Glu-460
15	-5.1	Ser-362, Asn-465	Leu-355, Met-467, Ile-359, Ala-358	Ser-354, Thr-353
16	-5.3	Gly-462, Glu-460	Val-456, Asn-465, Ile-359, Ala-358, Met-467	Ser-362, Leu-355, Thr-461, Thr-463
Amoxicillin	-4.9	Thr-464, Thr-463, Leu-355, Ala-358	Ile-359	Ser-362, Ile-361

Appendix XXII. Molecular docking studies of synthesized compounds (**8-16**) against *S. aureus* Pyruvate Kinase (PDB ID: 4XCH).

Synthesized compounds (Ligands)	Docking scores /Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-3.8	Ser-126	Cys-127, His-57	Glu-60, Gly-128, Asn-129, Pro-120
9	-4.5	Cys-127, Glu-60	His-57, His-61	Gly-128, Asn-129, Pro-120, Ser-126, Gly-121
10	-5.3	Glu-60	Ala-64, His-61, His-57	Gly-121, Ser-126, Gly-128, Asn-129
11	-5.6		Ser-126, His-61, Pro-79, Leu-56, His-57	Gly-128, Asn-129, Thr-53
12	-1.6		Ala-64, His-61, His-57, Leu-56, Cys-127, Pro-79, Ser-126, Gly-121	Pro-120, Glu-60, Thr-122, Thr-123
13	-2.1	Ser-126, Asn-129	Ala-64, Cys-127, Gly-121, Pro-79, Leu-56, His-57, His-61, Glu-60, Cys-77	Arg-68, Gly-128, Asp-132, Thr-53
14	-2.3	Asn-129	Ser-126, His-61, His-57, Glu-60, Ala-64, Cys-127	Gly-128, Pro-120, Gly-121
15	-3.1		Cys-127, Ala-64, His-57	Asn-129, Gly-128, Pro-120, Gly-121, Arg-68, Cys-77, Glu-60
16	-5.1		Pro-79, Glu-60, Ala-64, His-61, Pro-120, His-57	Ser-126, Gly-128, Gly-121, Asn-129
Amoxicillin	-2.9	His-61, Glu-60	His-57, Cys-127, Gly-121	Ser-126, Gly-128, Asn-129

Appendix XXIII. Molecular docking studies of synthesized compounds (**8-16**) against LuxS of *S. pyogenes* (PDB ID: 5OE3_RE2).

Synthesized compounds (Ligands)	Docking scores /Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-7.6	Thr-304	Asp-299, Gly-300, Ser-280, Gly-279, Ile-301, Ala-278, Phe-209	Thr-323, Pro-281, His-394, Asp-382, Gly-302, Arg-397
9	-8.1	Thr-304	Glu-305, Ala-303, Ser-280, Pro-281, Gly-279, Ile-301	Thr-164, Tyr-211, Gly-300, Gly-210, Arg-397
10	-7.6		His-308, Gly-307, Ala-303, Asp-382, Arg-397, His-394, Pro-281, Gly-302, Ala-278, Phe-209, Tyr-211	Thr-164, Thr-304, Gly-210, Gly-279
11	-8.6	Thr-304, Tyr-211, Asp-382	Pro-281, His-394, Ser-280, Ile-301, Gly-279, Arg-397	Gly-210, Phe-209, Thr-323, Asp-299, Gly-300, Gly-302, His-308
12	-5.7	Gly-307	Asp-382, Arg-397, Gly-279, Ile-301, Tyr-211, Ala-278, Val-309, His-308, Phe-209, Gly-210, Gly-302	Ala-303, Thr-304, Gly-300
13	-4.6	Thr-380, Arg-372, Arg-397	Glu-305, Ala-303, Gly-302, Phe-209, Tyr-211, Ala-278, His-308, Ile-301	Ser-380, Tyr-378, Thr-164, Val-309
14	-7.0	Tyr-378, Glu-305	Thr-164, Thr-304, Ala-303, His-308, Phe-209, Gly-302, Ala-278, Arg-397	Thr-380, Arg-372, Gly-210, Gly-307, Tyr-211
15	-8.8	Thr-304, Val-309	Ala-303, Arg-397, Ile-301, Gly-210, His-308, Gly-302	Thr-164, Arg-372, Thr-380, Tyr-378, Asp-382, Ser-280, Gly-279, Tyr-211
16	-9.1	Val-309	His-308, Gly-302, Asp-382, Ala-303, Ile-301, Gly-279, Asp-299, Ala-278, Gly-300, His-394, Phe-209	Thr-304, Thr-164, Arg-397, Thr-380, Ser-280, Asp-299, Ala-278, Gly-300, His-394, Phe-209
Amoxicillin	-7.9	Glu-305, Asp-299, Thr-323, Gly-302, Gly-279	Ser-280, Pro-281, Ile-301, Asp-382	Thr-304, Gly-300, Leu-282, Arg-397, Thr-380, Tyr-378

Appendix XXIV. Molecular docking studies of most active synthesized compounds (**8**, **11**, and **16**) against Penicillin binding proteins (PBPs) (PDB ID: 1VQQ).

Synthesized compounds (Ligands)	Docking scores/Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-6.7	Arg-241, Ser-240	Asp-295, Asp-275, Val-277	Lys-148, Glu-294, Lys-273, Val-256, Met-372, Try-373
11	-7.5	Ser-240	His-293, Val-277, Asp-295, Ala-276, Lys-273	Met-372, Glu-239, Ser-149, Lys-148, Glu-294
16	-6.9	Ser-149	His-293, Glu-150, Val-277, Thr-165, Pro-258, Met-372	Asp-295, Arg-241, Thr-165, Ser-240, Val-256, Gly-257, Tyr-373
Amoxicillin	-7.2	Lys-148, Asp-275	Val-277, His-293, Arg-241, Arg-151	Ala-276, Ser-149, Asn-164, Gly-166, Thr-165, Ser-240

Appendix XXV. Molecular docking studies of most active synthesized compounds (**8**, **11**, and **16**) against *β*-lactamases (PDB ID: 1IYS).

Synthesized compounds (Ligands)	Docking scores/Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-6.9	Tyr-105, Asn-104, Asn-170	Asn-132	Trr-129, Thr-215, Ser-218, Thr-126, Ala-219, Ser-130, Asn-132, Ser-132, Glu-166, Ser-70
11	-8.3	Ser-70	Tyr-105, Asp-240, Pro-167	Asn-132, Ser-237, Thy-168, Thr-171, Asn-104, Asn-170, Glu-166, Ser-130
16	-7.7	Arg-276, Thr-216, Ser-70, Lys-73	Gly-236, Tyr-105	Asn-132, Ser-130, Gly-236, Asn-104, Ser-237, Asn-170, Thr-235, Gly-236
Amoxicillin	-7.9	Thr-235, Ser-130, Ser-237, Asn-132, Glu-166, Asn-170, Thr-216	Arg-276, Tyr-105	Asn-104, Lys-234

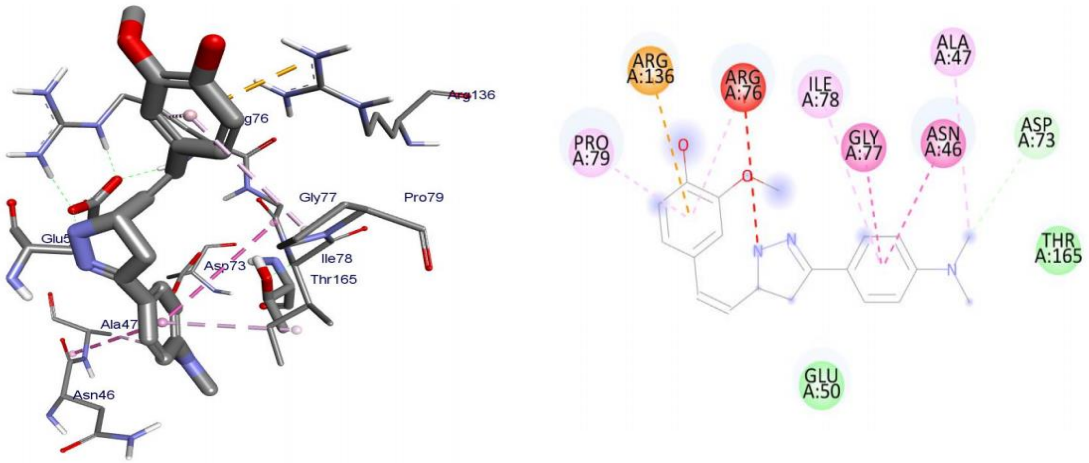
Appendix XXVI. Molecular docking studies of synthesized compounds (**8-16**) against Human peroxiredoxin 5 (PDB ID: 1HD2_M1).

Synthesized compounds (Ligands)	Docking scores/Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	Van der Waals interactions
8	-5.6	Thr-147	Leu-116	Arg-127, Asn-76, Arg-124, Phe-120, Thr-44, Ile-119
9	-5.4	Thr-147	Leu-116, Thr-44, Phe-120	Arg-127, Phe-43
10	-5.4	Ile-119, Gly-46	Leu-116, Thr-147, Pro-45	Thr-44, Ala-147
11	-5.5		Phe-120, Ile-119, Ala-42, Pro-45	Phe-43, Thr-44, Leu-149, Gly-46, Arg-127, Thr-147, Leu-116
12	-4.9	Thr-147, Gly-46, Ile-119	Leu-116, Phe-43, Pro-45	Arg-127, Gly-148, Asp-145, Thr-44
13	-4.6	Thr-147, Gly-46	Ile-119, Pro-45, Phe-120, Thr-44	Arg-127, Phe-43
14	-5.6	Thr-147, Arg-127, Ile-119	Ala-42, Pro-45	Gly-148, Gly-46, Thr-44
15	-4.8	Thr-44, Gly-46, Arg-127, Cys-47, Thr-147	Pro-45, Leu-116, Asp-145	
16	-4.9	Ile-119, Thr-44	Thr-147, Leu-116, Pro-45, Ala-42, Phe-120, Pro-40, Cys-47	Asp-145, Arg-124, Gly-46, Arg-127
Amox	-5.4	Thr-147, Arg-127, Gly-46	Ile-119, Phe-120, Pro-45	Thr-44, Cys-47, Leu-149
Vit C	-5.8	Thr-44, Arg-127, Thr-147, Gly-46, Cys-47		Leu-149, Pro-40

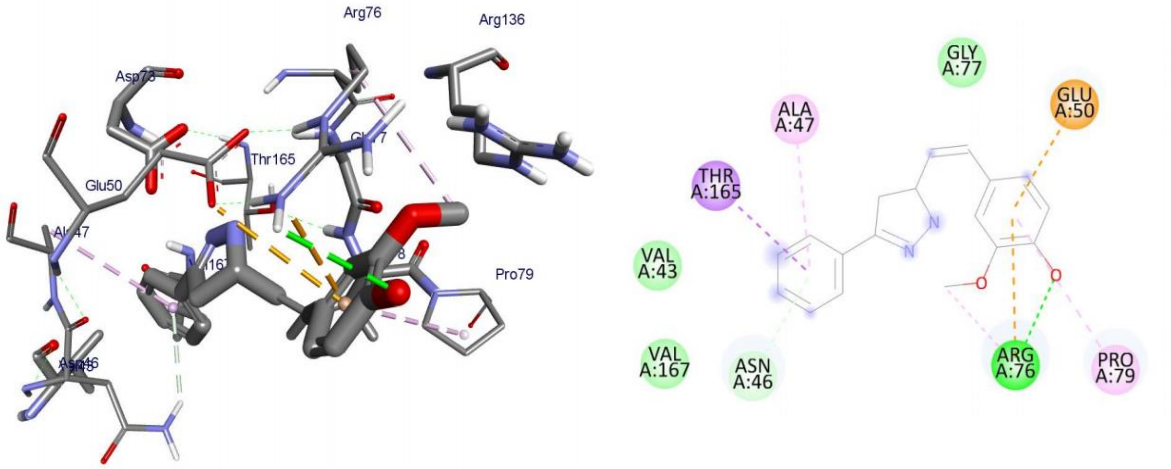
Appendix XXVII. Molecular docking studies of most active synthesized compounds (**8**, **11**, and **16**) against α-amylase enzyme (PDB ID: 4w93).

Synthesized compounds (Ligands)	Docking scores/Affinity (kcal/mol)	H-bonds	Amino acid residual interactions	
			Hydrophobic/π-cation/ π-anion/ π-alkyl interactions	**Van der Waals interactions**
8	-8.4	Glu-233	His-201, Trp-59, Trp-58, Ile-235	Arg-195, Ala-198, Lys-200, Tyr-151, Tyr-62, Gln-63
11	-7.4	His-299	Arg-195, Asp-197, His-201, Ile-235, Lys-200, Tyr-62, Leu-165	Typ-59, Gln-63, His-101, Tyr-151, Ala-198, Glu-233
16	-8.2	Glu-233	His-299, Typ-62, Ala-198, Leu-162	Tyr-58, Asp-300, Asn-298, Leu-165, Thr-163
Acarbose	-7.5	Asp-300, Ile-235, Trp-59, Glu-240	Ala-198, Leu-162	Gly-00, His-305, Trp-58, Ala-307, Leu-237, Leu-165, His-101, Asp-197

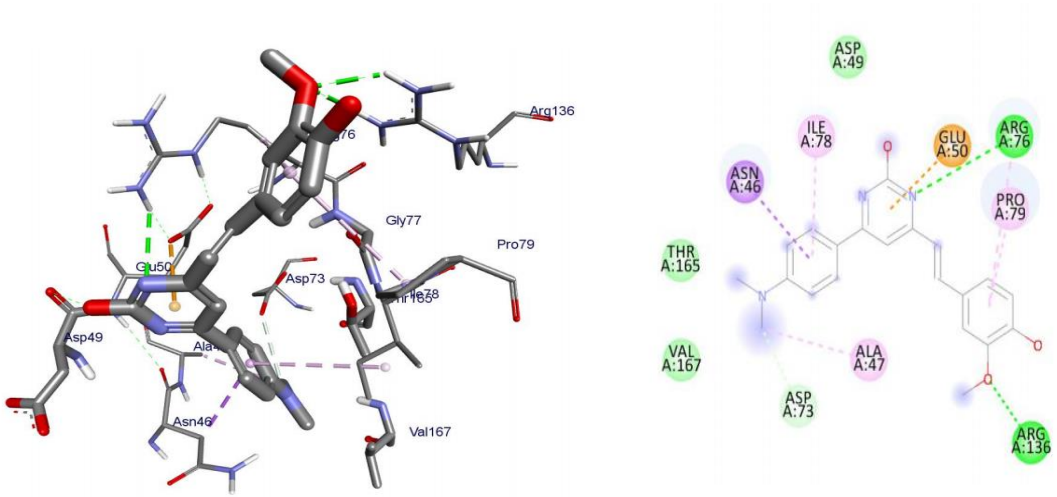
Appendix XXVIIIa. 3D (right) and 2D (left) representations of the binding interactions of **8** against *E. coli* DNA Gyrase B (PDB ID: 6f86)



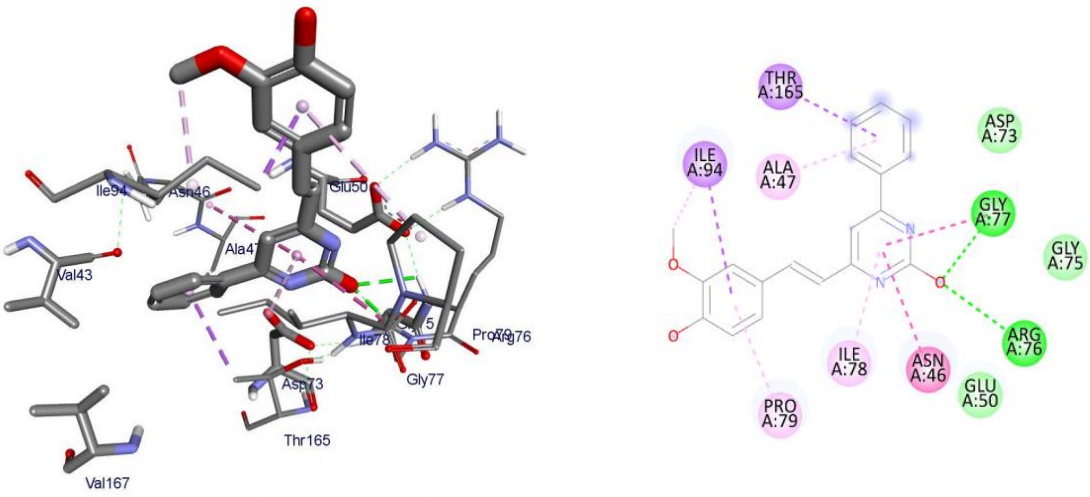
Appendix XXVIIIb. 3D (right) and 2D (left) representations of the binding interactions of **9** against *E. coli* DNA Gyrase B (PDB ID: 6f86)



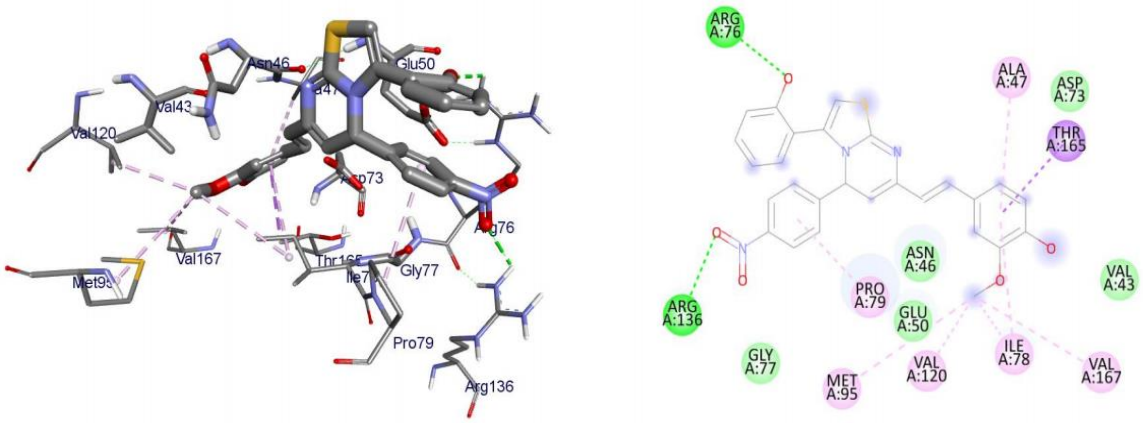
Appendix XXVIIIc. 3D (right) and 2D (left) representations of the binding interactions of **10** against *E. coli* DNA Gyrase B (PDB ID: 6f86)



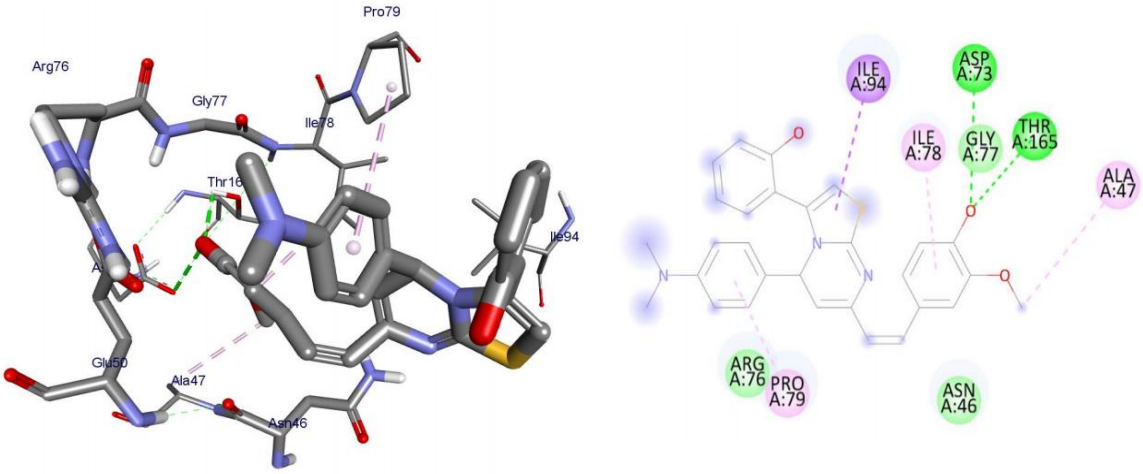
Appendix XXVIIId. 3D (right) and 2D (left) representations of the binding interactions of **11** against *E. coli* DNA Gyrase B (PDB ID: 6f86)



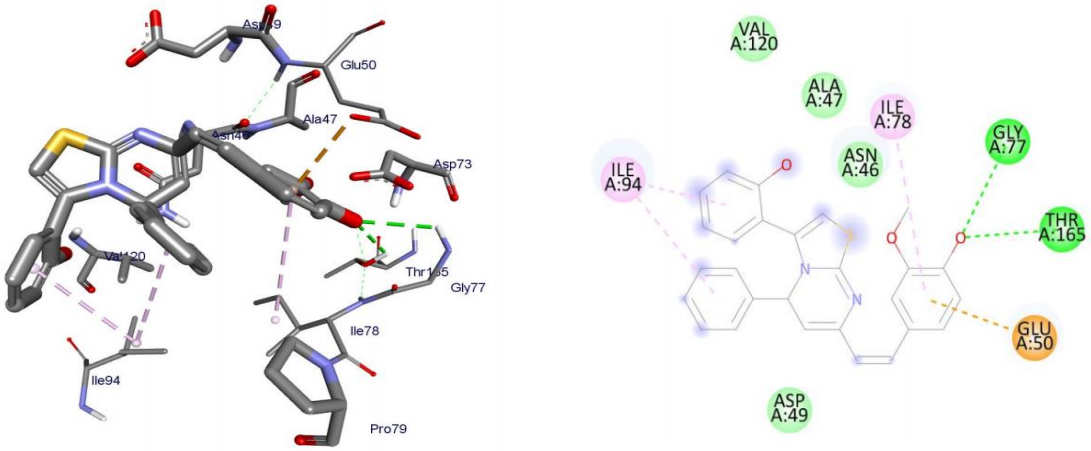
Appendix XXVIIIe. 3D (right) and 2D (left) representations of the binding interactions of **12** against *E. coli* DNA Gyrase B (PDB ID: 6f86)



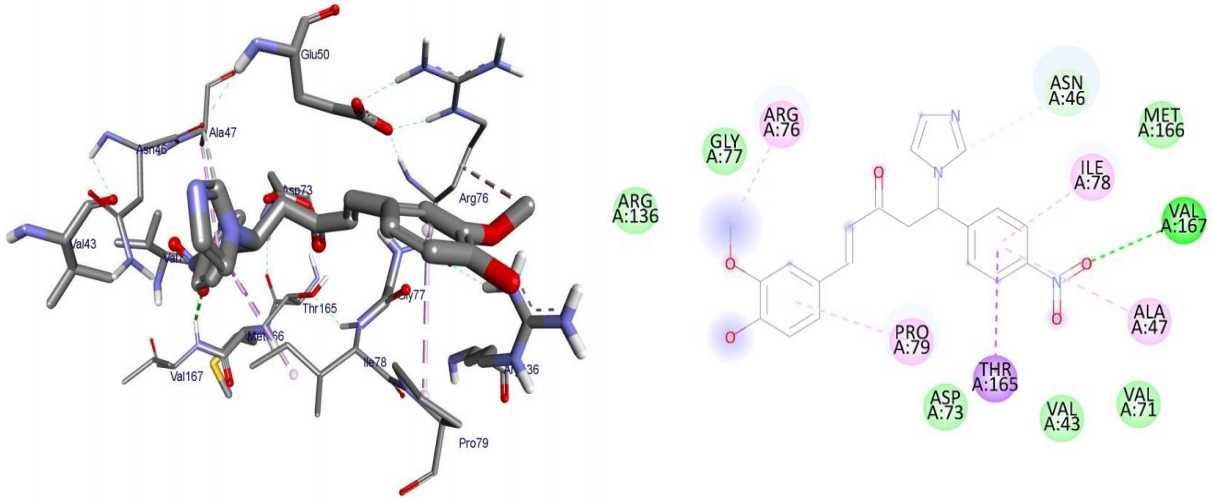
Appendix XXVIIIf. 3D (right) and 2D (left) representations of the binding interactions of **13** against *E. coli* DNA Gyrase B (PDB ID: 6f86).



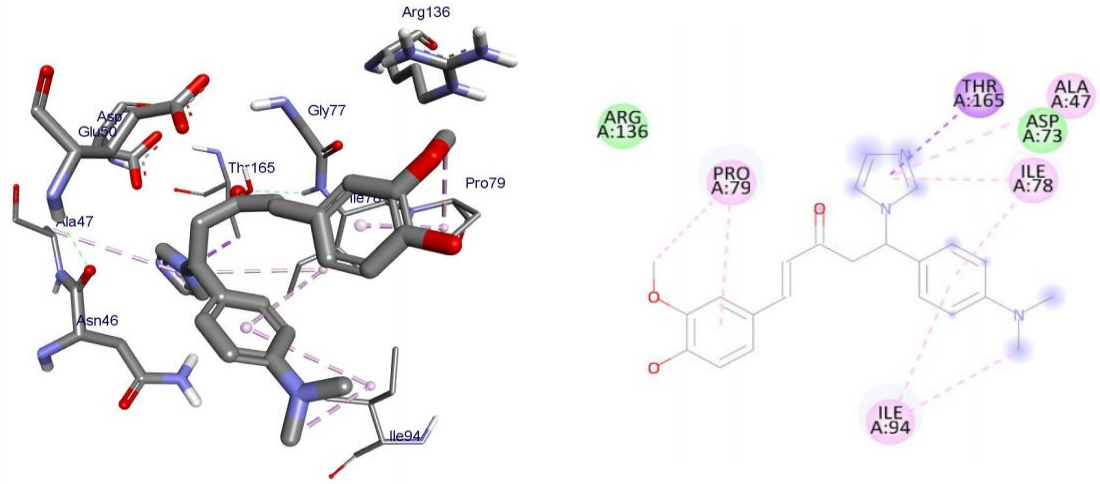
Appendix XXVIIIg. 3D (right) and 2D (left) representations of the binding interactions of **14** against *E. coli* DNA Gyrase B (PDB ID: 6f86).



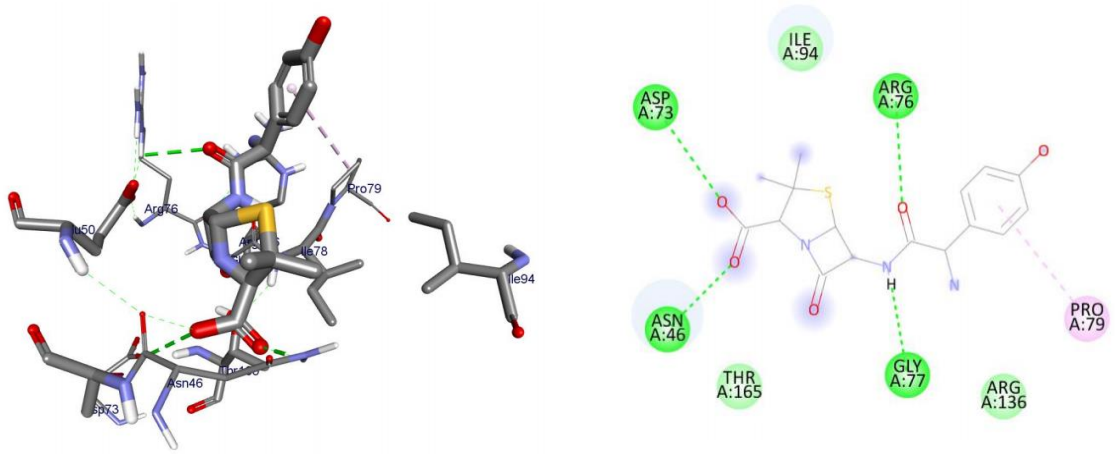
Appendix XXVIIIh. 3D (right) and 2D (left) representations of the binding interactions of **15** against *E. coli* DNA Gyrase B (PDB ID: 6f86).



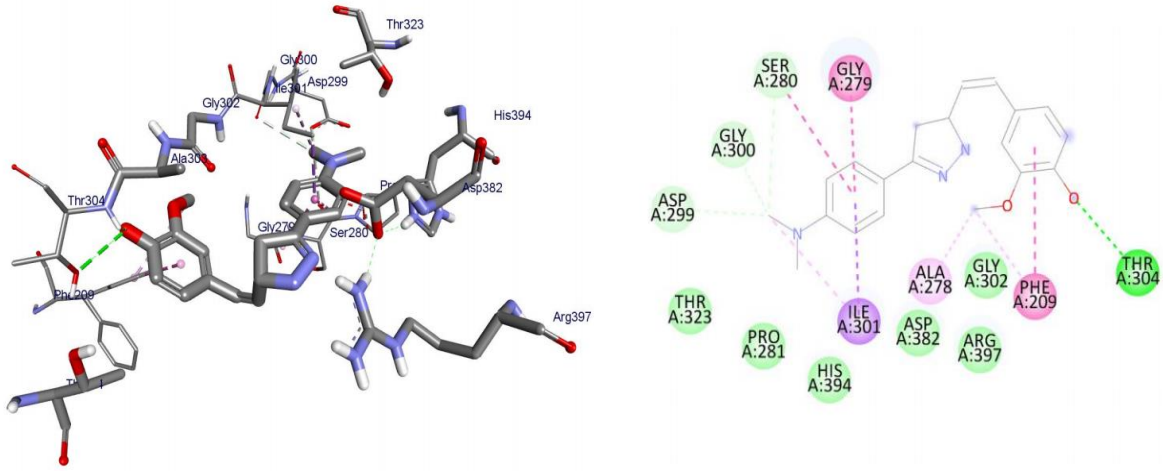
Appendix XXVIIIi. 3D (right) and 2D (left) representations of the binding interactions of **16** against *E. coli* DNA Gyrase B (PDB ID: 6f86).



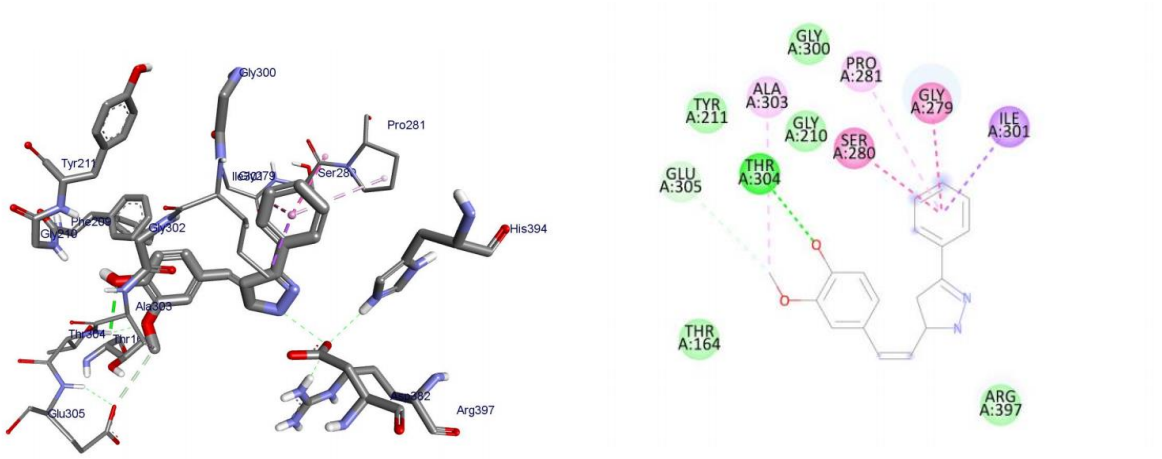
Appendix XXVIIIj. 3D (right) and 2D (left) representations of the binding interactions of **amoxicillin** against *E. coli* DNA Gyrase B (PDB ID: 6f86).



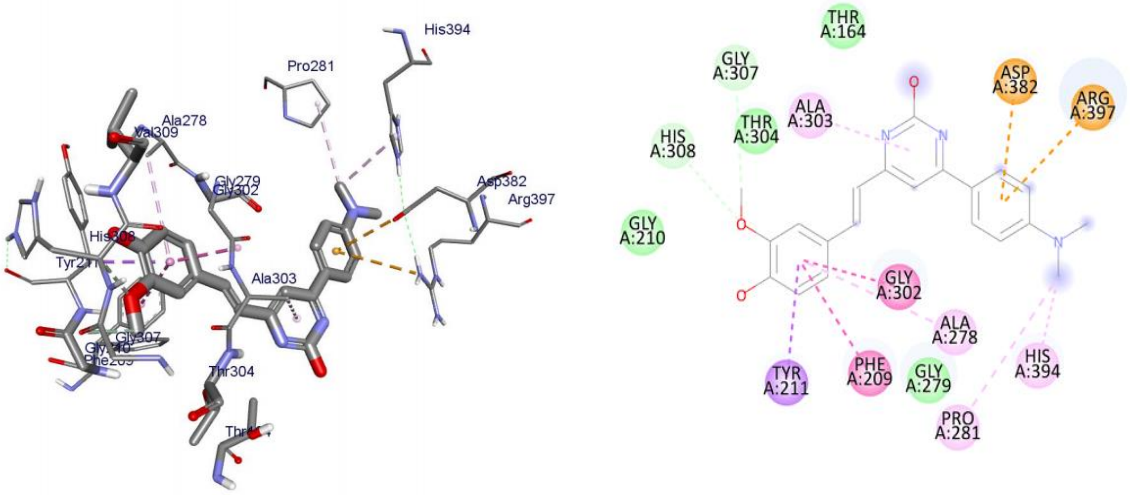
Appendix XXIXa. 3D (right) and 2D (left) representations of the binding interactions of **8** against N-terminal domain of PqsA (PDB ID: 5oe3).



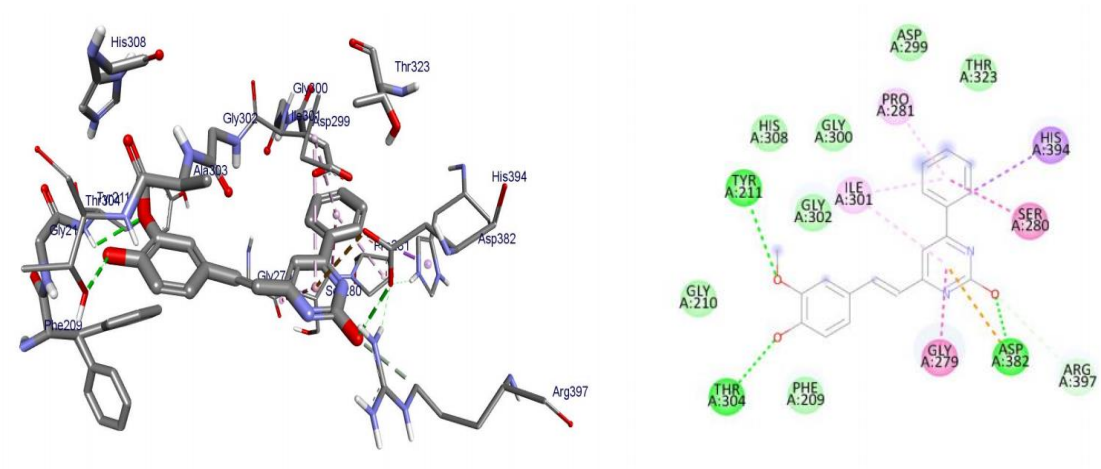
Appendix XXIXb. 3D (right) and 2D (left) representations of the binding interactions **9** of against N-terminal domain of PqsA (PDB ID: 5oe3).



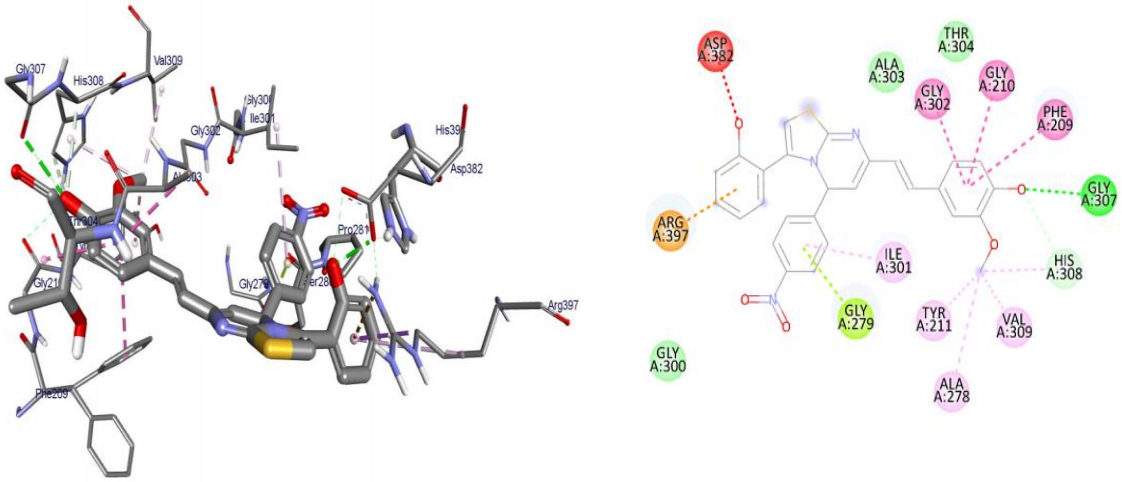
Appendix XXIXc. 3D (right) and 2D (left) representations of the binding interactions **10** of against N-terminal domain of PqsA (PDB ID: 5oe3).



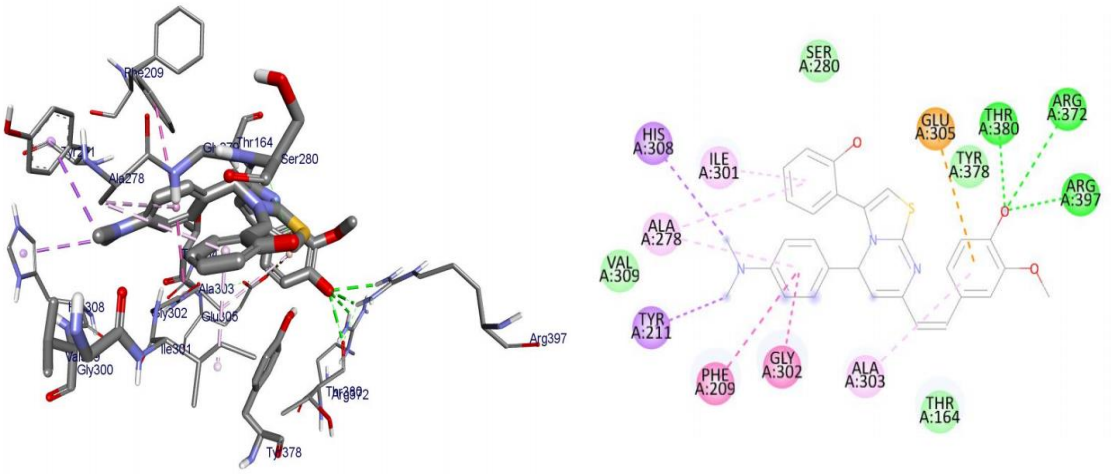
Appendix XXIXd. 3D (right) and 2D (left) representations of the binding interactions of **11** against N-terminal domain of PqsA (PDB ID: 5oe3).



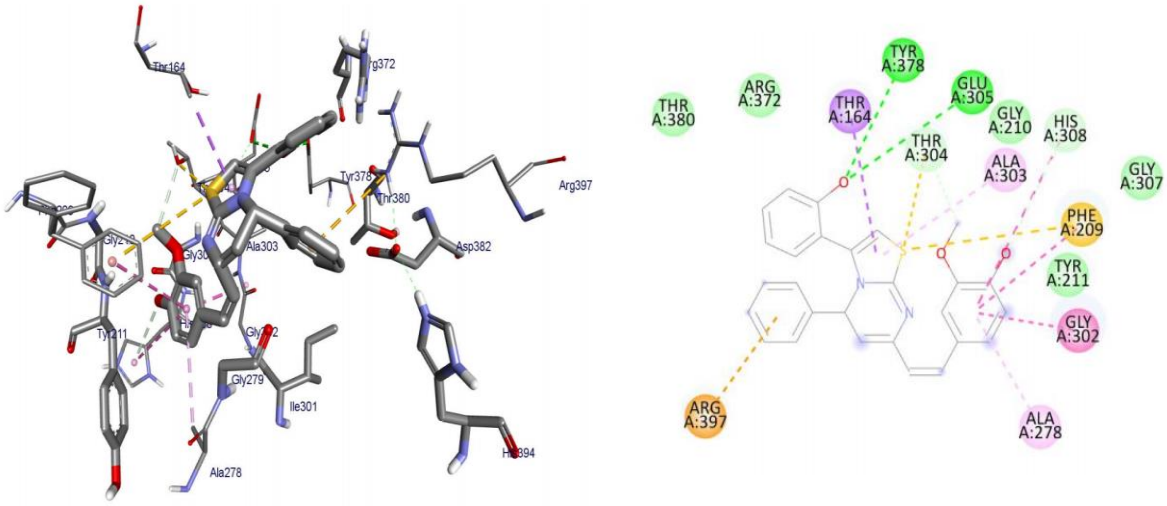
Appendix XXIXe. 3D (right) and 2D (left) representations of the binding interactions of **12** against N-terminal domain of PqsA (PDB ID: 5oe3).



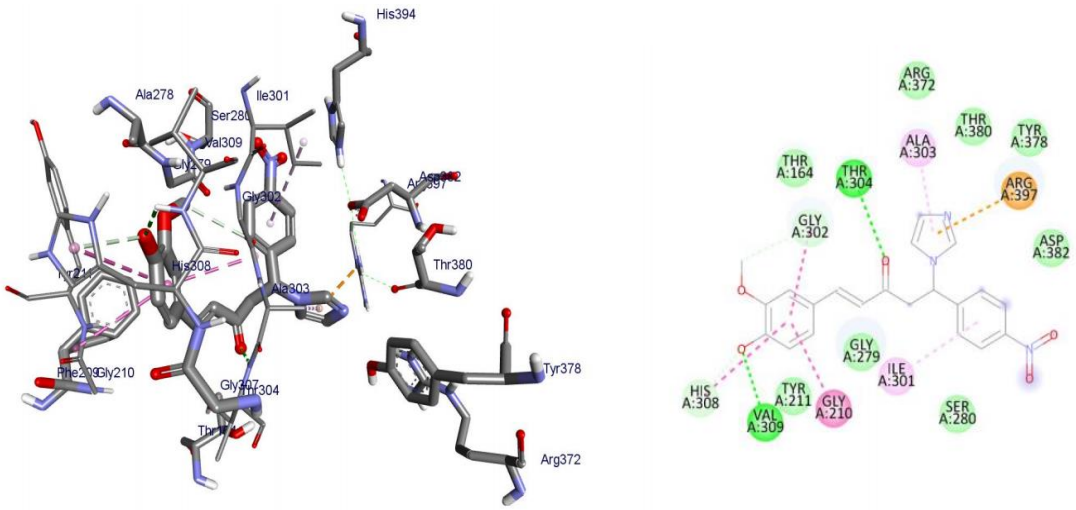
Appendix XXIXf. 3D (right) and 2D (left) representations of the binding interactions of **13** against N-terminal domain of PqsA (PDB ID: 5oe3).



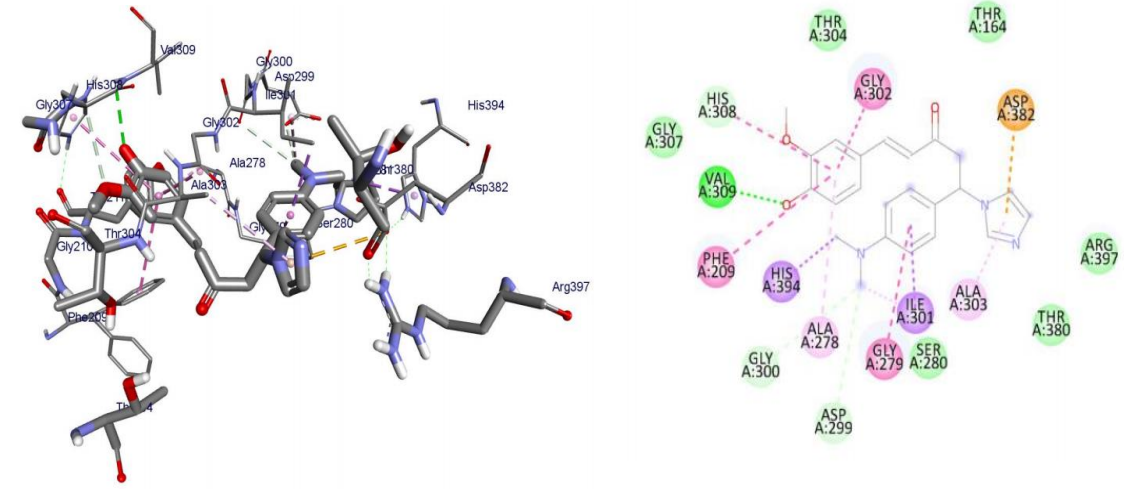
Appendix XXIXg. 3D (right) and 2D (left) representations of the binding interactions of **14** against N-terminal domain of PqsA (PDB ID: 5oe3).



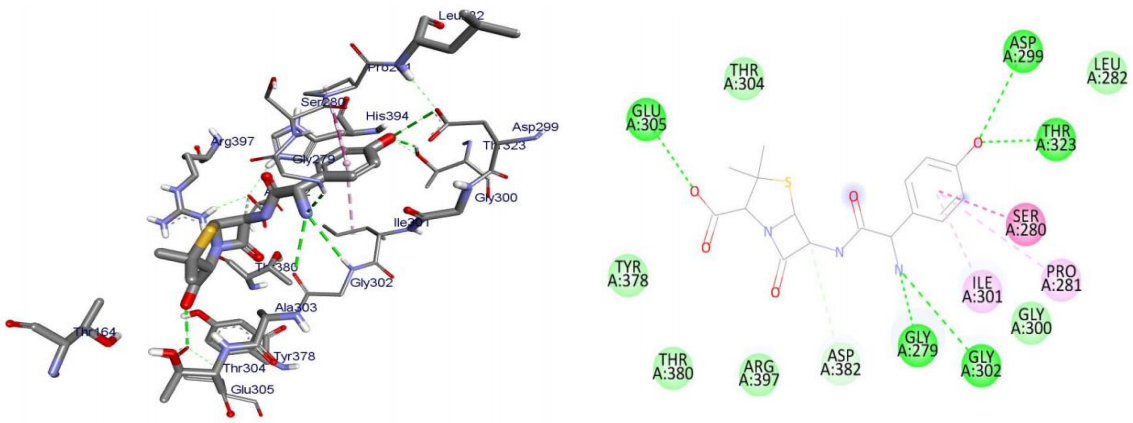
Appendix XXIXh. 3D (right) and 2D (left) representations of the binding interactions of **15** against N-terminal domain of PqsA (PDB ID: 5oe3).



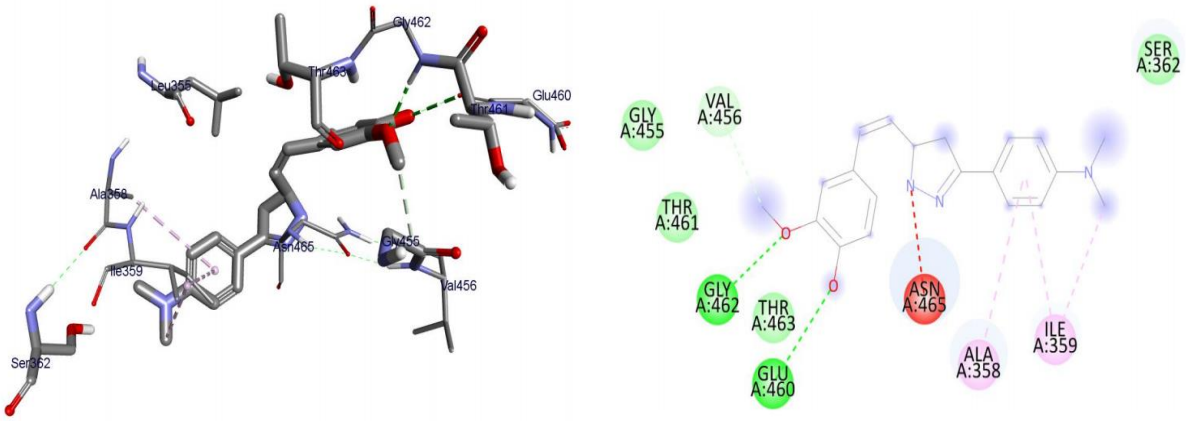
Appendix XXIXi. 3D (right) and 2D (left) representations of the binding interactions of **16** against N-terminal domain of PqsA (PDB ID: 5oe3).



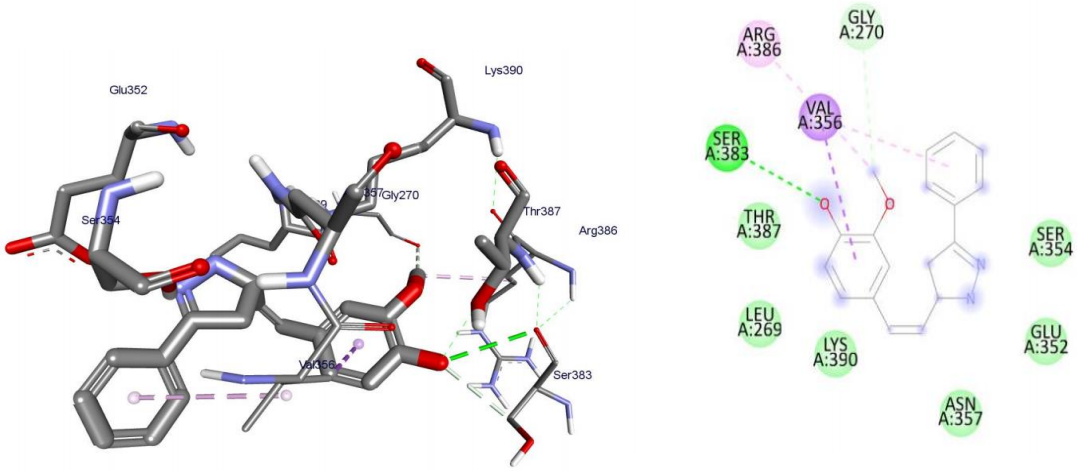
Appendix XXIXj. 3D (right) and 2D (left) representations of the binding interactions of **amoxicillin** against N-terminal domain of PqsA (PDB ID: 5oe3).



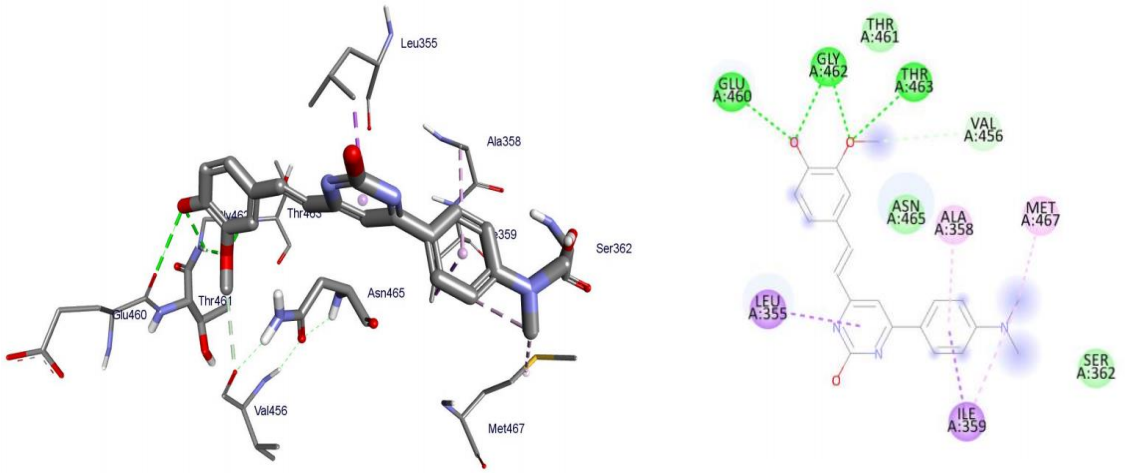
Appendix XXXa. 3D (right) and 2D (left) representations of the binding interactions of **8** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



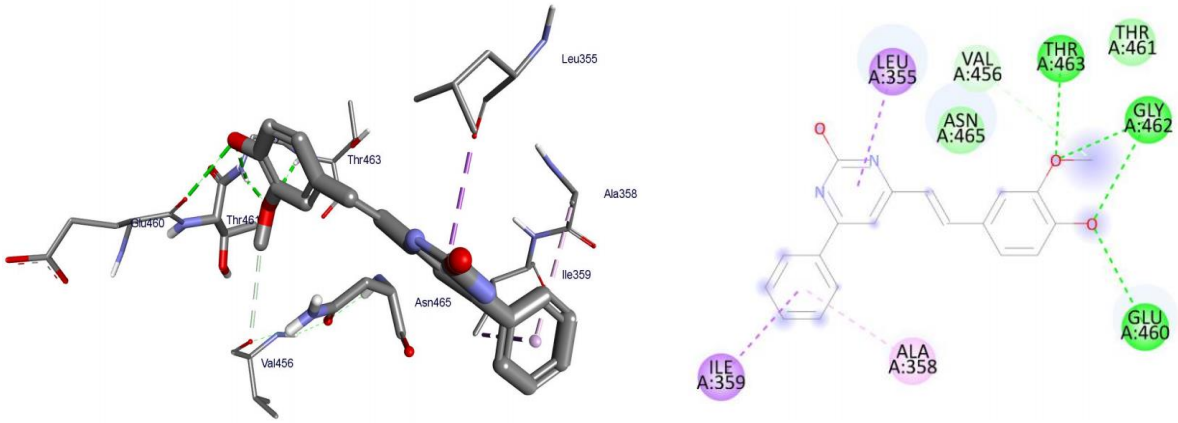
Appendix XXXb. 3D (right) and 2D (left) representations of the binding interactions of **9** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



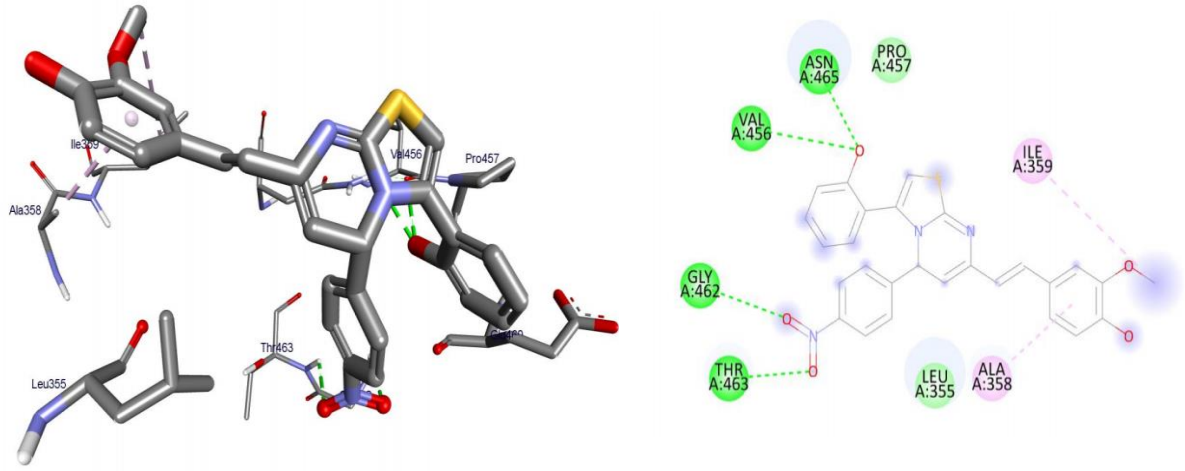
Appendix XXXc. 3D (right) and 2D (left) representations of the binding interactions of **10** against *S. aureus* Pyruvate Kinase in complex (PDB ID: 3t07).



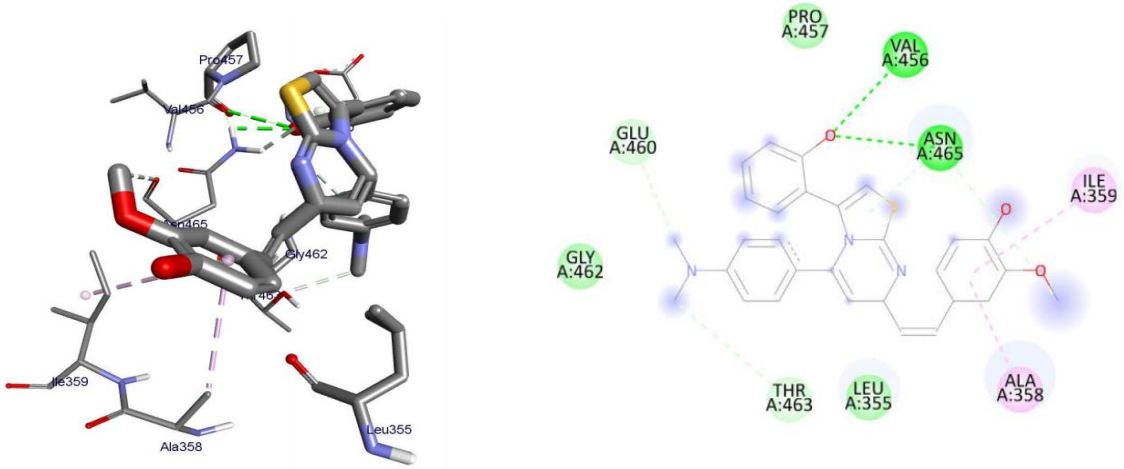
Appendix XXXd. 3D (right) and 2D (left) representations of the binding interactions of **11** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



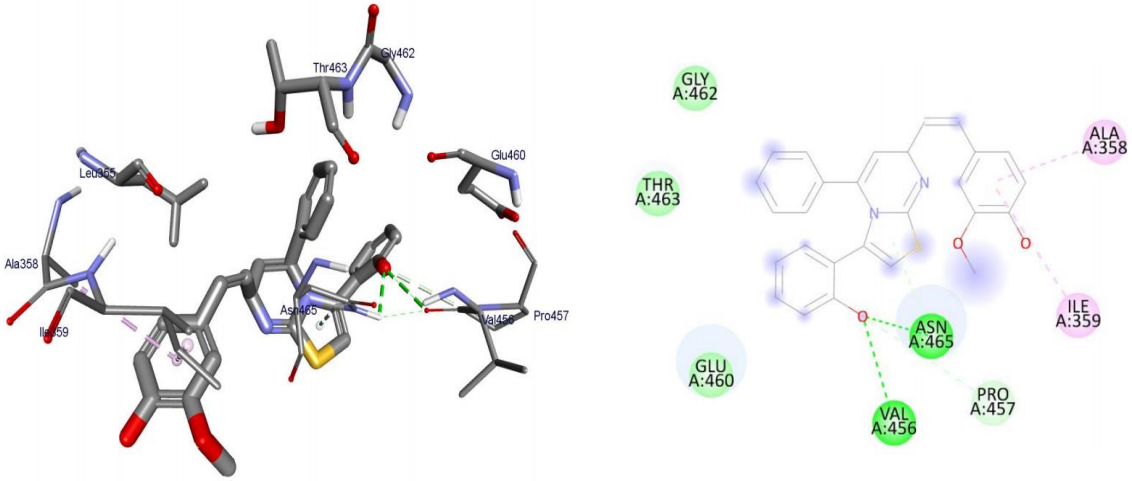
Appendix XXXe. 3D (right) and 2D (left) representations of the binding interactions of **12** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



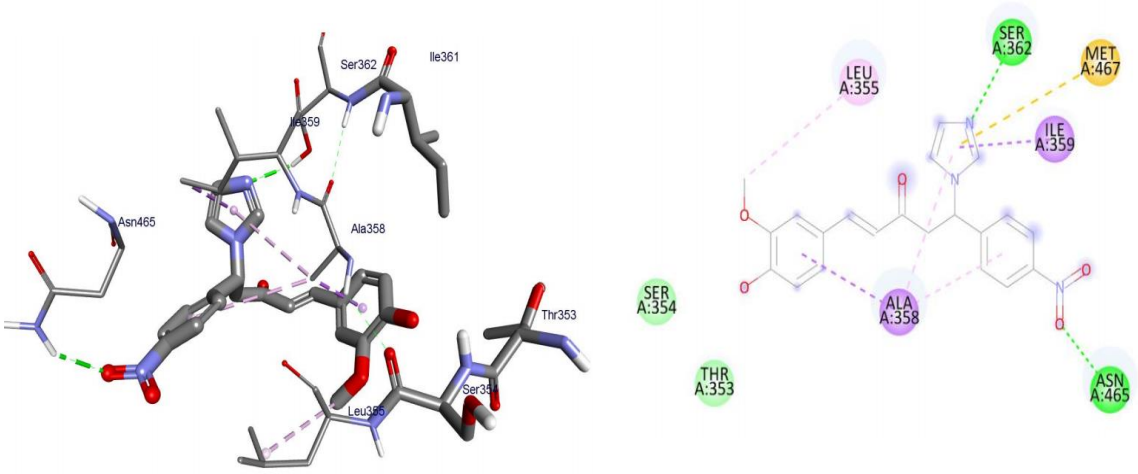
Appendix XXXf. 3D (right) and 2D (left) representations of the binding interactions of **13** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



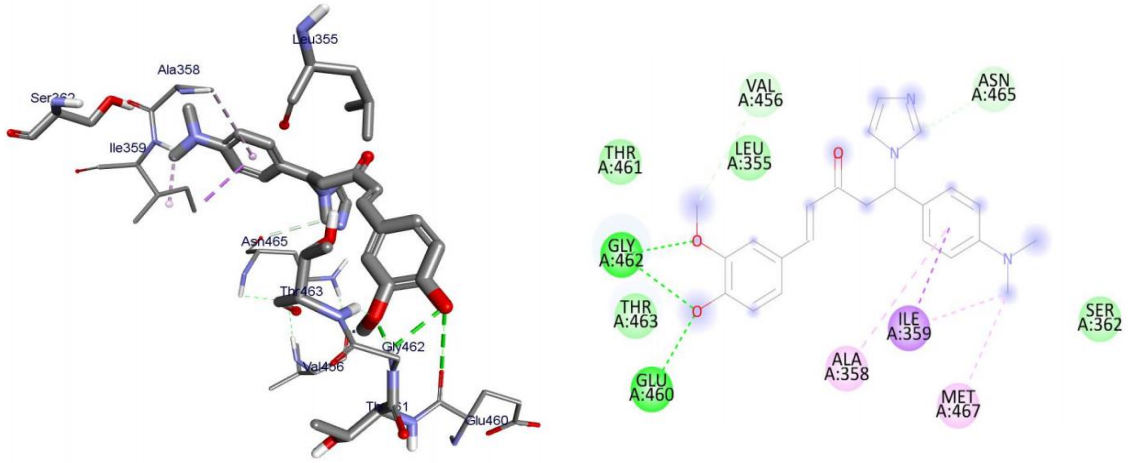
Appendix XXXg. 3D (right) and 2D (left) representations of the binding interactions of **14** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



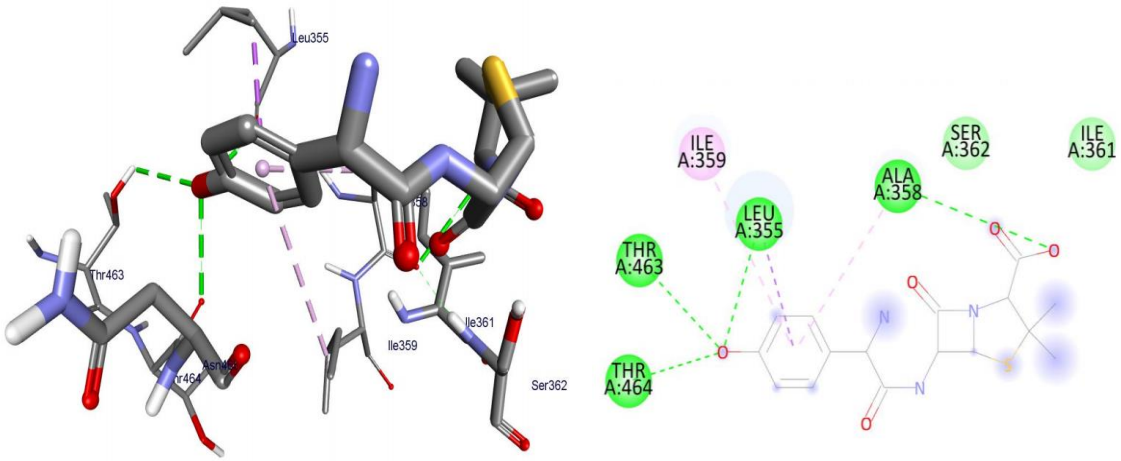
Appendix XXXh. 3D (right) and 2D (left) representations of the binding interactions of **15** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



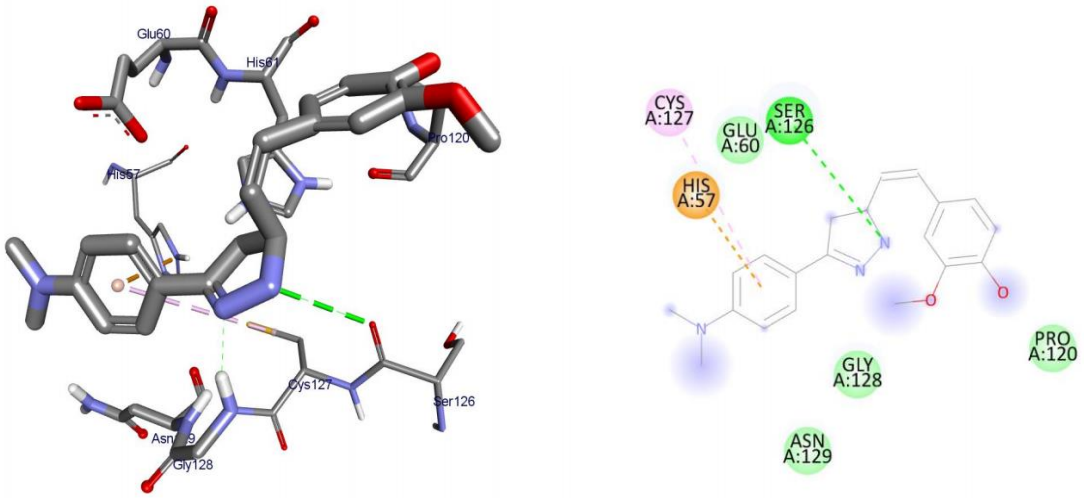
Appendix XXXi. 3D (right) and 2D (left) representations of the binding interactions of **16** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



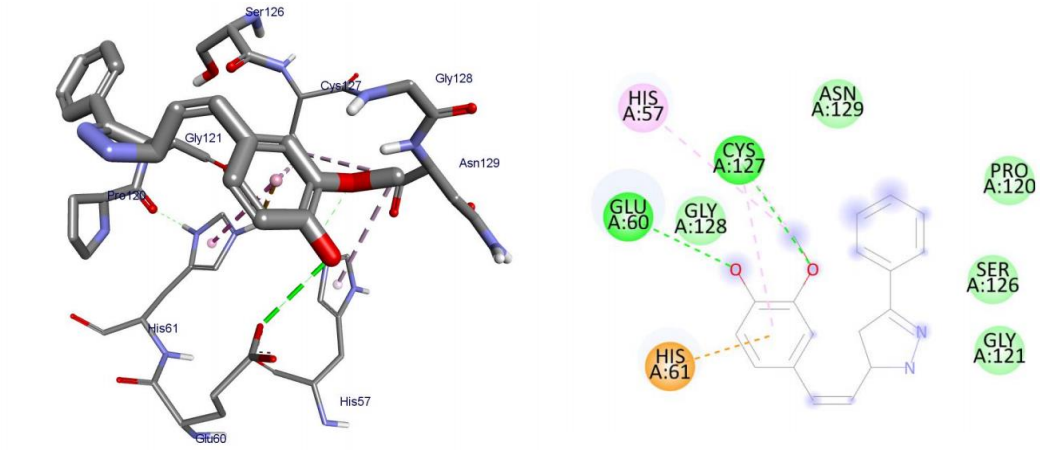
Appendix XXXj. 3D (right) and 2D (left) representations of the binding interactions of **amoxicillin** against *S. aureus* Pyruvate Kinase (PDB ID: 3t07).



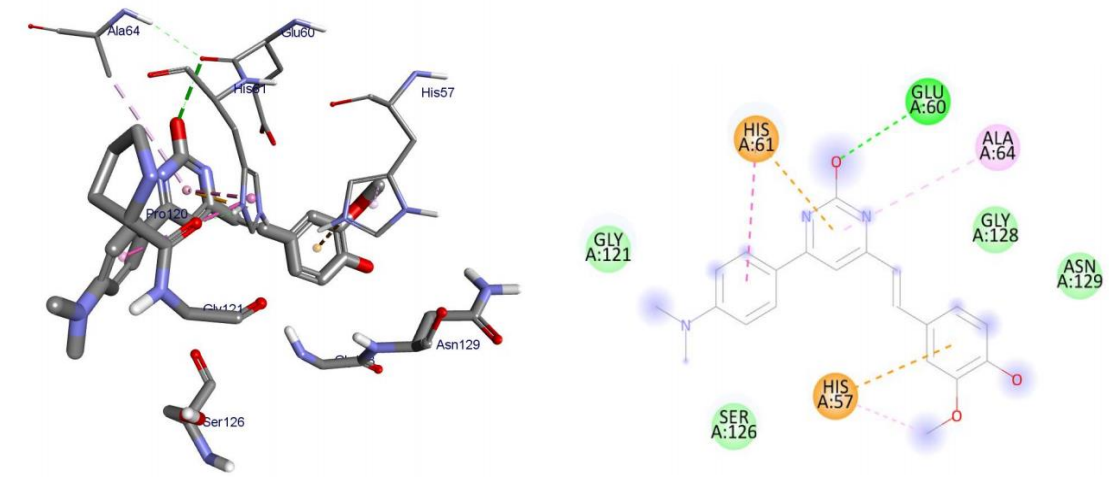
Appendix XXXIa. 3D (right) and 2D (left) representations of the binding interactions of **8** against against LuxS of *S. pyogenes* (PDB ID: 4xch)



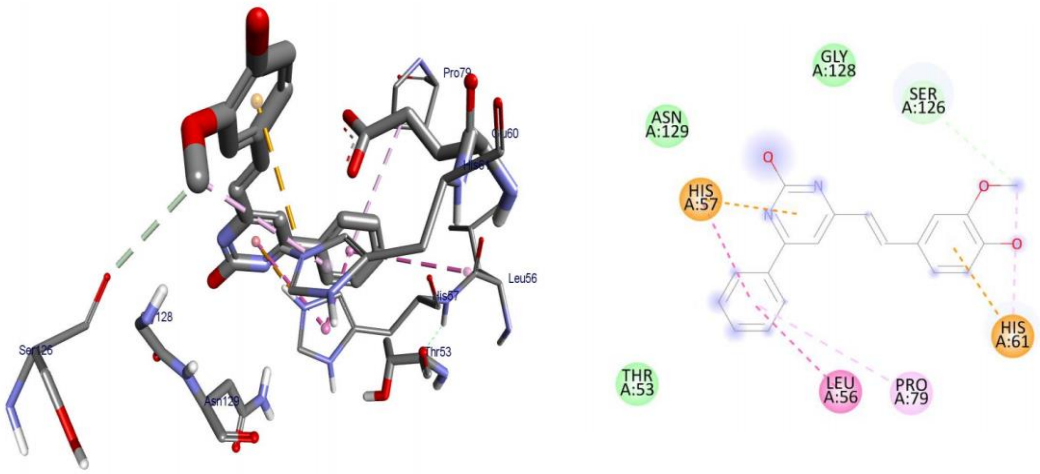
Appendix XXXIb. 3D (right) and 2D (left) representations of the binding interactions of **9** against LuxS of *S. pyogenes* (PDB ID: 4xch)



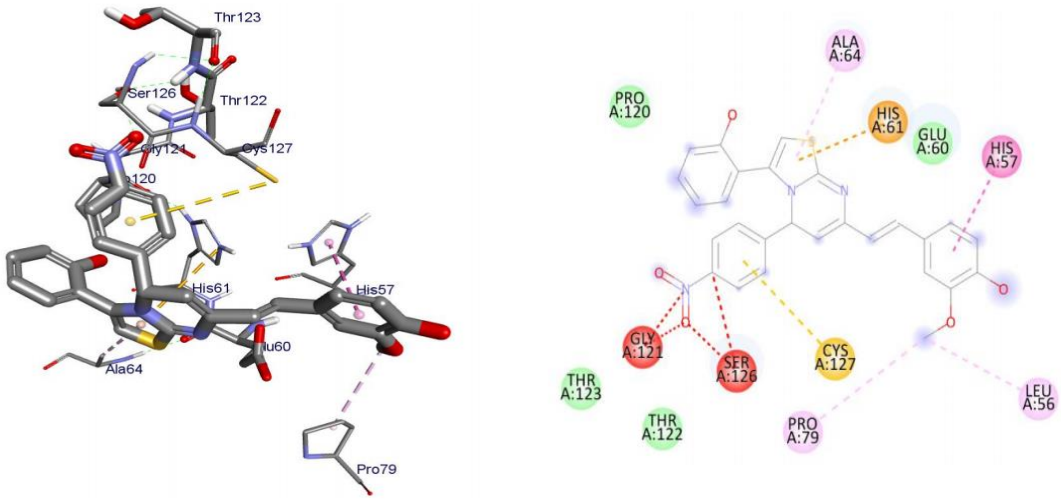
Appendix XXXIc. 3D (right) and 2D (left) representations of the binding interactions of **10** against LuxS of *S. pyogenes* (PDB ID: 4xch)



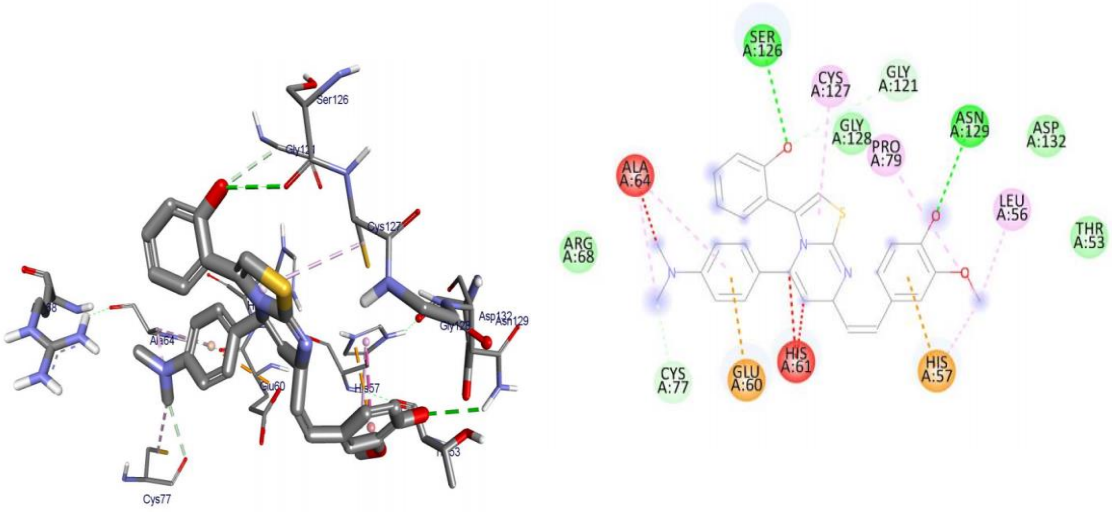
Appendix XXXId. 3D (right) and 2D (left) representations of the binding interactions of **11** against LuxS of *S. pyogenes* (PDB ID: 4xch)



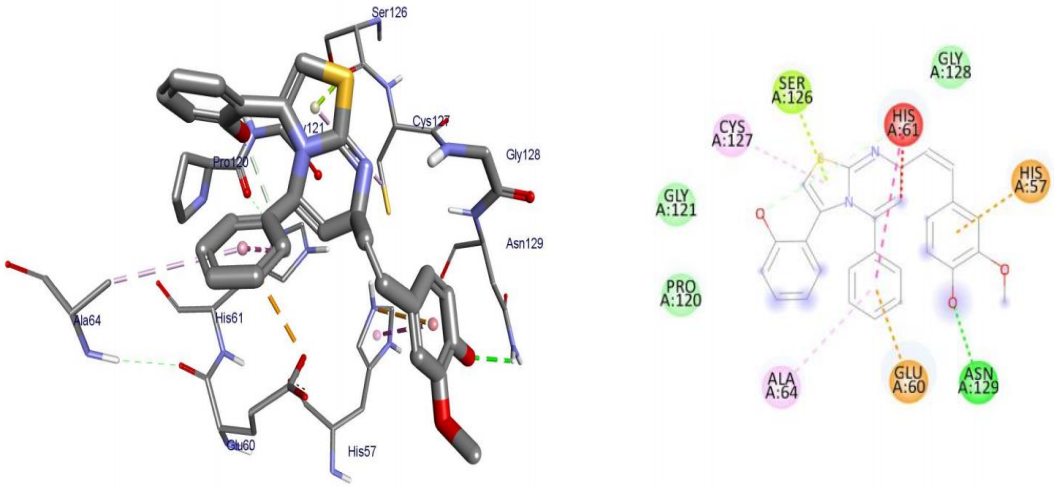
Appendix XXXIe. 3D (right) and 2D (left) representations of the binding interactions of **12** against LuxS of *S. pyogenes* (PDB ID: 4xch)



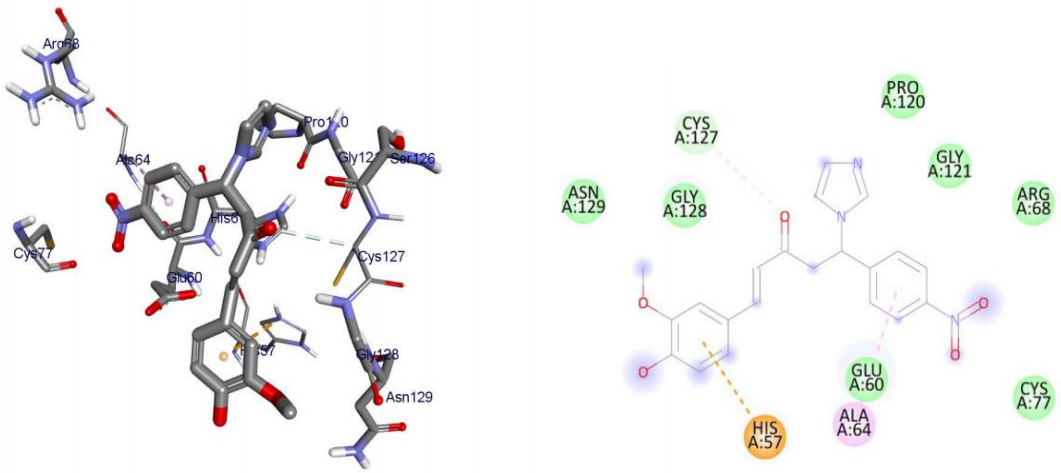
Appendix XXXIf. 3D (right) and 2D (left) representations of the binding interactions of **13** against LuxS of *S. pyogenes* (PDB ID: 4xch)



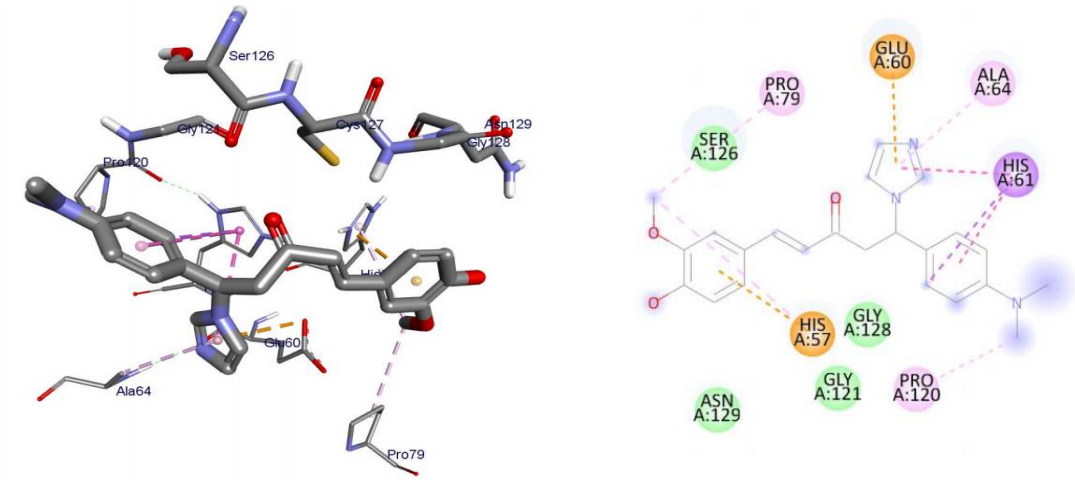
Appendix XXXIg. 3D (right) and 2D (left) representations of the binding interactions of **14** against LuxS of *S. pyogenes* (PDB ID: 4xch)



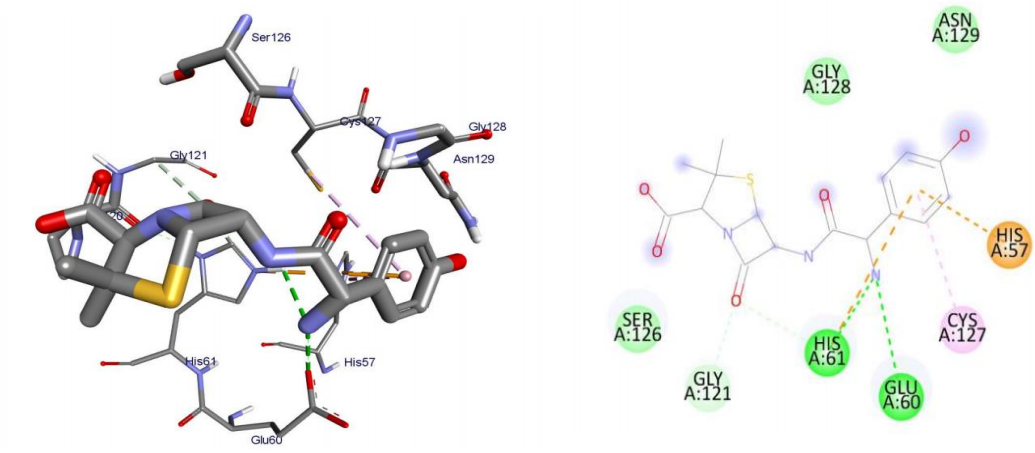
Appendix XXXIh. 3D (right) and 2D (left) representations of the binding interactions of **15** against LuxS of *S. pyogenes* (PDB ID: 4xch)



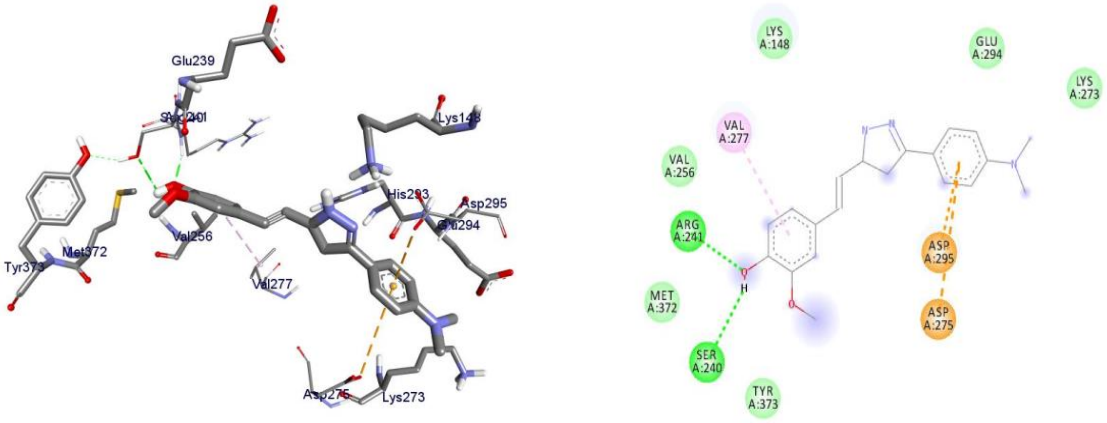
Appendix XXXIi. 3D (right) and 2D (left) representations of the binding interactions of **16** against LuxS of *S. pyogenes* (PDB ID: 4xch)



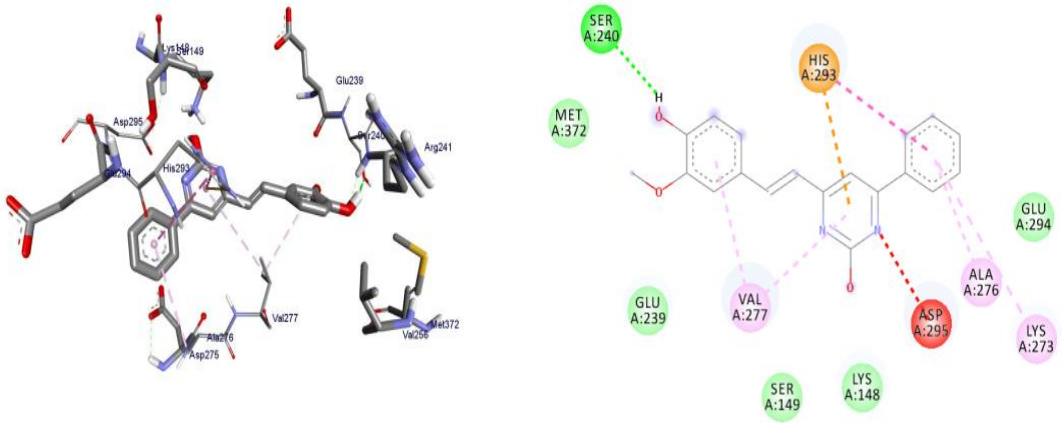
Appendix XXXIj. 3D (right) and 2D (left) representations of the binding interactions of **amoxicillin** against LuxS of *S. pyogenes* (PDB ID: 4xch)



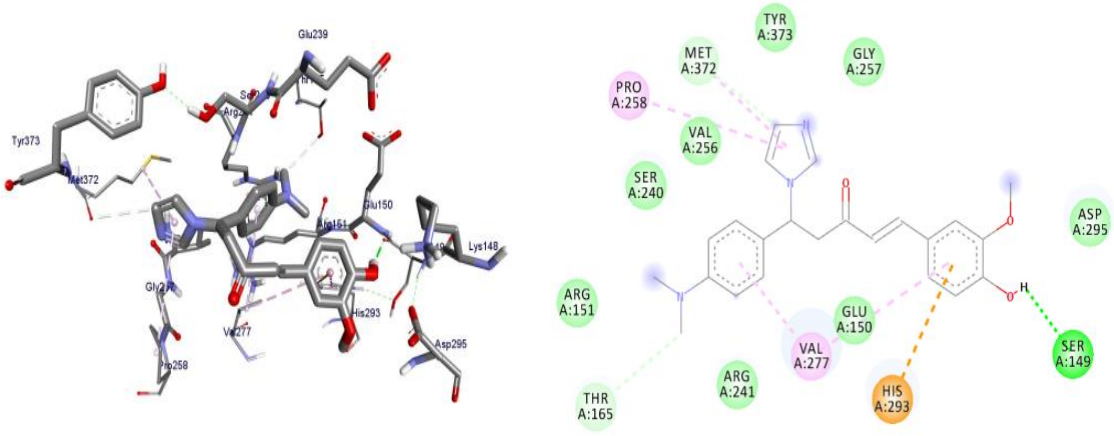
Appendix XXXIIa. 3D (right) and 2D (left) representations of the binding interactions of **8** against Penicillin binding proteins (PBPs) (PDB ID: 1VQQ).



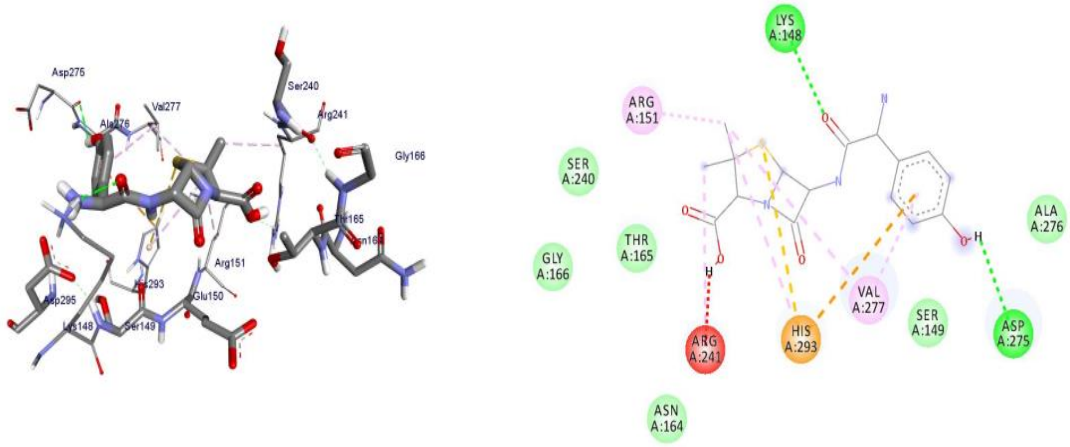
Appendix XXXIIb. 3D (right) and 2D (left) representations of the binding interactions of **11** against Penicillin binding proteins (PBPs) (PDB ID: 1VQQ).



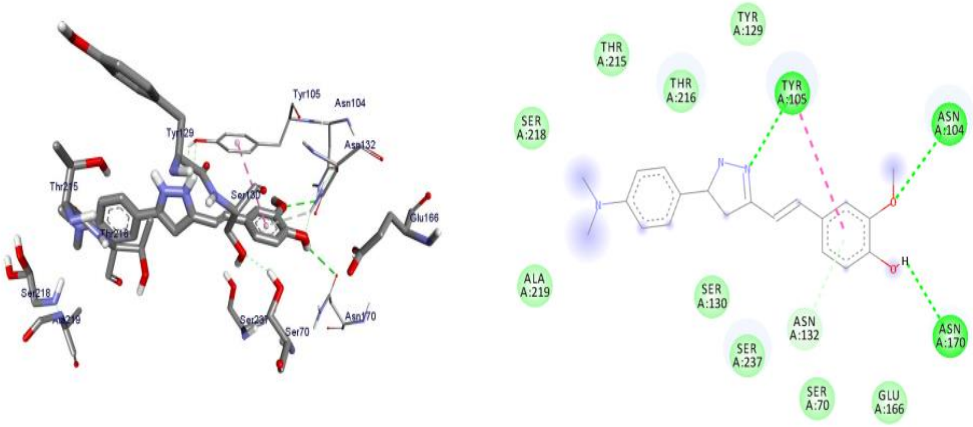
Appendix XXXIIc. 3D (right) and 2D (left) representations of the binding interactions of **16** against Penicillin binding proteins (PBPs) (PDB ID: 1VQQ).



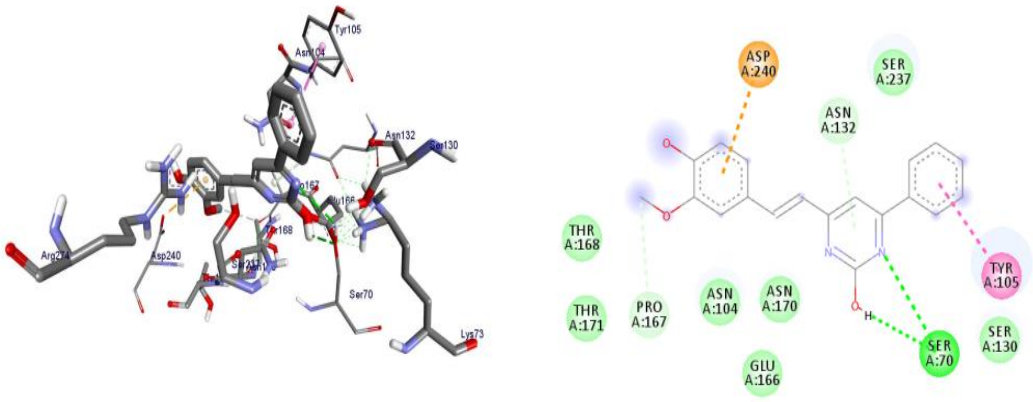
Appendix XXXIId. 3D (right) and 2D (left) representations of the binding interactions of **amoxicillin** against Penicillin binding proteins (PBPs) (PDB ID: 1VQQ).



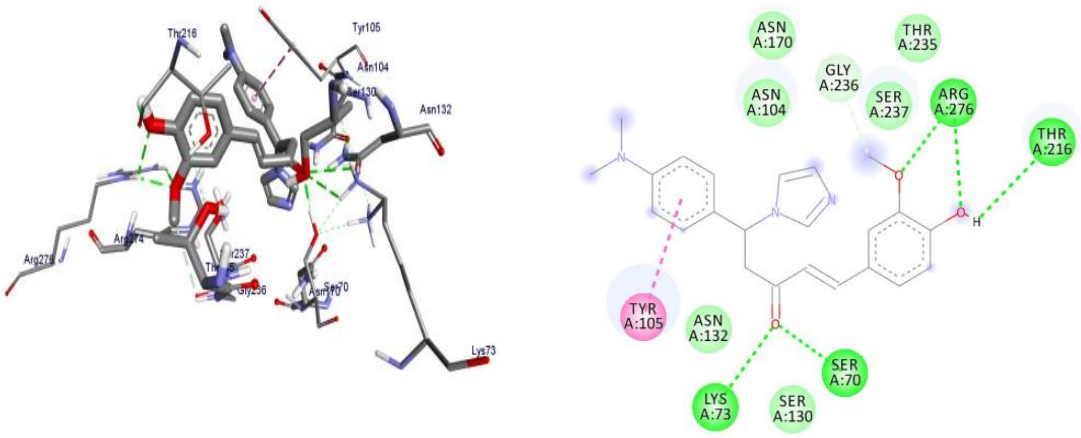
Appendix XXXIIIa. 3D (right) and 2D (left) representations of the binding interactions of **8** against β-lactamases (PDB ID: 1IYS)



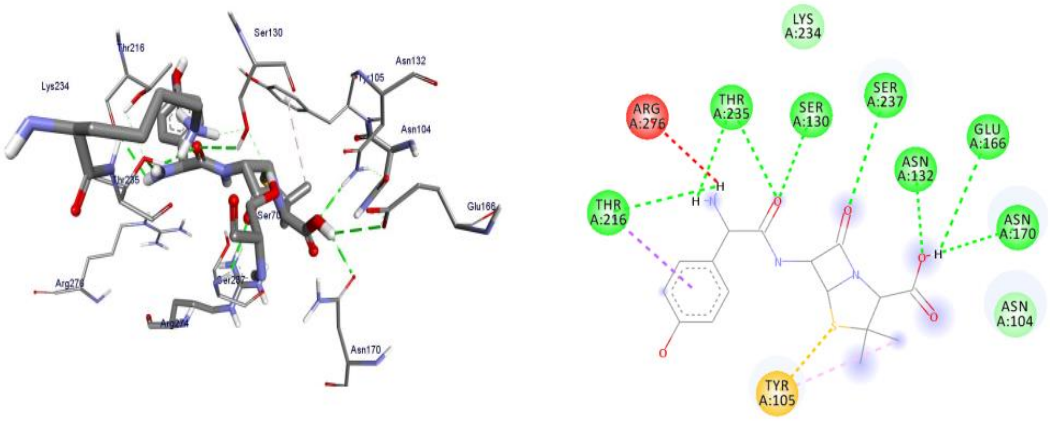
Appendix XXXIIIb. 3D (right) and 2D (left) representations of the binding interactions of **11** against β-lactamases (PDB ID: 1IYS)



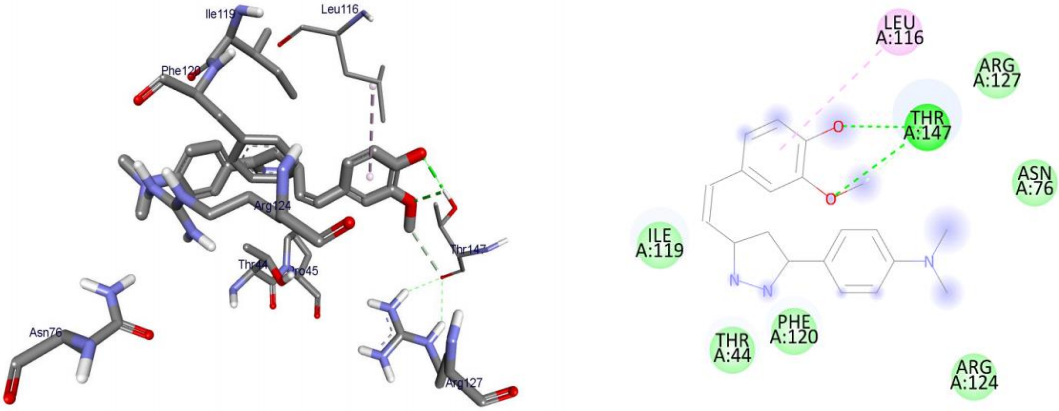
Appendix XXXIIIc. 3D (right) and 2D (left) representations of the binding interactions of **16** against β-lactamases (PDB ID: 1IYS)



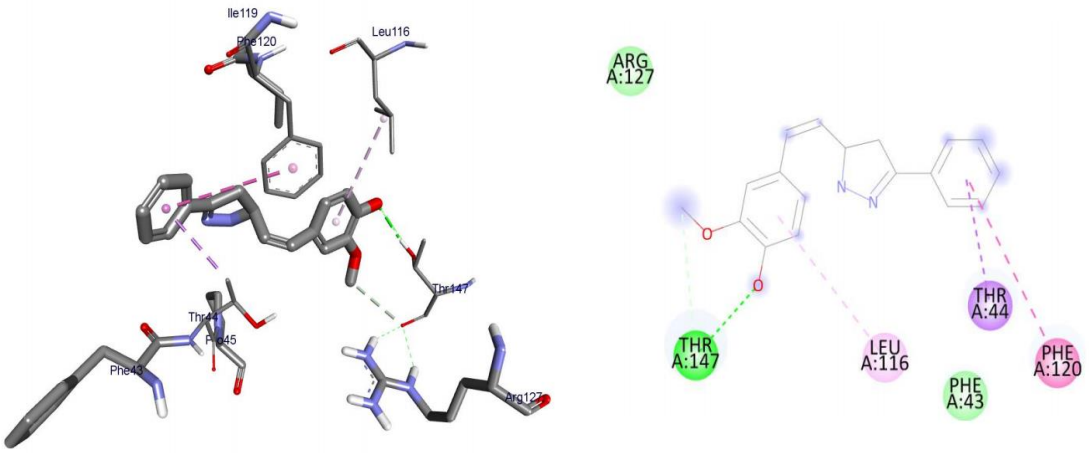
Appendix XXXIIId. 3D (right) and 2D (left) representations of the binding interactions of **amoxicillin** against β-lactamases (PDB ID: 1IYS)



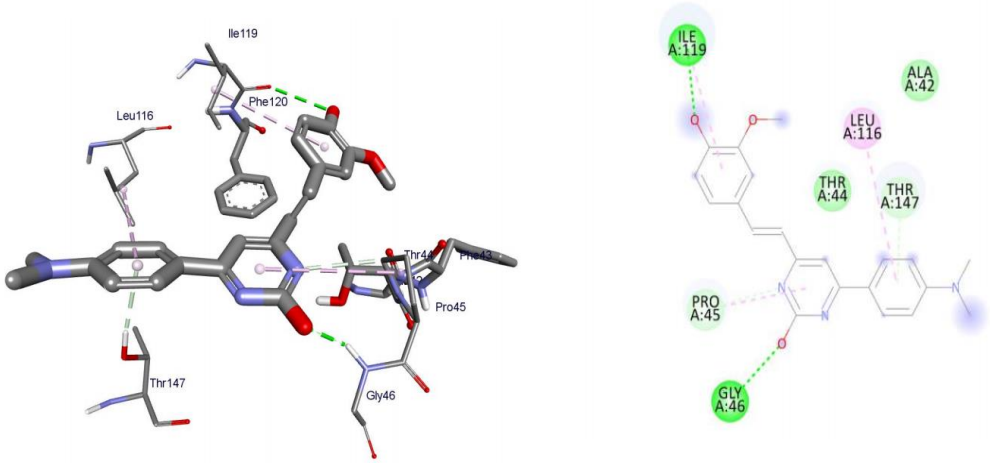
Appendix XXXIVa. 3D (right) and 2D (left) representations of the binding interactions of **8** against Human peroxiredoxin 5 (PDB ID: 1hd2).



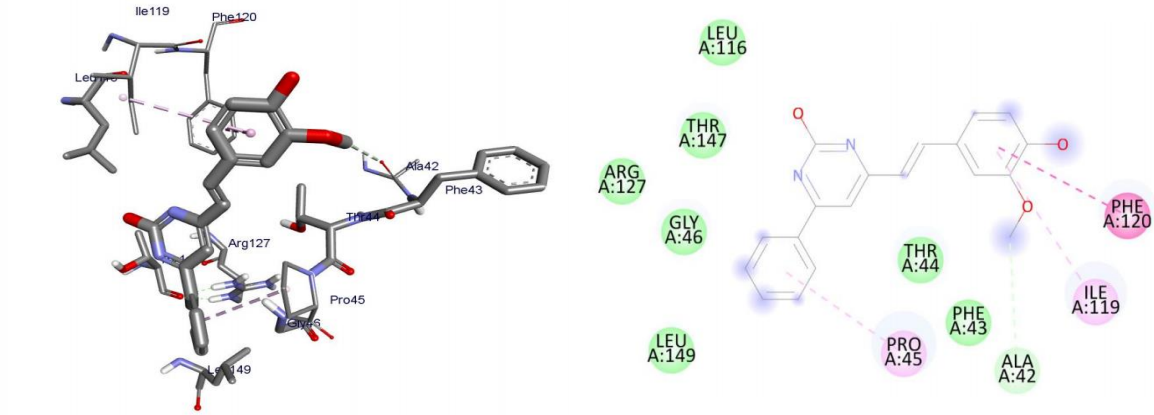
Appendix XXXIVb. 3D (right) and 2D (left) representations of the binding interactions of **9** against Human peroxiredoxin 5 (PDB ID: 1hd2).



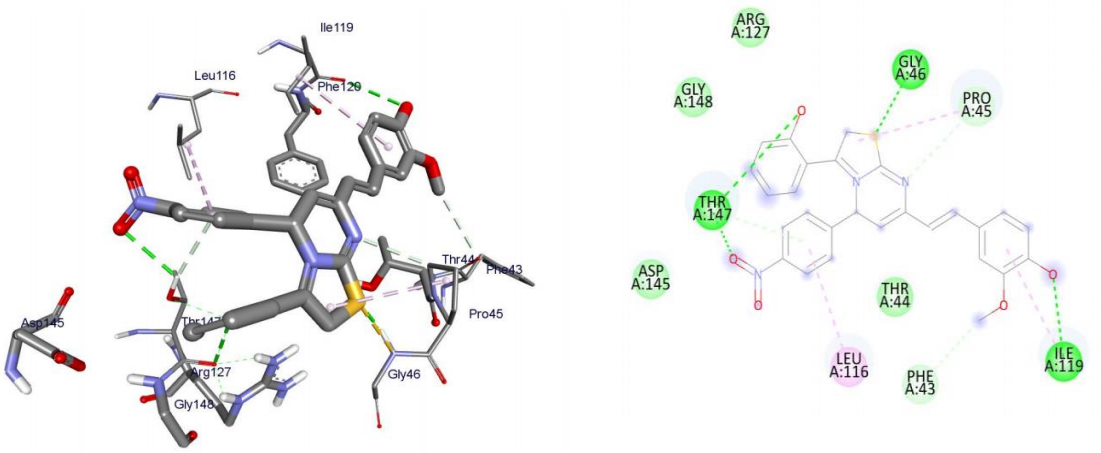
Appendix XXXIVc. 3D (right) and 2D (left) representations of the binding interactions of **10** against Human peroxiredoxin 5 (PDB ID: 1hd2).



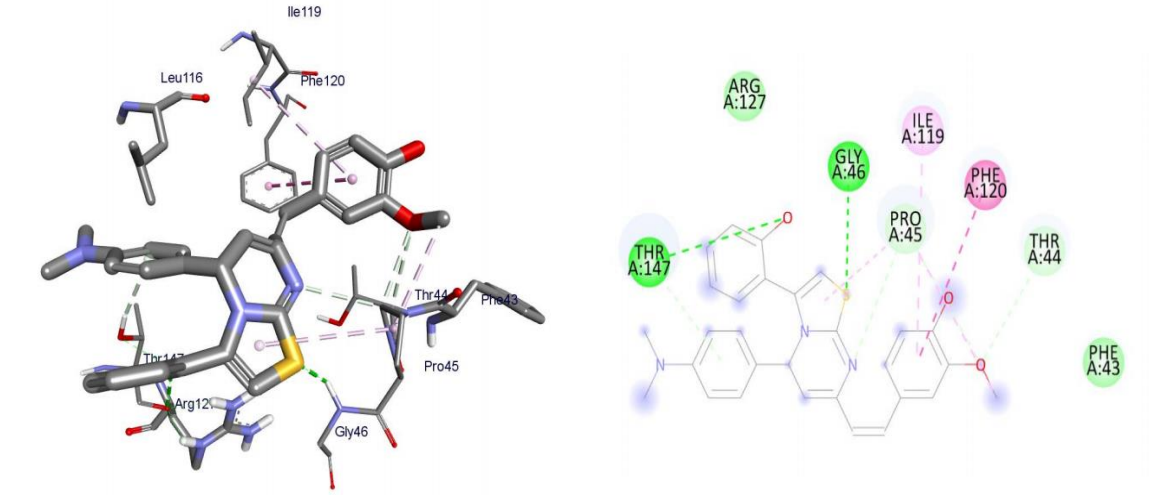
Appendix XXXIVd. 3D (right) and 2D (left) representations of the binding interactions of **11** against Human peroxiredoxin 5 (PDB ID: 1hd2).



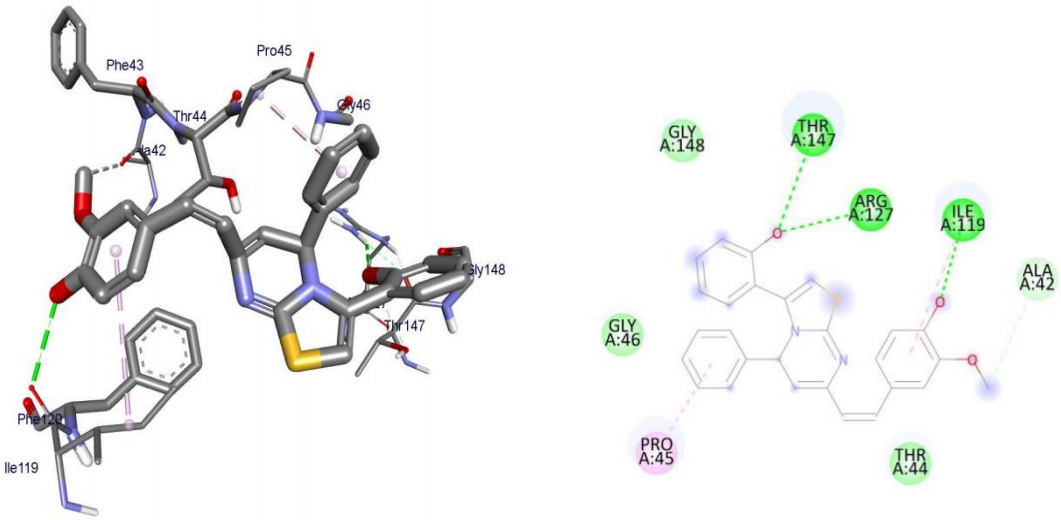
Appendix XXXIVe. 3D (right) and 2D (left) representations of the binding interactions of **12** against Human peroxiredoxin 5 (PDB ID: 1hd2).



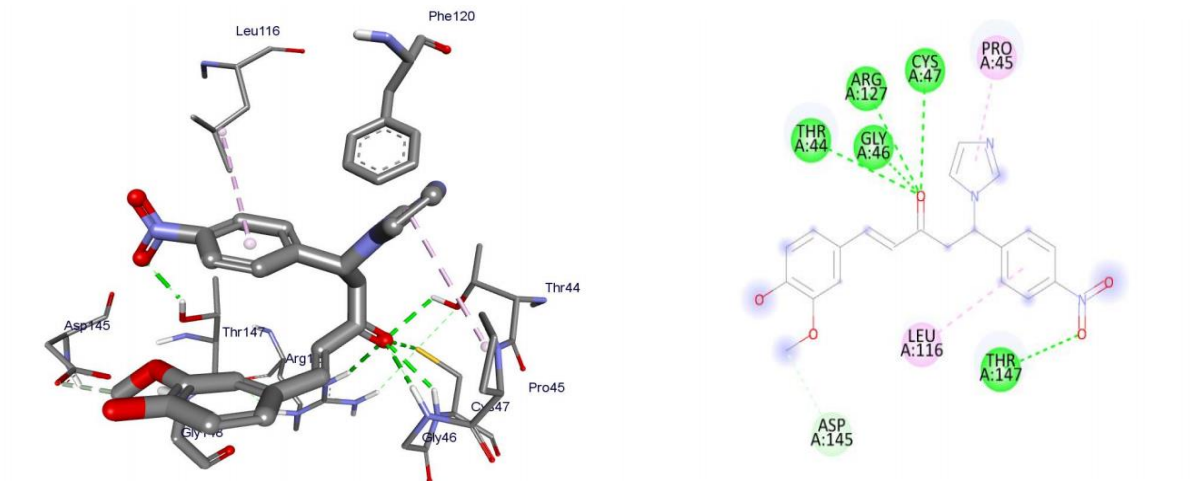
Appendix XXXIVf. 3D (right) and 2D (left) representations of the binding interactions of **13** against Human peroxiredoxin 5 (PDB ID: 1hd2).



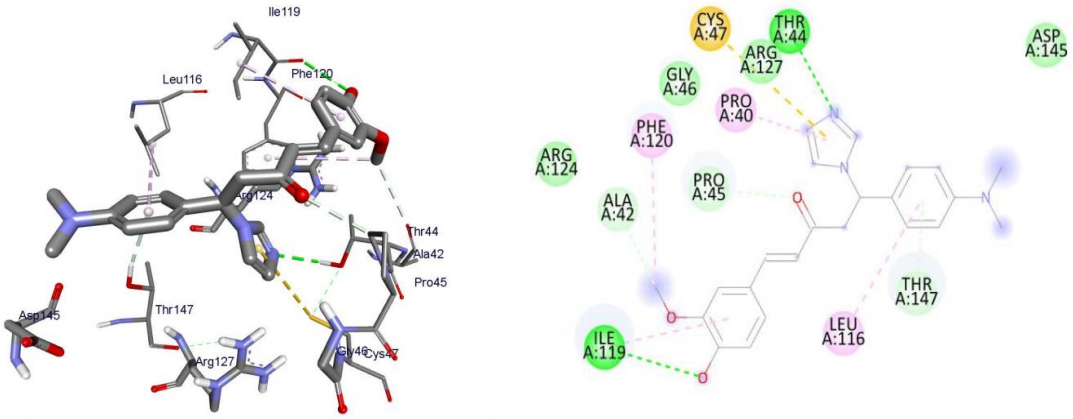
Appendix XXXIVg. 3D (right) and 2D (left) representations of the binding interactions of **14** against Human peroxiredoxin 5 (PDB ID: 1hd2).



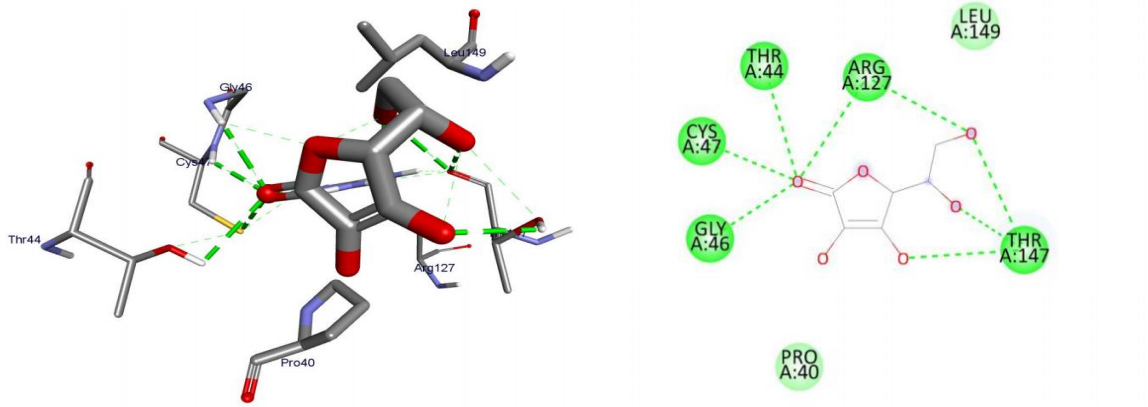
Appendix XXXIVh. 3D (right) and 2D (left) representations of the binding interactions of **15** against Human peroxiredoxin 5 (PDB ID: 1hd2).



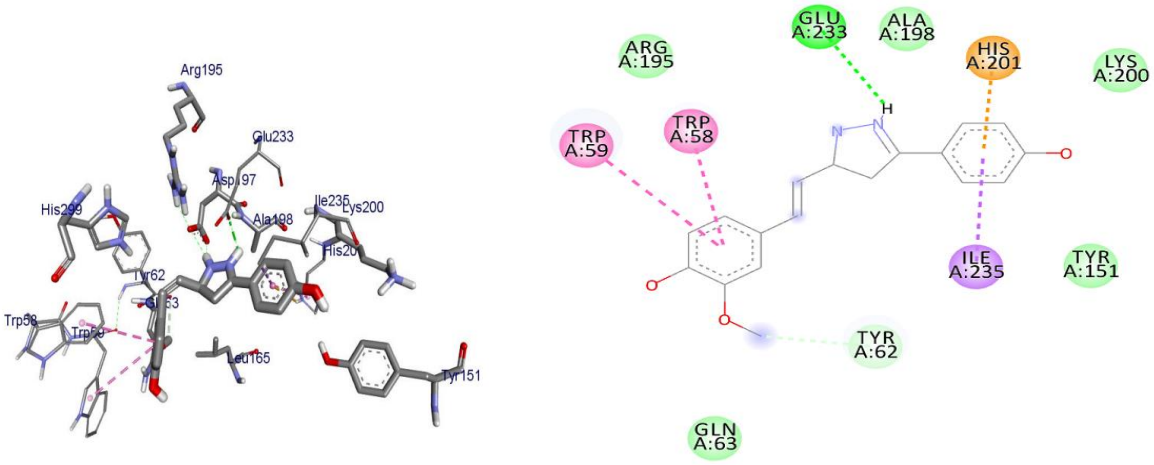
Appendix XXXIVi. 3D (right) and 2D (left) representations of the binding interactions of **16** against Human peroxiredoxin 5 (PDB ID: 1hd2).



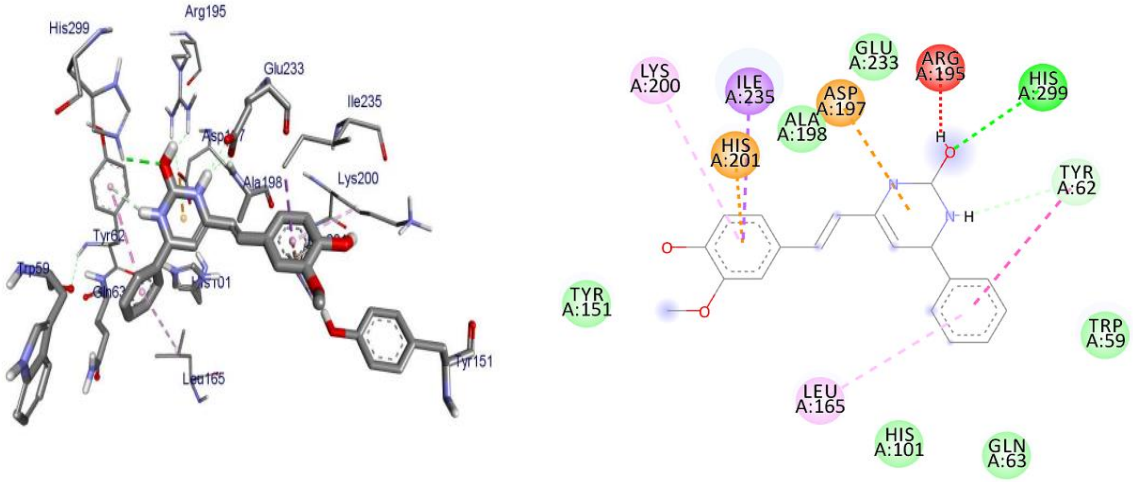
Appendix XXXIVj. 3D (right) and 2D (left) representations of the binding interactions of **vitamin C** against Human peroxiredoxin 5 (PDB ID: 1hd2).



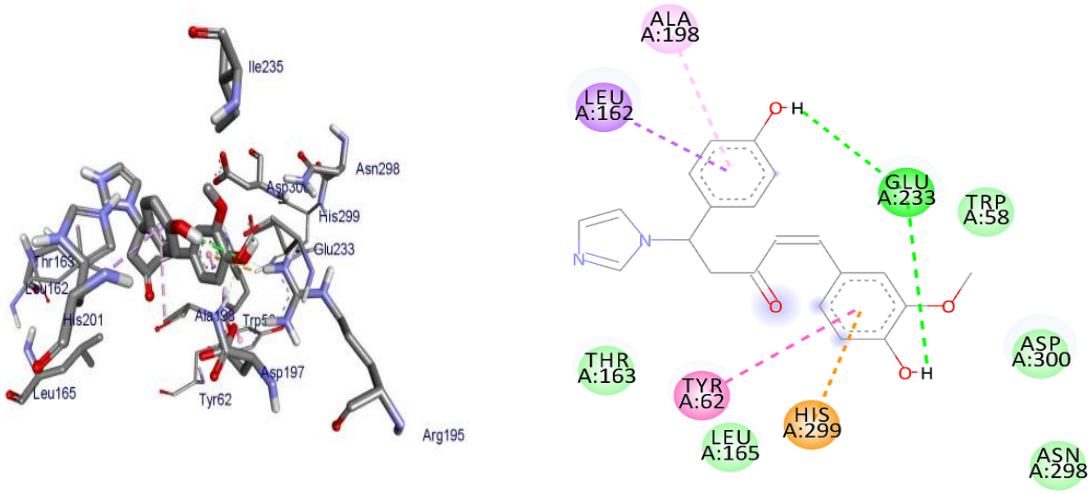
Appendix XXXVa. 3D (right) and 2D (left) representations of the binding interactions of **8** against α-amylase enzyme (PDB ID: 4w93)



Appendix XXXVb. 3D (right) and 2D (left) representations of the binding interactions of **11** against α-amylase enzyme (PDB ID: 4w93)



Appendix XXXVc. 3D (right) and 2D (left) representations of the binding interactions of **16** against α-amylase enzyme (PDB ID: 4w93)



Appendix XXXVd. 3D (right) and 2D (left) representations of the binding interactions of **acarbose** against α-amylase enzyme (PDB ID: 4w93)