Electronic Supplementary Material (ESI) for RSC Advances.

THE SUPPORTING INFORMATION

N,2,6-Trisubstituted 1*H*-benzimidazole derivatives as a new scaffold of antimicrobial and anticancer agents: Design, synthesis, *in vitro* evaluation, and *in silico* studies

Table S1 ADMET profile of the most active compounds, ciprofloxacin, fluconazole, and paclitaxel

Parameter	3k	3l	4c	4g	4j	Cipro	Flu	PTX
Absorption								
Caco-2 permeability	-4.666	-4.788	-4.808	-4.711	-4.776	-5.269	-4.950	-5.461
MDCK permeability	$1.6x10^{-4}$	$7.4x10^{-6}$	$9.5x10^{-6}$	$1.2x10^{-4}$	$3.2x10^{-5}$	$3.0x10^{-6}$	$2.8x10^{-5}$	$5.4x10^{-5}$
Pgp-inhibitor	++	+++	+++	+++	+++	---	---	+++
Pgp-substrate	---	---	---	---	---	+++	---	+++
HIA	+++	+++	+++	+++	+++	+++	+++	+++
$F_{20\%}$	+	--	---	+++	+++	+++	+++	---
$F_{30\%}$	+++	++	+	+++	+++	+++	+++	---
Distribution								
PPB (%)	98.833	99.442	99.207	99.093	99.873	37.456	61.763	94.571
VD (L/kg)	0.505	0.988	0.960	0.456	0.463	2.324	0.835	0.907
BBB penetration	-	+	++	--	--	---	+++	--
Fu (%)	1.556	1.313	1.304	1.325	1.013	78.856	51.002	6.779
Log Kp (cm/s)	-5.100	-4.230	-4.290	-4.920	-4.690	-9.090	-7.920	
Metabolism								
CYP1A2 inhibitor	+++	+++	++	++	++	--	-	---
CYP1A2 substrate	--	--	--	--	--	--	-	---
CYP2C19 inhibitor	+++	++	++	++	++	---	+	---
CYP2C19 substrate	---	---	---	---	---	--	---	---
CYP2C9 inhibitor	++	++	++	++	++	---	--	++
CYP2C9 substrate	+	--	--	++	++	---	+	---
CYP2D6 inhibitor	-	++	++	+	+	---	-	---
CYP2D6 substrate	++	--	-	++	++	--	--	---
CYP3A4 inhibitor	+	-	-	+	-	---	-	++
CYP3A4 substrate	--	+	-	-	+	--	--	+
Excretion								
CL (mL/min/kg)	5.908	5.822	6.936	6.148	5.054	3.214	5.960	3.416
$T_{1/2}$	0.080	0.039	0.059	0.068	0.042	0.056	0.228	0.028
Toxicity								
hERG blockers	++	+	+	++	++	--	---	--
H-HT	--	---	--	--	---	+++	+++	+++
DILI	--	-	--	--	-	+++	+++	+++

AMES toxicity	+++	-	-	+++	+++	--	++	---
Rat oral acute toxicity	--	--	--	---	---	--	+++	-
FDAMDD	+	+	++	++	++	++	++	++
Skin sensitization	+	---	---	-	--	+	+++	---
Carcinogenicity	++	++	++	++	++	-	+++	---
Eye corrosion	---	---	---	---	---	---	---	---
Eye irritation	+++	++	++	+++	++	---	--	---
Respiratory toxicity	-	---	---	+	-	++	++	+++
Tox21 Pathway								
NR-AR	--	---	--	--	-	++	---	--
NR-AR-LBD	--	---	---	---	---	---	---	+++
NR-AhR	+	--	-	+	-	--	+	---
NR-Aromatase	+	++	--	-	+	---	+++	++
NR-ER	++	++	++	++	++	-	---	+
NR-ER-LBD	--	--	---	--	-	---	---	+
NR-PPAR-gamma	---	---	---	---	---	---	---	+++
SR-ARE	++	++	++	++	++	-	--	++
SR-ATAD5	--	--	--	--	---	---	---	+++
SR-HSE	---	---	---	---	---	---	---	-
SR-MMP	++	++	+	++	++	---	--	+++
SR-p53	+	++	+	+	++	---	---	+++
Toxicophore Rules								
Acute Toxicity Rule	0 alert	0 alert	0 alert	0 alert	0 alert	1 alert	0 alert	0 alert
Genotoxic Carcinogenicity Rule	5 alerts	0 alert	0 alert	5 alerts	5 alerts	1 alert	0 alert	1 alert
NonGenotoxic Carcinogenicity Rule	0 alert	1 alert	1 alert	0 alert	1 alert	1 alert	0 alert	0 alert
Skin Sensitization Rule	1 alert	1 alert	1 alert	1 alert	1 alert	0 alert	0 alert	6 alerts
Aquatic Toxicity Rule	0 alert	1 alert	1 alert	0 alert	1 alert	1 alert	1 alert	2 alerts
NonBiodegradable Rule	2 alerts	1 alert	1 alert	2 alerts	3 alerts	2 alerts	1 alert	2 alerts
SureChEMBL Rule	0 alert	0 alert	0 alert	0 alert	0 alert	0 alert	0 alert	0 alert
FAF-Drugs4 Rule	4 alerts	2 alerts	2 alerts	4 alerts	4 alerts	1 alert	1 alert	1 alert

Cipro *- ciprofloxacin,* ***Flu*** *- fluconazole,* ***PTX*** *- paclitaxel,* ***Caco-2 permeability*** *(optimal: higher than -5.15 Log unit),* ***MDCK permeability*** *(low permeability: <2x10^{-6} cm/s, medium permeability: 2-20x10^{-6} cm/s, high passive permeability: > 20x10^{-6} cm/s),* ***Pgp*** *- P-glycoprotein,* ***HIA*** *- human intestinal absorption (-: <30%, +: ≥30%),* ***F*** *- bioavailability (-: <percent value, +: ≥percent value),* ***PPB*** *- plasma protein binding (optimal: <90%),* ***VD*** *- volume distribution (optimal: 0.04-20 L/kg),* ***BBB*** *- blood-brain barrier,* ***Fu*** *- the fraction unbound in plasms (low: <5%, middle: 5-20%, high: >20%),* ***Log Kp*** *(skin permeation),* ***CL*** *- clearance (low: <5 mL/min/kg, moderate: 5-15 mL/min/kg, high: >15 mL/min/kg),* ***T$_{1/2}$*** *(category 1: long half-life (>3 h), category 0: short half-life (<3 h)),* ***H-HT*** *- human hepatotoxicity,* ***DILI*** *- drug-induced liver injury,* ***FDAMDD*** *- maximum recommended daily dose,* ***AR*** *- androgen receptor,* ***AR-LBD*** *- androgen receptor ligand-binding domain,* ***AhR*** *- aryl hydrocarbon receptor,* ***ER*** *- estrogen receptor,* ***ER-LBD*** *- estrogen receptor ligand-binding domain,* ***PPAR-gamma*** *- peroxisome proliferator-activated receptor gamma,* ***ARE*** *- antioxidant response element,* ***ATAD5*** *- ATPase family AAA domain-containing protein 5,* ***HSE*** *- heat shock factor response element,* ***MMP*** *- mitochondrial membrane potential.*

The output value is the probability of being inhibitor/substrate/active/positive/high-toxicity/sensitizer/carcinogens/corrosives/irritants (category 1) or non-inhibitor/non-substrate/inactive/negative/low-toxicity/non-sensitizer/non-carcinogens/noncorrosives/nonirritants (category 0). For the classification endpoints, the prediction probability values are transformed into six symbols: 0-0.1(---), 0.1-0.3(--), 0.3-0.5(-), 0.5-0.7(+), 0.7-0.9(++), and 0.9-1.0(+++).

COMPUTATIONAL DATA IN SUPPLEMENTARY INFORMATION

```
receptor = 3fyvDHFRB.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = 23.972
center_y = 17.083
center_z = 41.528

size_x = 30
size_y = 35
size_z = 30

energy_range = 4
exhaustiveness = 8
```

Figure S1. Grid box volume – Autodock Vina for Dihydrofolate Reductase – Bacteria (DHFR-B, PDB: 3FYV)

```
#############################################################################
# If you used AutoDock Vina in your work, please cite:                      #
#                                                                           #
# O. Trott, A. J. Olson,                                                    #
# AutoDock Vina: improving the speed and accuracy of docking                #
# with a new scoring function, efficient optimization and                   #
# multithreading, Journal of Computational Chemistry 31 (2010)              #
# 455-461                                                                   #
#                                                                           #
# DOI 10.1002/jcc.21334                                                     #
#                                                                           #
# Please see http://vina.scripps.edu for more information.                  #
#############################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1020872224
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.6      0.000      0.000
   2         -9.3      3.198      6.059
   3         -9.1      1.500      4.237
   4         -8.8      3.824      6.976
   5         -8.7      3.404      6.972
   6         -8.7      4.963      7.300
   7         -8.5      3.326      5.834
   8         -8.4      3.194      5.980
   9         -8.4      3.719      5.851
Writing output ... done.
```

Figure S2. Affinity result of compound **3k** with DHFR-B receptor

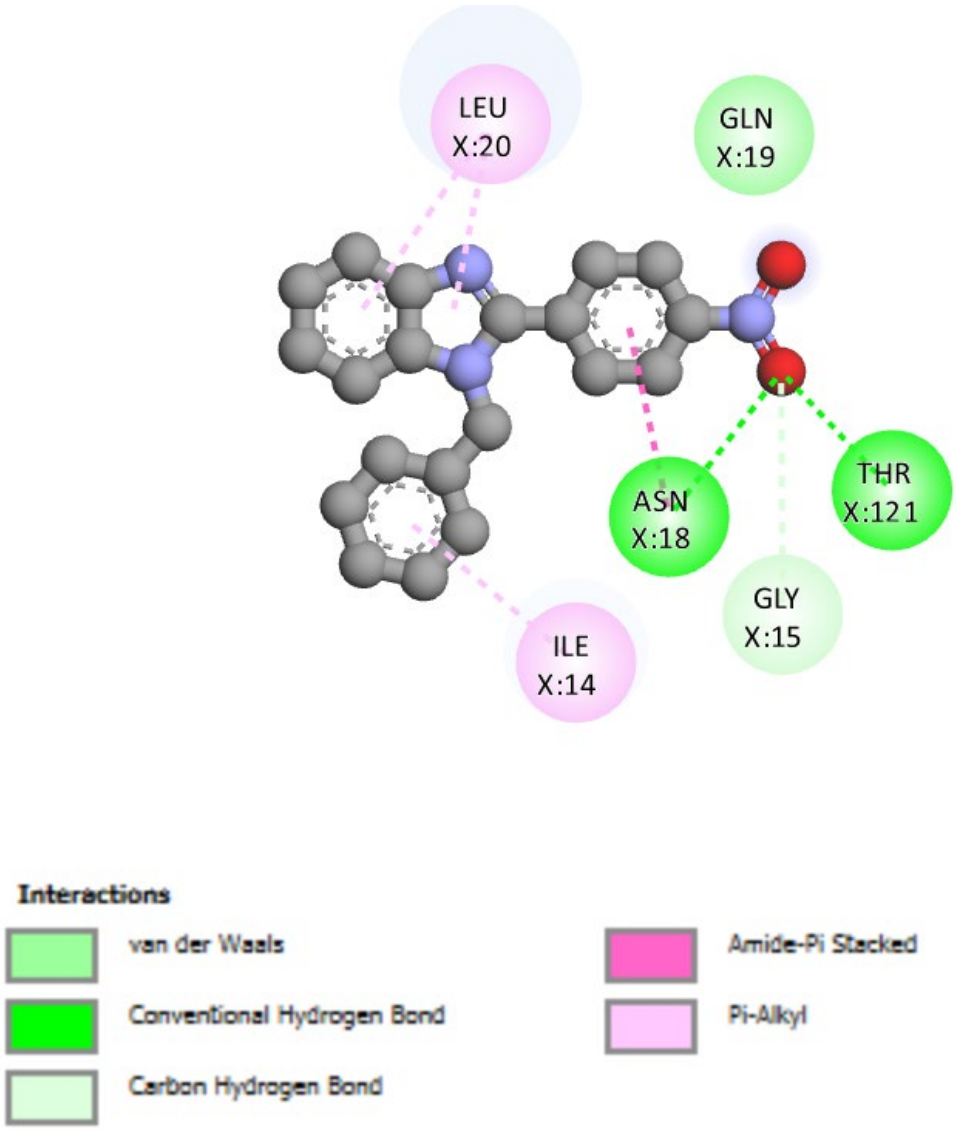


Figure S3. 2D representation of the interaction of compound **3k** with DHFR-B receptor

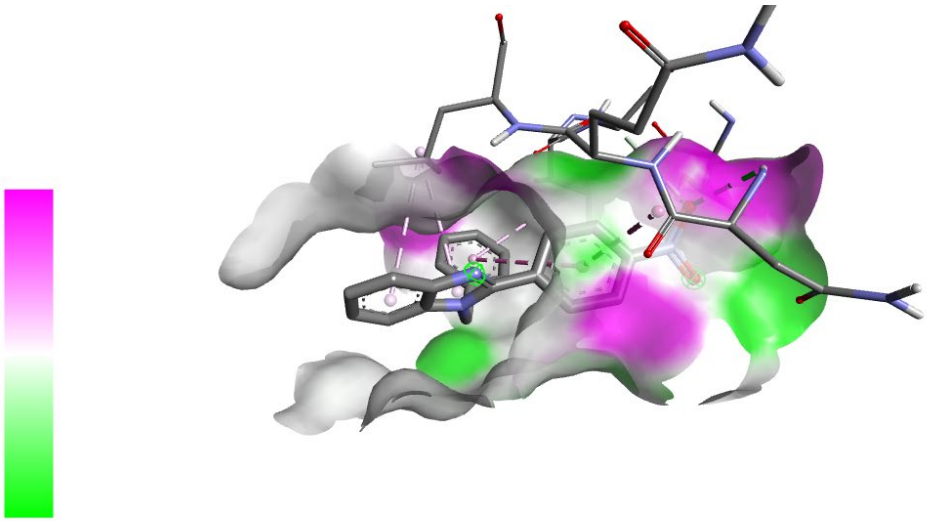


Figure S4. 3D representation of the interaction of compound **3k** with DHFR-B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -978072136
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.5      0.000      0.000
   2         -8.9      3.012      4.587
   3         -8.8      2.807      6.409
   4         -8.8      4.056      5.934
   5         -8.6      2.934      6.008
   6         -8.5      2.120      5.350
   7         -8.5      2.625      5.946
   8         -8.2      3.583      6.504
   9         -8.0      3.467      7.601
Writing output ... done.
```

Figure S5. Affinity result of compound **3l** with DHFR-B receptor

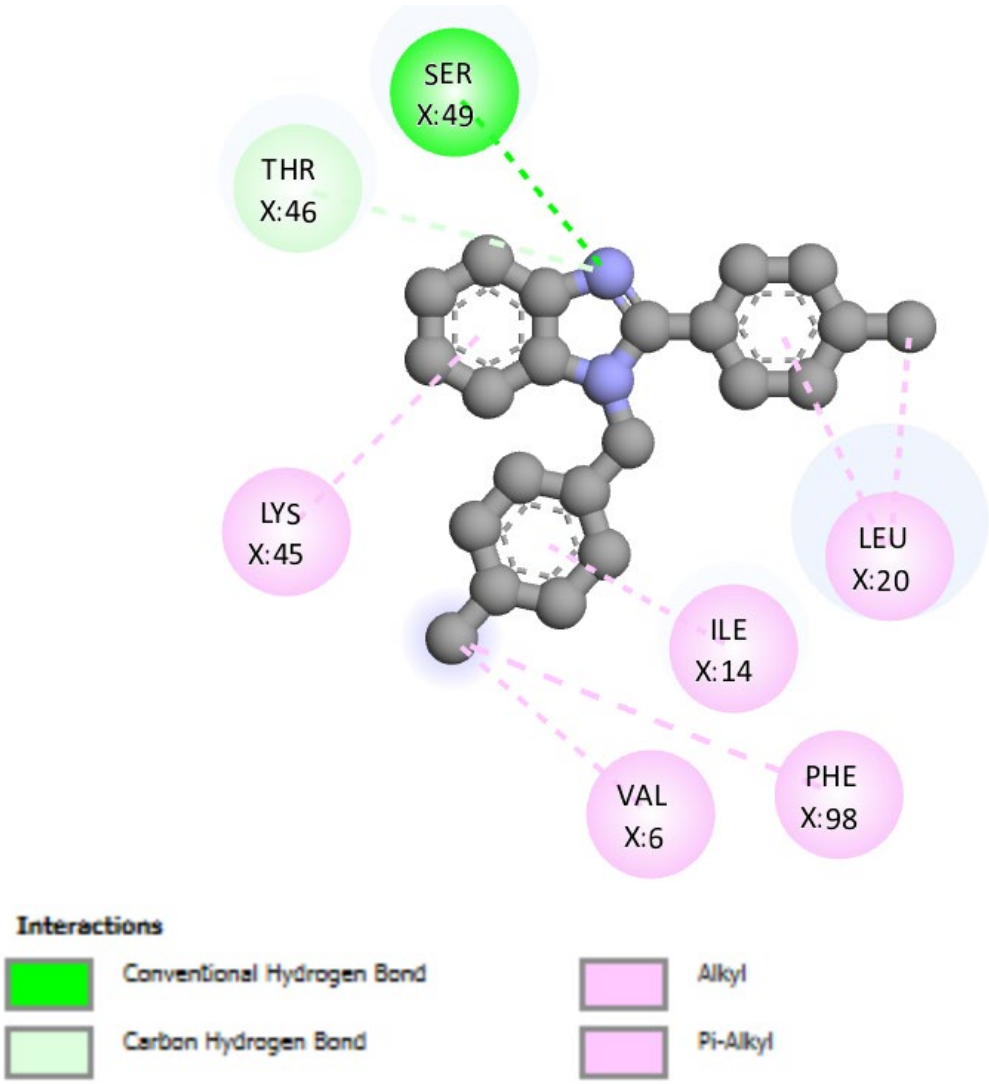


Figure S6. 2D representation of the interaction of compound **3l** with DHFR-B receptor

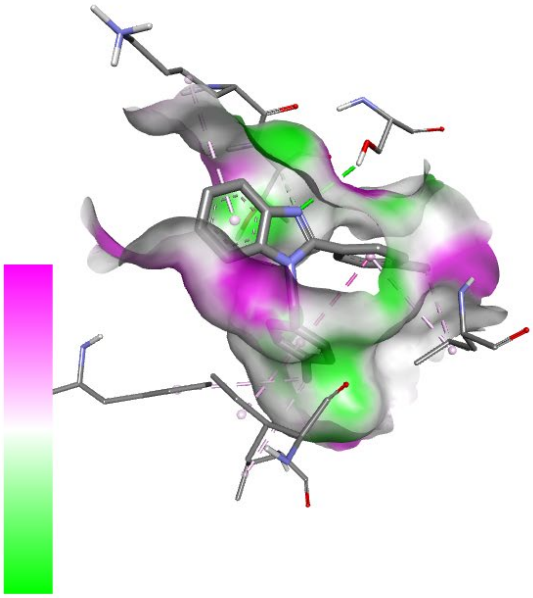


Figure S7. 3D representation of the interaction of compound **3l** with DHFR-B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1588645616
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.0      0.000      0.000
   2         -9.7      1.932      3.027
   3         -9.4      3.393      6.807
   4         -9.2      2.874      5.585
   5         -9.1      2.765      5.703
   6         -9.0      1.428      4.429
   7         -8.9      4.115      6.919
   8         -8.8      2.143      3.275
   9         -8.6      4.413      8.059
Writing output ... done.
```

Figure S8. Affinity result of compound **4c** with DHFR-B receptor

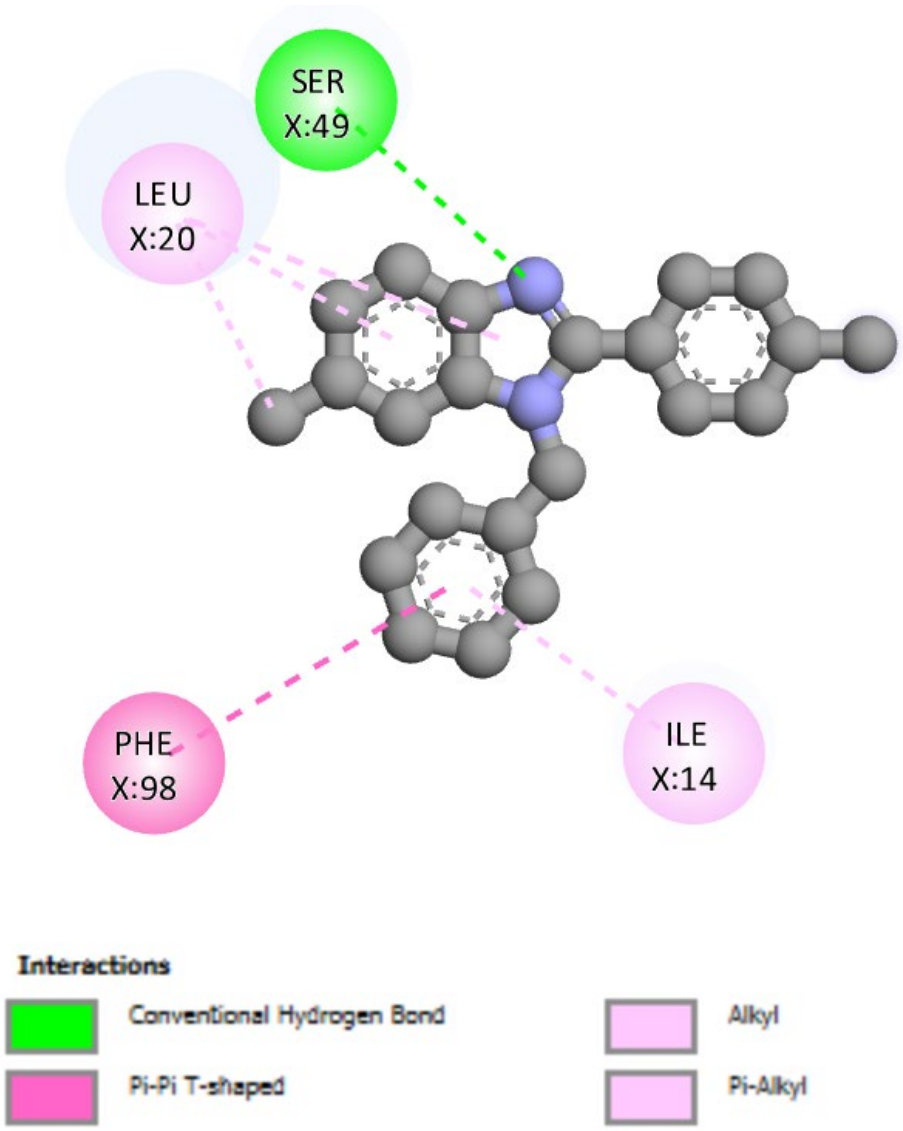


Figure S9. 2D representation of the interaction of compound **4c** with DHFR-B receptor

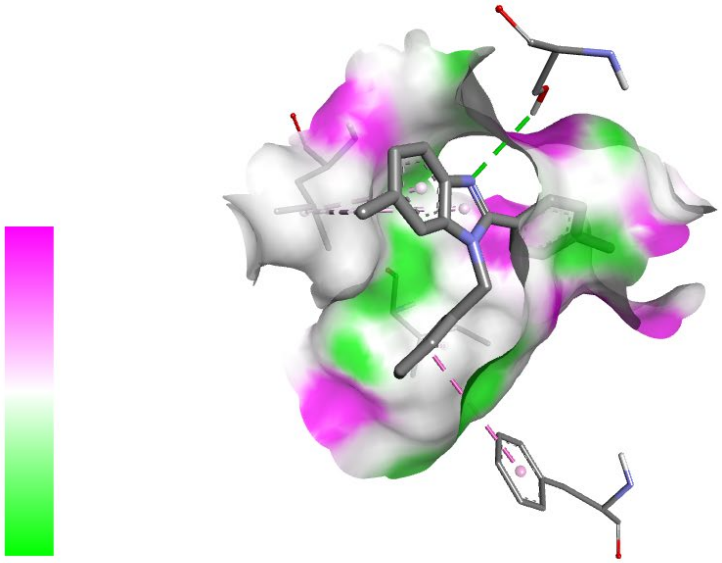


Figure S10. 3D representation of the interaction of compound **4c** with DHFR-B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 2107646336
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.0      0.000      0.000
   2         -9.4      1.675      4.040
   3         -9.3      1.967      2.871
   4         -9.0      1.005      1.779
   5         -8.9      3.425      6.797
   6         -8.9      3.659      6.461
   7         -8.8      1.853      4.165
   8         -8.7      3.442      6.342
   9         -8.5      4.390      6.854
Writing output ... done.
```

Figure S11. Affinity result of compound **4g** with DHFR-B receptor

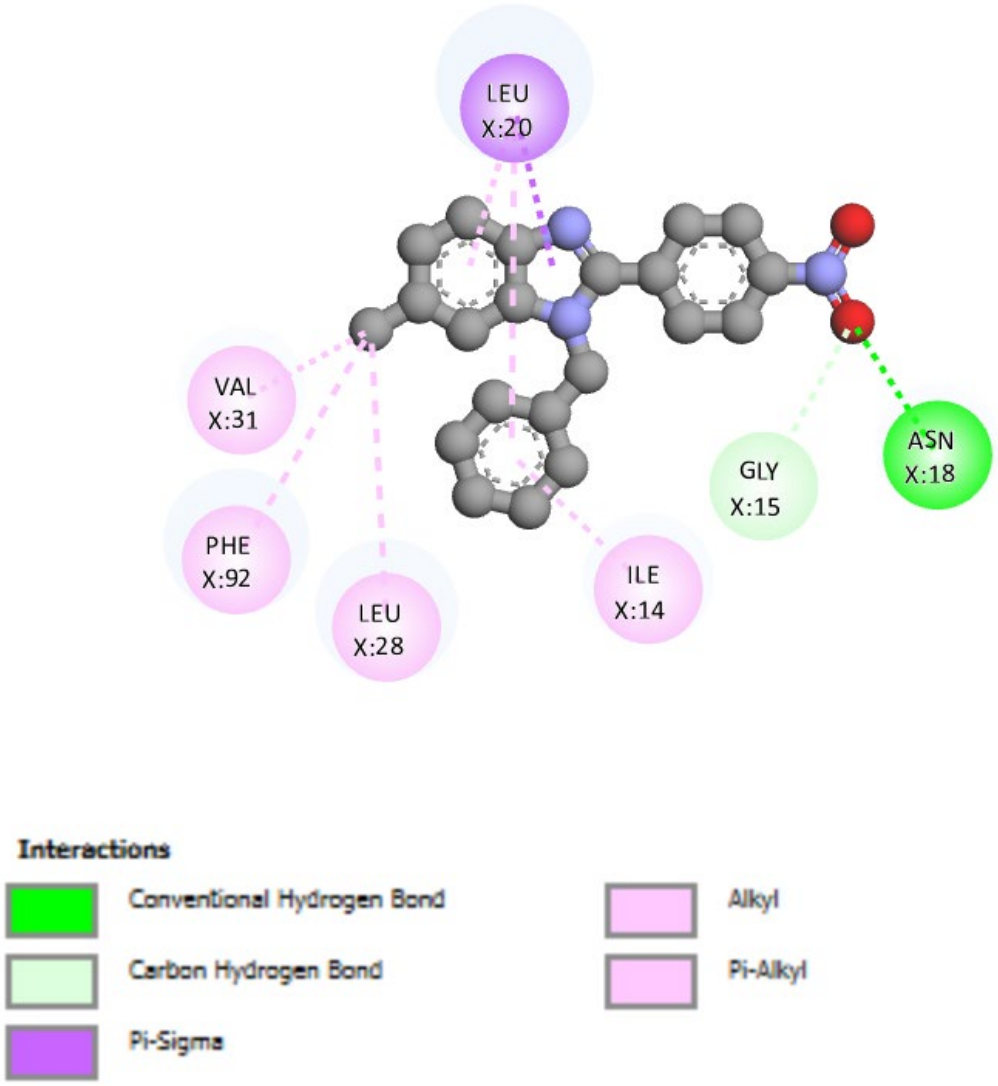


Figure S12. 2D representation of the interaction of compound **4g** with DHFR-B receptor

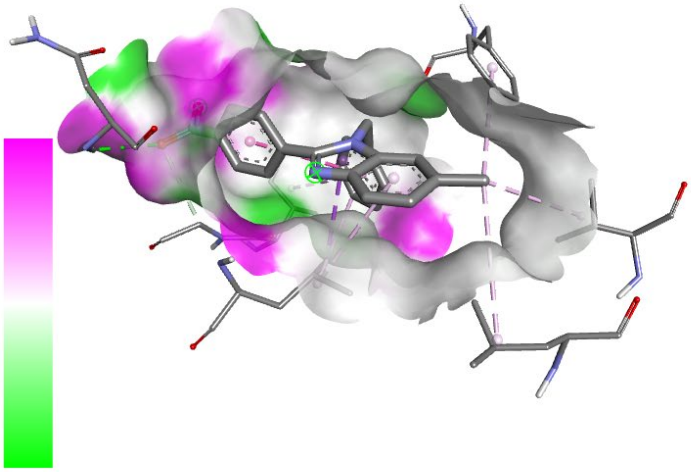


Figure S13. 3D representation of the interaction of compound **4g** with DHFR-B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1457842096
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.9      0.000      0.000
   2         -9.6      3.813      6.936
   3         -9.6      2.571      5.008
   4         -9.5      2.752      4.993
   5         -9.4      1.849      2.617
   6         -9.4      5.752      8.717
   7         -9.3      4.164      6.541
   8         -9.0      2.744      5.240
   9         -8.7      5.202      8.012
Writing output ... done.
```

Figure S14. Affinity result of compound **4j** with DHFR-B receptor

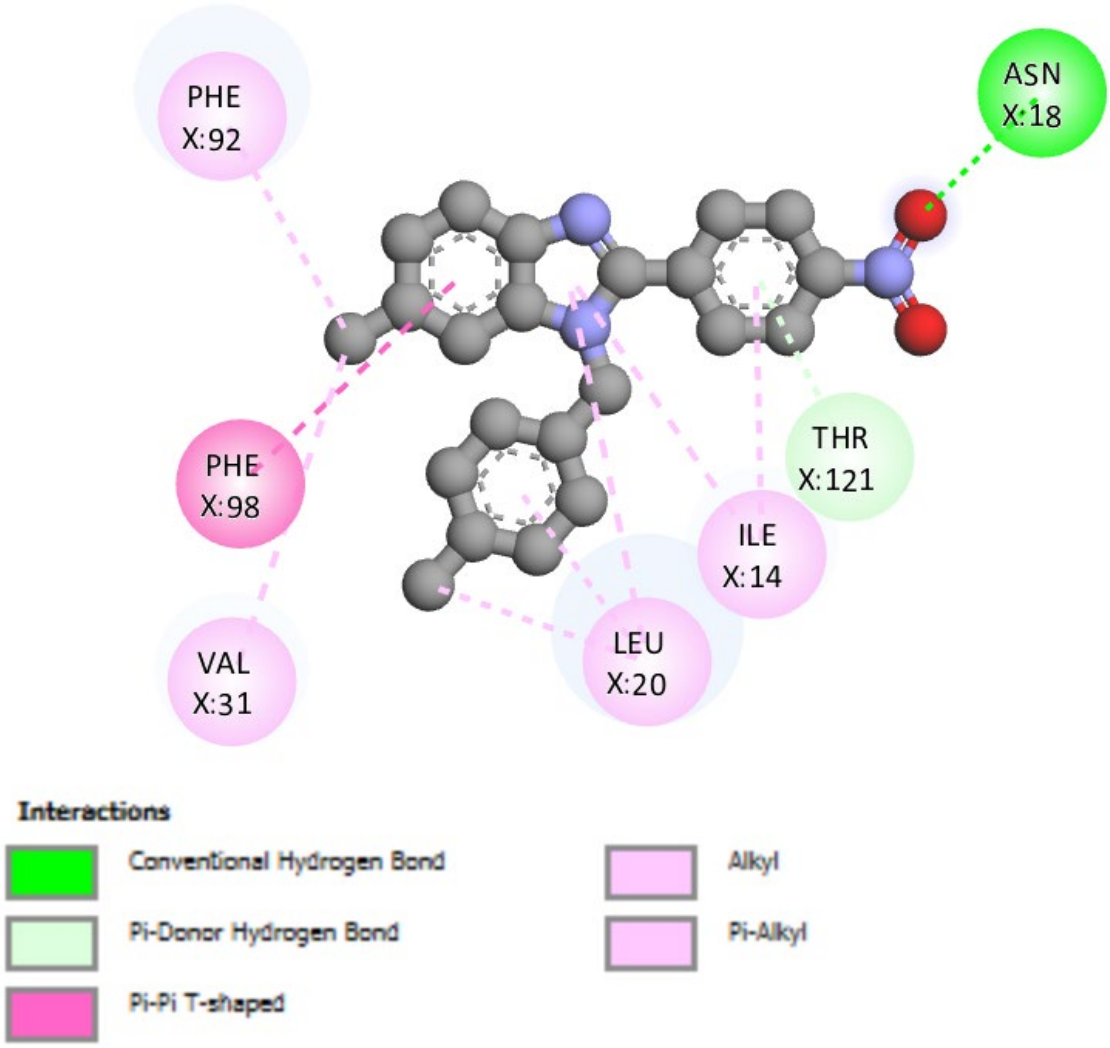


Figure S15. 2D representation of the interaction of compound **4j** with DHFR-B receptor

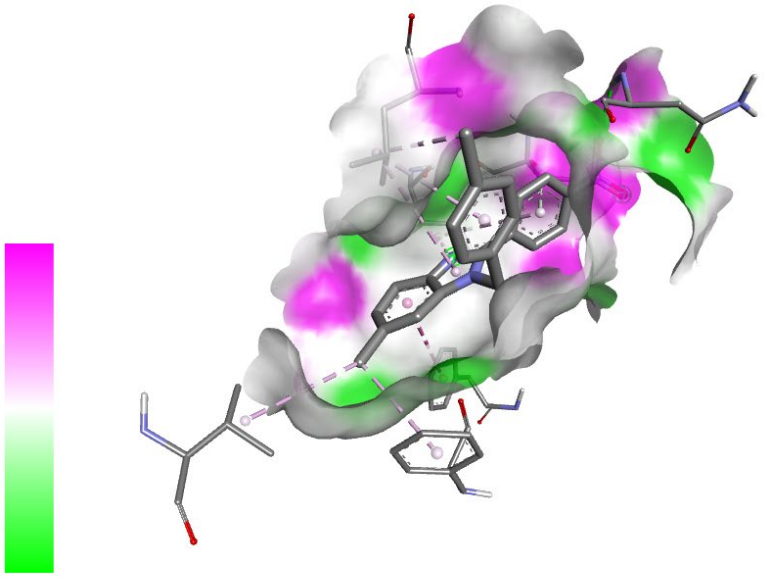


Figure S16. 3D representation of the interaction of compound **4j** with DHFR-B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -215246968
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.1      0.000      0.000
   2         -8.7      3.423      6.648
   3         -8.6      3.981      7.327
   4         -8.4      3.575      6.566
   5         -8.1      2.874      4.619
   6         -8.0      4.052      5.964
   7         -7.8      4.025      7.178
   8         -7.7      8.845     12.410
   9         -7.6      3.533      6.043
Writing output ... done.
```

Figure S17. Affinity result of compound **Cipro** with DHFR-B receptor

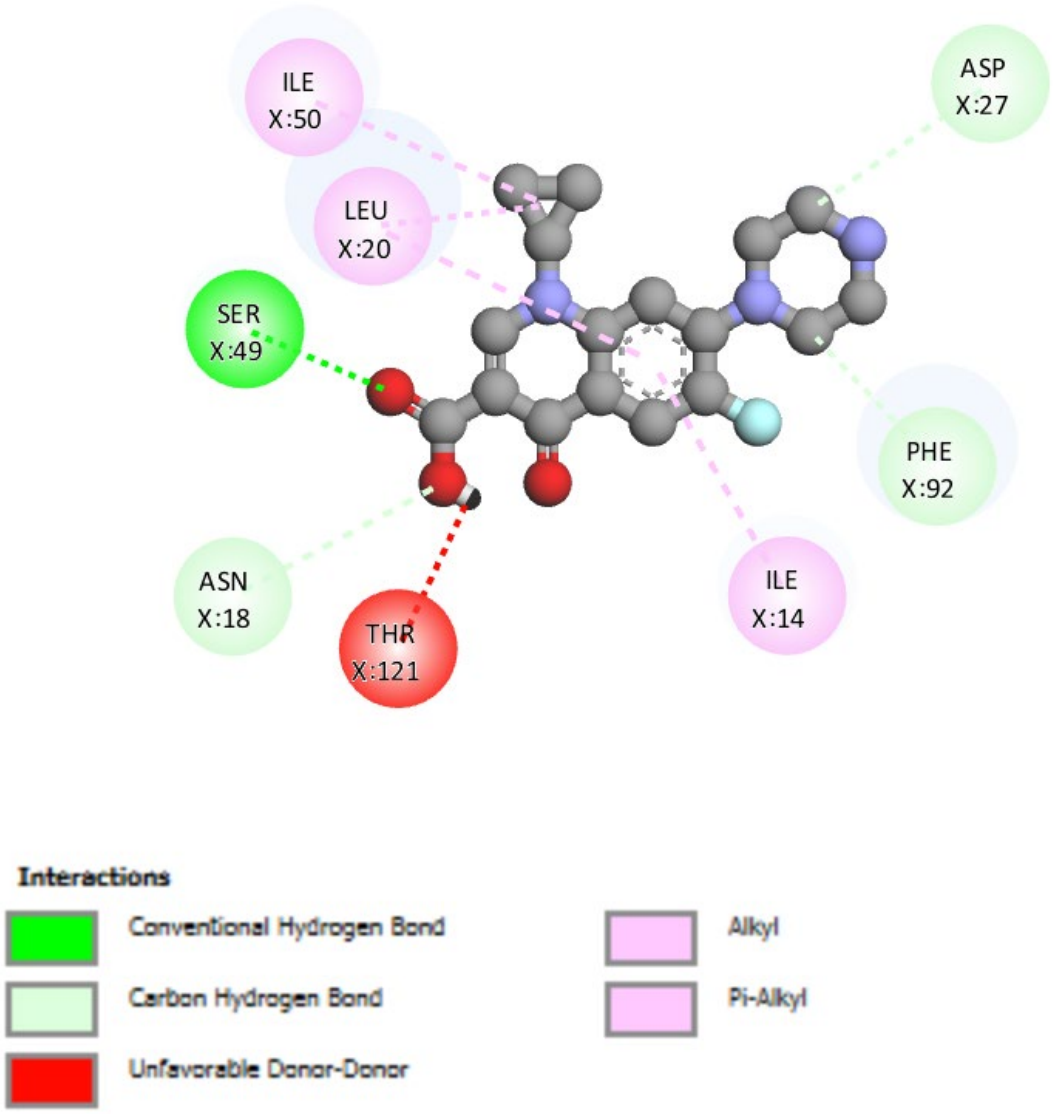


Figure S18. 2D representation of the interaction of compound **Cipro** with DHFR-B receptor

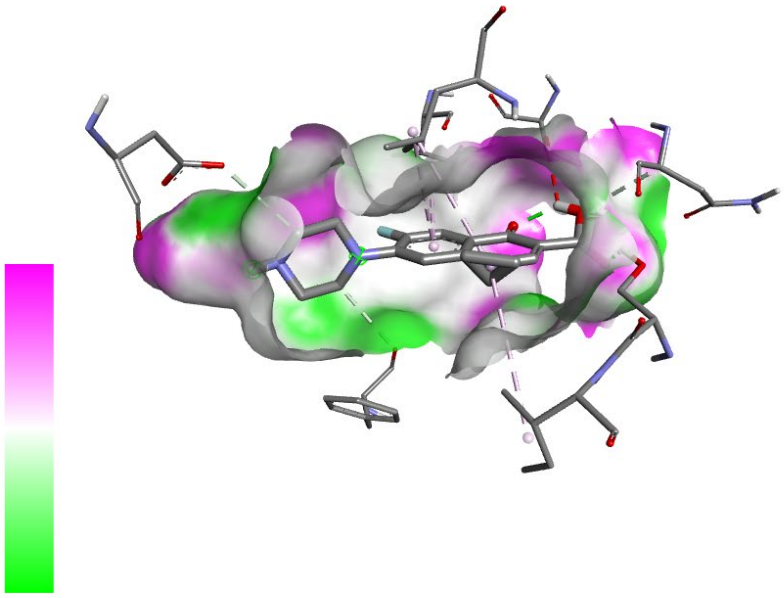


Figure S19. 3D representation of the interaction of compound **Cipro** with DHFR-B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2051321328
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.0      0.000      0.000
   2         -8.1      1.596      5.444
   3         -8.1      0.944      3.622
   4         -8.0     10.018     18.422
   5         -7.6     10.188     17.799
   6         -7.5      8.739     18.280
   7         -7.3      2.112      5.745
   8         -7.2     10.636     19.300
   9         -7.1      2.459      7.199
Writing output ... done.
```

Figure S20. Affinity result of compound **PTX** with DHFR-B receptor

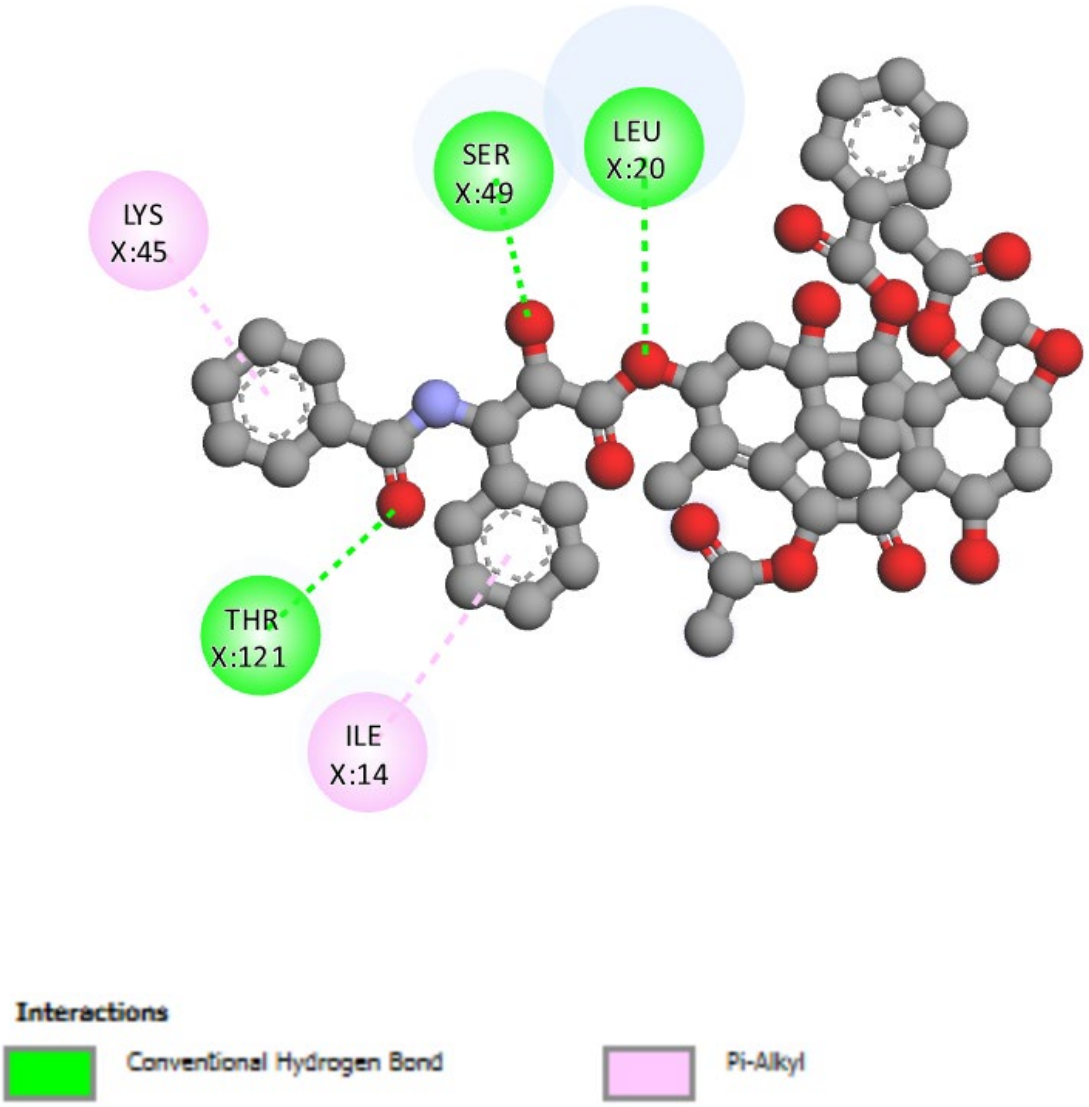


Figure S21. 2D representation of the interaction of compound **PTX** with DHFR-B receptor

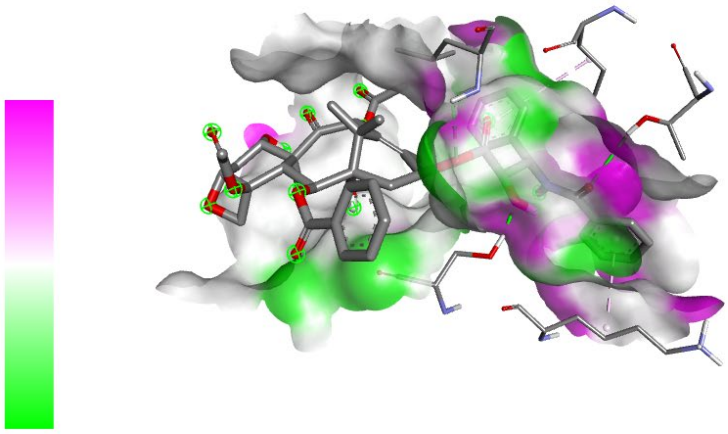


Figure S22. 3D representation of the interaction of compound **PTX** with DHFR-B receptor

```
receptor = 4urmGyrB.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = 23.9228
center_y = 7.94566
center_z = 90.4085

size_x = 30
size_y = 30
size_z = 30

energy_range = 4
exhaustiveness = 8
```

Figure S23. Grid box volume – Autodock Vina for Gyrase B (PDB: 4URM)

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 430978864
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.0      0.000      0.000
   2         -8.0      3.568      6.612
   3         -8.0      1.792      2.954
   4         -7.6      2.111      2.879
   5         -7.6      3.363      6.042
   6         -7.4      1.661      2.690
   7         -7.3      2.122      4.793
   8         -7.3      3.578      6.389
   9         -6.9      4.070      6.343
Writing output ... done.
```

Figure S24. Affinity result of compound **3k** with Gyrase B receptor

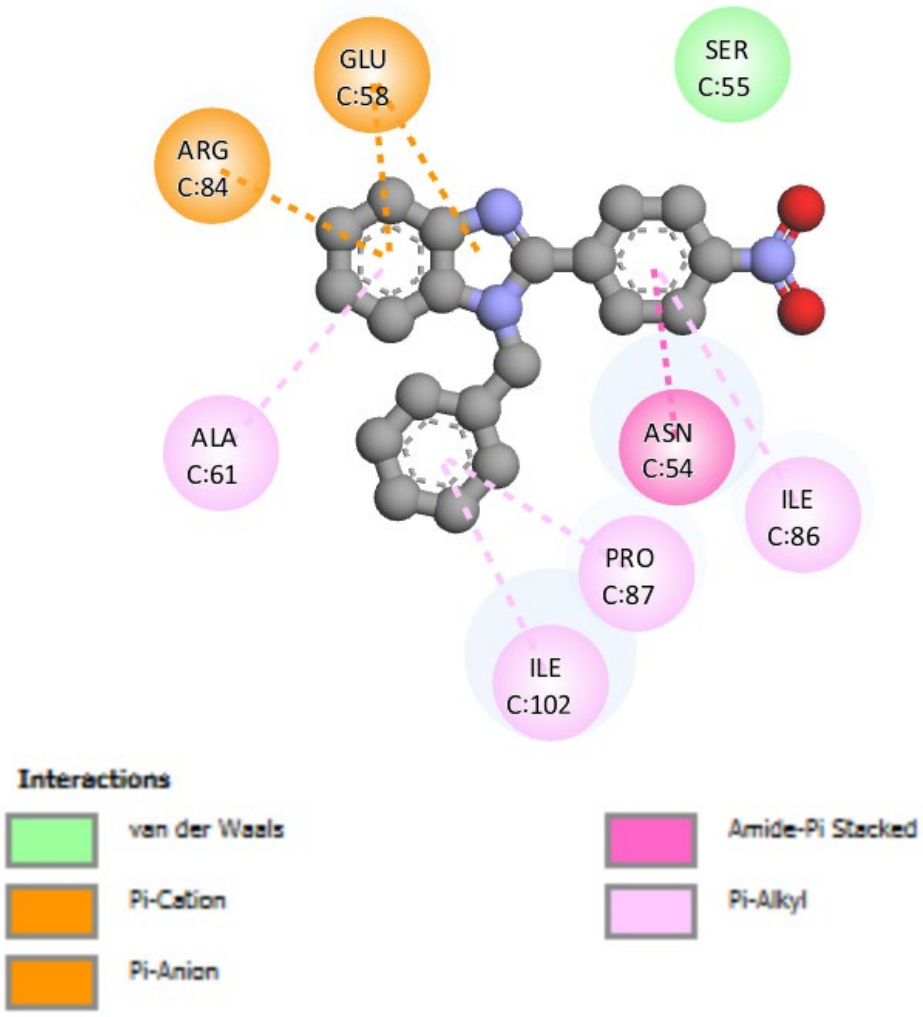


Figure S25. 2D representation of the interaction of compound **3k** with Gyrase B receptor

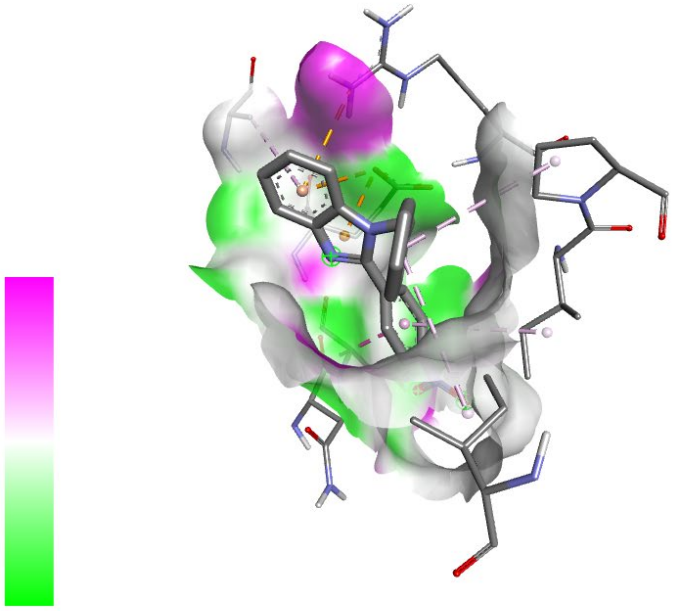


Figure S26. 3D representation of the interaction of compound **3k** with Gyrase B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1457996380
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.9      0.000      0.000
   2         -7.7      2.982      6.097
   3         -7.4      1.910      4.086
   4         -7.0      3.343      6.568
   5         -6.7      2.924      4.574
   6         -6.6      2.863      6.584
   7         -6.5      1.892      2.813
   8         -6.5      3.080      6.069
   9         -6.4      3.077      4.784
Writing output ... done.
```

Figure S27. Affinity result of compound **3l** with Gyrase B receptor

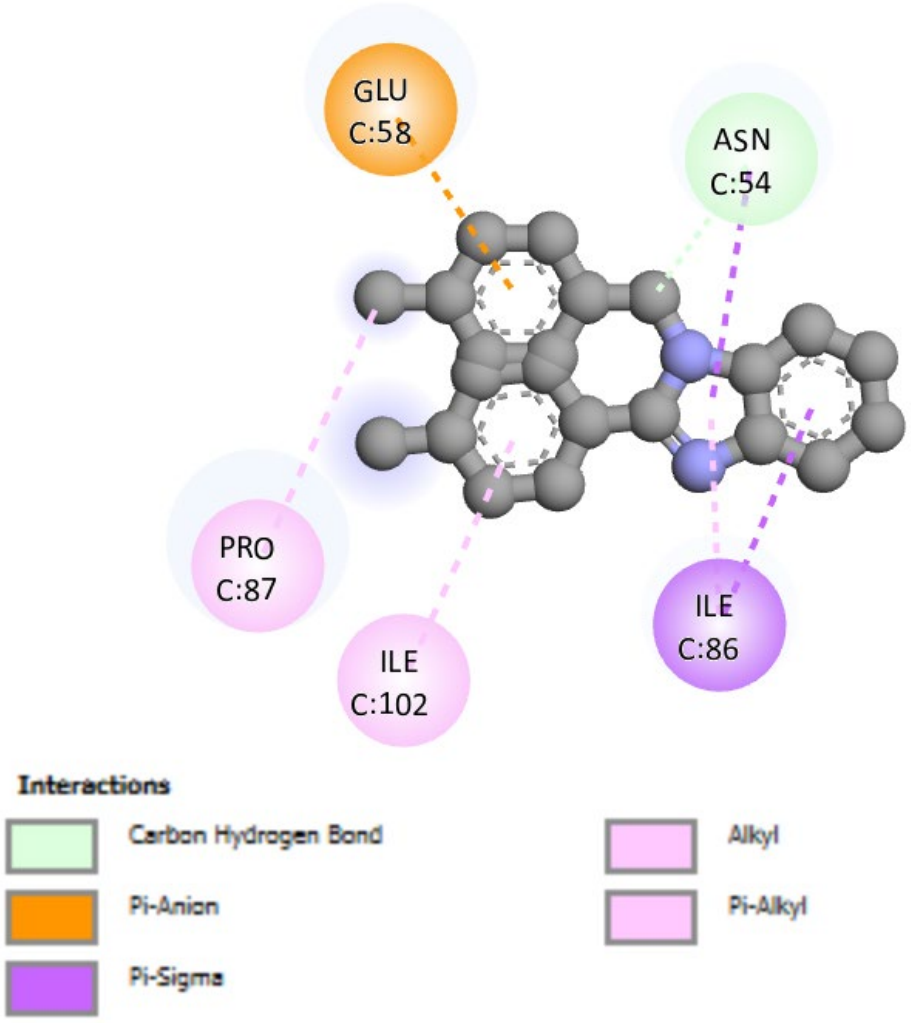


Figure S28. 2D representation of the interaction of compound **3l** with Gyrase B receptor

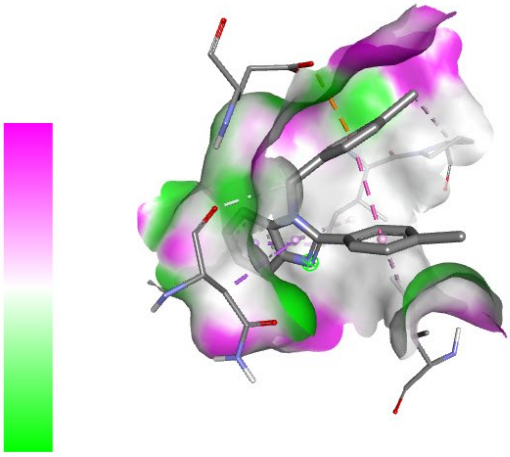


Figure S29. 3D representation of the interaction of compound **3l** with Gyrase B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1163912448
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.9      0.000      0.000
   2         -7.7      1.605      4.096
   3         -7.5      2.886      6.687
   4         -7.4      3.164      6.770
   5         -7.4      1.387      2.227
   6         -7.2      1.771      3.695
   7         -7.1      2.918      6.518
   8         -7.0      3.124      6.436
   9         -6.8      3.395      7.196
Writing output ... done.
```

Figure S30. Affinity result of compound **4c** with Gyrase B receptor

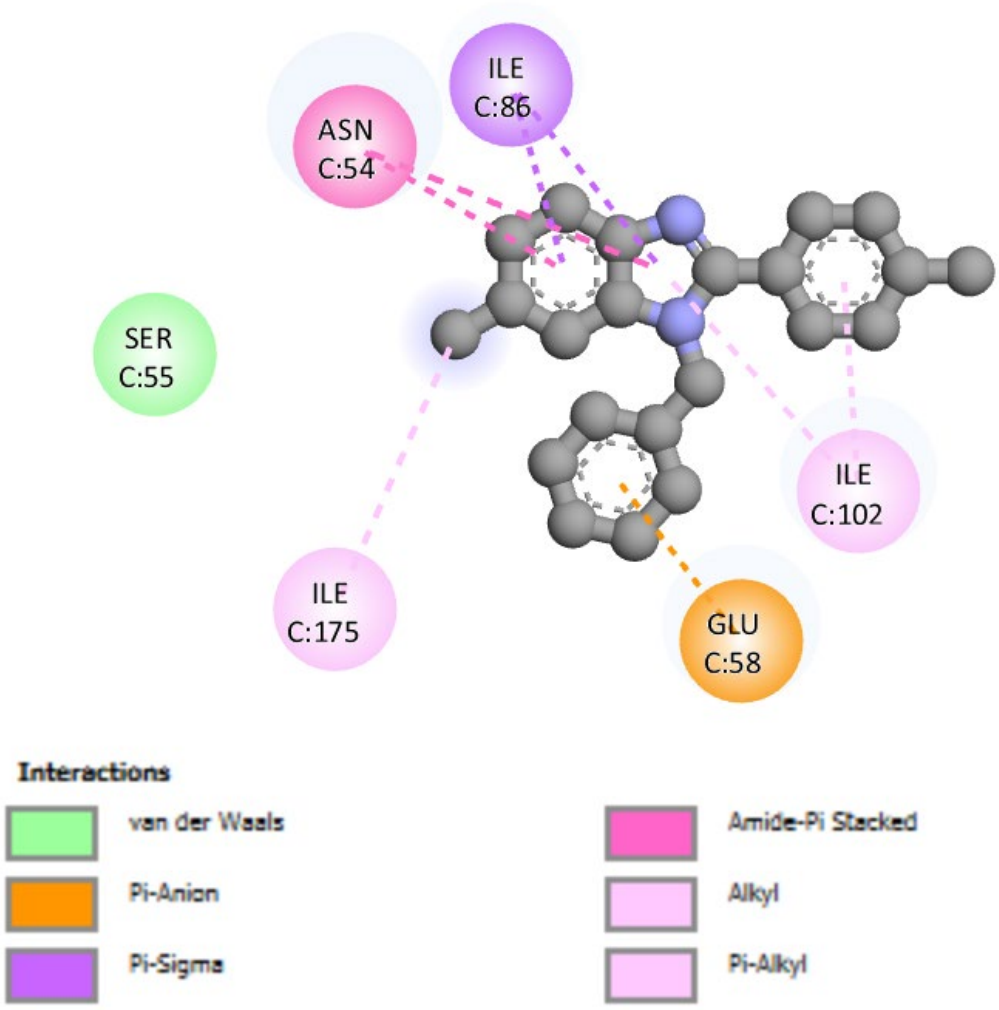


Figure S31. 2D representation of the interaction of compound **4c** with Gyrase B receptor

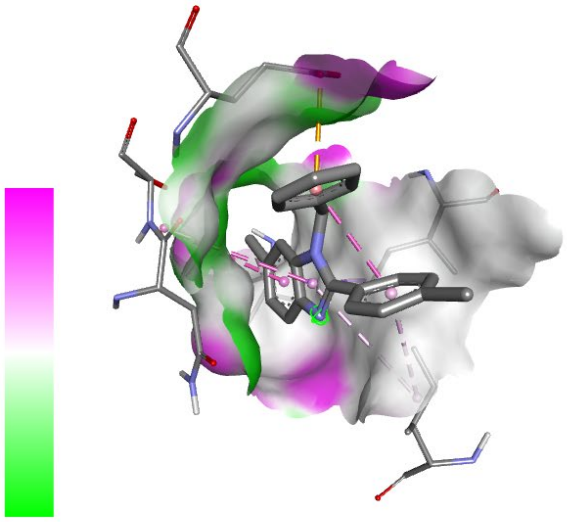


Figure S32. 3D representation of the interaction of compound **4c** with Gyrase B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2027696004
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.1      0.000      0.000
   2         -8.1      1.337      2.255
   3         -8.1      2.351      3.963
   4         -8.0      3.919      7.011
   5         -7.9      1.378      3.994
   6         -7.8      3.918      6.908
   7         -7.1      4.004      7.204
   8         -7.0      4.264      7.370
   9         -6.5      4.032      7.482
Writing output ... done.
```

Figure S33. Affinity result of compound **4g** with Gyrase B receptor

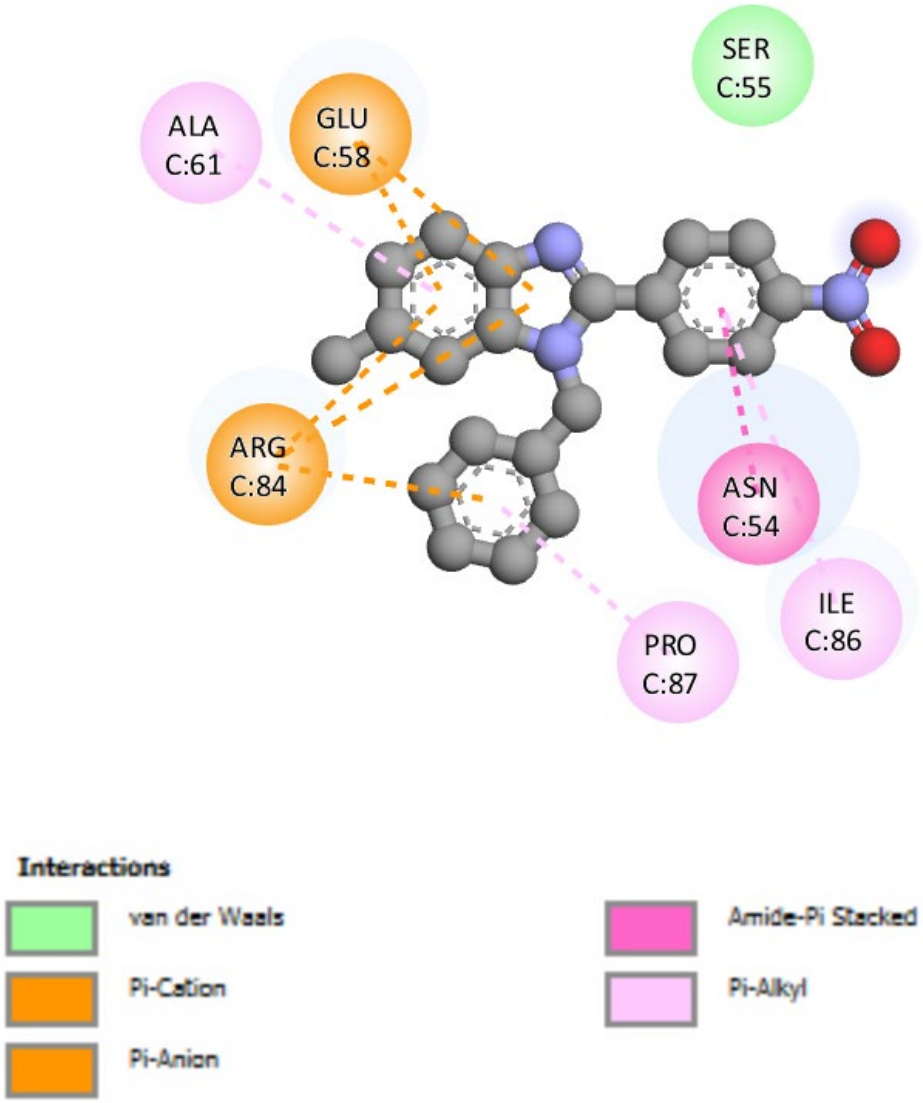


Figure S34. 2D representation of the interaction of compound **4g** with Gyrase B receptor

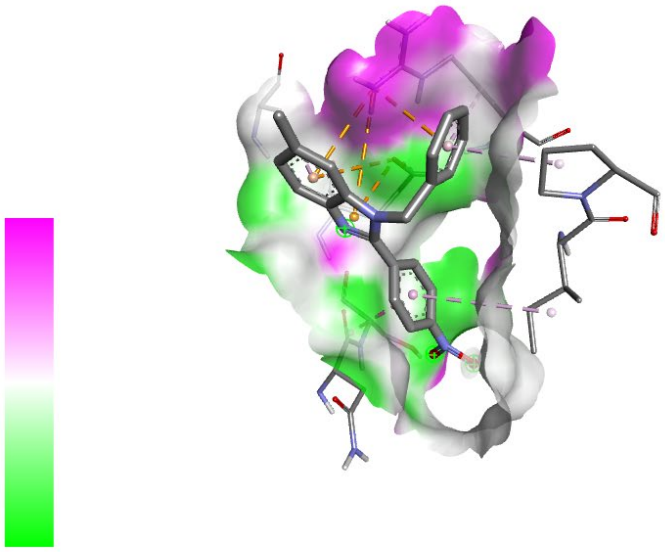


Figure S35. 3D representation of the interaction of compound **4g** with Gyrase B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 626833024
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.0      0.000      0.000
   2         -7.9      3.846      6.889
   3         -7.7      2.520      4.131
   4         -7.5      1.465      1.880
   5         -7.3      1.038      1.527
   6         -7.0      2.972      4.674
   7         -6.9      3.932      6.965
   8         -6.7      2.774      4.505
   9         -6.6      3.942      7.043
Writing output ... done.
```

Figure S36. Affinity result of compound **4j** with Gyrase B receptor

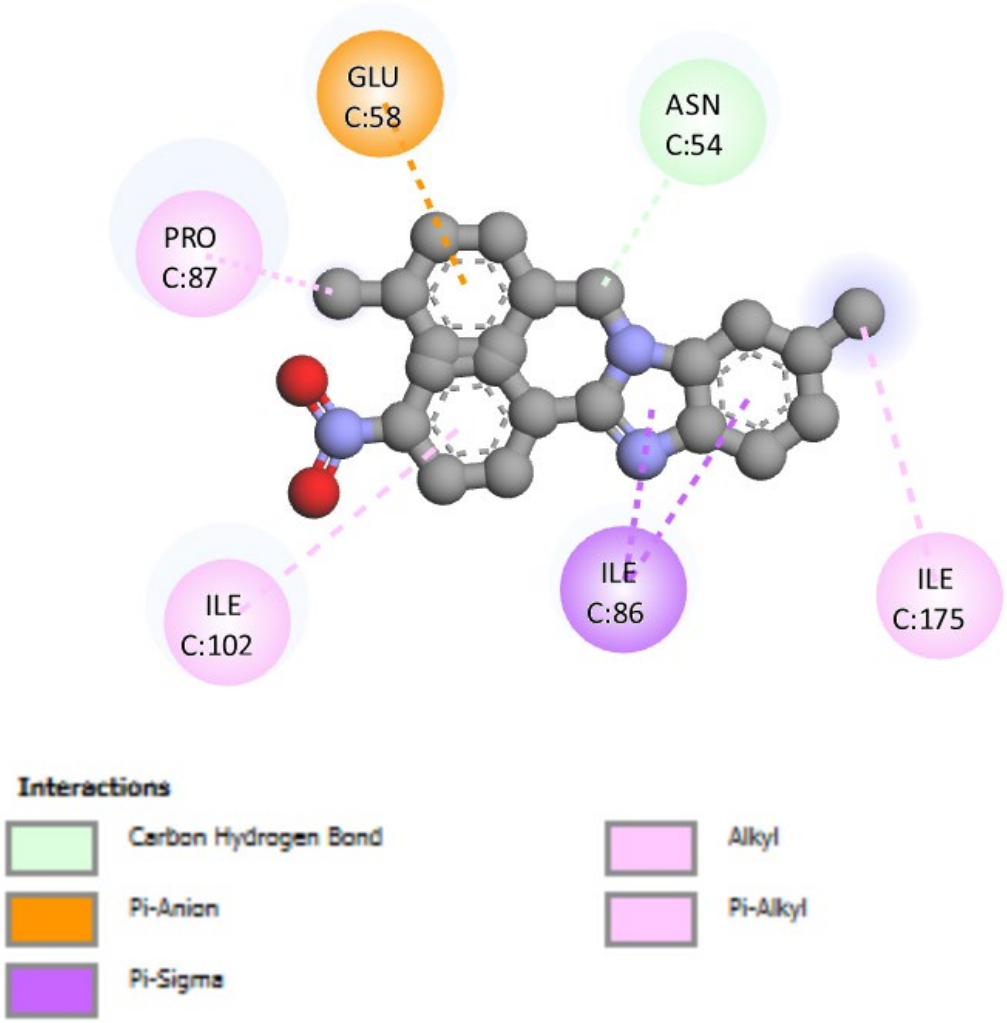


Figure S37. 2D representation of the interaction of compound **4j** with Gyrase B receptor

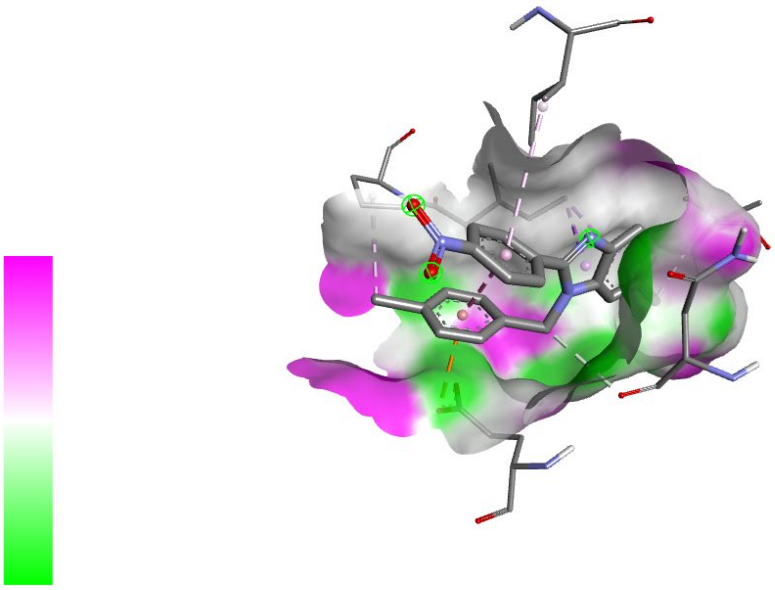


Figure S38. 3D representation of the interaction of compound **4j** with Gyrase B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -260904248
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.3      0.000      0.000
   2         -6.9      2.891      4.494
   3         -6.8      3.615      6.726
   4         -6.8      2.343      3.878
   5         -6.3      3.850      7.243
   6         -6.3      4.582      7.334
   7         -6.1      4.079      7.491
   8         -6.1      5.292      8.112
   9         -5.9      4.651      7.100
Writing output ... done.
```

Figure S39. Affinity result of compound **Cipro** with Gyrase B receptor

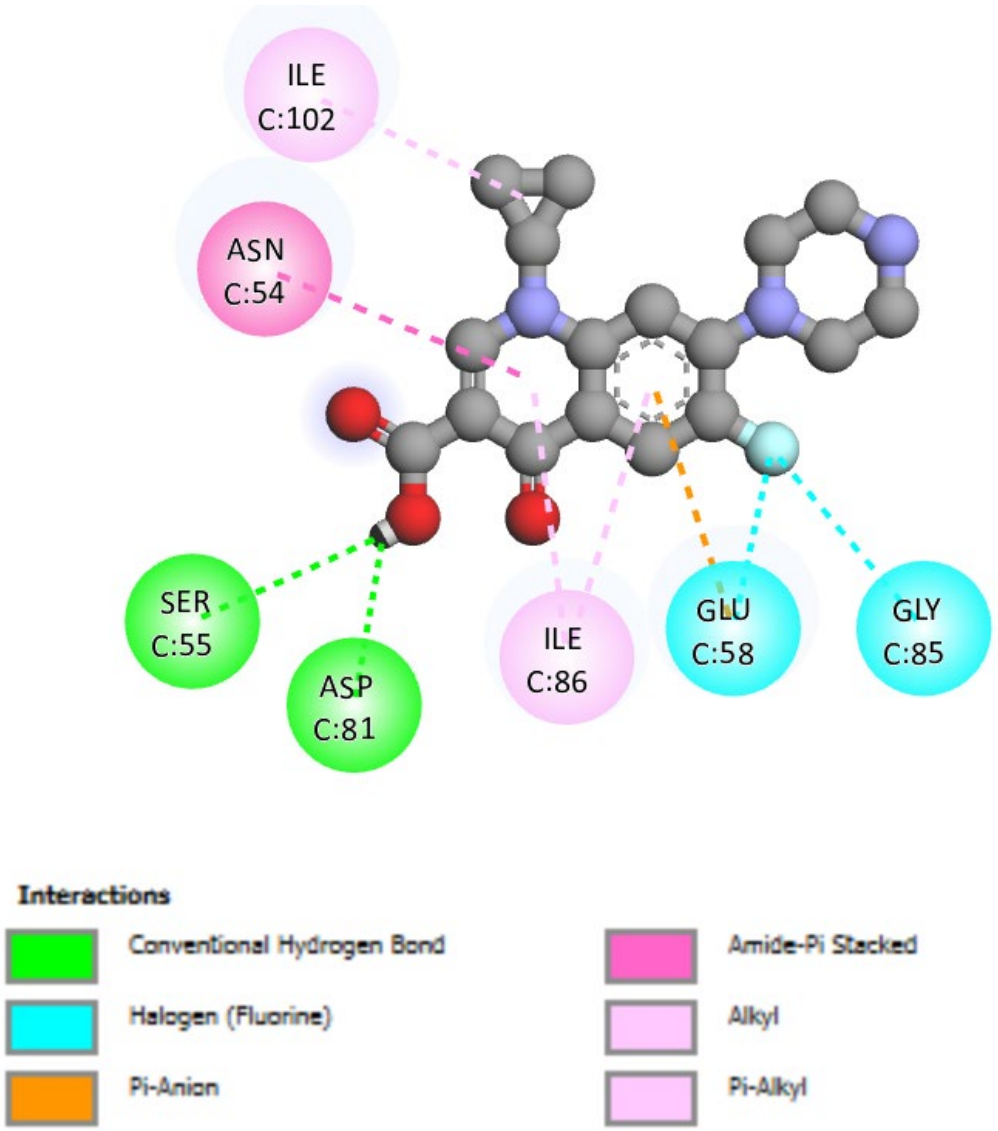


Figure S40. 2D representation of the interaction of compound **Cipro** with Gyrase B receptor

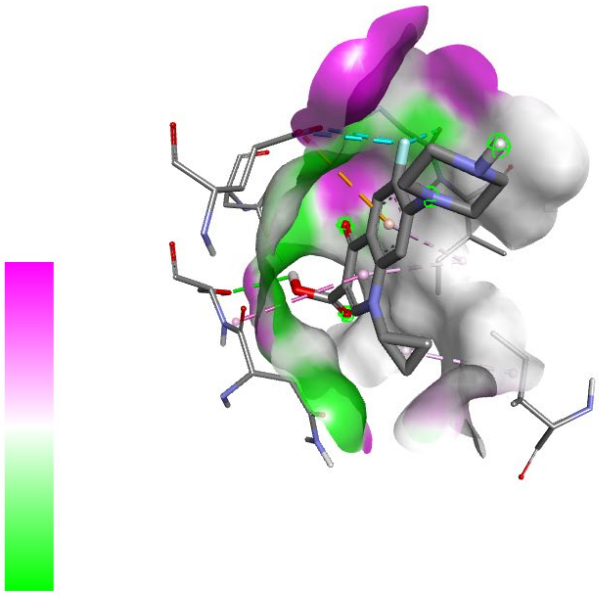


Figure S41. 3D representation of the interaction of compound **Cipro** with Gyrase B receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 934984084
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.8      0.000      0.000
   2         -7.6      2.335      4.921
   3         -7.5      2.945      8.770
   4         -7.4      3.629      9.582
   5         -7.4      3.099      6.925
   6         -7.3      2.977      7.101
   7         -7.3      4.177     10.014
   8         -7.3      3.805      7.256
   9         -7.2      2.564      5.400
Writing output ... done.
```

Figure S42. Affinity result of compound **PTX** with Gyrase B receptor

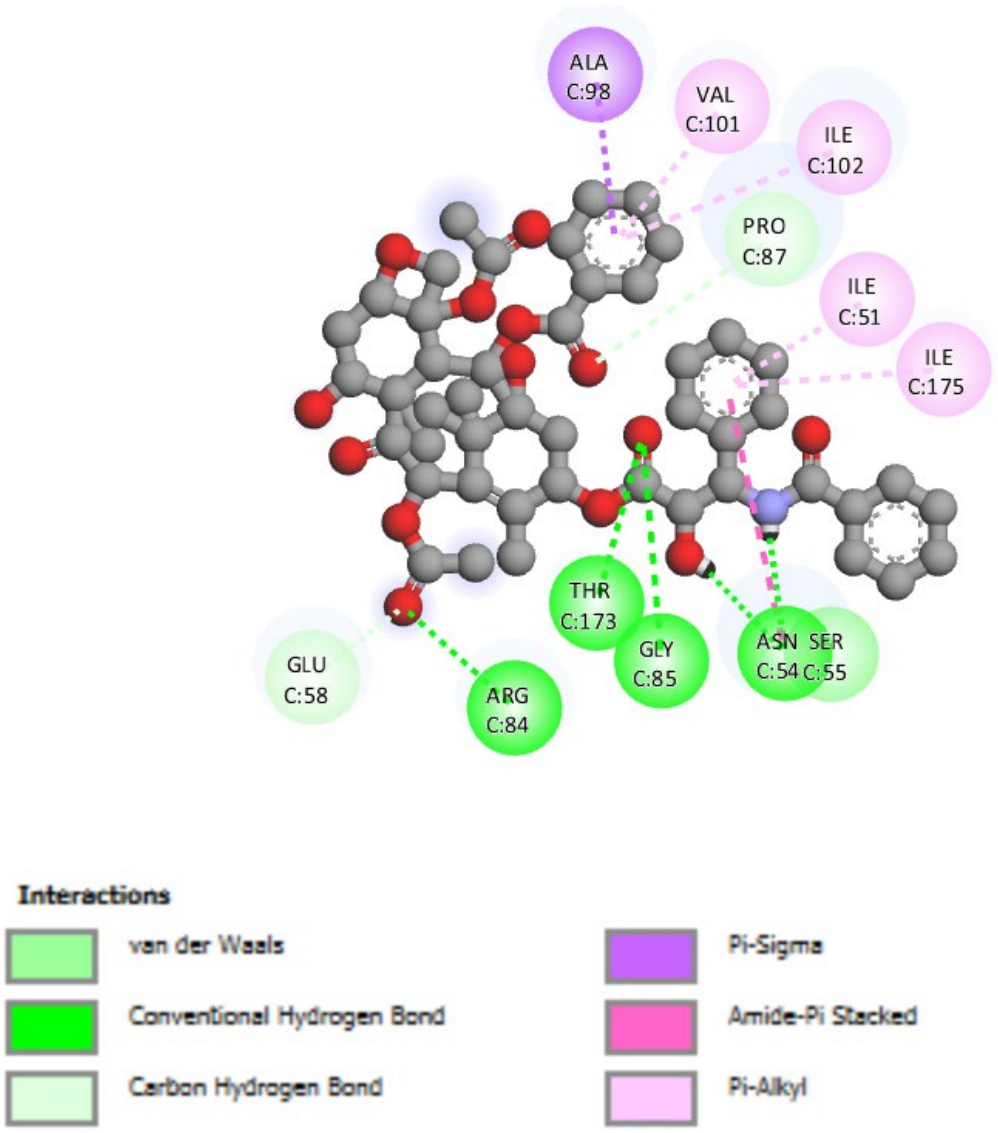


Figure S43. 2D representation of the interaction of compound **PTX** with Gyrase B receptor

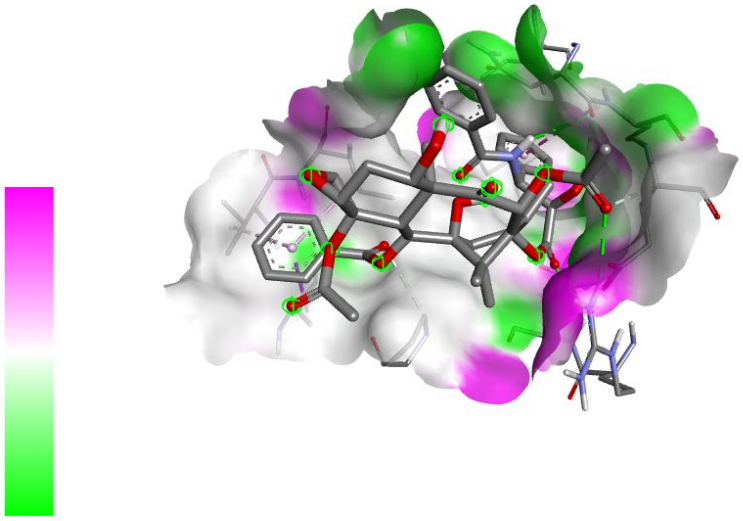


Figure S44. 3D representation of the interaction of compound **PTX** with Gyrase B receptor

```
receptor = 4hofDHFRF.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = 11.44
center_y = -32.6283
center_z = 17.3865

size_x = 30
size_y = 30
size_z = 30

energy_range = 4

exhaustiveness = 8
```

Figure S45. Grid box volume – Autodock Vina for Dihydrofolate Reductase - Fungi (DHFR-F, PDB: 4HOF)

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2067082648
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.5      0.000      0.000
   2         -8.2      3.261      4.505
   3         -8.1     10.784     14.348
   4         -7.9     16.051     19.048
   5         -7.9     12.067     14.718
   6         -7.5      3.930      6.281
   7         -7.3     12.387     15.308
   8         -7.1     14.092     17.415
   9         -6.9      3.783      5.848
Writing output ... done.
```

Figure S46. Affinity result of compound **3k** with DHFR-F receptor

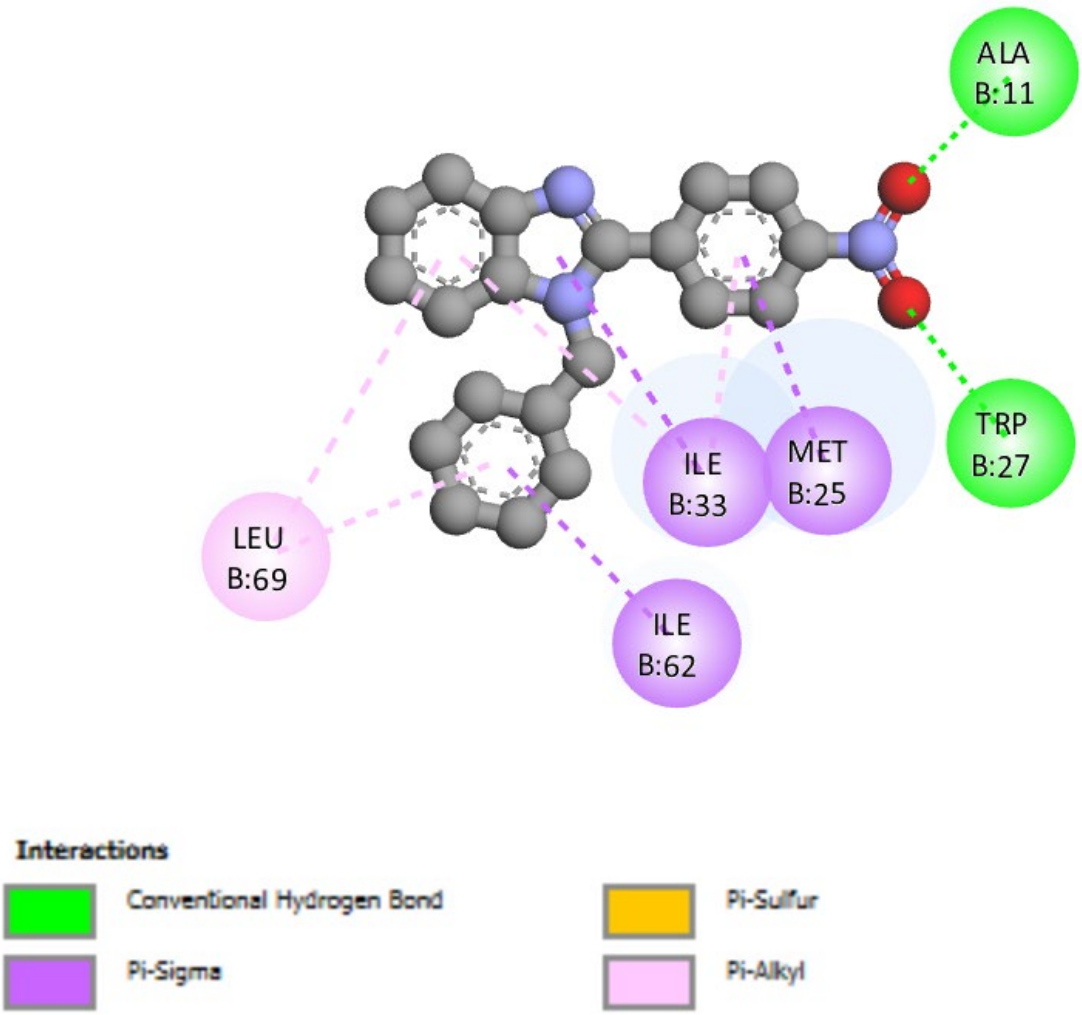


Figure S47. 2D representation of the interaction of compound **3k** with DHFR-F receptor

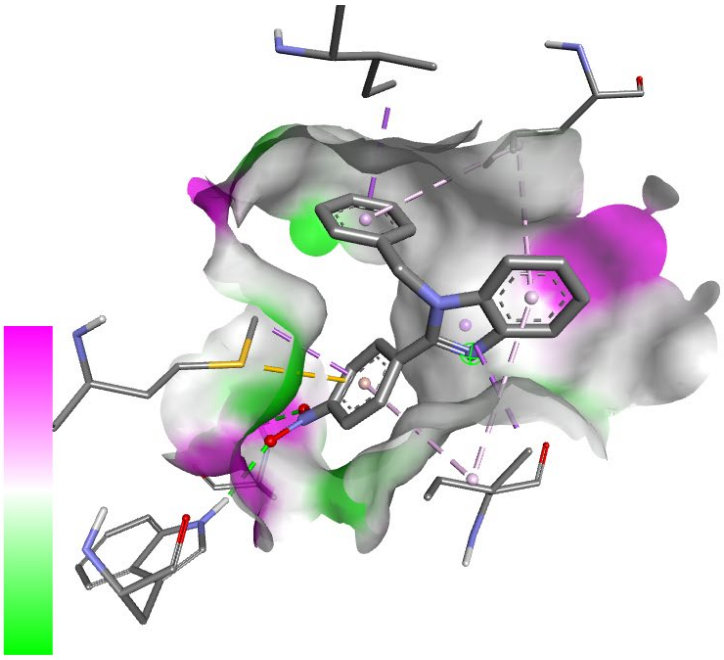


Figure S48. 3D representation of the interaction of compound **3k** with DHFR-F receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1071739692
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.0      0.000      0.000
   2         -7.9     11.677     14.547
   3         -7.9     11.242     13.573
   4         -7.9      2.162      5.027
   5         -7.9     12.540     15.231
   6         -7.8     11.774     15.304
   7         -7.8     12.500     14.687
   8         -7.7      2.505      6.069
   9         -7.7      6.188      9.653
Writing output ... done.
```

Figure S49. Affinity result of compound **3l** with DHFR-F receptor

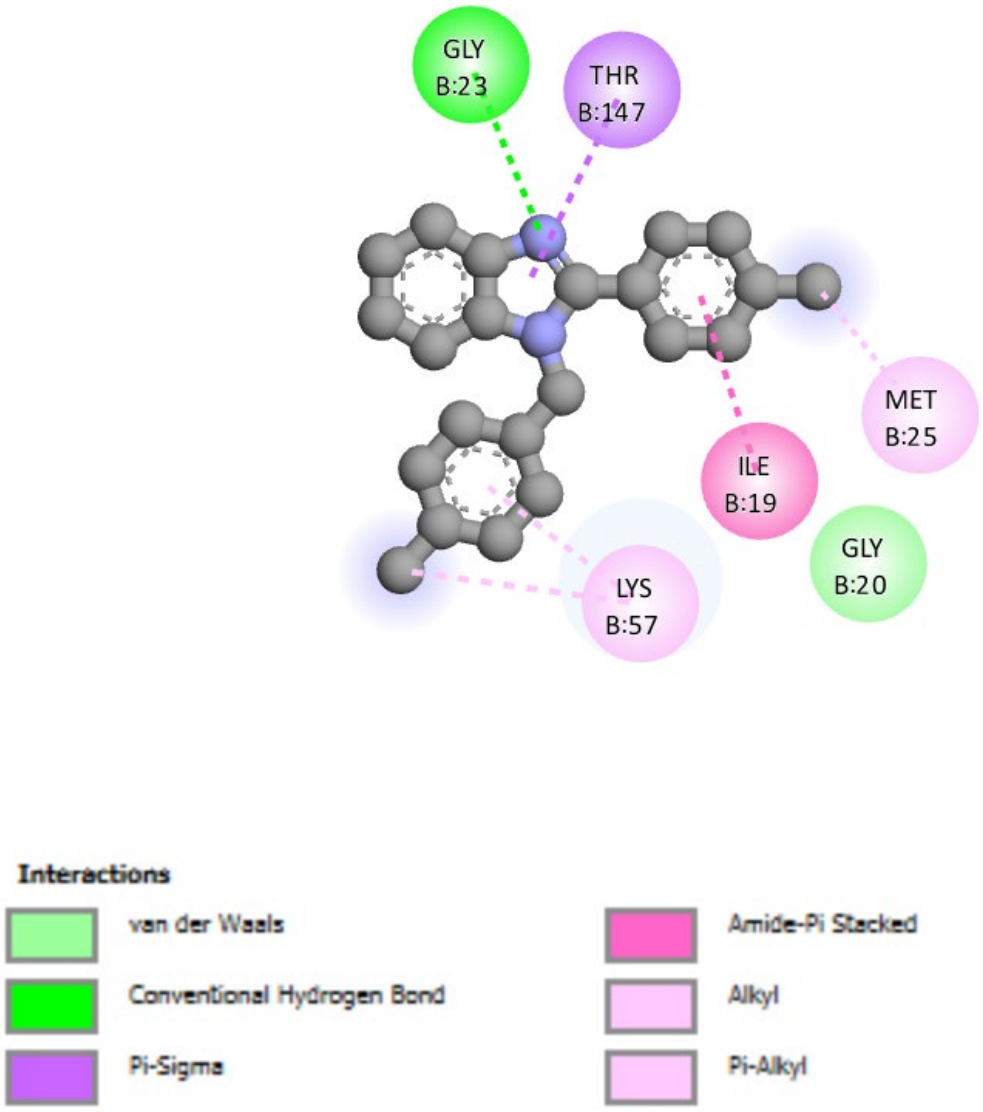


Figure S50. 2D representation of the interaction of compound **3l** with DHFR-F receptor

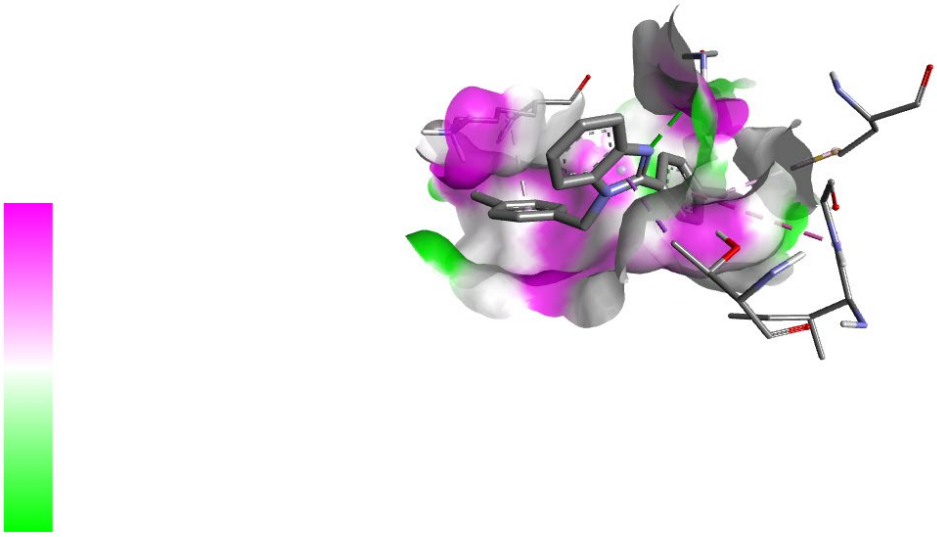


Figure S51. 3D representation of the interaction of compound **3l** with DHFR-F receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1573657864
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.4      0.000      0.000
   2         -8.1      2.776      5.817
   3         -8.1      2.175      4.598
   4         -7.9      2.789      5.650
   5         -7.9     11.925     14.139
   6         -7.9      2.715      5.775
   7         -7.8      2.897      4.703
   8         -7.6      2.760      5.853
   9         -7.5     11.487     13.879
Writing output ... done.
```

Figure S52. Affinity result of compound **4c** with DHFR-F receptor

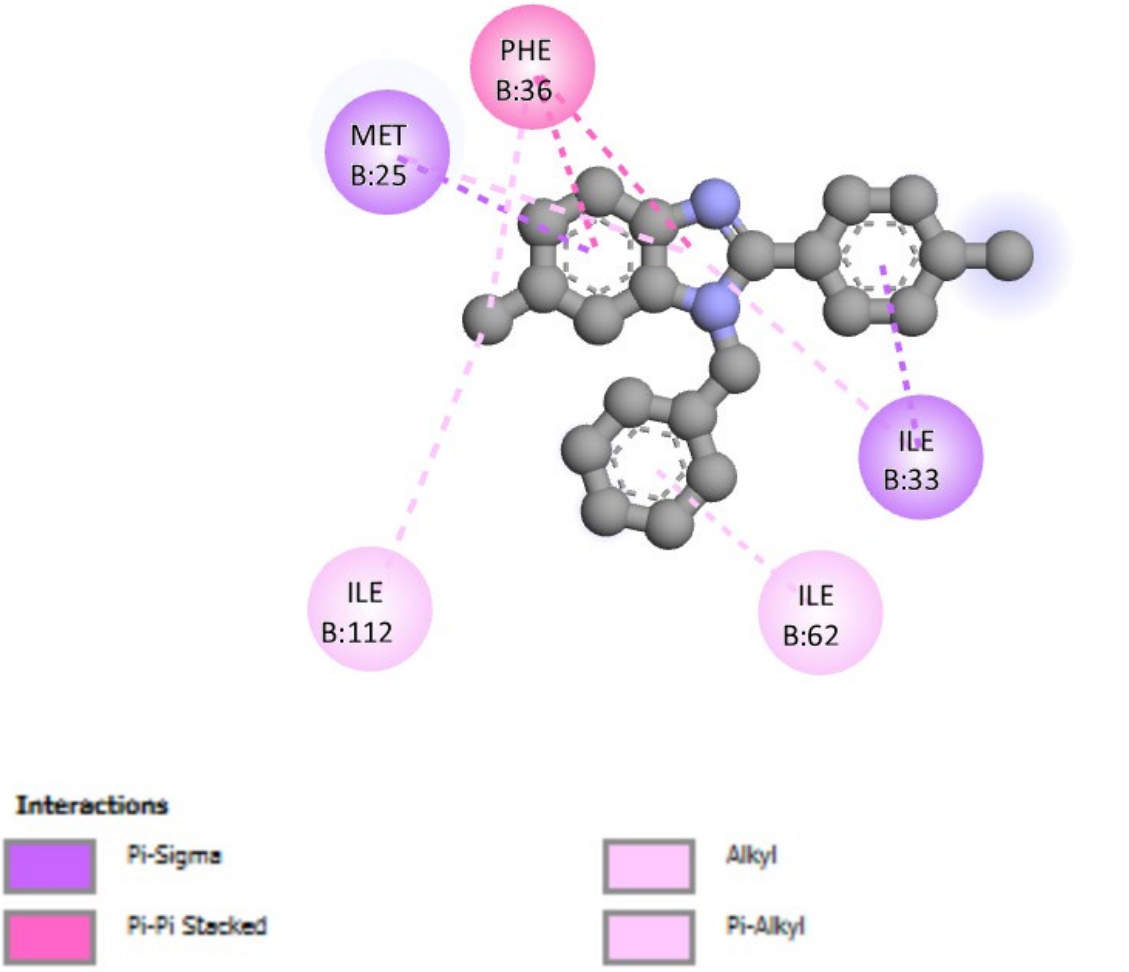


Figure S53. 2D representation of the interaction of compound **4c** with DHFR-F receptor

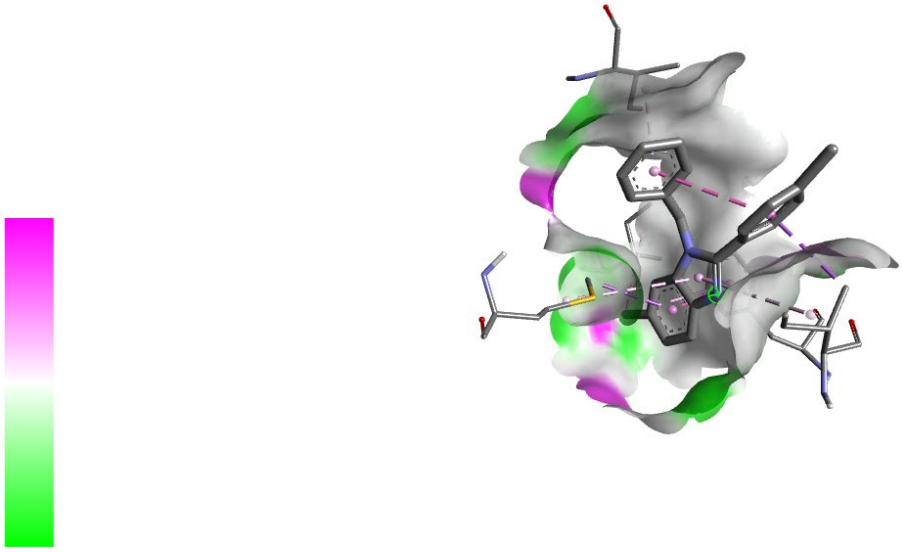


Figure S54. 3D representation of the interaction of compound **4c** with DHFR-F receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 75226880
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.8      0.000      0.000
   2         -8.5      3.132      4.333
   3         -8.0      1.586      2.551
   4         -7.9     11.307     15.144
   5         -7.9      3.805      6.546
   6         -7.7      3.969      6.030
   7         -7.6     10.706     14.205
   8         -7.4      3.455      4.867
   9         -7.4     12.635     15.720
Writing output ... done.
```

Figure S55. Affinity result of compound **4g** with DHFR-F receptor

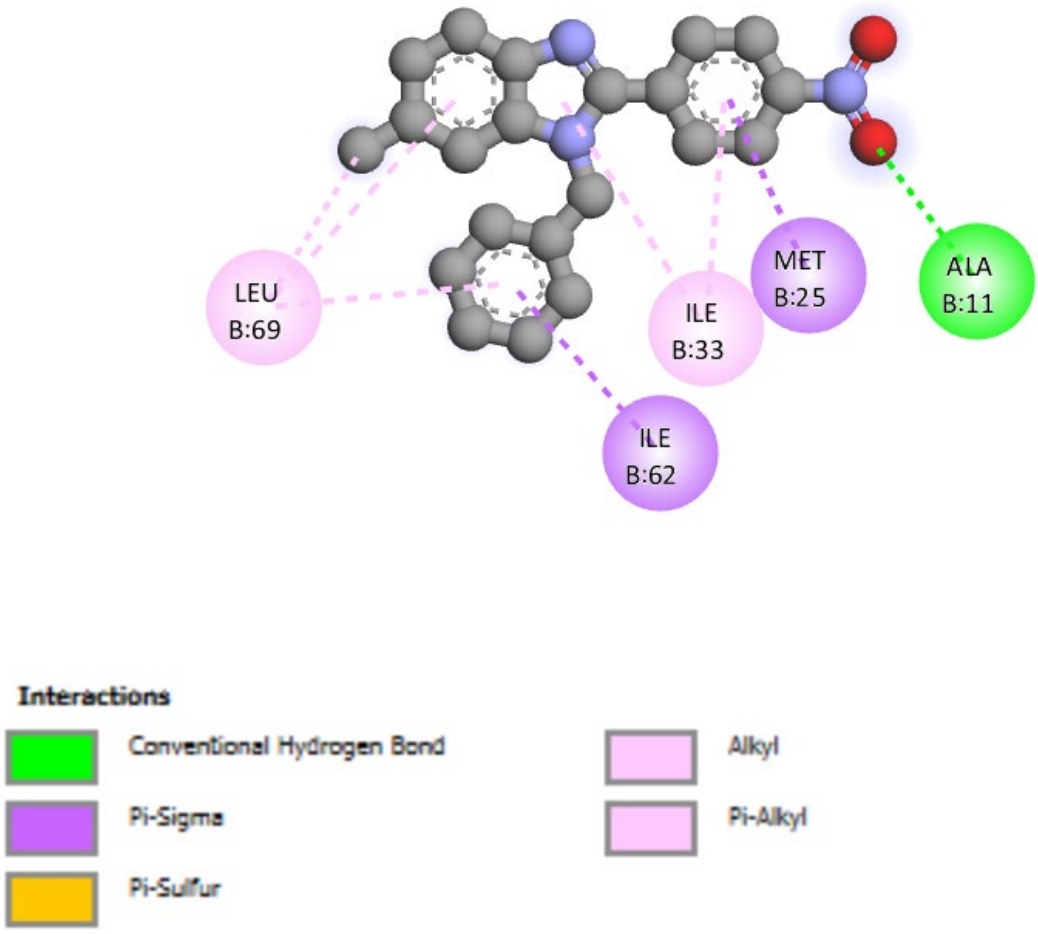


Figure S56. 2D representation of the interaction of compound **4g** with DHFR-F receptor

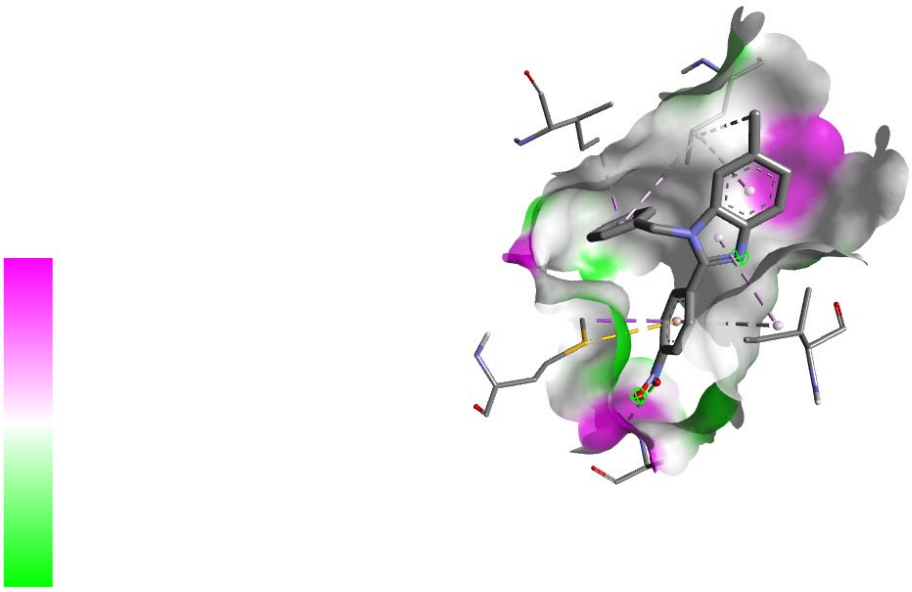


Figure S57. 3D representation of the interaction of compound **4g** with DHFR-F receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -83376064
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.5      0.000      0.000
   2         -8.3     10.989     14.342
   3         -8.2     10.955     14.868
   4         -7.9     12.633     14.859
   5         -7.6      4.108      6.447
   6         -7.4      7.616     10.503
   7         -7.1      3.307      5.314
   8         -7.1      3.570      5.214
   9         -7.0      3.896      6.195
Writing output ... done.
```

Figure S58. Affinity result of compound **4j** with DHFR-F receptor

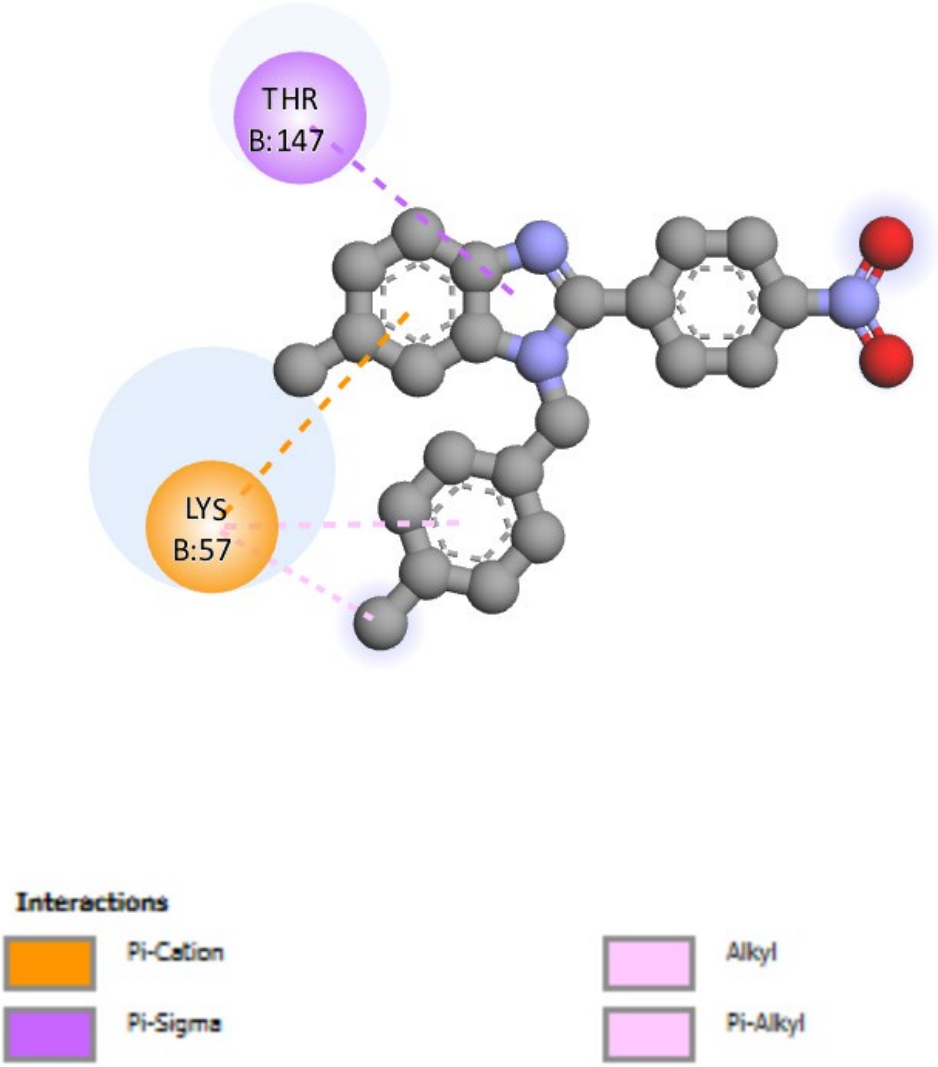


Figure S59. 2D representation of the interaction of compound **4j** with DHFR-F receptor

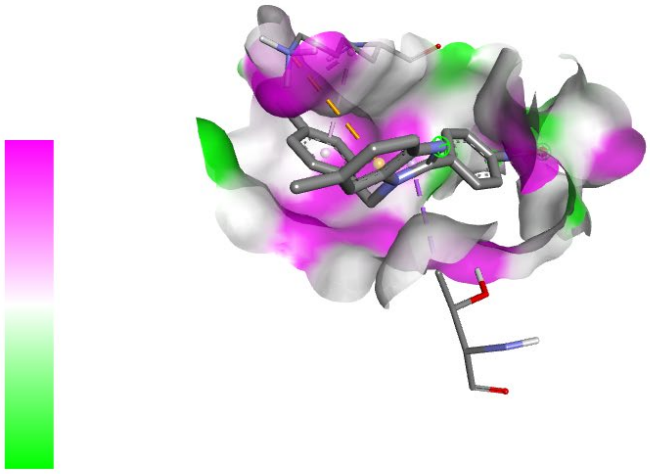


Figure S60. 3D representation of the interaction of compound **4j** with DHFR-F receptor

```
#############################################################################
# If you used AutoDock Vina in your work, please cite:                      #
#                                                                           #
# O. Trott, A. J. Olson,                                                    #
# AutoDock Vina: improving the speed and accuracy of docking                #
# with a new scoring function, efficient optimization and                   #
# multithreading, Journal of Computational Chemistry 31 (2010)              #
# 455-461                                                                   #
#                                                                           #
# DOI 10.1002/jcc.21334                                                     #
#                                                                           #
# Please see http://vina.scripps.edu for more information.                  #
#############################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1446104232
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.0      0.000      0.000
   2         -6.9      0.967      3.654
   3         -6.6      6.812      8.965
   4         -6.5     15.477     17.482
   5         -6.3      6.744      9.198
   6         -6.3      6.201      8.334
   7         -6.3      6.133      8.712
   8         -6.2     16.145     17.921
   9         -6.2      5.952      8.003
Writing output ... done.
```

Figure S61. Affinity result of **Flu** with DHFR-F receptor

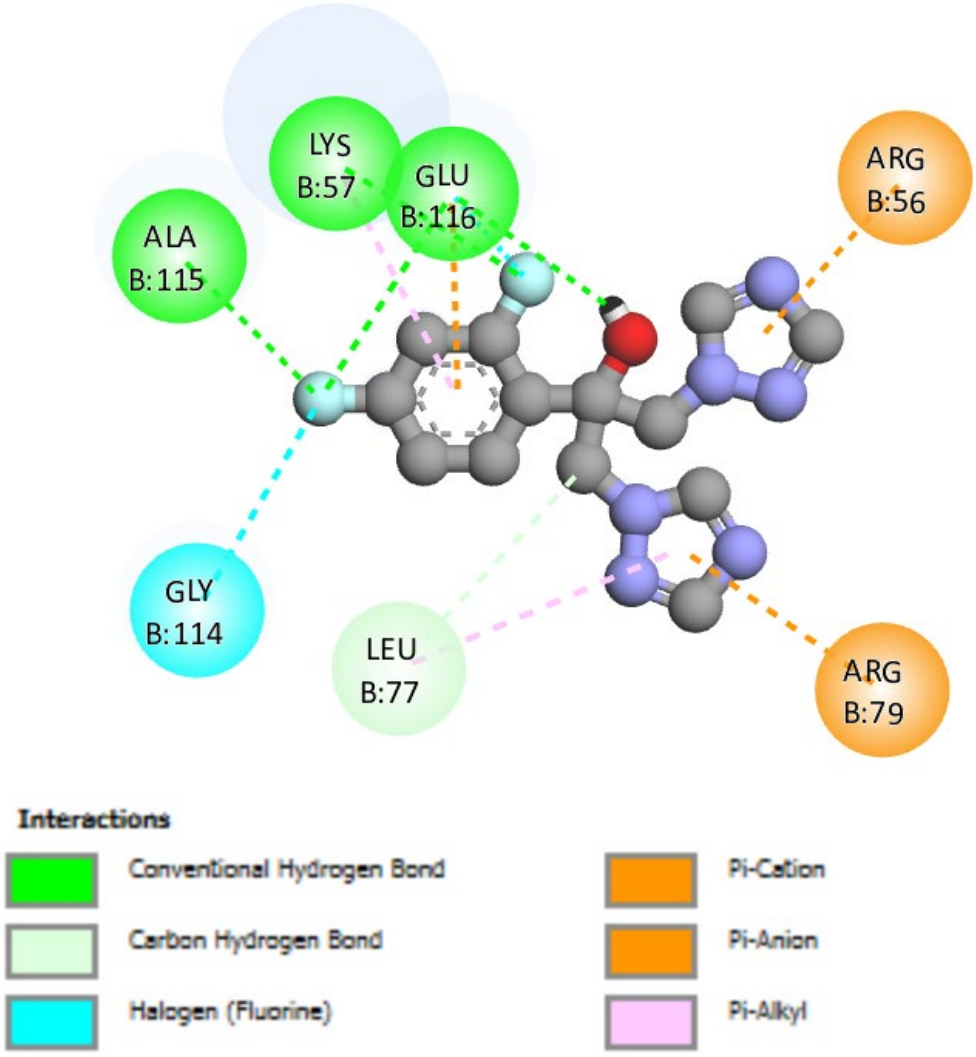


Figure S62. 2D representation of the interaction of **Flu** with DHFR-F receptor

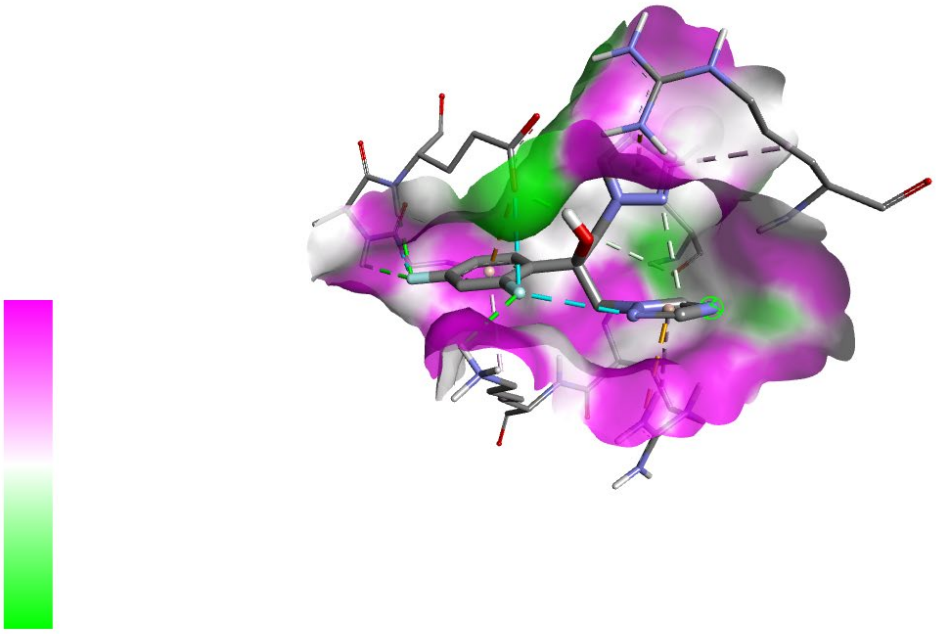


Figure S63. 3D representation of the interaction of **Flu** with DHFR-F receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1298481664
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.5      0.000      0.000
   2         -8.4     11.499     19.266
   3         -8.3     14.515     22.467
   4         -8.1     11.057     19.824
   5         -7.9      9.306     14.573
   6         -7.7     11.349     17.544
   7         -7.7     10.169     14.970
   8         -7.5      9.634     17.562
   9         -7.5     14.073     22.233
Writing output ... done.
```

Figure S64. Affinity result of **PTX** with DHFR-F receptor

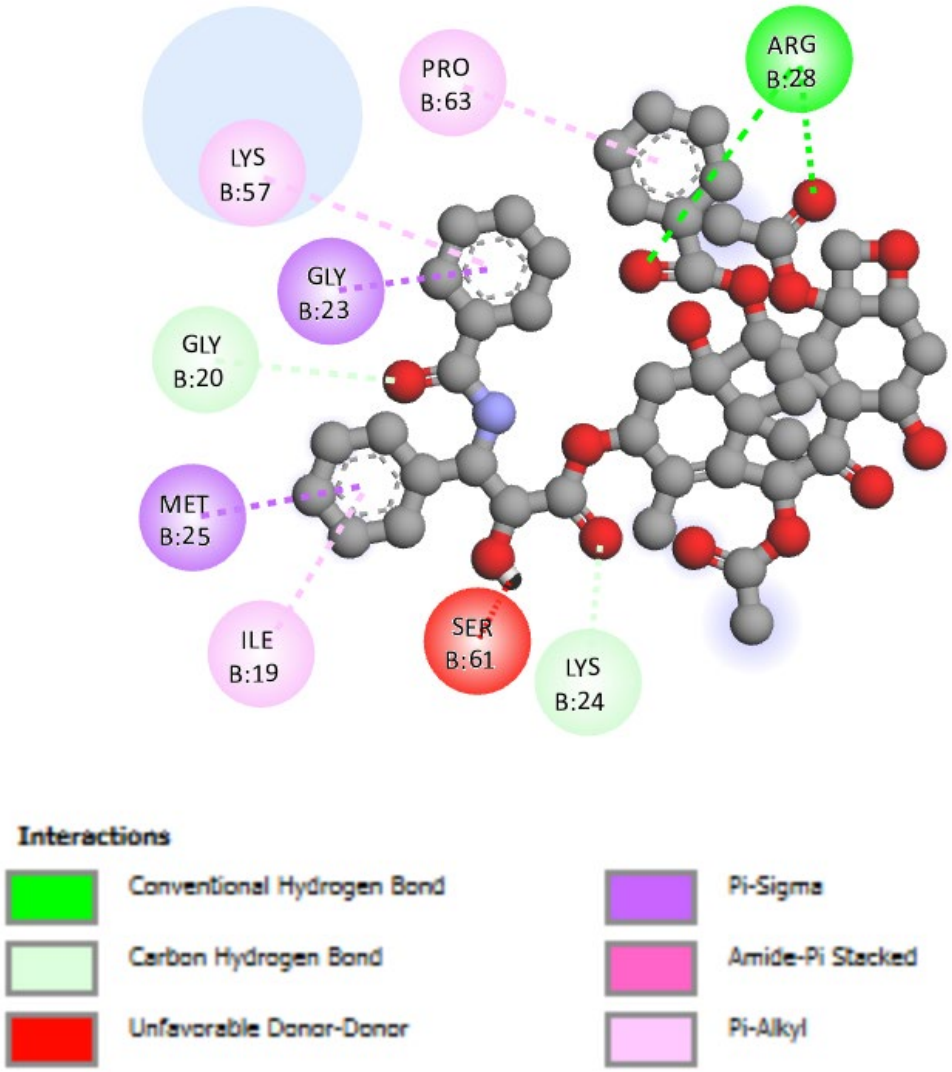


Figure S65. 2D representation of the interaction of **PTX** with DHFR-F receptor

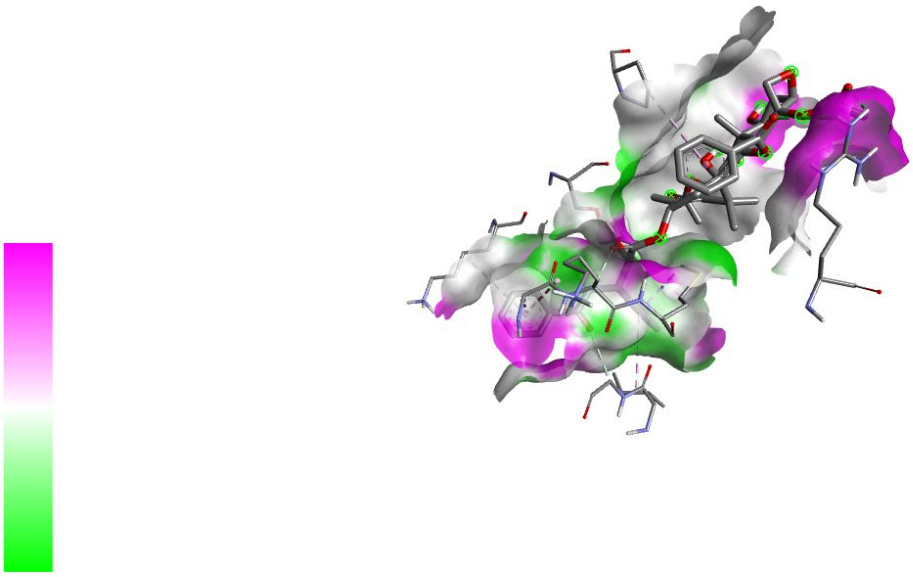


Figure S66. 2D representation of the interaction of **PTX** with DHFR-F receptor

```
receptor = 1iylNMTF.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = 12.6146
center_y = 47.7652
center_z = -0.440754

size_x = 25
size_y = 25
size_z = 25

energy_range = 4
exhaustiveness = 8
```

Figure S67. Grid box volume – Autodock Vina for *N*-myristoyl Transferase (PDB: 1IYL)

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1830617628
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -11.0      0.000      0.000
   2        -10.5      4.488      7.883
   3        -10.5      5.021      8.210
   4        -10.4      4.337      7.416
   5        -10.4      5.147      7.609
   6        -10.4      5.196      8.494
   7        -10.2      4.008      6.386
   8         -9.8      3.931      8.047
   9         -9.6      3.413      5.518
Writing output ... done.
```

Figure S68. Affinity result of compound **3k** with *N*-myristoyl Transferase receptor

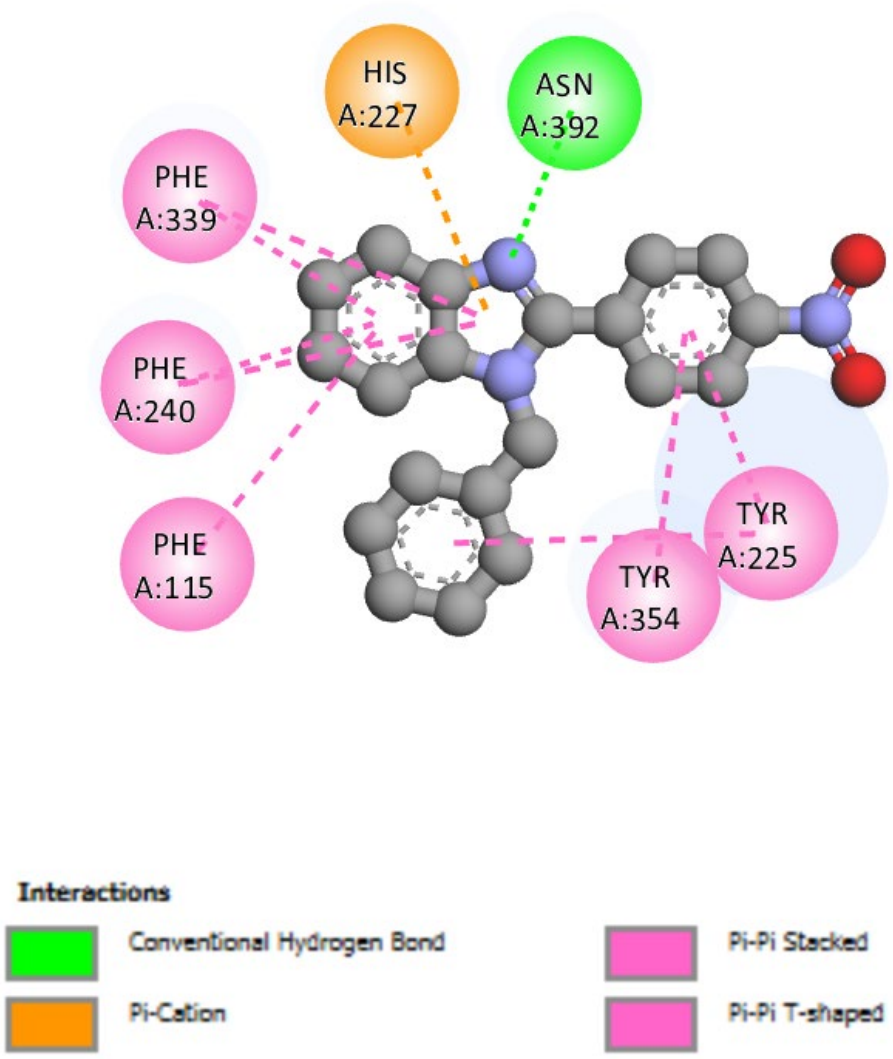


Figure S69. 2D representation of the interaction of compound **3k** with *N*-myristoyl Transferase receptor

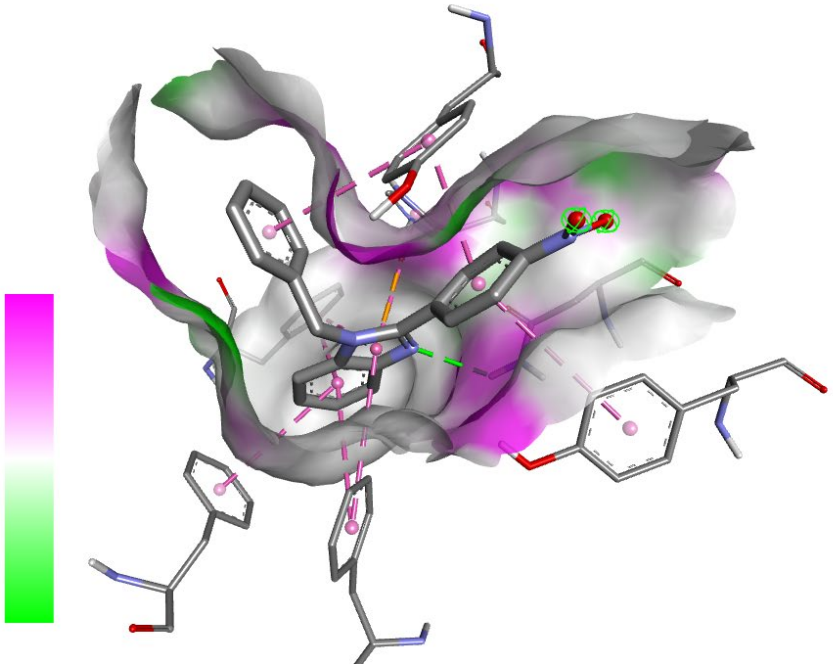


Figure S70. 3D representation of the interaction of compound **3k** with *N*-myristoyl Transferase receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1327543296
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -11.3      0.000      0.000
   2        -10.8      3.105      6.119
   3        -10.7      2.111      2.871
   4        -10.6      4.961      8.409
   5        -10.6      4.741      8.026
   6        -10.2      4.659      7.601
   7        -10.1      1.472      5.063
   8         -9.9      3.513      5.786
   9         -9.7      4.669      7.204
Writing output ... done.
```

Figure S71. Affinity result of compound **3l** with *N*-myristoyl Transferase receptor

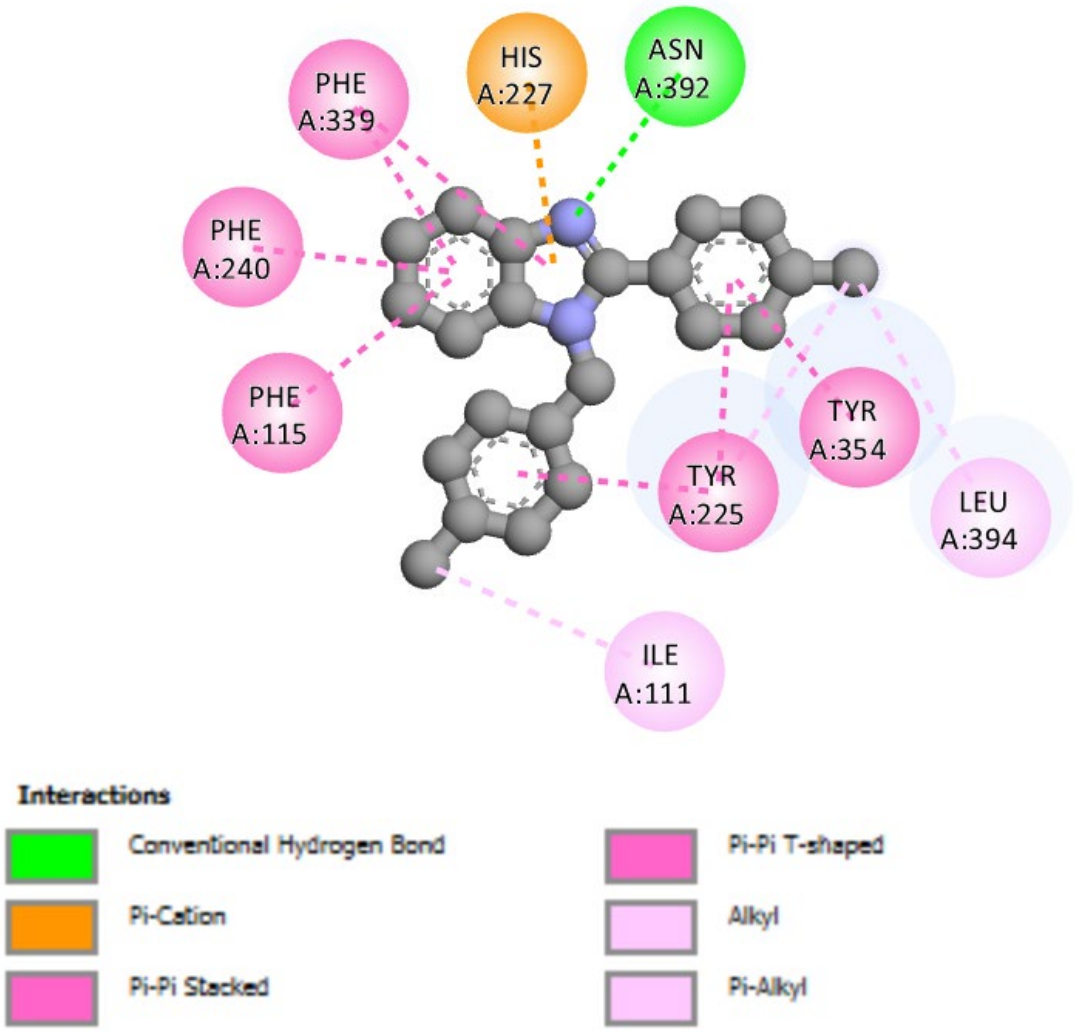


Figure S72. 2D representation of the interaction of compound **3l** with *N*-myristoyl Transferase receptor

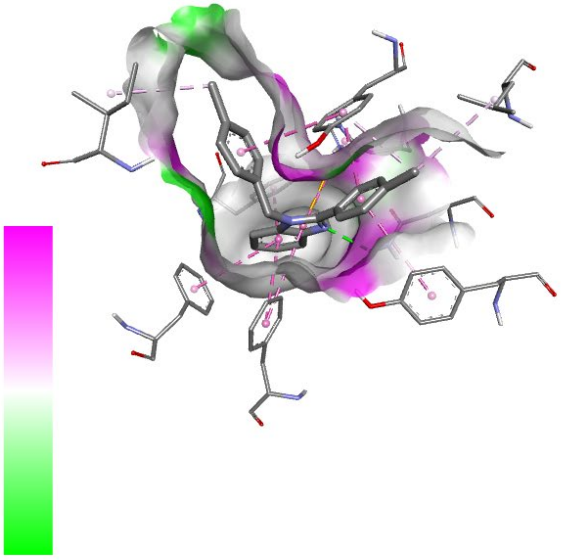


Figure S73. 3D representation of the interaction of compound **3l** with *N*-myristoyl Transferase receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1569994888
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -11.1      0.000      0.000
   2        -10.0      2.280      4.896
   3         -9.9      3.130      5.830
   4         -9.6      2.741      4.685
   5         -9.6      4.051      6.873
   6         -9.5      3.440      6.122
   7         -9.2      2.662      5.784
   8         -8.9      1.039      1.374
   9         -8.8      2.088      4.928
Writing output ... done.
```

Figure S74. Affinity result of compound **4c** with *N*-myristoyl Transferase receptor

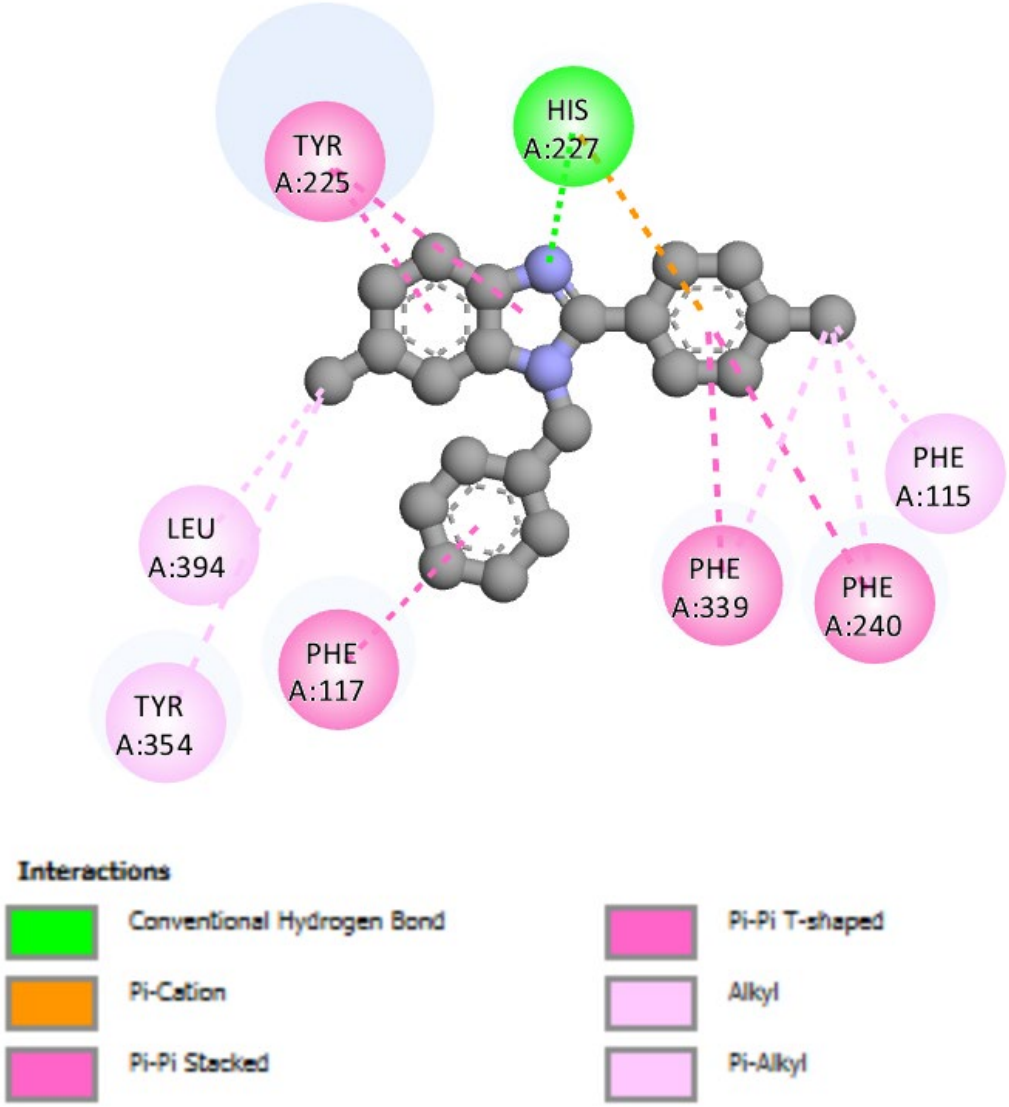


Figure S75. 2D representation of the interaction of compound **4c** with *N*-myristoyl Transferase receptor

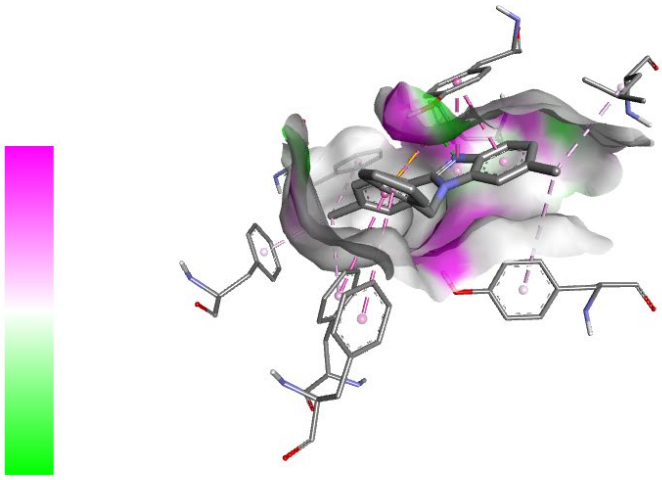


Figure S76. 3D representation of the interaction of compound **4c** with *N*-myristoyl Transferase receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 599659224
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.3      0.000      0.000
   2        -10.1      2.536      5.226
   3         -9.9      4.568      6.594
   4         -9.8      4.223      6.866
   5         -9.8      3.966      6.250
   6         -9.6      4.248      7.392
   7         -9.6      4.553      7.264
   8         -9.6      4.350      6.939
   9         -9.3      1.932      4.507
Writing output ... done.
```

Figure S77. Affinity result of compound **4g** with *N*-myristoyl Transferase receptor

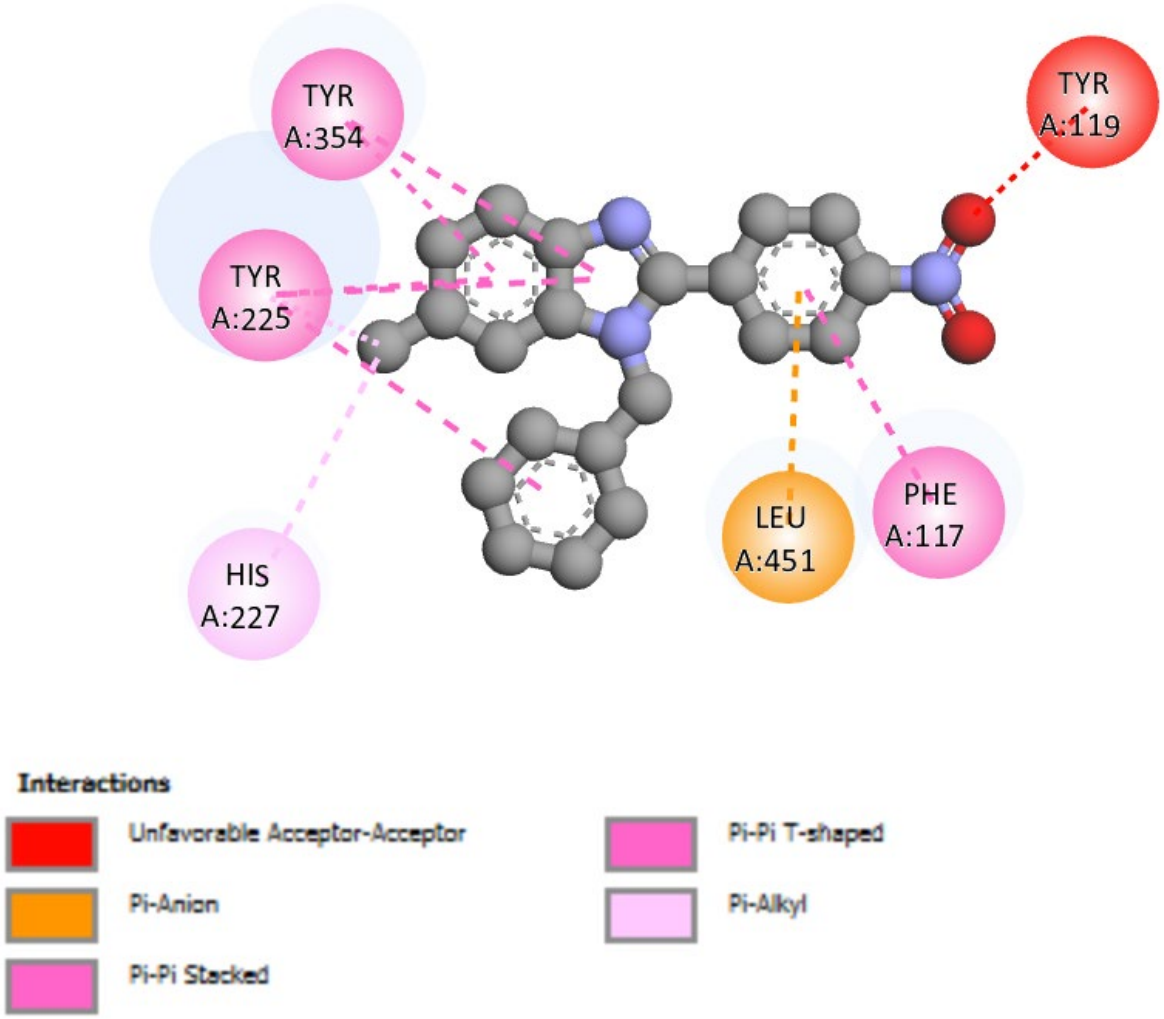


Figure S78. 2D representation of the interaction of compound **4g** with *N*-myristoyl Transferase receptor

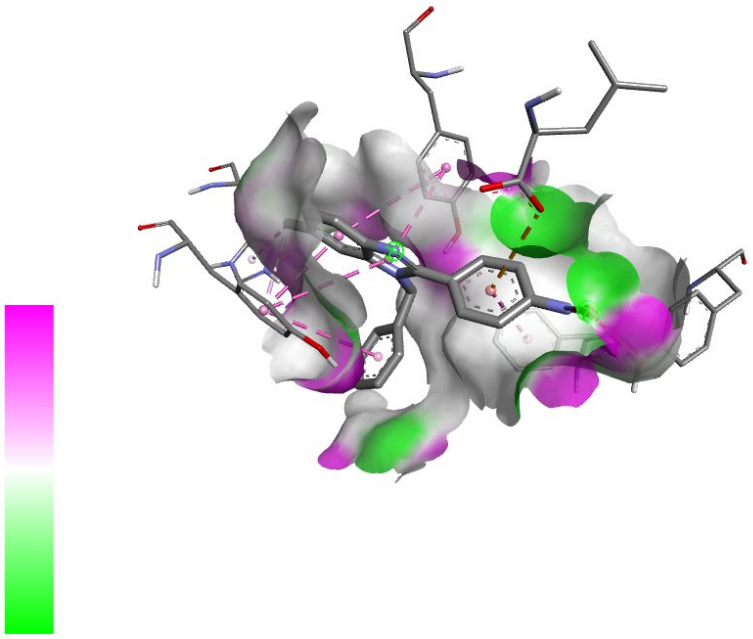


Figure S79. 3D representation of the interaction of compound **4g** with *N*-myristoyl Transferase receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -149691628
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.6      0.000      0.000
   2        -10.3      4.503      6.447
   3        -10.2      3.890      6.072
   4        -10.1      3.584      5.596
   5        -10.0      4.653      7.546
   6         -9.9      2.717      5.038
   7         -9.9      4.055      6.646
   8         -9.7      4.375      6.888
   9         -9.6      4.378      7.438
Writing output ... done.
```

Figure S80. Affinity result of compound **4j** with *N*-myristoyl Transferase receptor

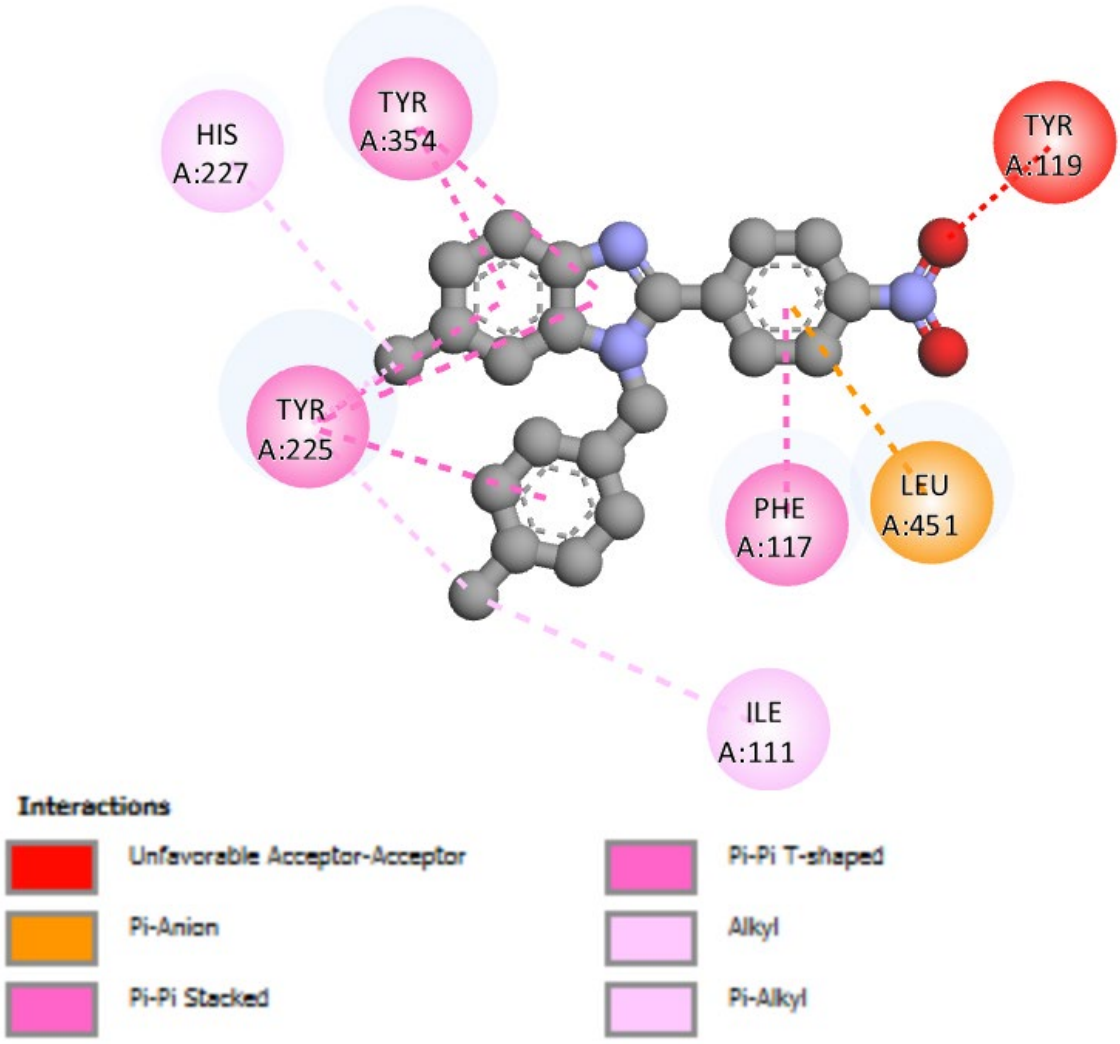


Figure S81. 2D representation of the interaction of compound **4j** with *N*-myristoyl Transferase receptor

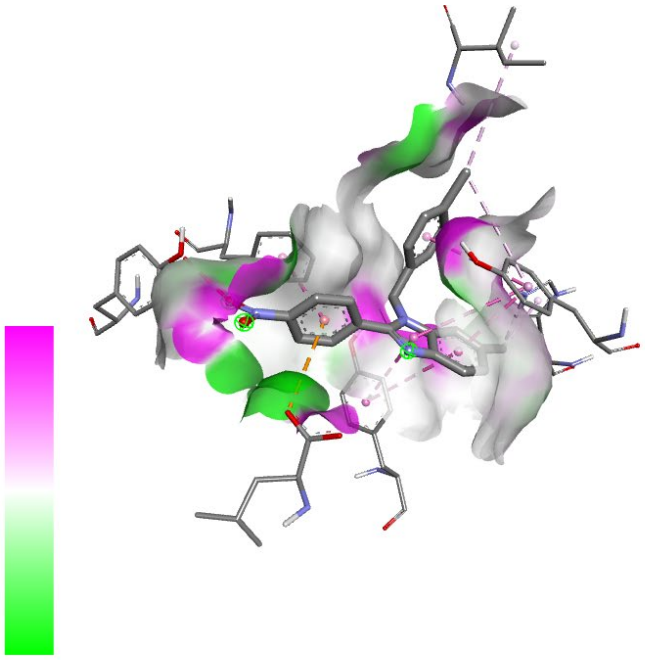


Figure S82. 2D representation of the interaction of compound **4j** with *N*-myristoyl Transferase receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1075688508
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.9      0.000      0.000
   2         -7.8      2.200      2.868
   3         -7.8      1.126      3.929
   4         -7.3      5.388      7.088
   5         -7.3      6.029      8.223
   6         -7.1      6.700      8.796
   7         -7.1      7.616      9.573
   8         -7.1      5.968      7.483
   9         -7.0      5.800      8.368
Writing output ... done.
```

Figure S83. Affinity result of **Flu** with *N*-myristoyl Transferase receptor

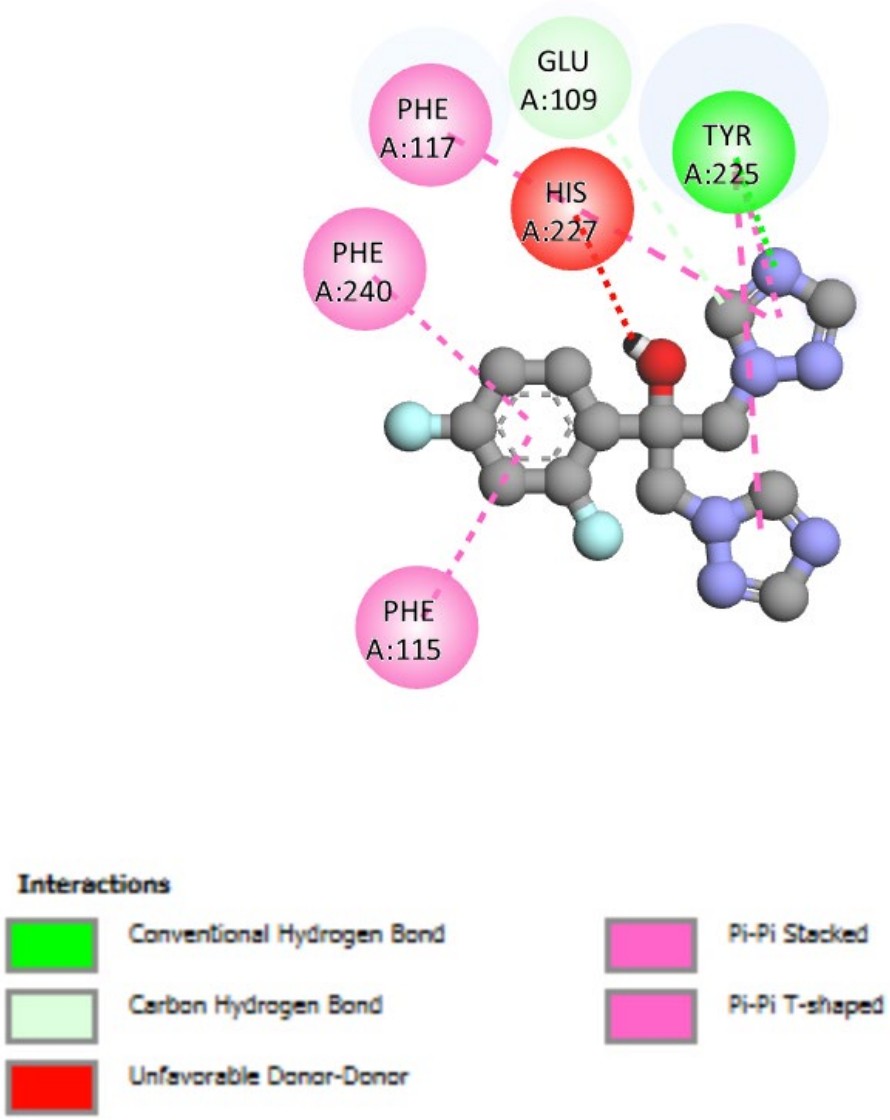


Figure S84. 2D representation of the interaction of **Flu** with *N*-myristoyl Transferase receptor

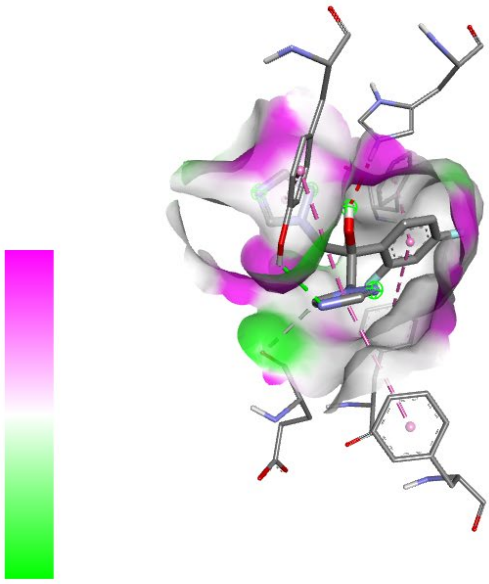


Figure S85. 3D representation of the interaction of **Flu** with *N*-myristoyl Transferase receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1697931708
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -11.4      0.000      0.000
   2        -10.8      1.142      3.784
   3        -10.0      3.254      7.148
   4         -9.7      1.651      4.239
   5         -9.5      3.229     10.323
   6         -9.4      3.191      7.252
   7         -9.3      3.160      9.844
   8         -9.3      2.344      3.916
   9         -8.5      3.061      9.289
Writing output ... done.
```

Figure S86. Affinity result of **PTX** with *N*-myristoyl Transferase receptor

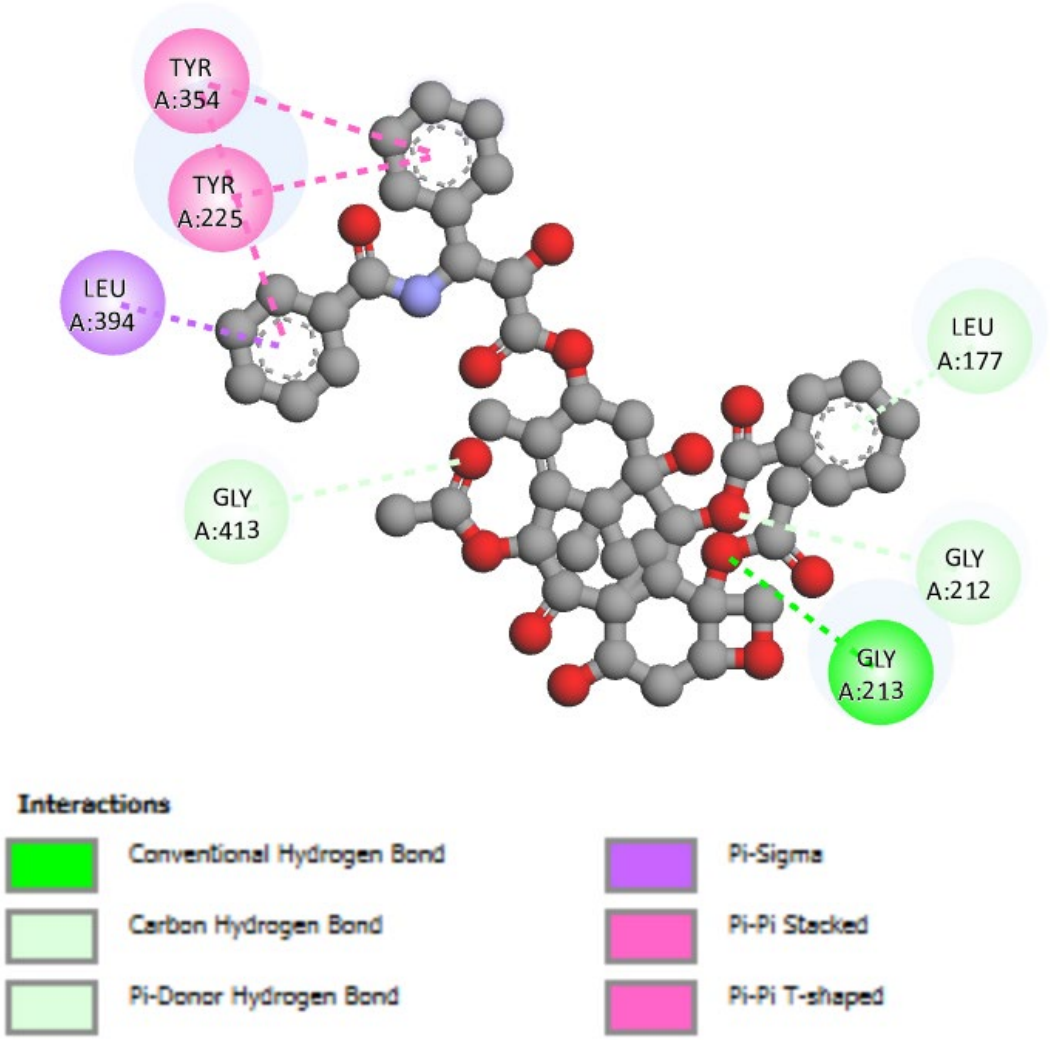


Figure S87. 2D representation of the interaction of **PTX** with *N*-myristoyl Transferase receptor

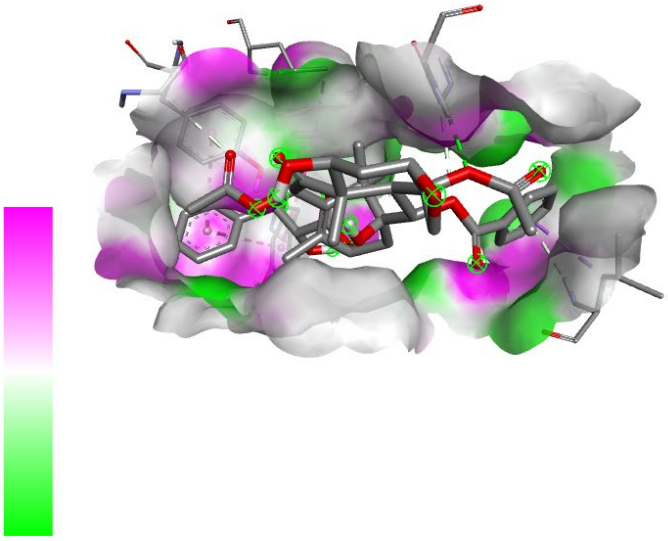


Figure S88. 3D representation of the interaction of **PTX** with *N*-myristoyl Transferase receptor

```
receptor = 5ew3VEGFR2.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = 18.728
center_y = 9.165
center_z = 12.278

size_x = 36
size_y = 34
size_z = 34

energy_range = 4
exhaustiveness = 8
```

Figure S89. Grid box volume – Autodock Vina for Vascular endothelial growth factor receptor 2 (VEGFR-2, PDB: 5EW3)

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -573662100
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.3      0.000      0.000
   2         -8.1      2.731      4.748
   3         -7.8      2.793      4.857
   4         -7.6      1.909      4.264
   5         -7.6     12.336     13.728
   6         -7.6      3.809      7.165
   7         -7.6      3.358      6.053
   8         -7.6      3.282      6.695
   9         -7.1      3.517      5.882
Writing output ... done.
```

Figure S90. Affinity result of compound **3k** with VEGFR-2 receptor

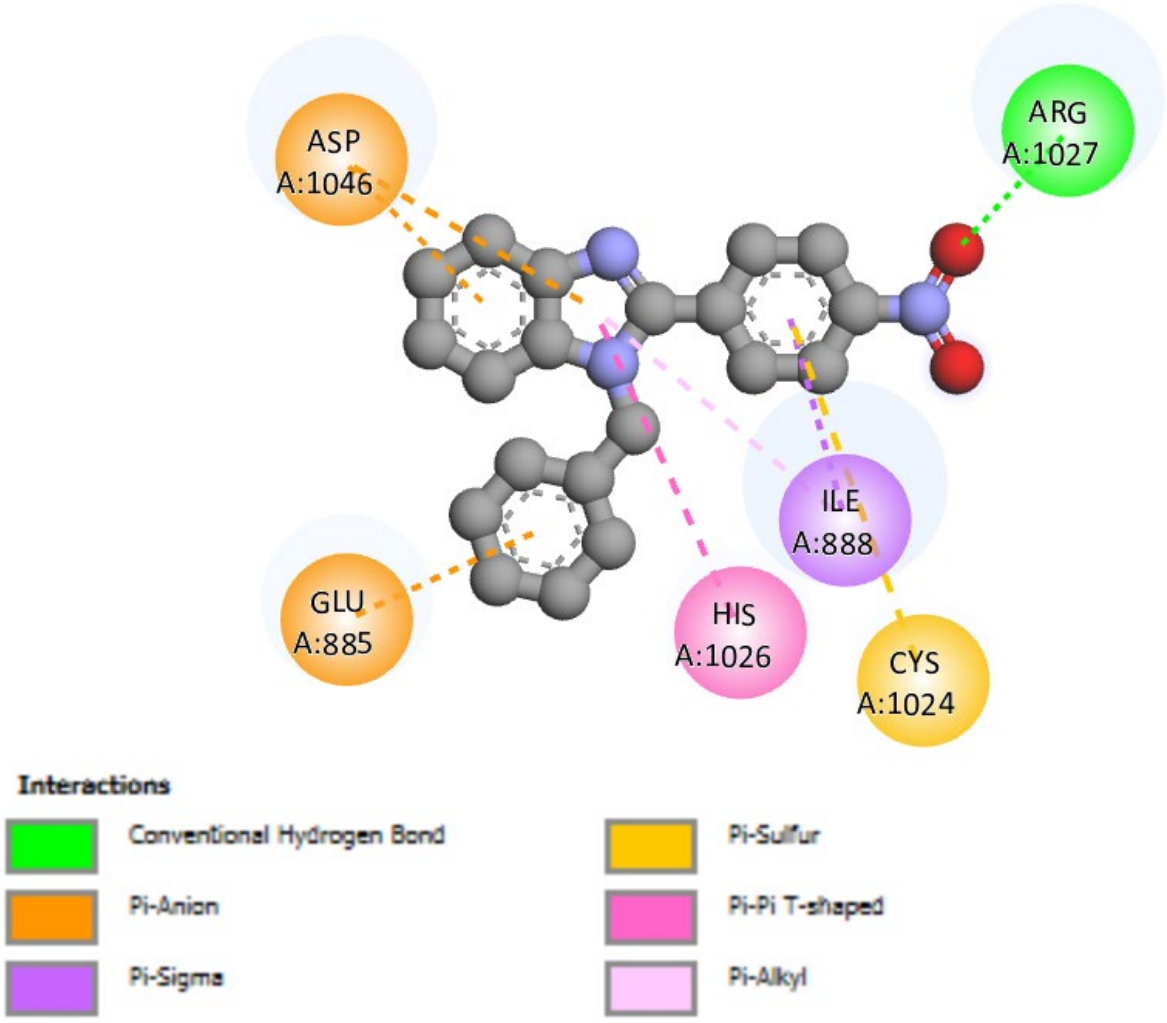


Figure S91. 2D representation of the interaction of compound **3k** with VEGFR-2 receptor

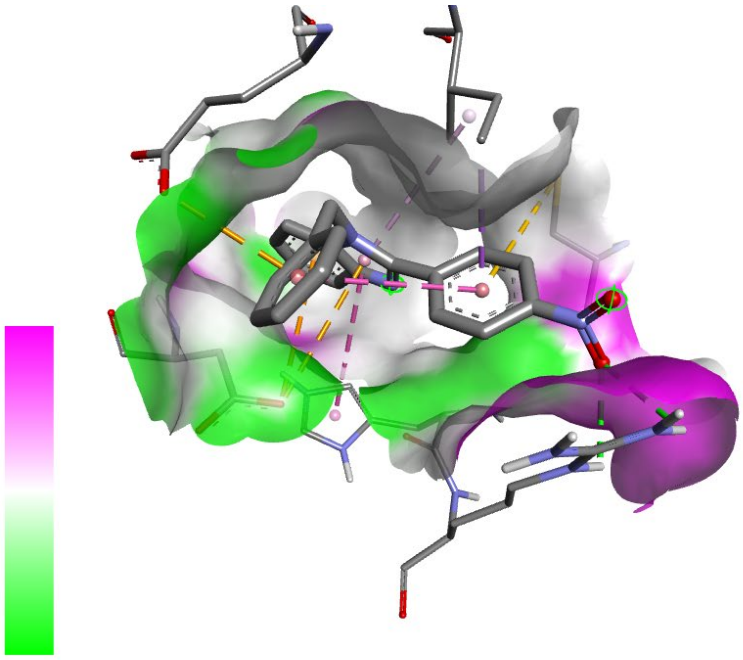


Figure S92. 3D representation of the interaction of compound **3k** with VEGFR-2 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1623088224
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.6      0.000      0.000
   2         -8.4      0.999      1.143
   3         -8.3      0.993      1.520
   4         -8.2      1.091      4.186
   5         -7.8      1.412      4.663
   6         -7.7      2.918      6.629
   7         -7.5      2.782      5.767
   8         -7.4      3.094      6.040
   9         -7.4      2.596      6.383
Writing output ... done.
```

Figure S93. Affinity result of compound **3l** with VEGFR-2 receptor

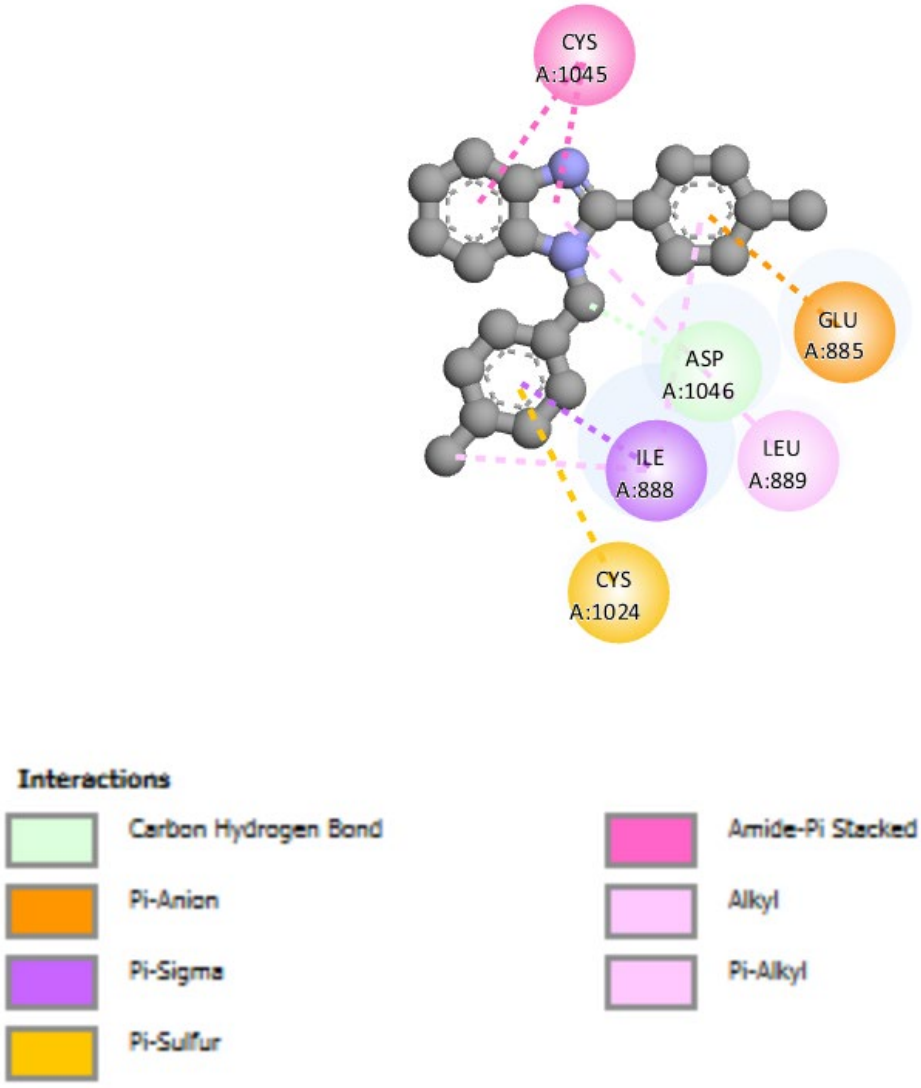


Figure S94. 2D representation of the interaction of compound **3l** with VEGFR-2 receptor

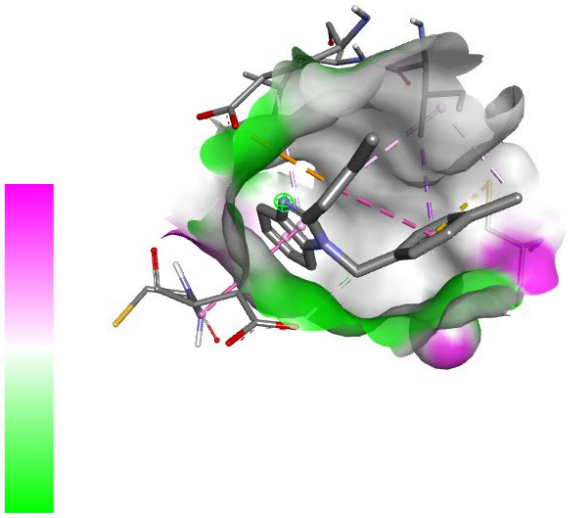


Figure S95. 3D representation of the interaction of compound **3l** with VEGFR-2 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -959184616
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.7      0.000      0.000
   2         -8.3      1.833      4.223
   3         -8.0      1.172      1.907
   4         -7.9      2.854      6.476
   5         -7.1      2.834      6.034
   6         -6.9      3.084      6.513
   7         -6.8      1.967      3.089
   8         -6.7     14.729     16.175
   9         -6.7      3.004      6.293
Writing output ... done.
```

Figure S96. Affinity result of compound **4c** with VEGFR-2 receptor

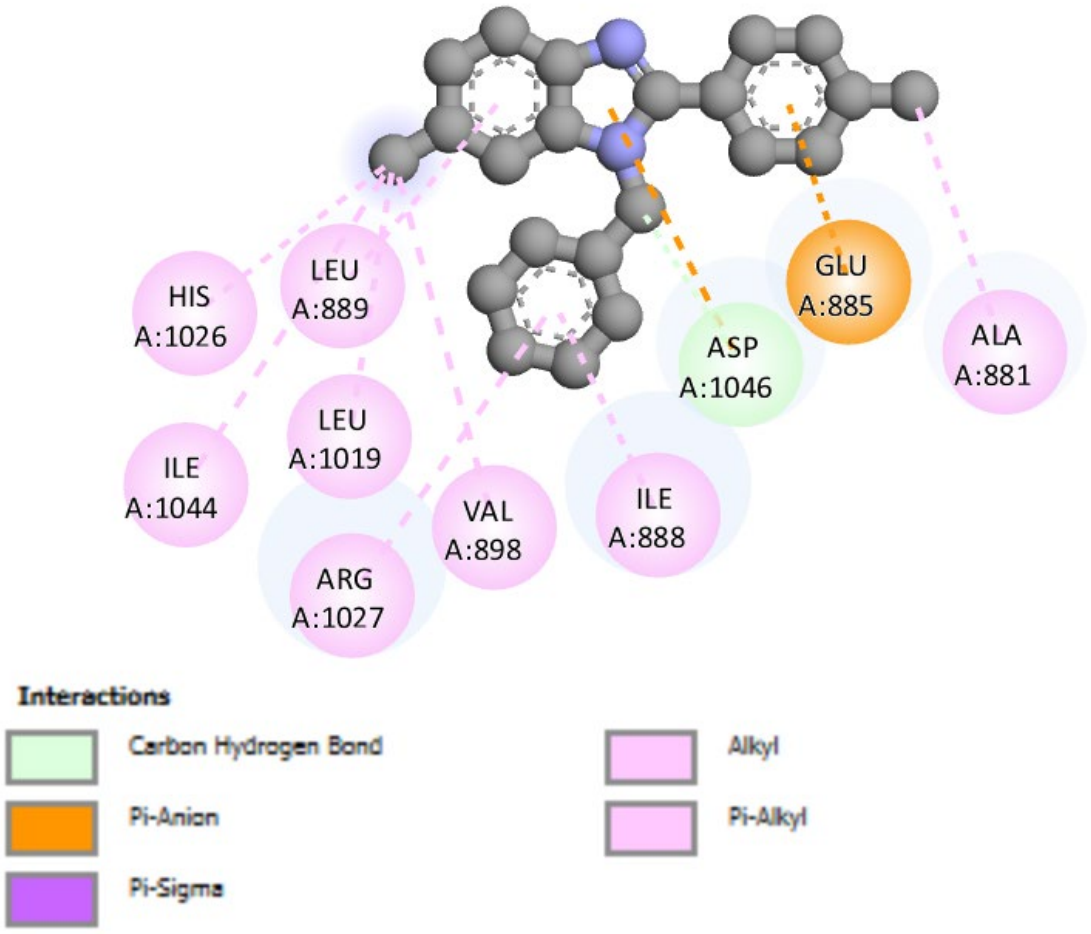


Figure S97. 2D representation of the interaction of compound **4c** with VEGFR-2 receptor

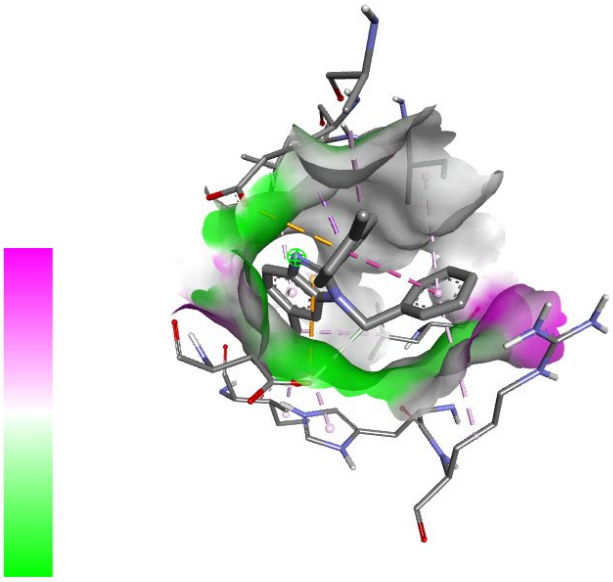


Figure S98. 3D representation of the interaction of compound **4c** with VEGFR-2 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -236140300
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.7      0.000      0.000
   2         -8.3      2.619      4.849
   3         -8.1      2.645      4.680
   4         -7.7      3.734      6.718
   5         -7.6      3.402      6.879
   6         -7.2      3.731      7.556
   7         -7.1     20.391     22.268
   8         -7.0      4.140      7.444
   9         -7.0     11.513     13.280
Writing output ... done.
```

Figure S99. Affinity result of compound **4g** with VEGFR-2 receptor

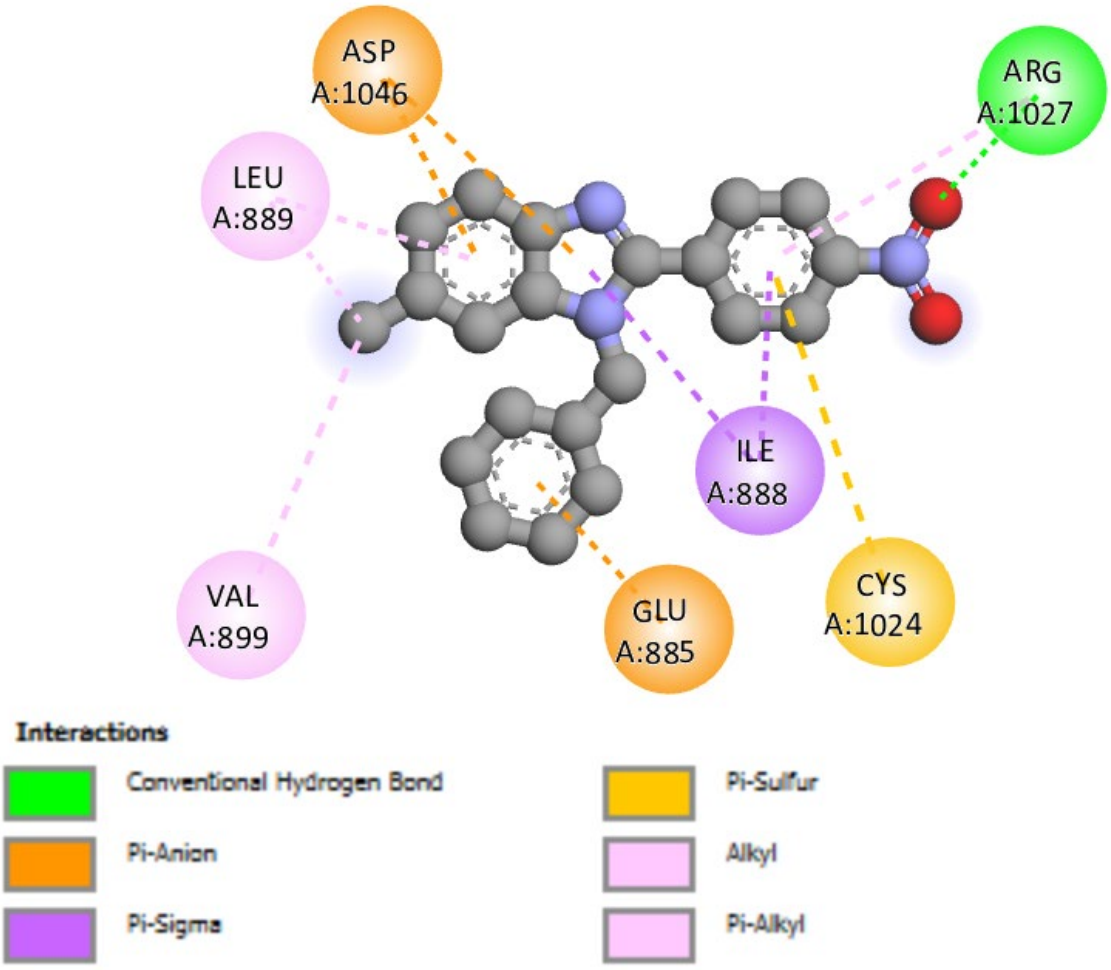


Figure S100. 2D representation of the interaction of compound **4g** with VEGFR-2 receptor

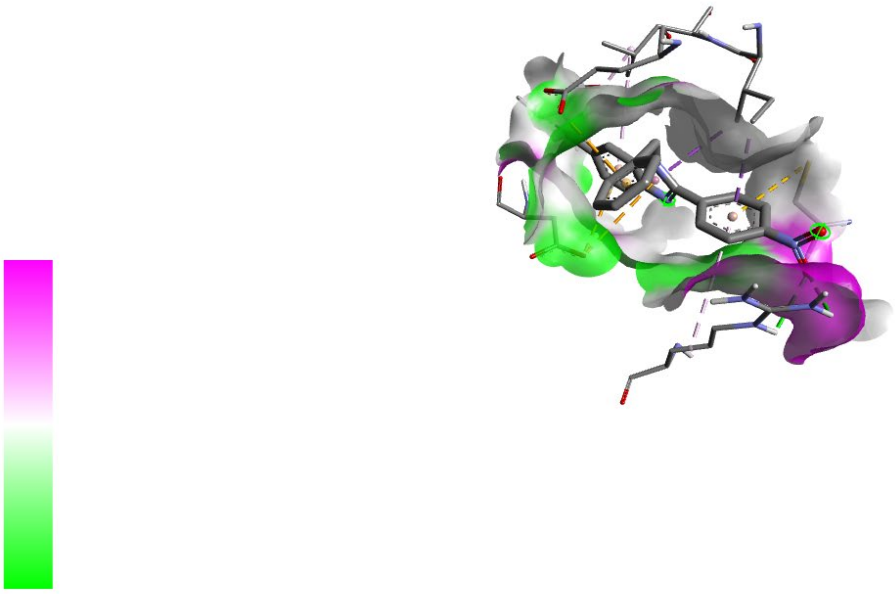


Figure S101. 3D representation of the interaction of compound **4g** with VEGFR-2 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 2138138172
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.0      0.000      0.000
   2         -8.9      3.112      5.072
   3         -8.1      3.082      4.878
   4         -7.7      3.978      7.202
   5         -7.5      3.459      6.328
   6         -7.3      4.181      7.518
   7         -7.1     14.304     16.755
   8         -7.1      4.320      7.658
   9         -7.0      4.091      7.430
Writing output ... done.
```

Figure S102. Affinity result of compound **4j** with VEGFR-2 receptor

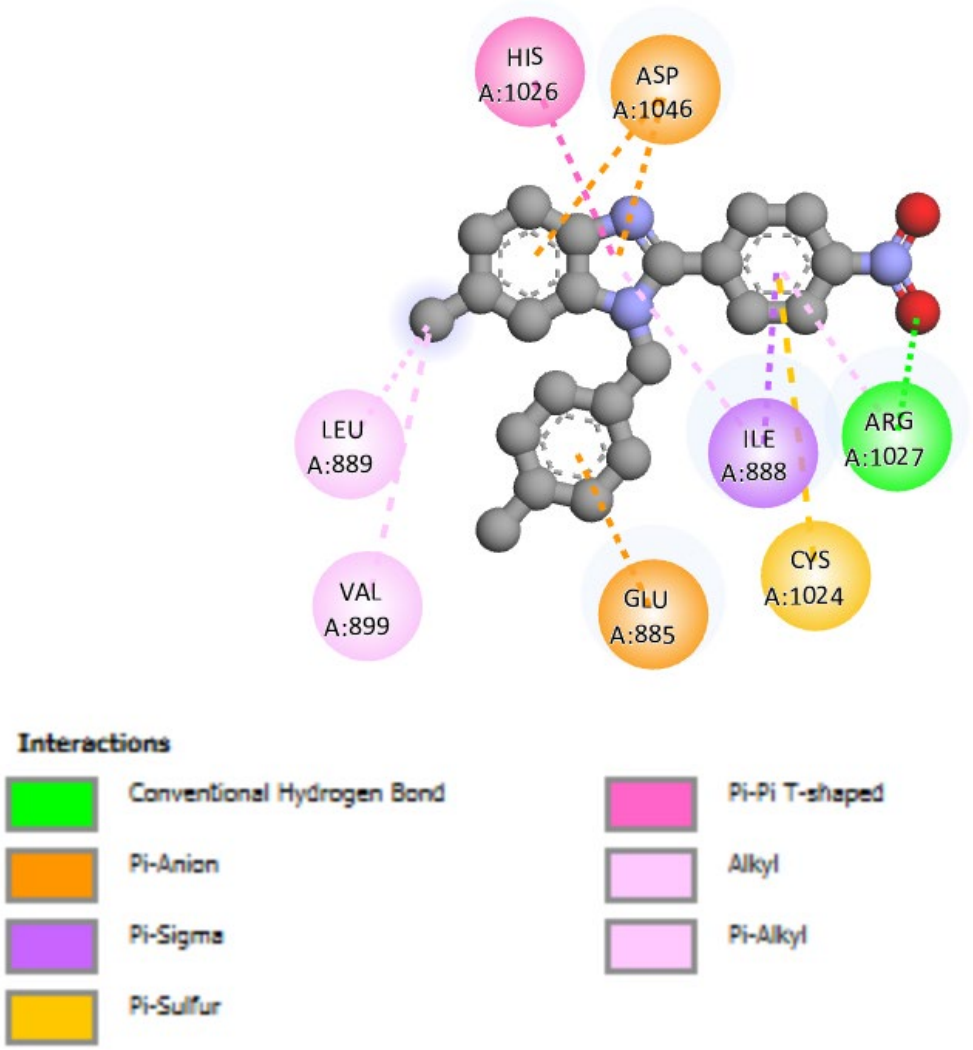


Figure S103. 2D representation of the interaction of compound **4j** with VEGFR-2 receptor

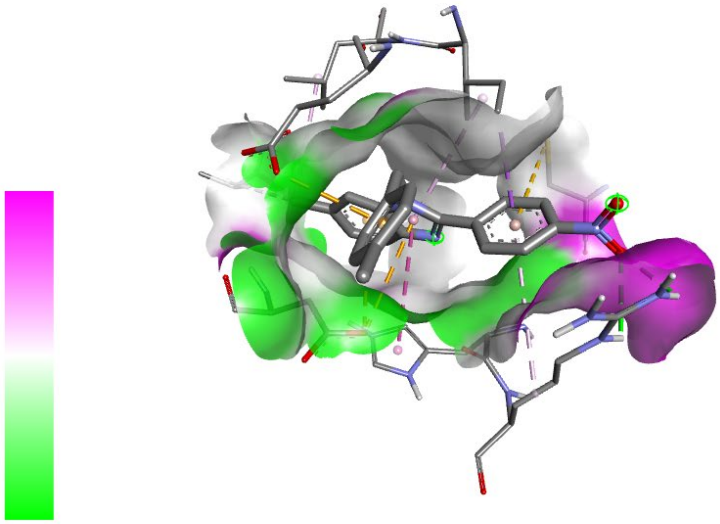


Figure S104. 3D representation of the interaction of compound **4j** with VEGFR-2 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 830497308
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.8      0.000      0.000
   2         -7.6      1.432      3.556
   3         -7.3      2.745      4.845
   4         -7.3      3.505      7.224
   5         -7.1      2.472      4.817
   6         -7.0      3.374      7.920
   7         -6.8      5.740      9.612
   8         -6.7      3.257      6.261
   9         -6.7      8.865     12.688
Writing output ... done.
```

Figure S105. Affinity result of **PTX** with VEGFR-2 receptor

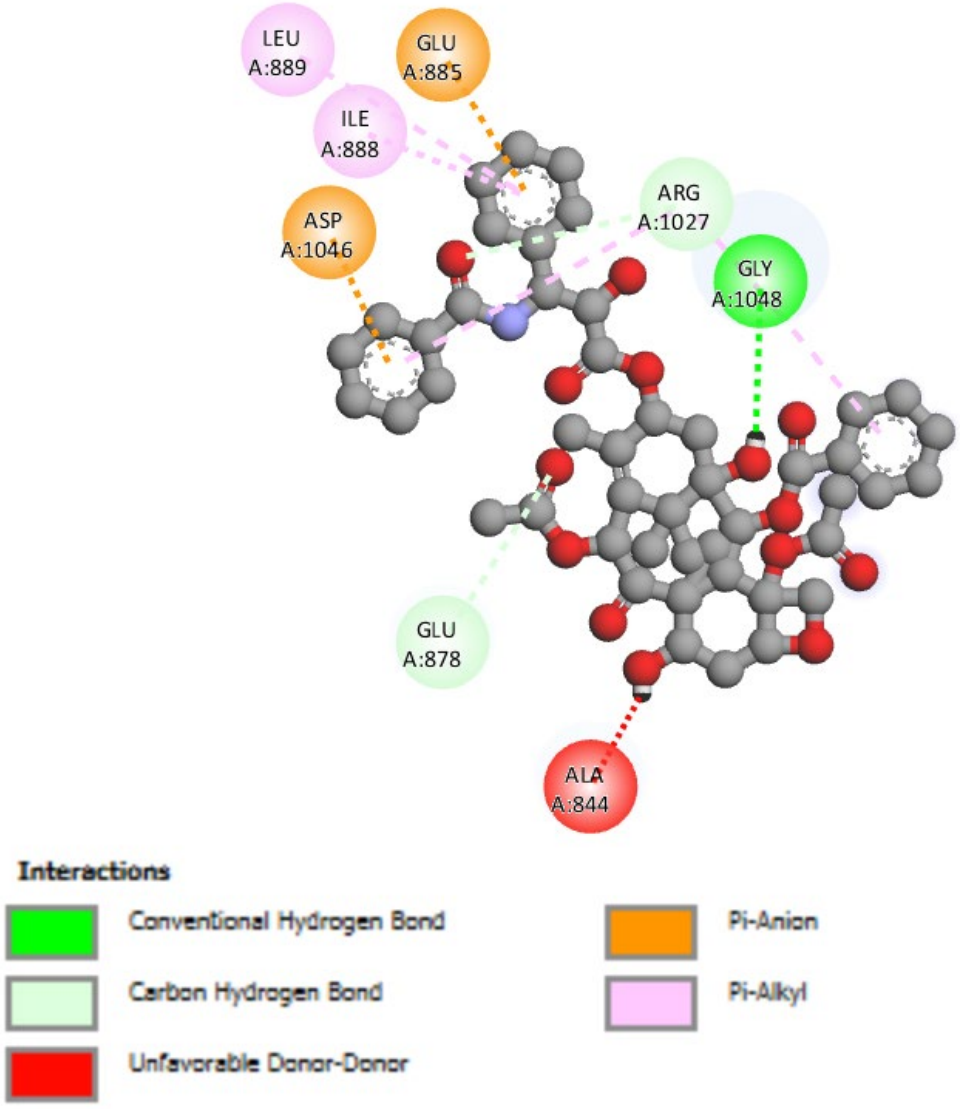


Figure S106. 2D representation of the interaction of **PTX** with VEGFR-2 receptor

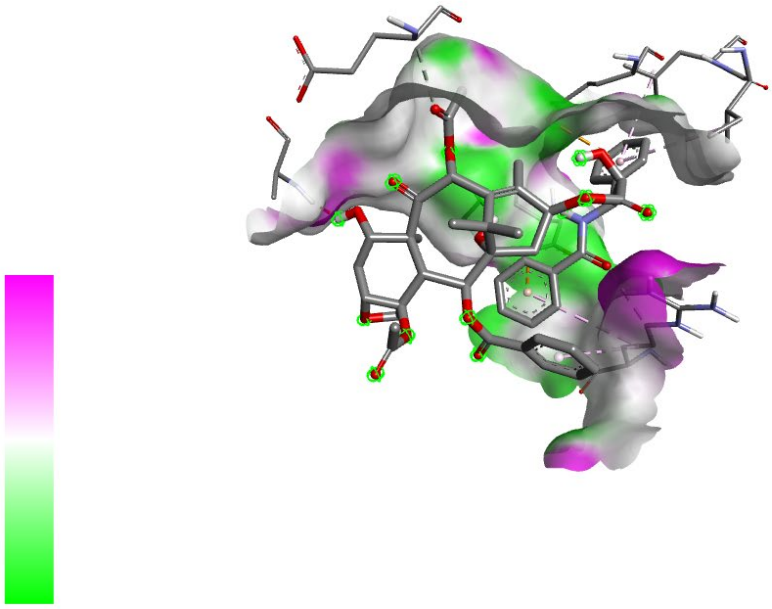


Figure S107. 3D representation of the interaction of **PTX** with VEGFR-2 receptor

```
receptor = 5a46FGFR1.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = 85.27
center_y = 1.20
center_z = 8.409

size_x = 52
size_y = 42
size_z = 48

energy_range = 4
exhaustiveness = 8
```

Figure S108. Grid box volume – Autodock Vina for Fibroblast growth factor receptor 1 (FGFR1, PDB: 5A46)

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1469268588
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.7      0.000      0.000
   2         -8.9      1.159      4.117
   3         -8.8      1.482      2.128
   4         -8.3      3.123      5.095
   5         -8.2      4.144      6.990
   6         -7.9      2.018      4.489
   7         -7.9      4.364      6.735
   8         -7.8      3.369      5.314
   9         -7.7     25.729     27.466
Writing output ... done.
```

Figure S109. Affinity result of compound **3k** with FGFR1 receptor

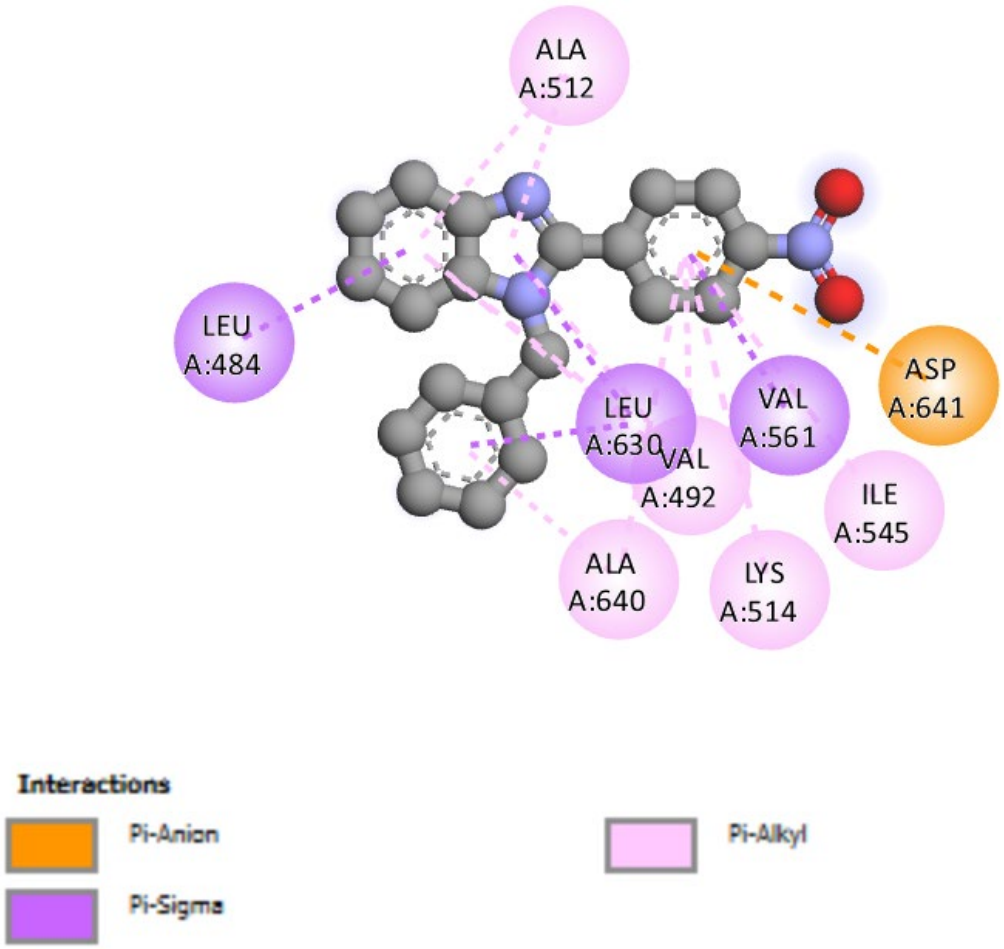


Figure S110. 2D representation of the interaction of compound **3k** with FGFR1 receptor

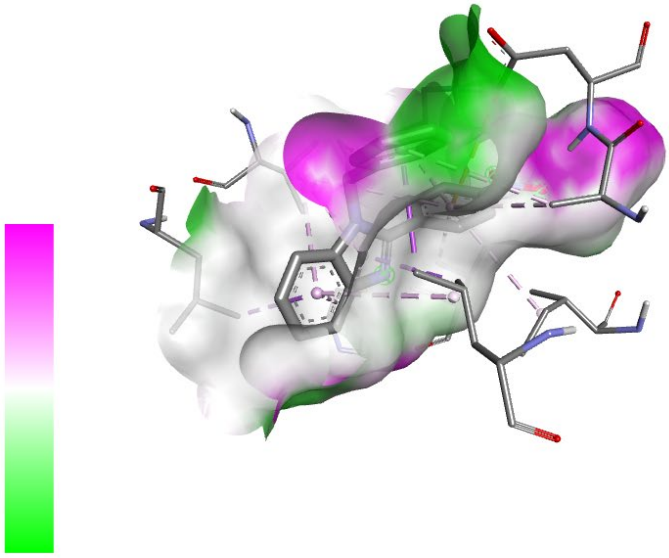


Figure S111. 3D representation of the interaction of compound **3k** with FGFR1 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -785473136
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.3      0.000      0.000
   2         -9.2      1.595      2.220
   3         -8.9      2.215      2.919
   4         -8.2      3.370      6.774
   5         -8.1      2.900      6.984
   6         -8.1      1.658      5.549
   7         -8.0      2.929      5.970
   8         -8.0      2.818      3.985
   9         -7.9      8.465     10.184
Writing output ... done.
```

Figure S112. Affinity result of compound **3j** with FGFR1 receptor

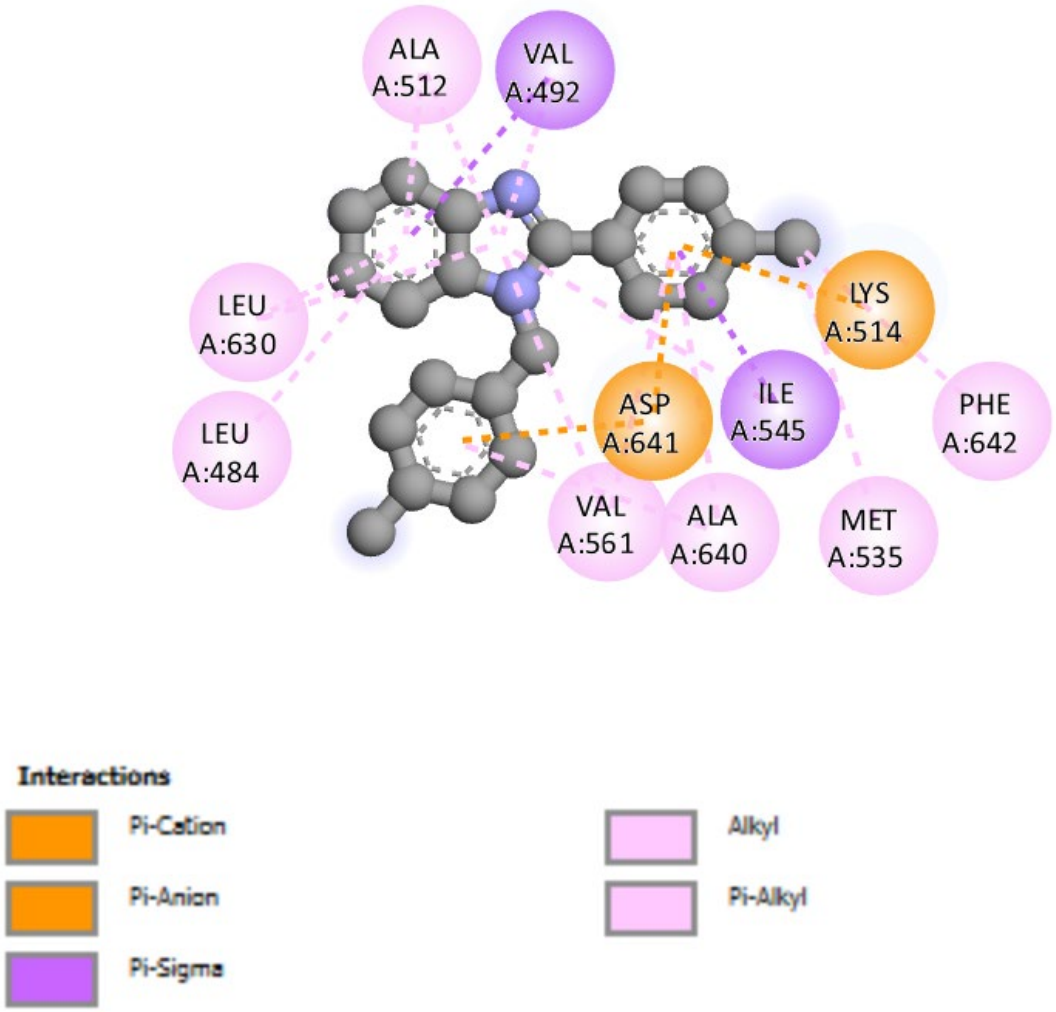


Figure S113. 2D representation of the interaction of compound **3j** with FGFR1 receptor

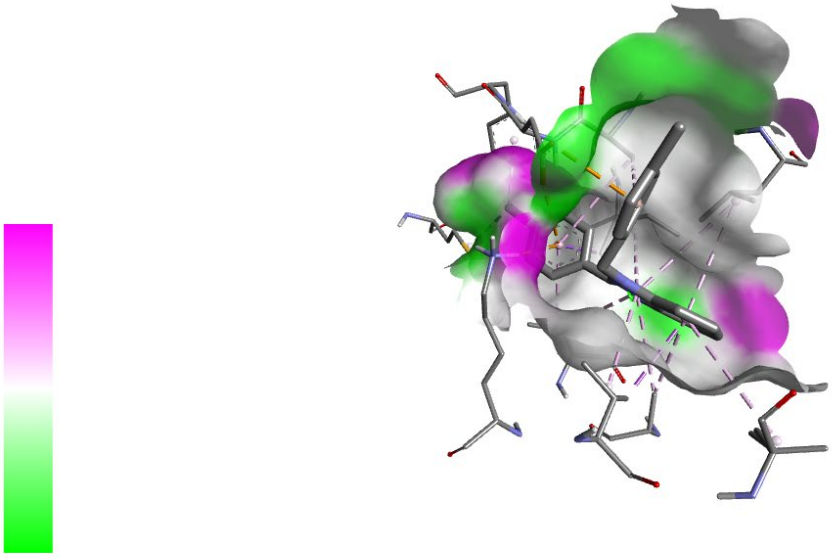


Figure S114. 3D representation of the interaction of compound **3j** with FGFR1 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1521636996
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.6      0.000      0.000
   2         -8.7      1.475      4.443
   3         -7.8      4.132      7.799
   4         -7.8      3.315      6.546
   5         -7.7      3.587      7.164
   6         -7.6      2.010      2.983
   7         -7.5     25.126     27.577
   8         -7.4     24.274     27.356
   9         -7.3     24.535     26.988
Writing output ... done.
```

Figure S115. Affinity result of compound **4c** with FGFR1 receptor

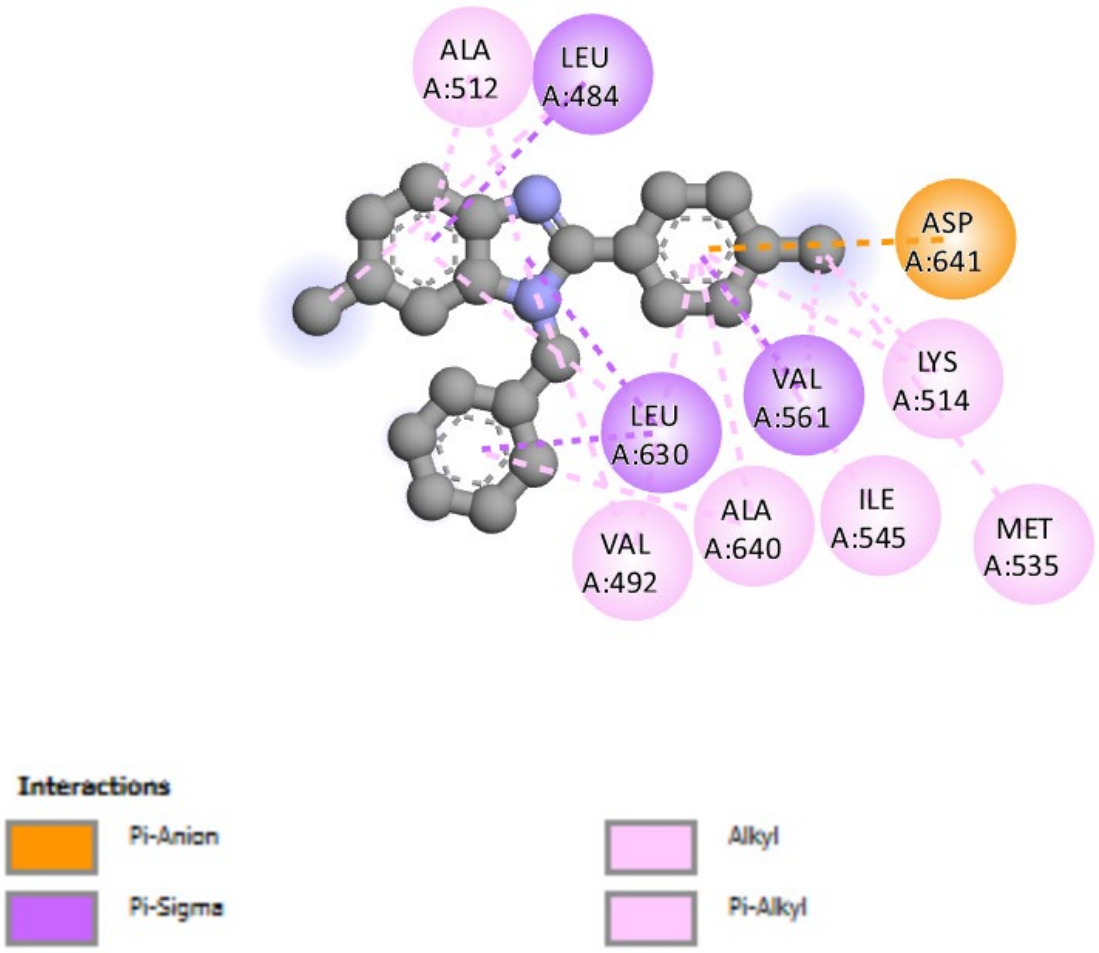


Figure S116. 2D representation of the interaction of compound **4c** with FGFR1 receptor

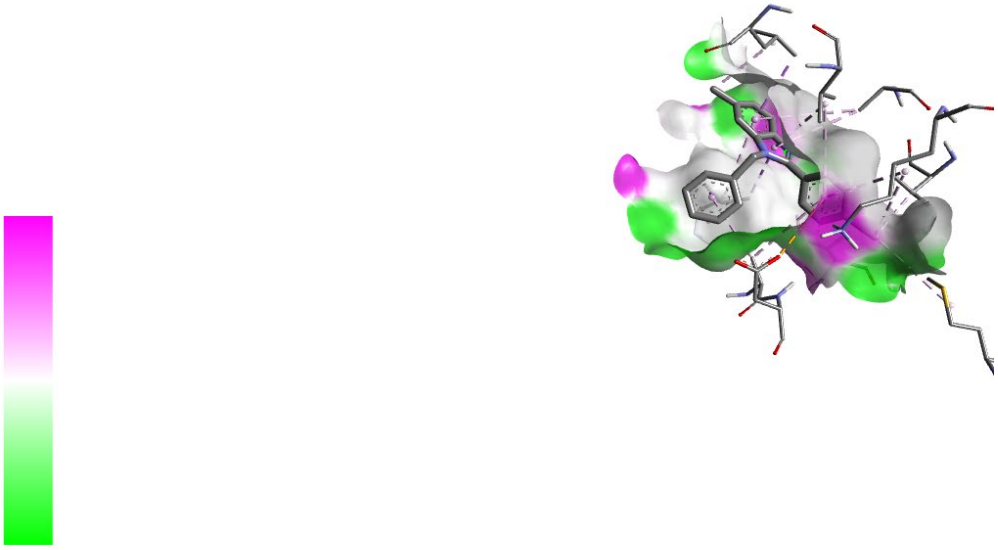


Figure S117. 3D representation of the interaction of compound **4c** with FGFR1 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -522603556
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.0      0.000      0.000
   2         -9.1      1.485      2.211
   3         -9.0      1.357      4.114
   4         -8.3      4.776      7.320
   5         -8.3      5.445      8.692
   6         -8.1      1.501      2.159
   7         -7.9     24.575     26.994
   8         -7.8      4.419      7.466
   9         -7.8      2.105      4.517
Writing output ... done.
```

Figure S118. Affinity result of compound **4g** with FGFR1 receptor

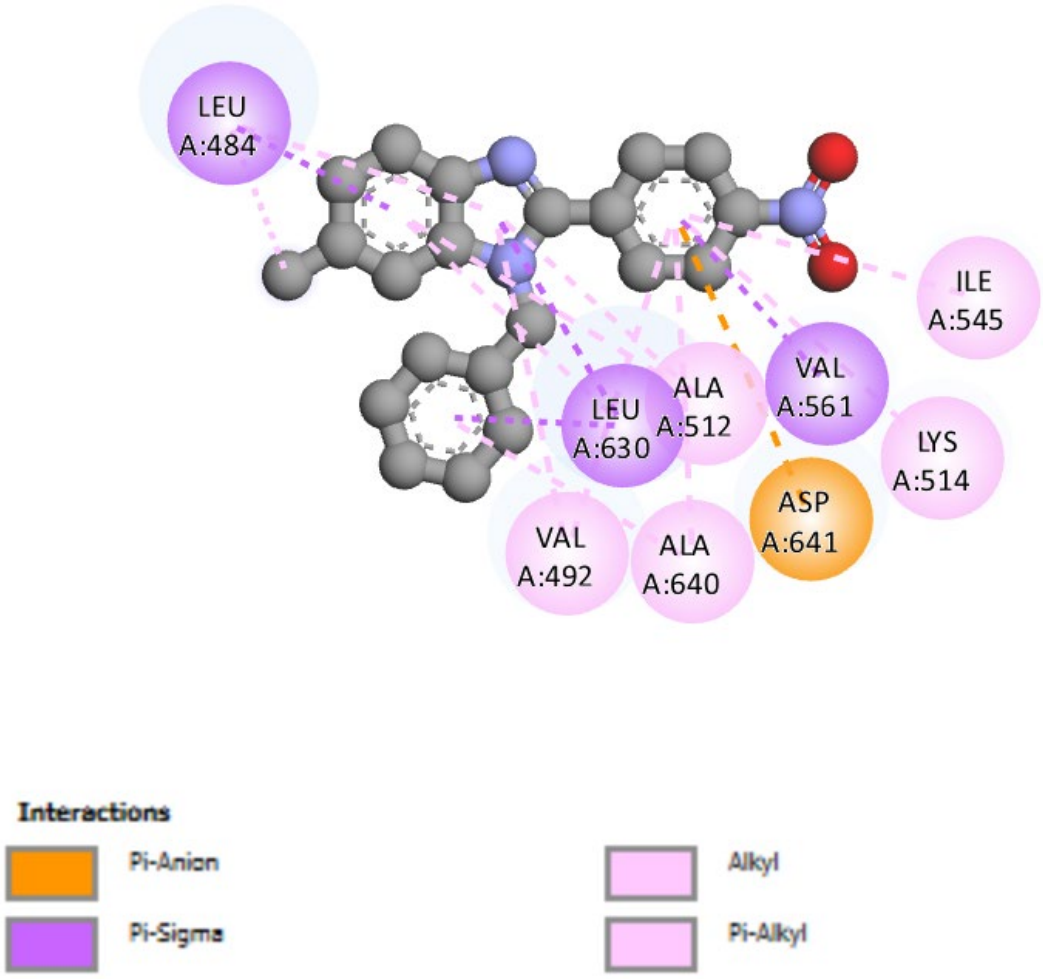


Figure S119. 2D representation of the interaction of compound **4g** with FGFR1 receptor

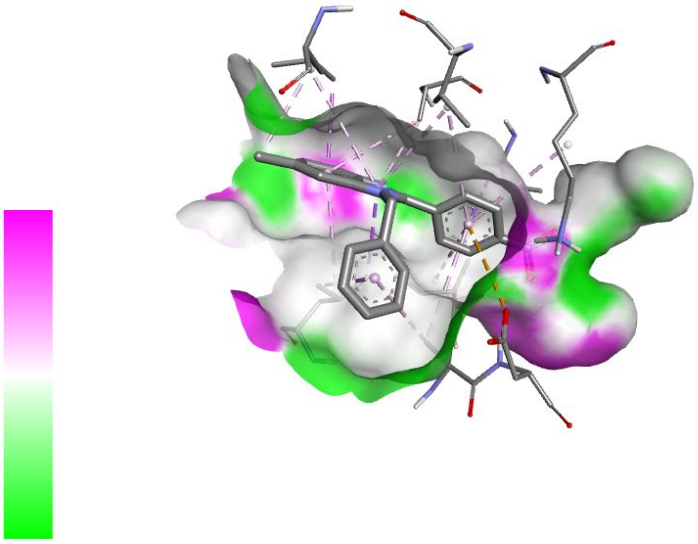


Figure S120. 3D representation of the interaction of compound **4g** with FGFR1 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 808097024
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.5      0.000      0.000
   2         -9.2      2.359      2.806
   3         -8.5      4.497      6.920
   4         -8.2      2.825      5.262
   5         -8.1      4.723      7.596
   6         -8.1      5.115      8.118
   7         -8.0     24.430     26.705
   8         -7.9     25.356     27.778
   9         -7.7      4.949      7.229
Writing output ... done.
```

Figure S121. Affinity result of compound **4j** with FGFR1 receptor

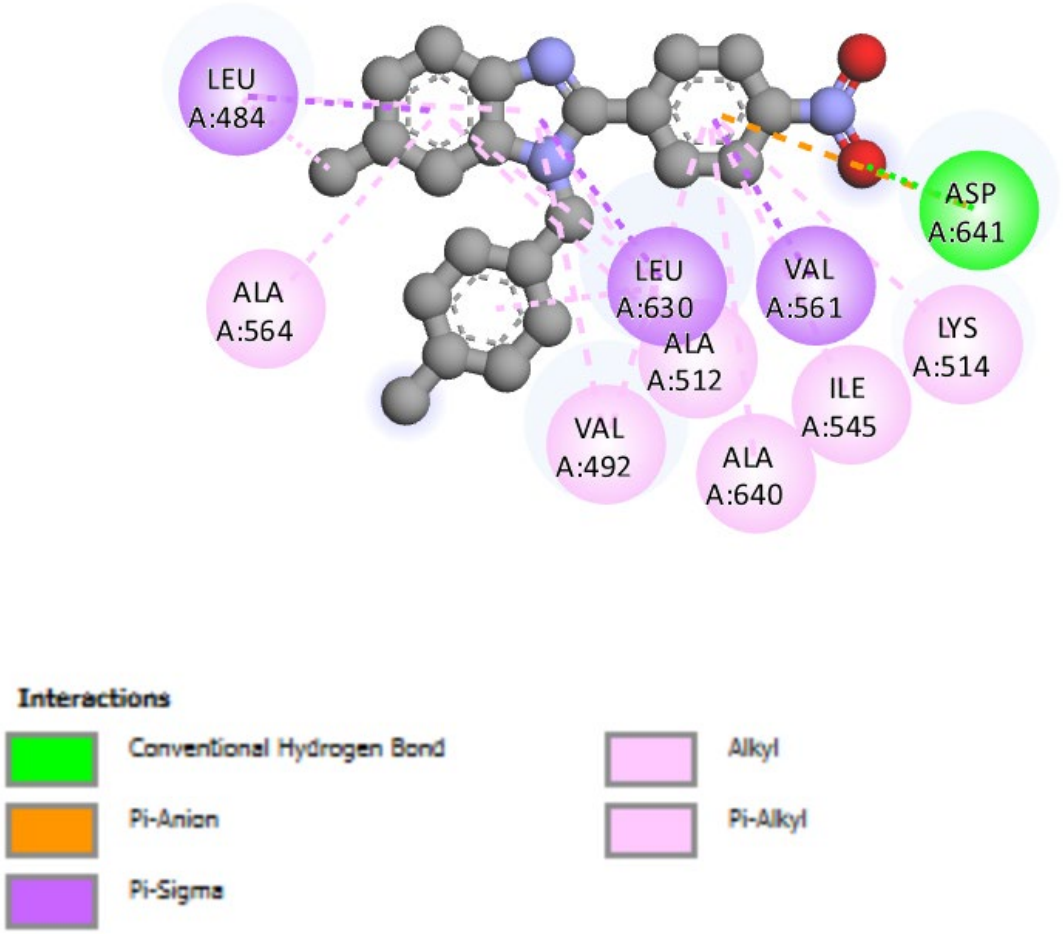


Figure S122. 2D representation of the interaction of compound **4j** with FGFR1 receptor

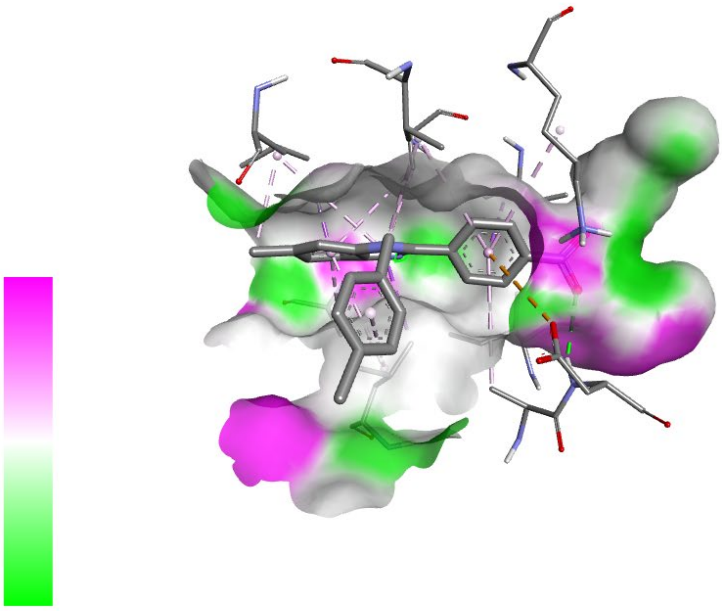


Figure S123. 3D representation of the interaction of compound **4j** with FGFR1 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 156777752
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.5      0.000      0.000
   2         -9.8      2.913      4.940
   3         -9.5      1.946      4.442
   4         -9.4      3.558     10.426
   5         -9.4      2.684      4.388
   6         -9.3      3.141      5.010
   7         -9.2      4.014      9.926
   8         -9.2      3.942      9.070
   9         -9.1      3.016      6.438
Writing output ... done.
```

Figure S124. Affinity result of **PTX** with FGFR1 receptor

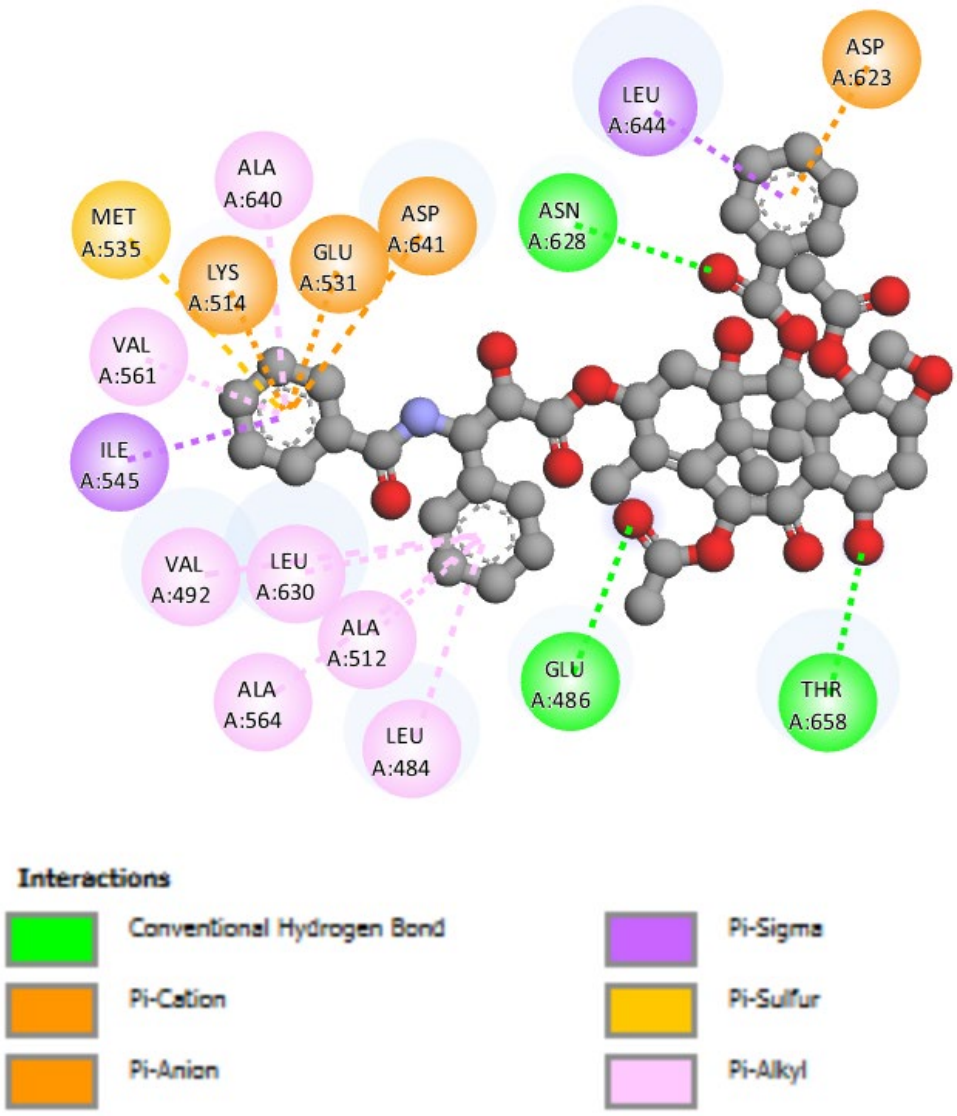


Figure S125. 2D representation of the interaction of **PTX** with FGFR1 receptor

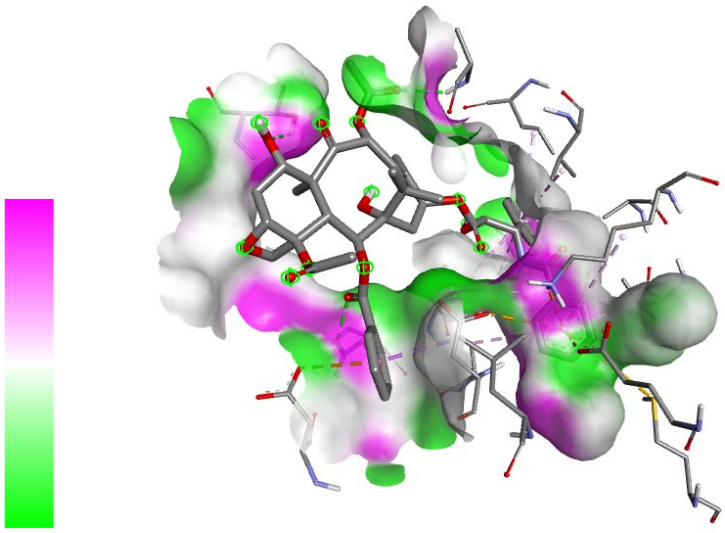


Figure S126. 3D representation of the interaction of **PTX** with FGFR1 receptor

```
receptor = 5eefHDAC6.pdbqt
ligand = ligand.pdbqt

out = out.pdbqt

center_x = -18.649
center_y = -42.547
center_z = -12.834

size_x = 30
size_y = 42
size_z = 30

energy_range = 4
exhaustiveness = 8
```

Figure S127. Grid box volume – Autodock Vina for Histone deacetylase 6 (HDAC6, PDB: 5EEF)

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1022254048
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.4      0.000      0.000
   2         -9.3      1.338      2.057
   3         -9.1      3.498      6.342
   4         -8.5      2.256      4.489
   5         -8.4      3.749      6.587
   6         -8.2      3.835      6.190
   7         -7.7      4.259      6.823
   8         -7.7      2.387      3.294
   9         -7.5      4.269      6.525
Writing output ... done.
```

Figure S128. Affinity result of compound **3k** with HDAC6 receptor

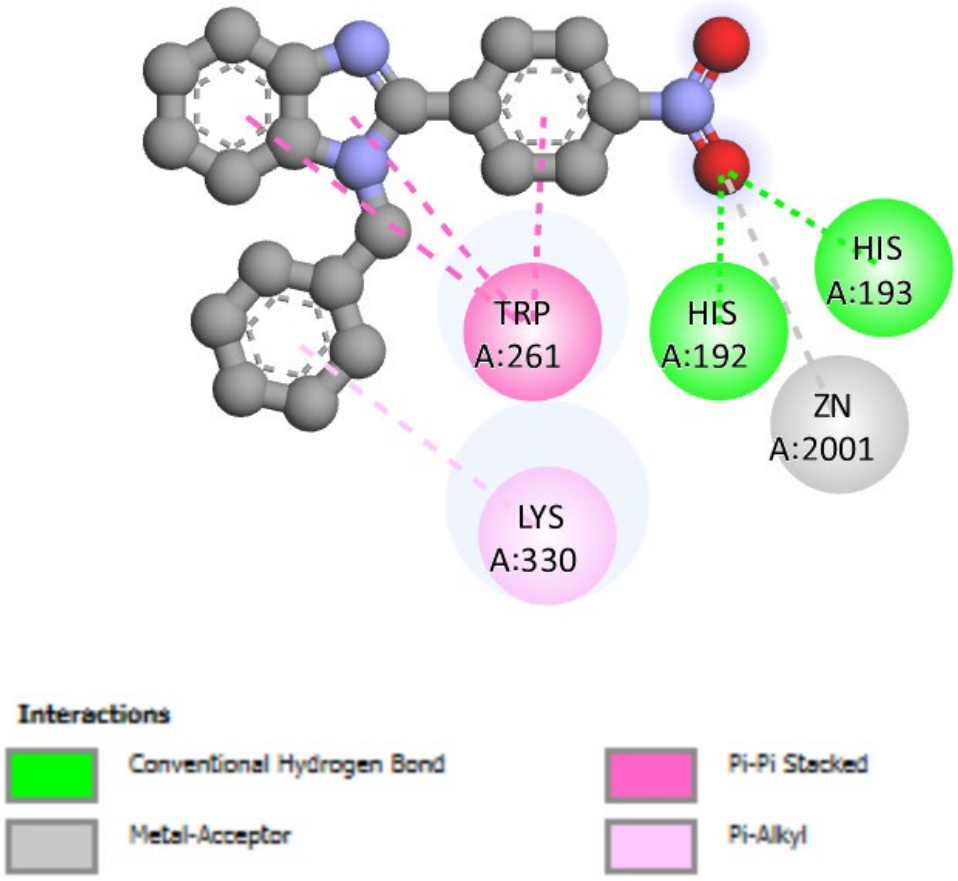


Figure S129. 2D representation of the interaction of compound **3k** with HDAC6 receptor

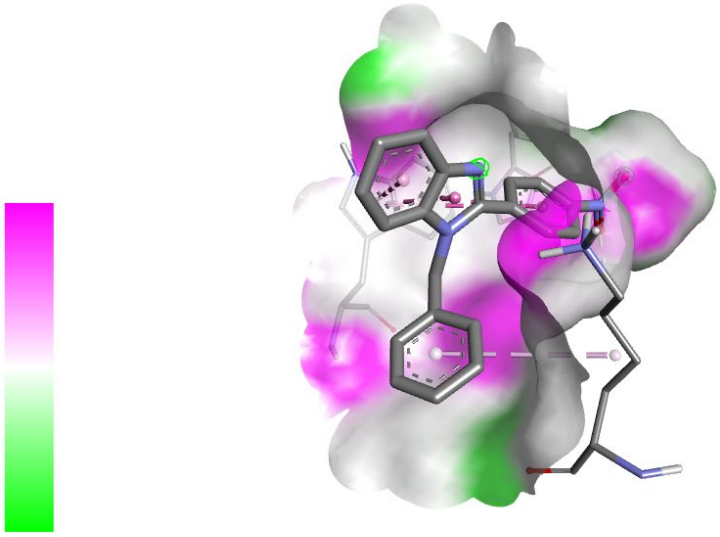


Figure S130. 3D representation of the interaction of compound **3k** with HDAC6 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1573869712
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.1      0.000      0.000
   2         -8.7      2.993      5.434
   3         -8.6      2.749      6.086
   4         -8.4      2.525      6.285
   5         -8.1      1.390      2.030
   6         -8.0      4.102      7.138
   7         -7.9      2.548      5.215
   8         -7.8      2.994      6.144
   9         -7.6      3.817      6.729
Writing output ... done.
```

Figure S131. Affinity result of compound **3l** with HDAC6 receptor

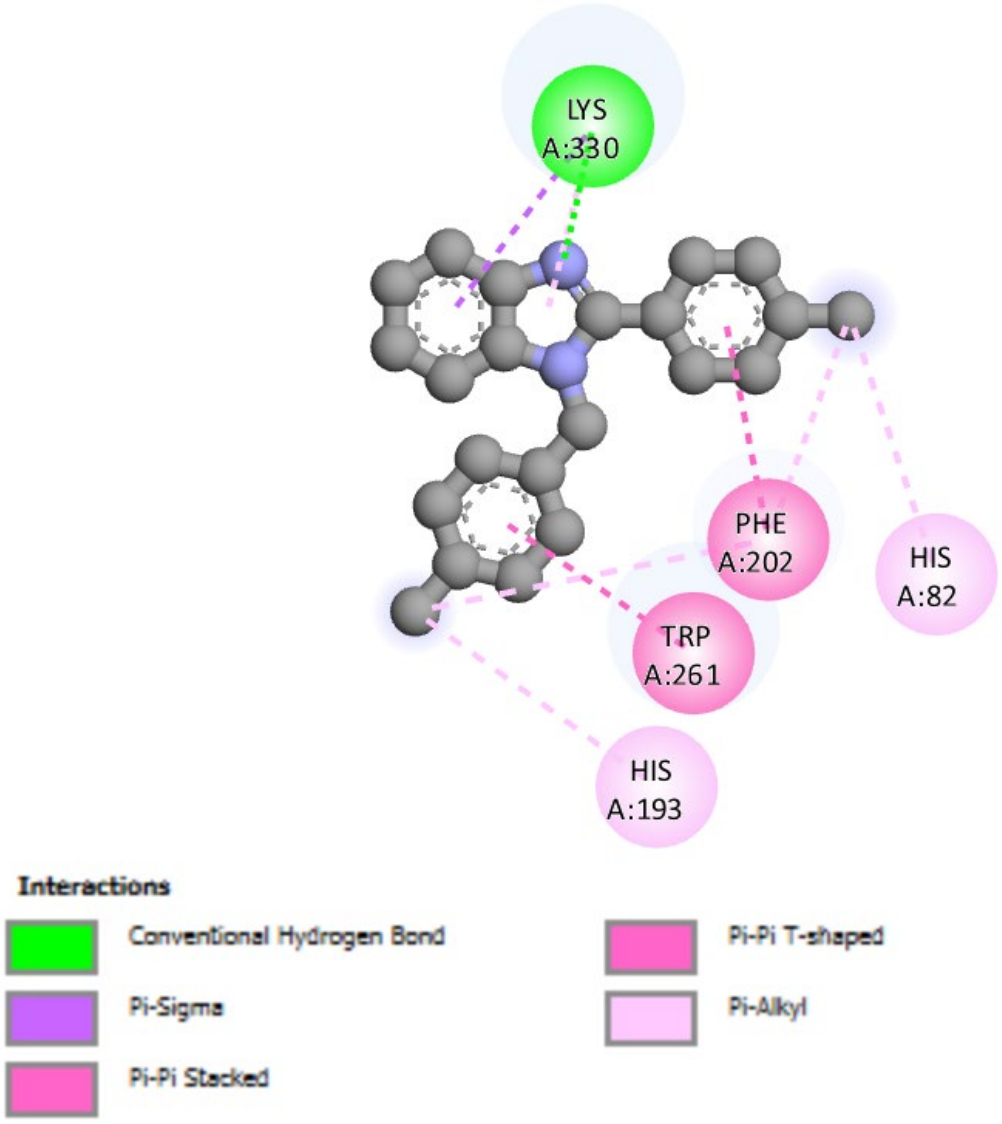


Figure S132. 2D representation of the interaction of compound **3l** with HDAC6 receptor

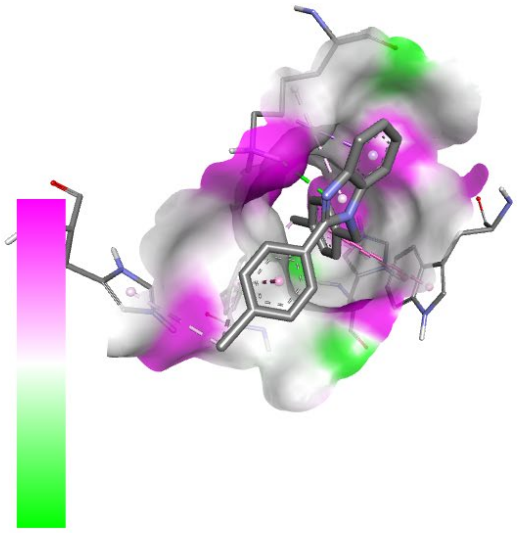


Figure S133. 3D representation of the interaction of compound **3l** with HDAC6 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 220100332
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.6      0.000      0.000
   2         -8.3      2.816      5.985
   3         -8.3      3.138      6.683
   4         -8.3      1.951      4.388
   5         -8.2      1.576      3.914
   6         -7.6      1.578      2.279
   7         -7.6      2.487      5.075
   8         -7.6      2.450      5.109
   9         -7.4      2.774      5.398
Writing output ... done.
```

Figure S134. Affinity result of compound **4c** with HDAC6 receptor

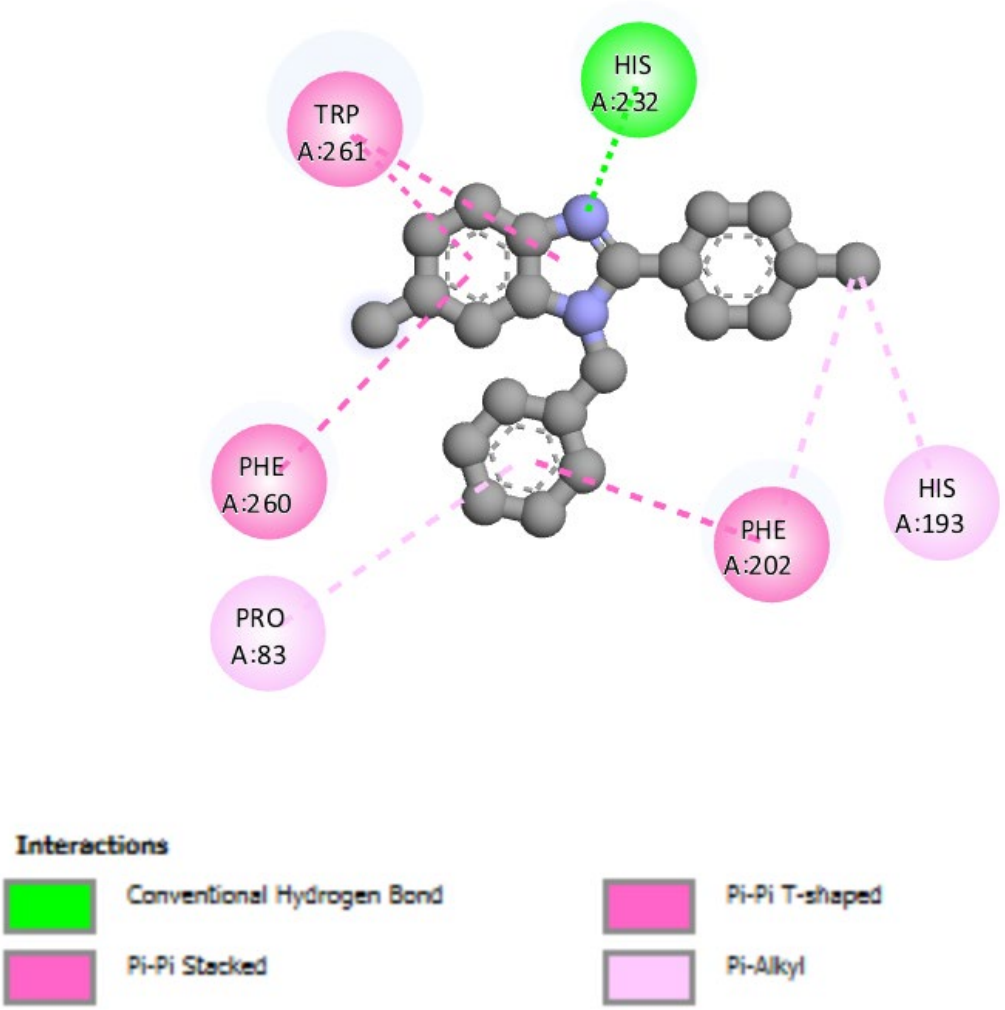


Figure S135. 2D representation of the interaction of compound **4c** with HDAC6 receptor

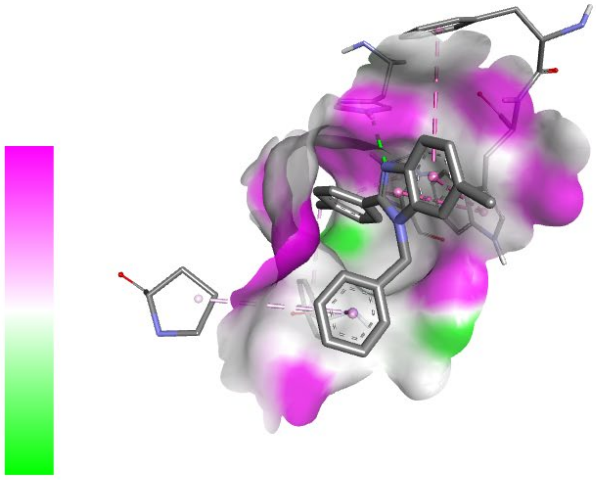


Figure S136. 3D representation of the interaction of compound **4c** with HDAC6 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1558642072
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.5      0.000      0.000
   2         -9.1      1.249      1.802
   3         -8.8      1.420      3.718
   4         -8.7      2.085      4.223
   5         -8.6      1.116      1.801
   6         -8.2      3.794      6.566
   7         -7.7      3.943      6.548
   8         -7.7      3.739      6.166
   9         -7.6      1.785      2.671
Writing output ... done.
```

Figure S137. Affinity result of compound **4g** with HDAC6 receptor

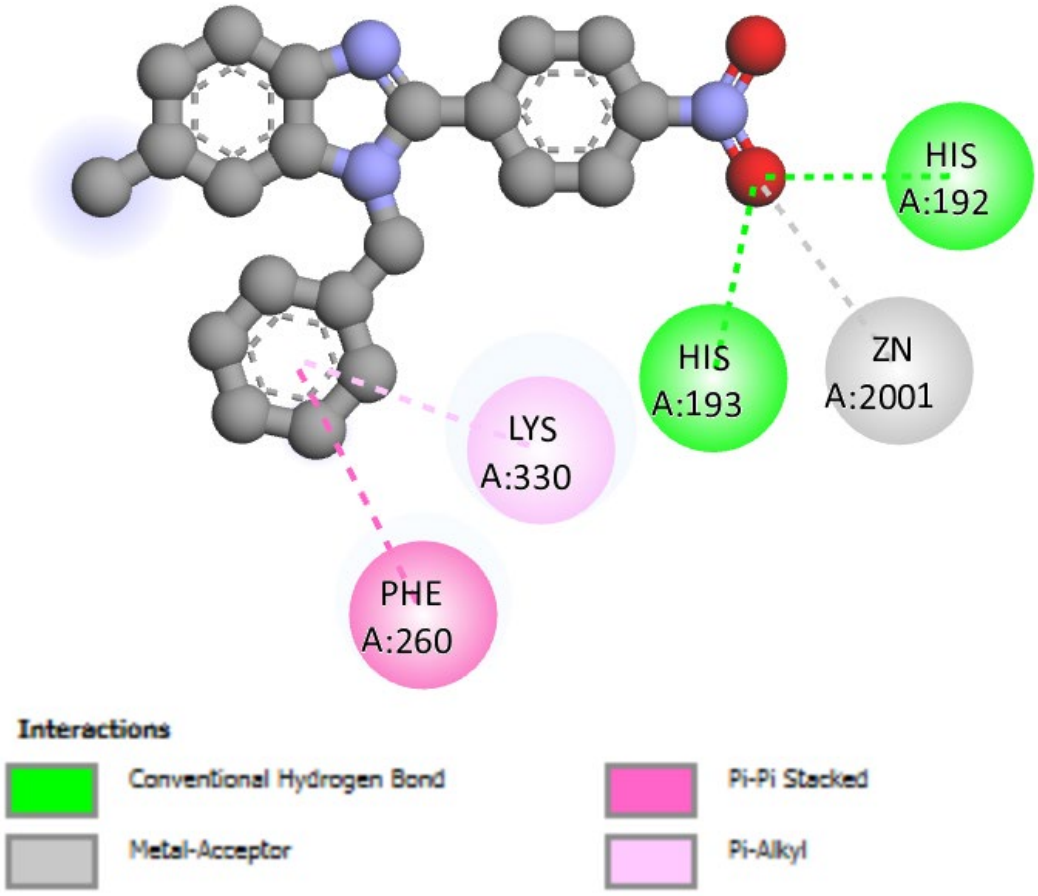


Figure S138. 2D representation of the interaction of compound **4g** with HDAC6 receptor

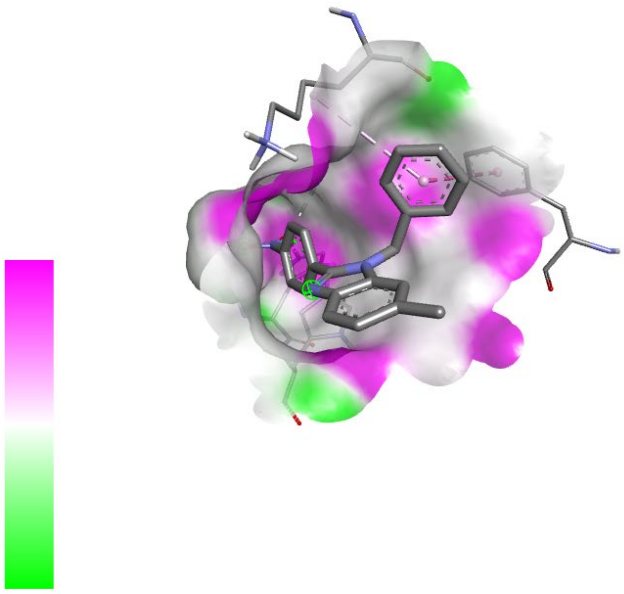


Figure S139. 3D representation of the interaction of compound **4g** with HDAC6 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -714589224
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.4      0.000      0.000
   2         -8.8      3.184      4.917
   3         -8.8      1.763      2.140
   4         -8.7      2.567      4.348
   5         -8.2      4.033      6.512
   6         -8.0      2.959      4.868
   7         -8.0      2.591      4.770
   8         -7.7      4.678      7.011
   9         -7.6      4.360      6.649
Writing output ... done.
```

Figure S140. Affinity result of compound **4j** with HDAC6 receptor

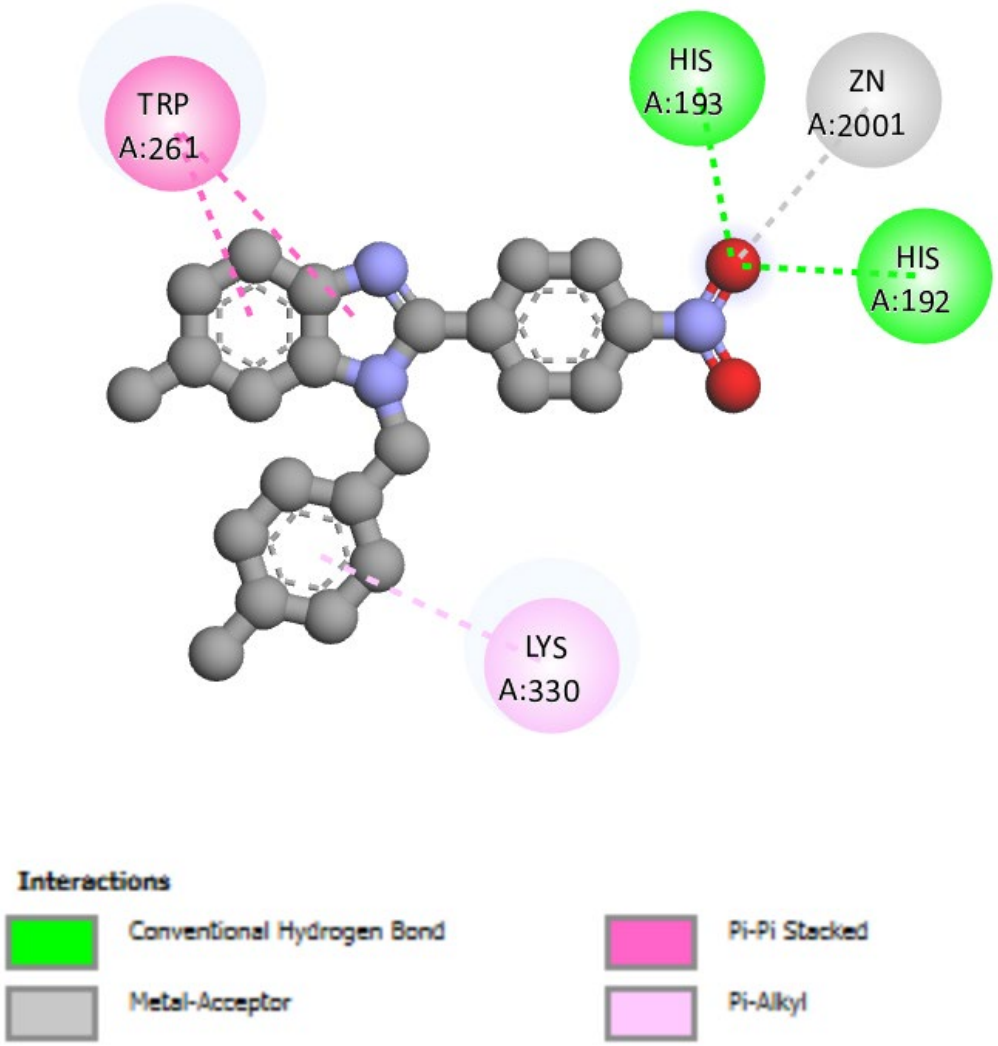


Figure S141. 2D representation of the interaction of compound **4j** with HDAC6 receptor

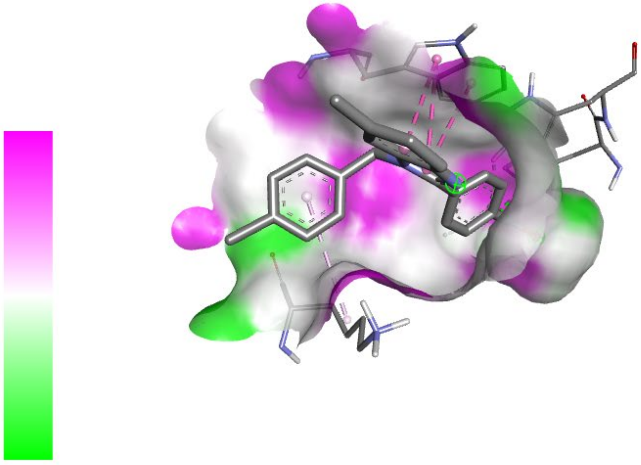


Figure S142. 3D representation of the interaction of compound **4j** with HDAC6 receptor

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 8 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1815704864
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.8      0.000      0.000
   2         -8.6      1.433      3.830
   3         -8.6      2.045      4.464
   4         -8.2      3.041     10.618
   5         -8.2      1.686      2.402
   6         -8.1      2.727     10.379
   7         -8.0      2.358      4.290
   8         -7.9      2.207      4.677
   9         -7.8      2.552      9.861
Writing output ... done.
```

Figure S143. Affinity result of **PTX** with HDAC6 receptor

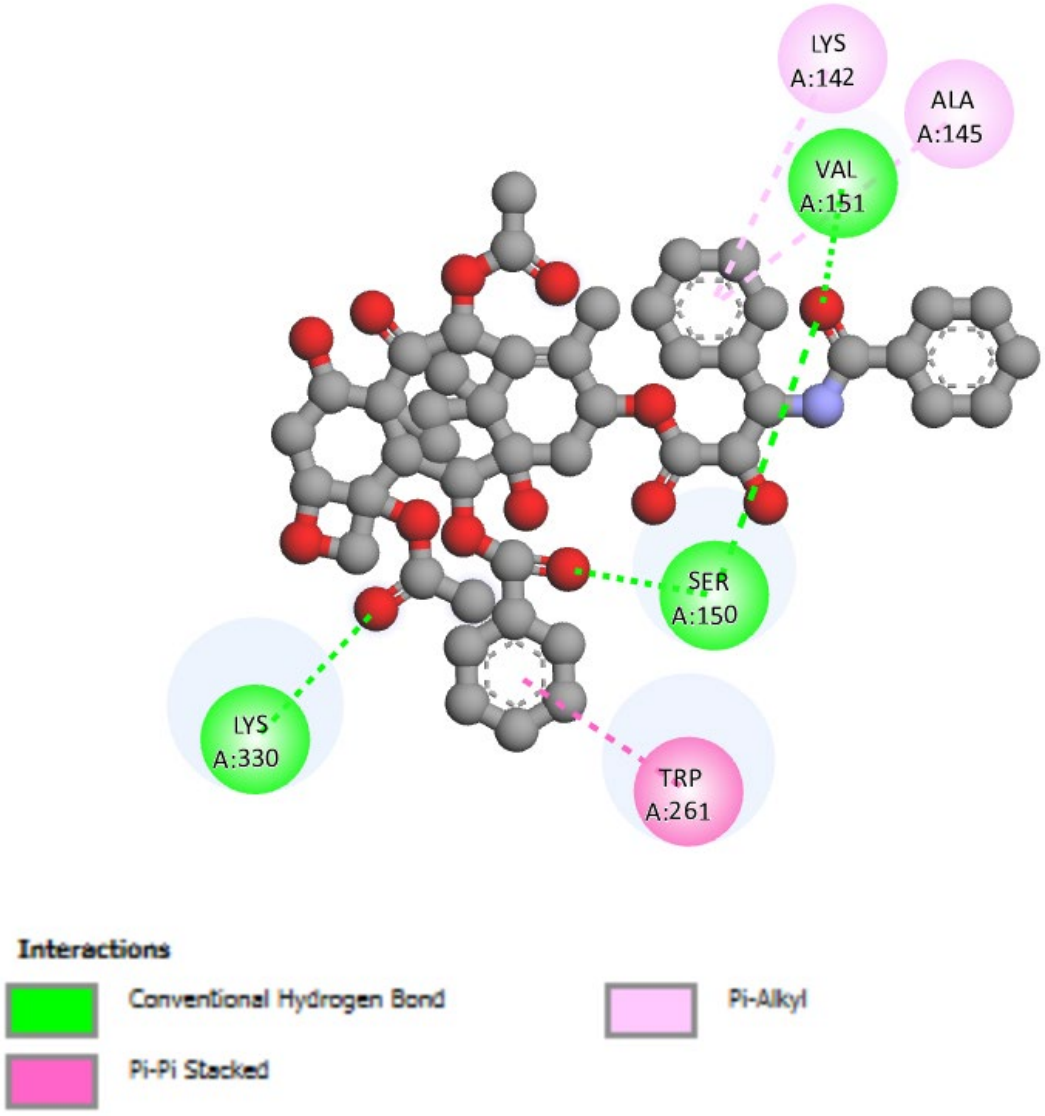


Figure S144. 2D representation of the interaction of **PTX** with HDAC6 receptor

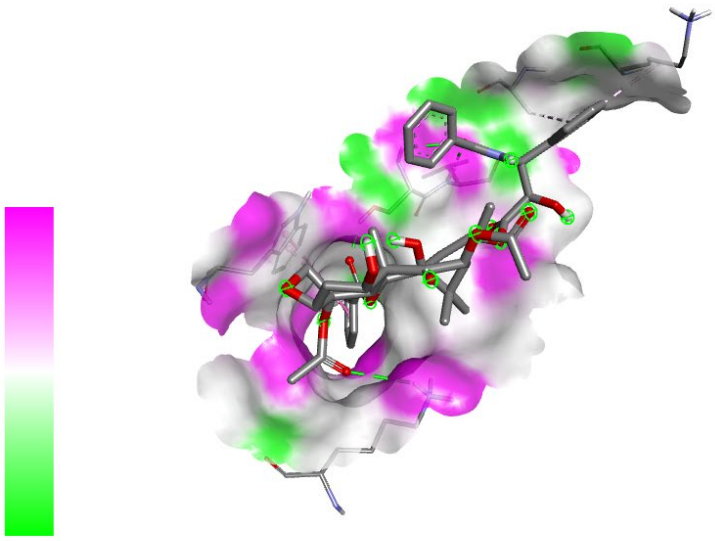


Figure S145. 3D representation of the interaction of **PTX** with HDAC6 receptor

^{1}H NMR SPECTRA

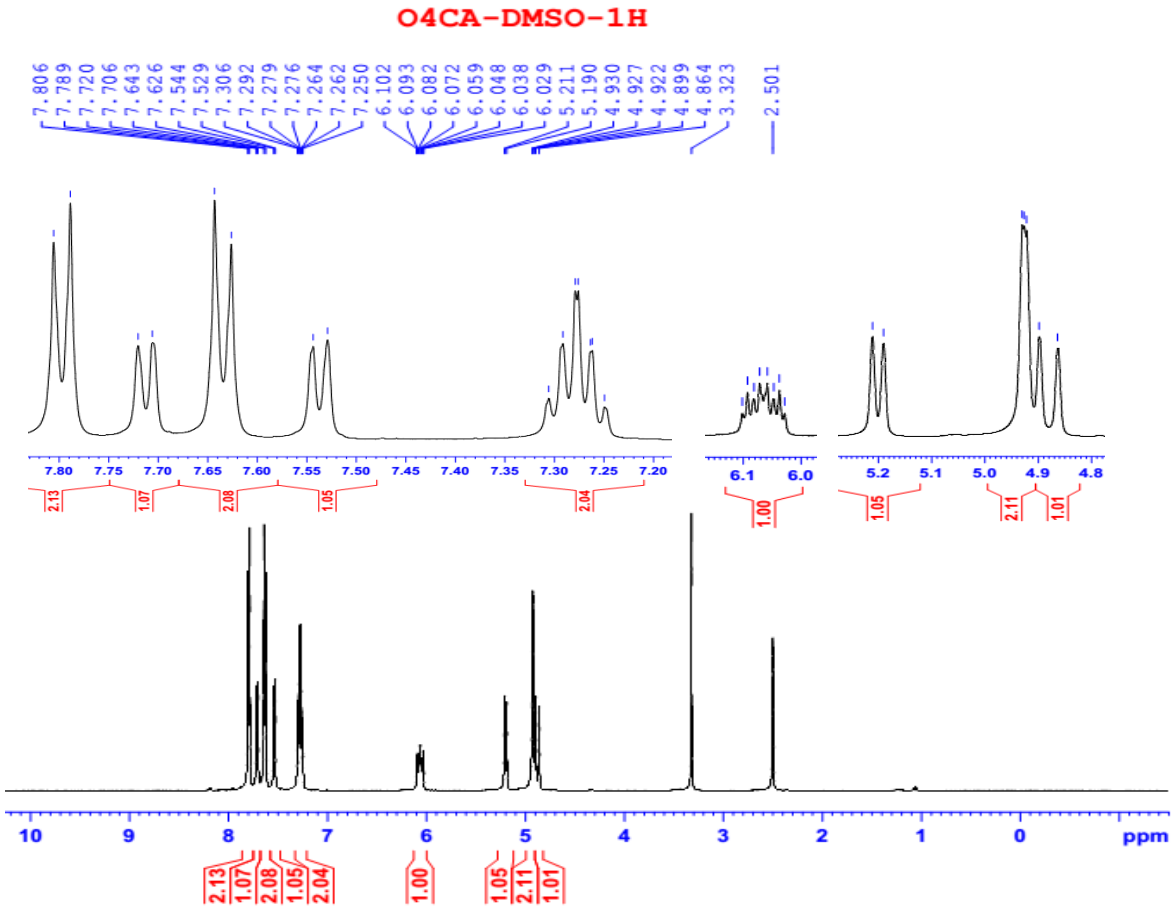


Figure S146. ^{1}H NMR spectra of compound **3a**

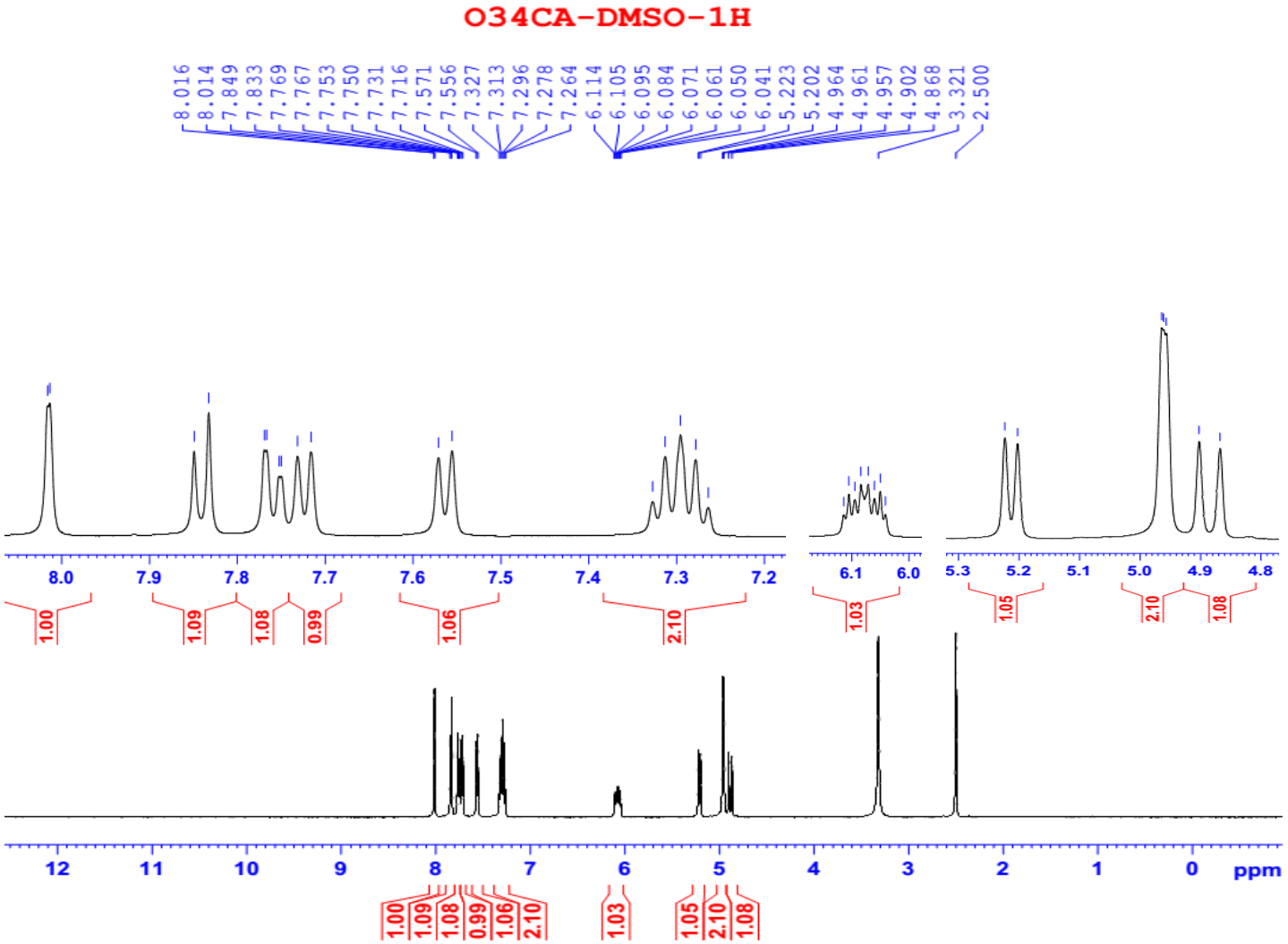


Figure S147. ^{1}H NMR spectra of compound **3b**

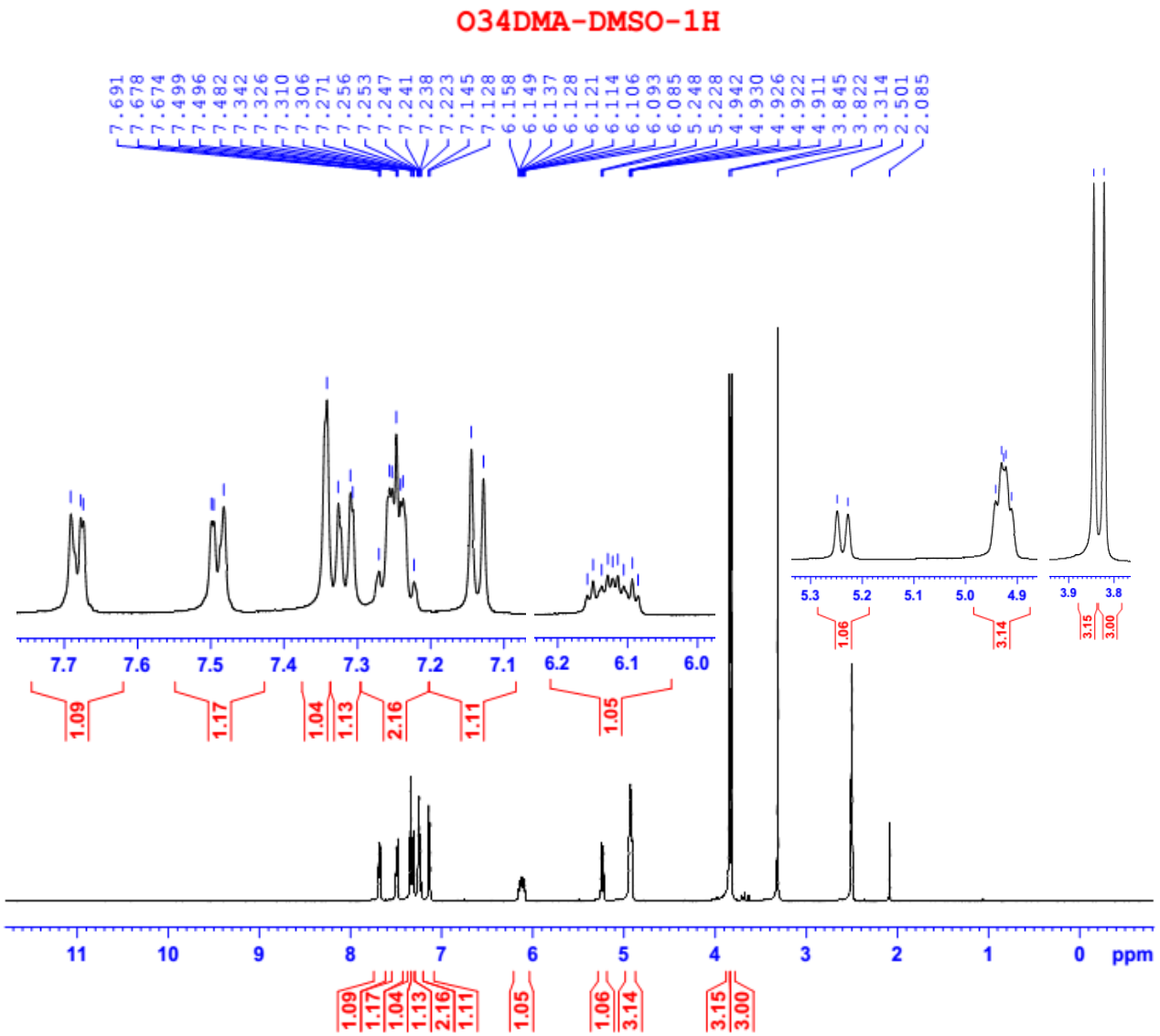


Figure S148. ^{1}H NMR spectra of compound **3c**

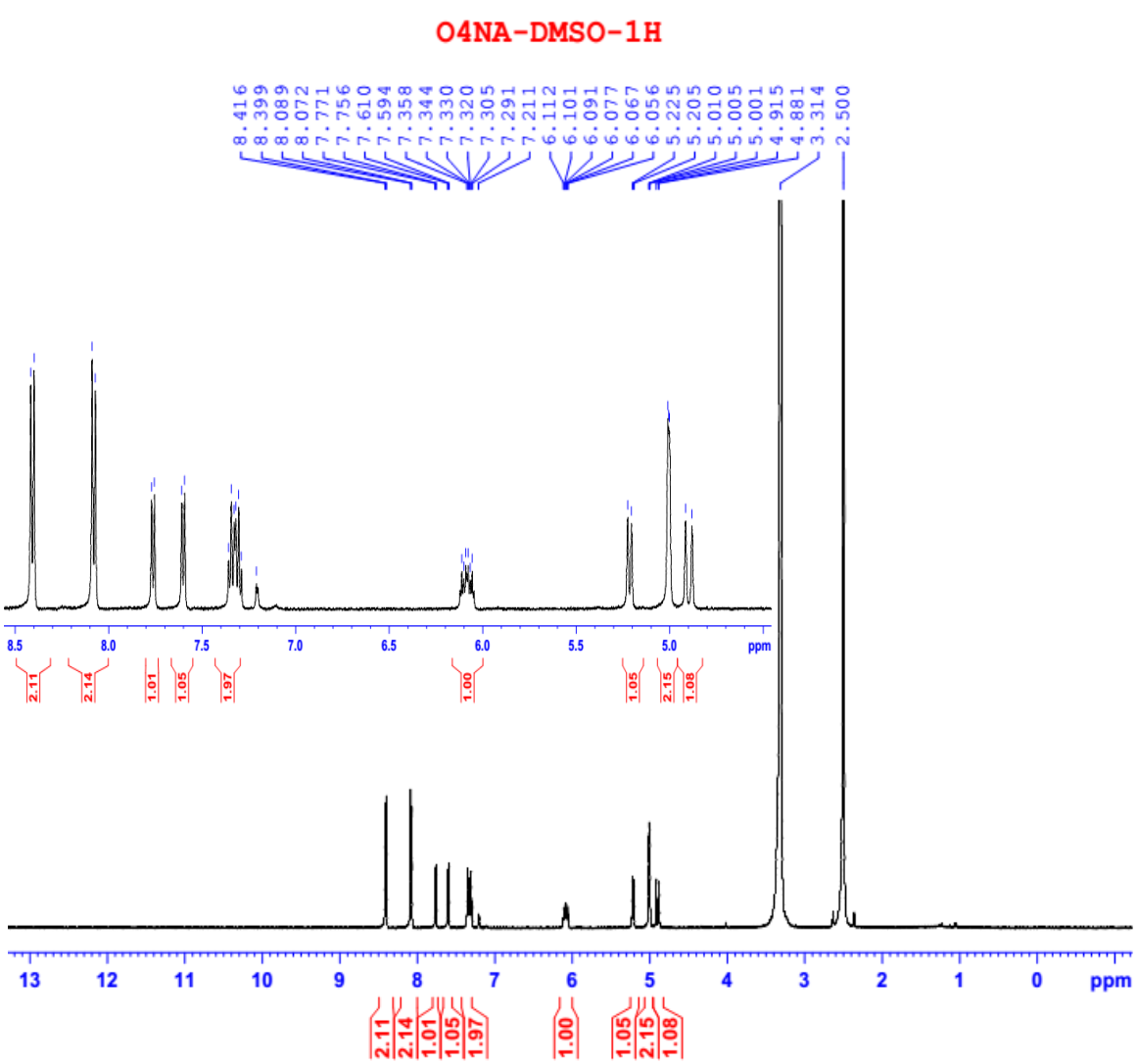


Figure S149. ^{1}H NMR spectra of compound **3d**

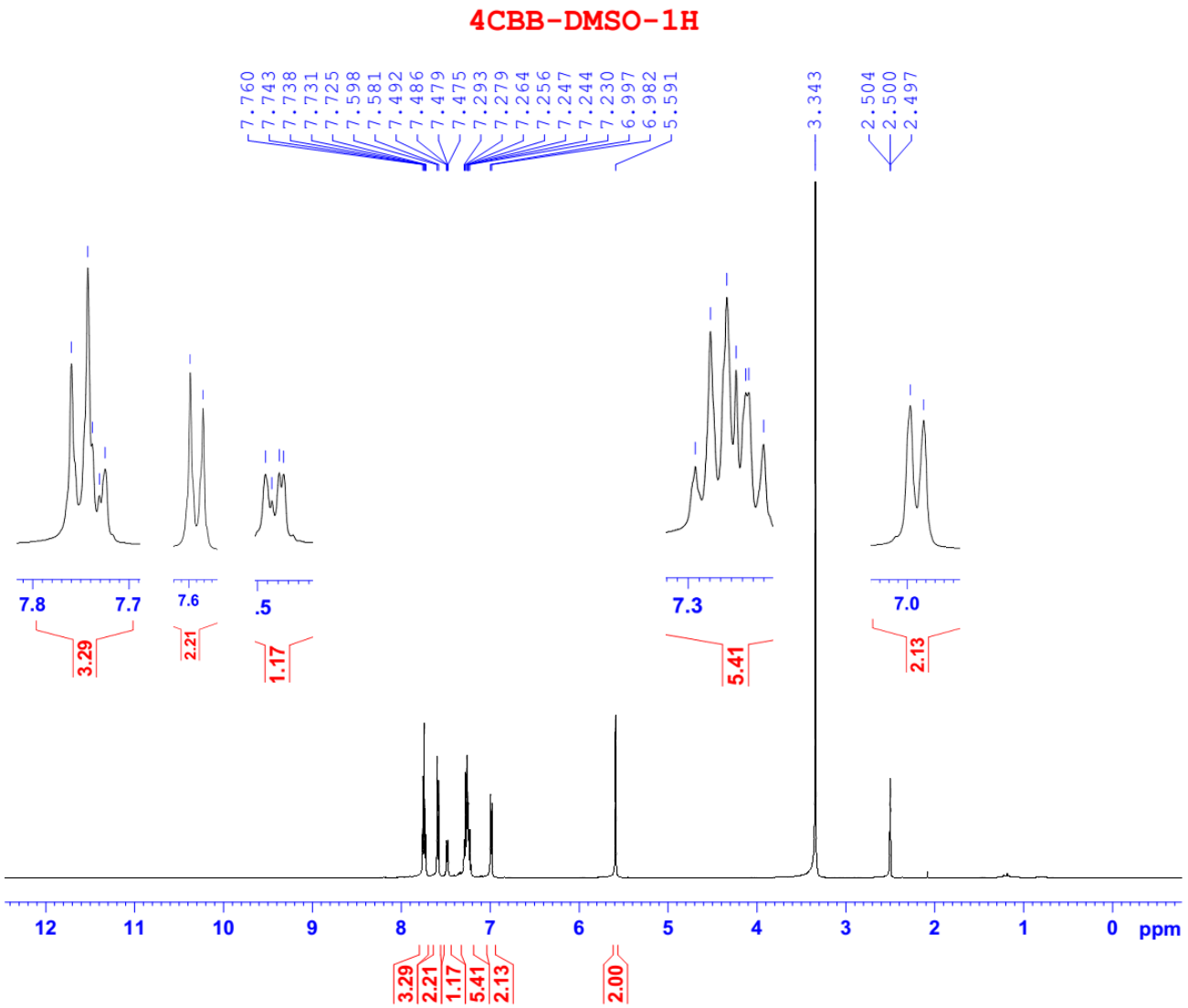


Figure S150. ^{1}H NMR spectra of compound **3e**

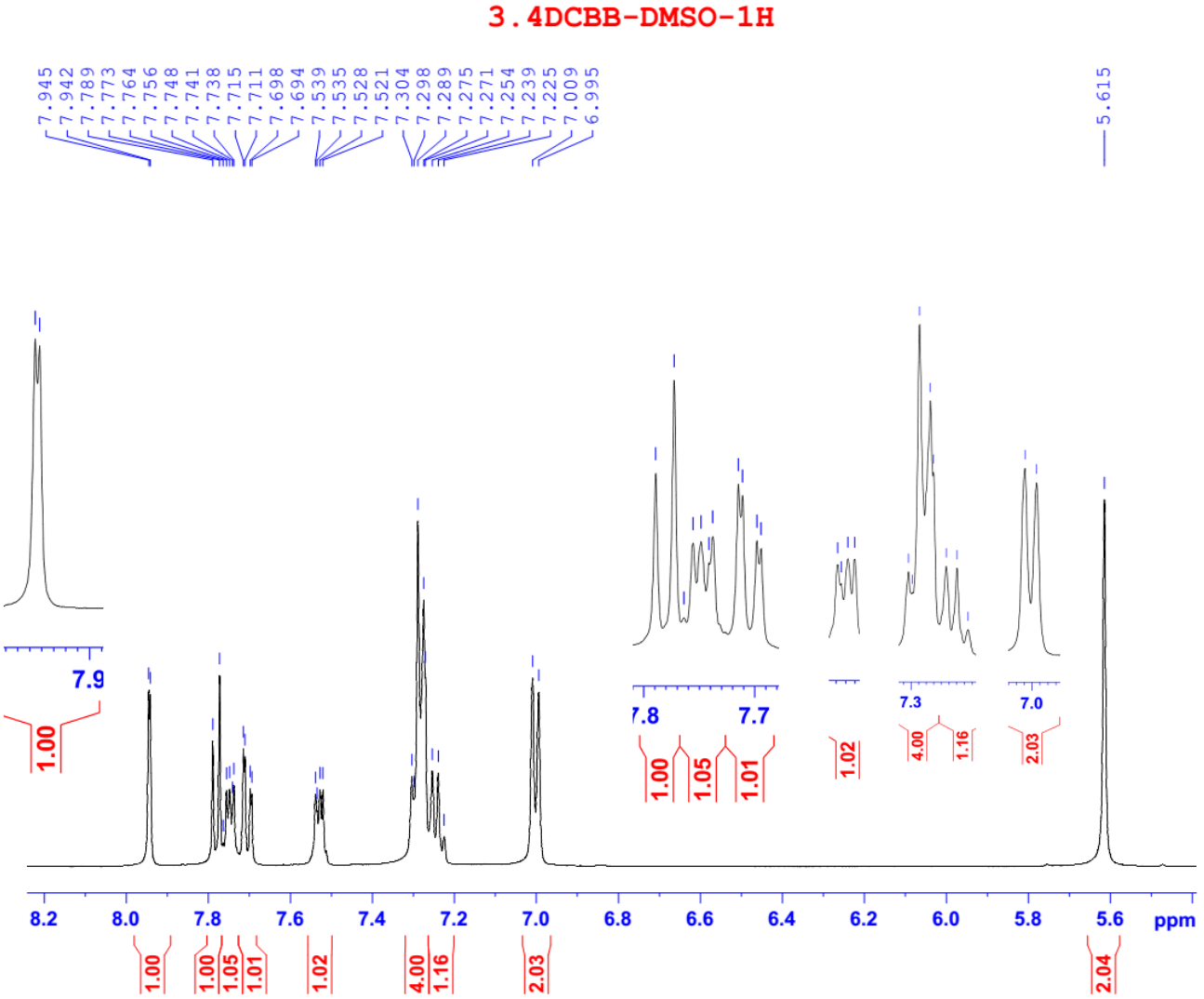


Figure S151. ^{1}H NMR spectra of compound **3f**

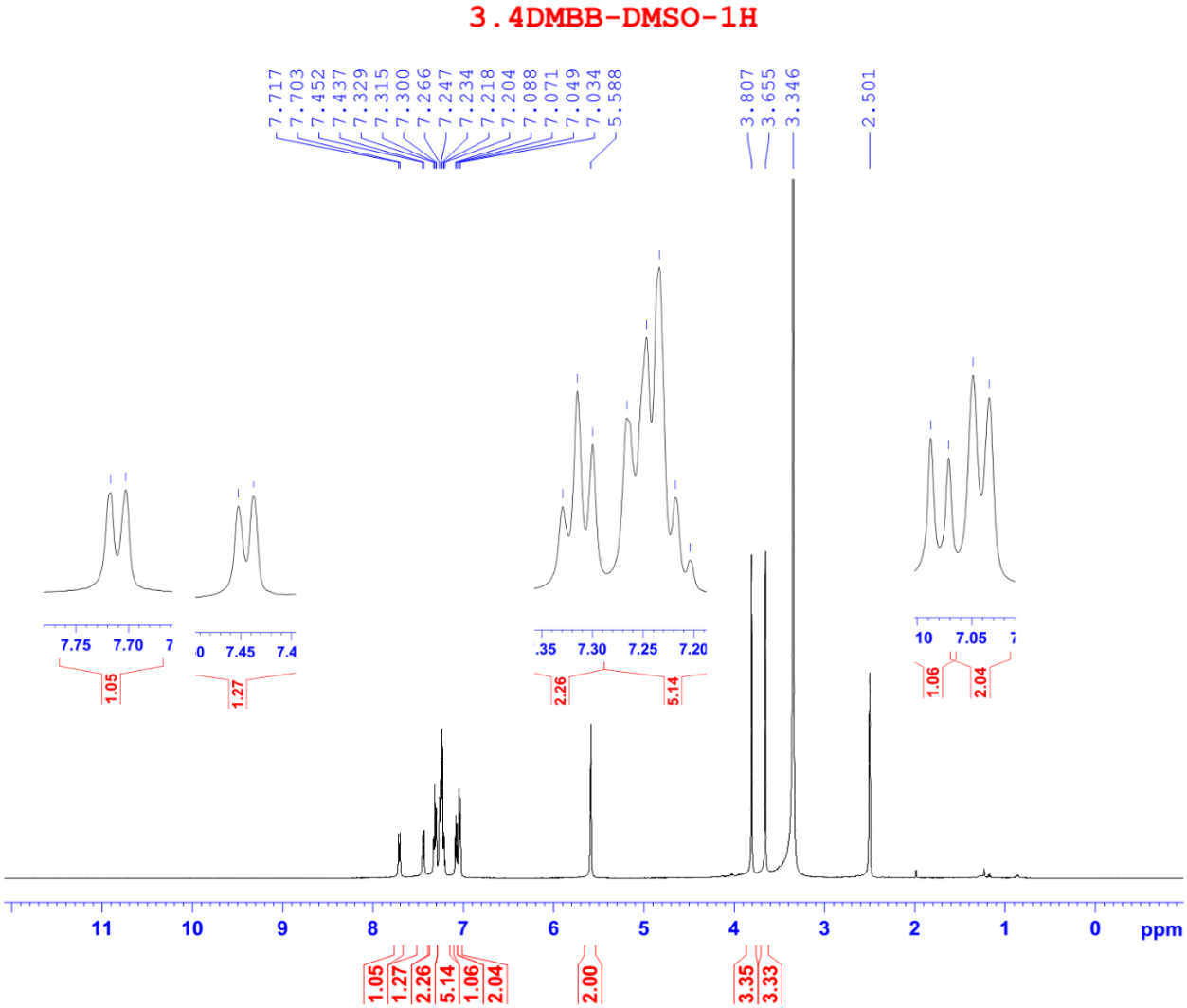


Figure S152. ^{1}H NMR spectra of compound **3g**

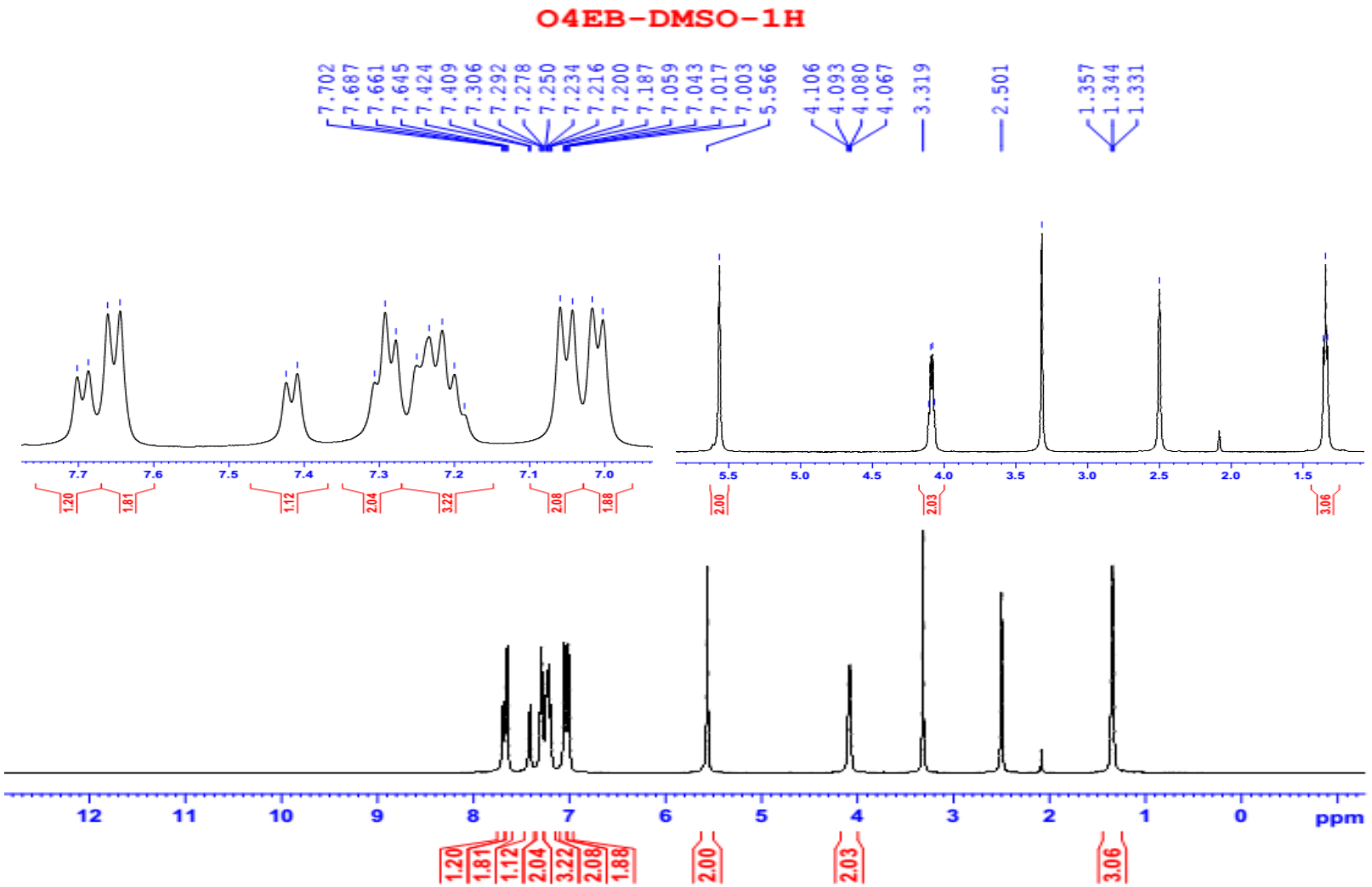


Figure S153. ^{1}H NMR spectra of compound **3**

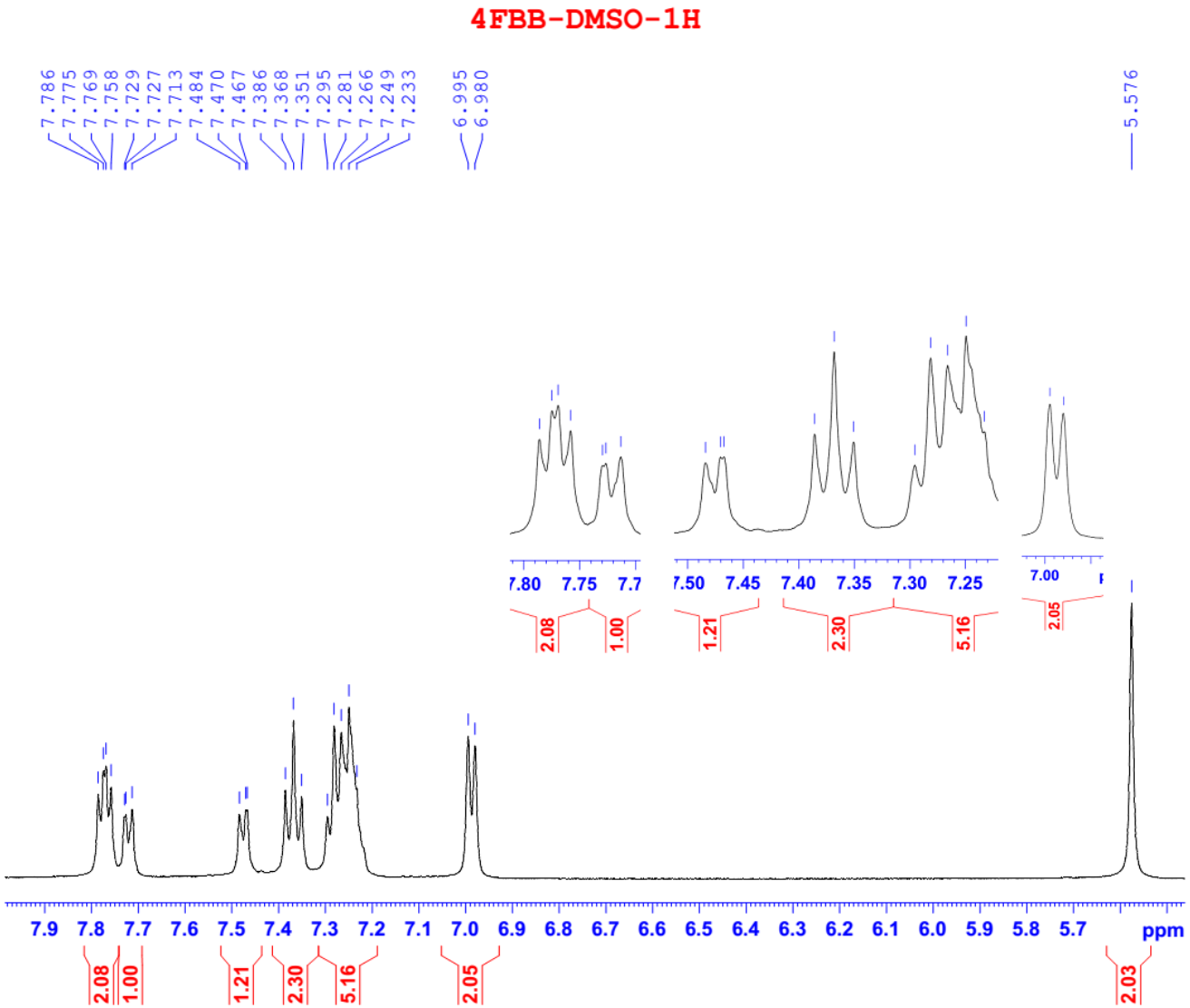


Figure S154. ^{1}H NMR spectra of compound **3i**

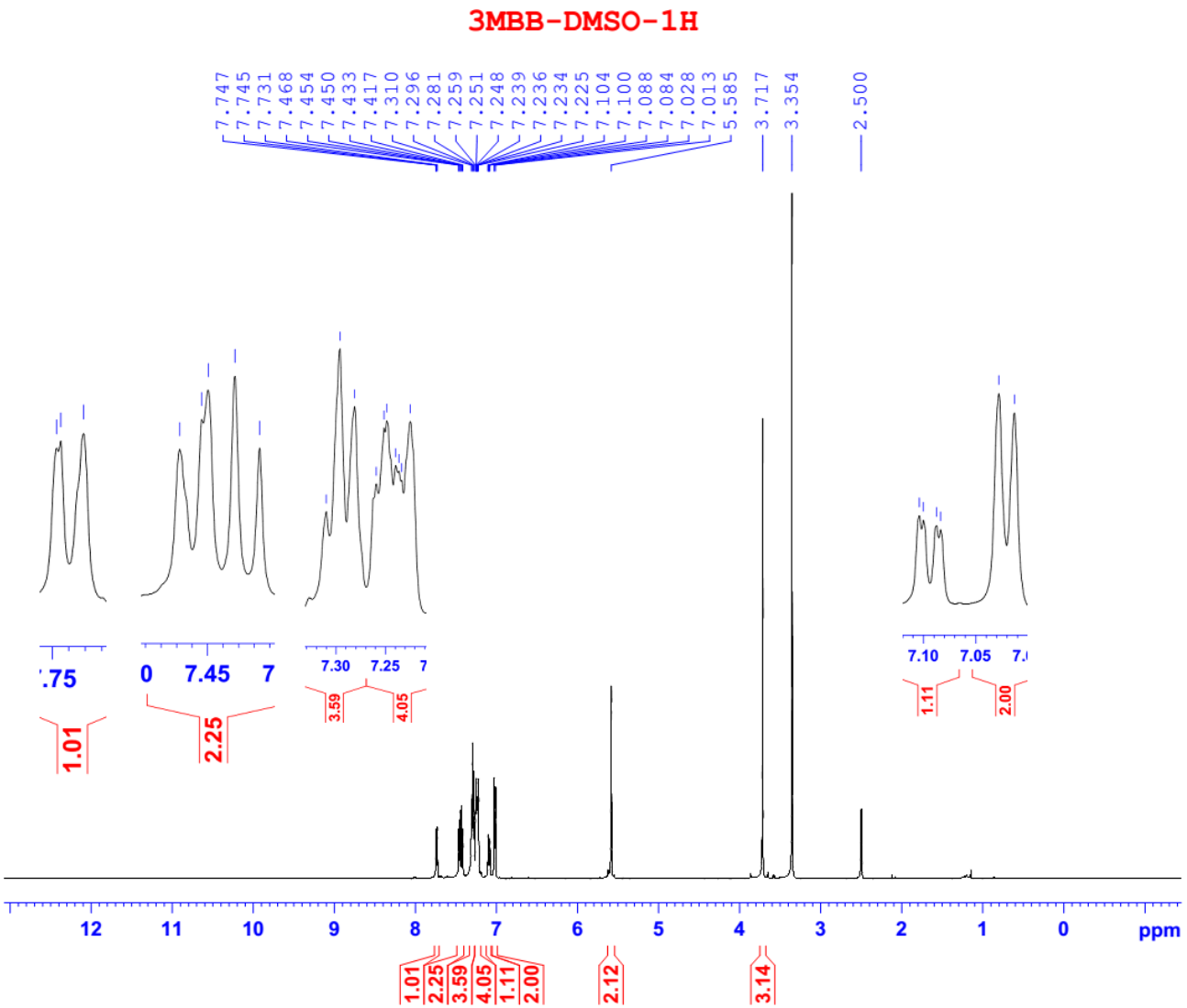


Figure S155. ^{1}H NMR spectra of compound **3j**

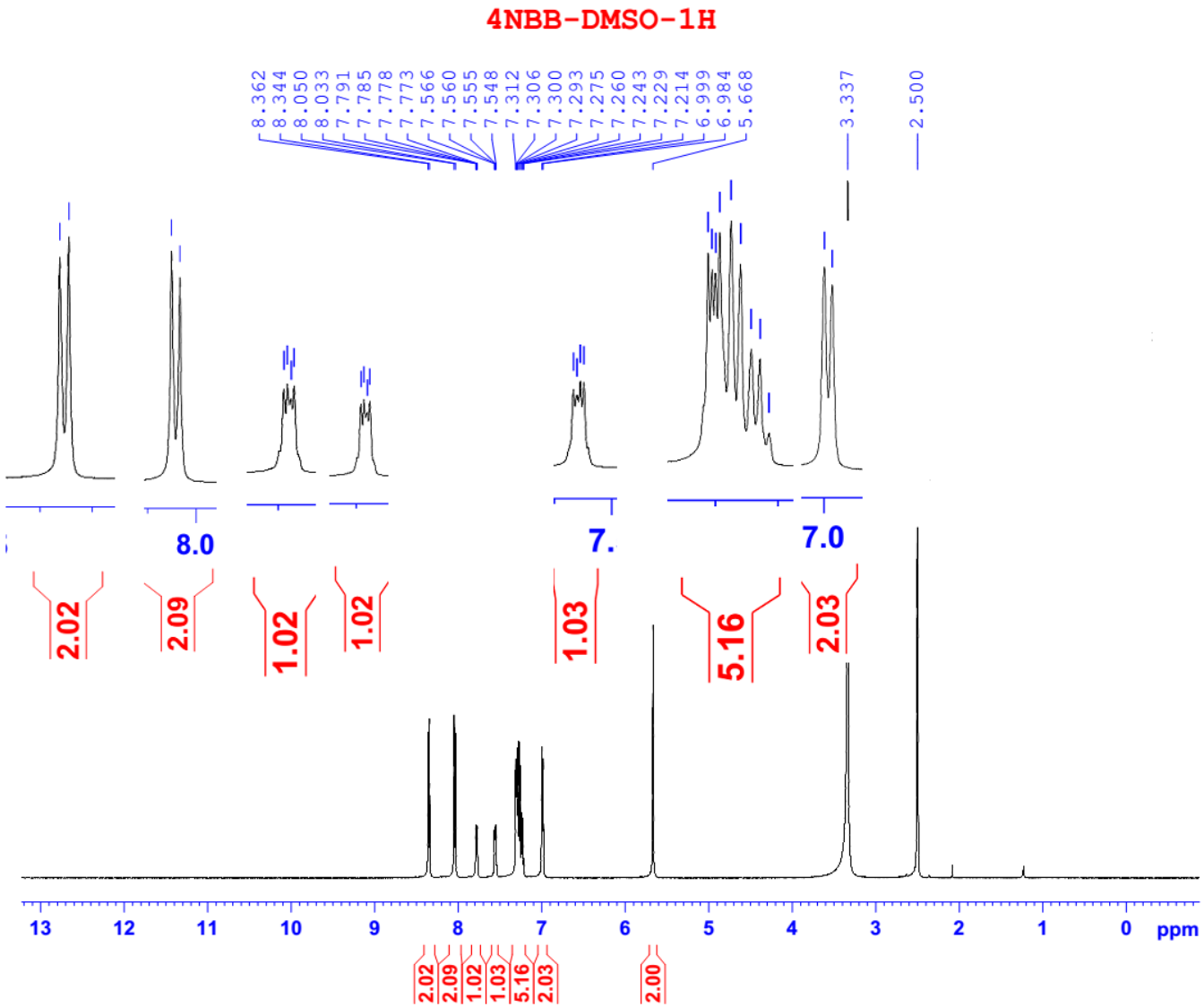


Figure S156. ^{1}H NMR spectra of compound **3k**

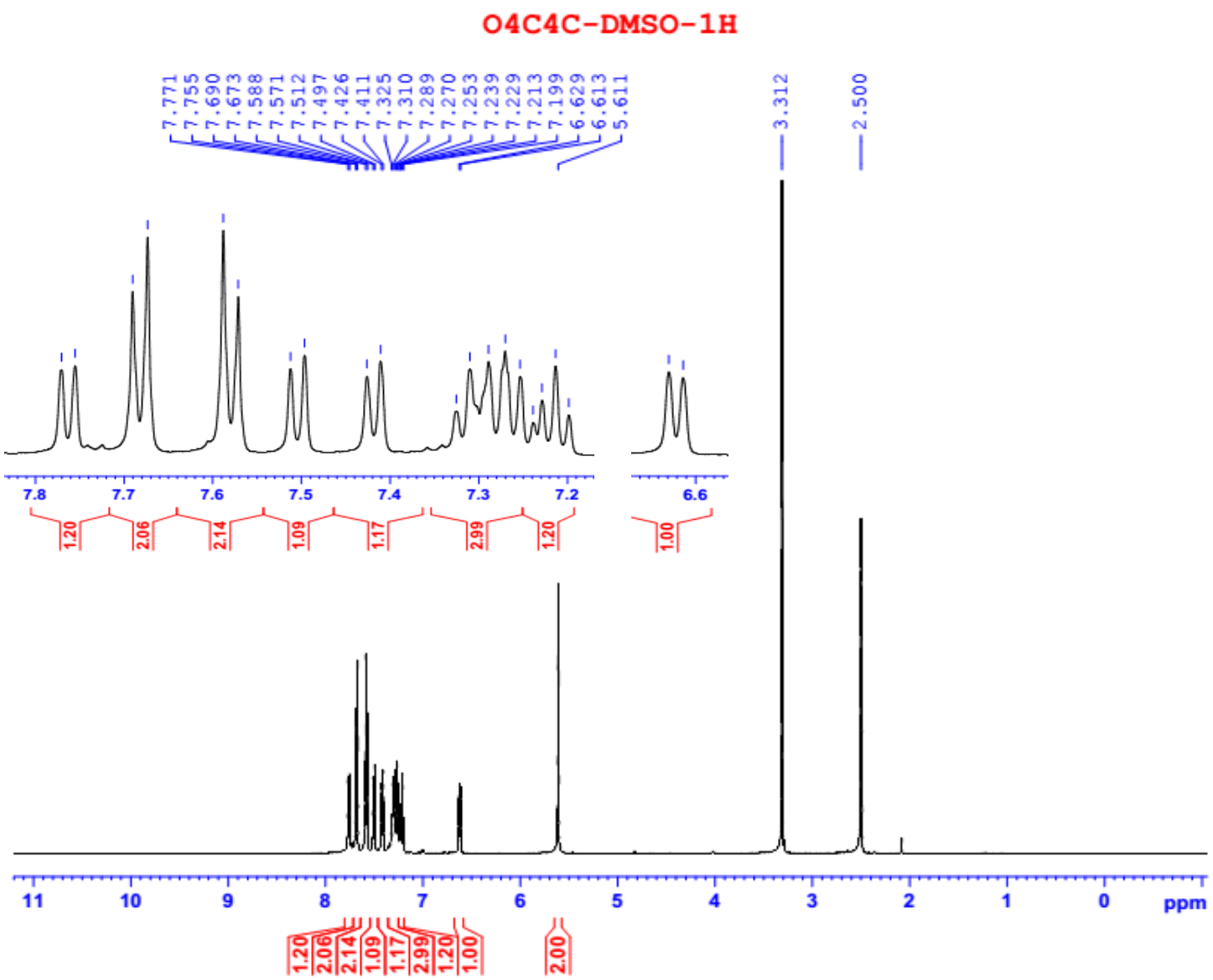


Figure S157. ^{1}H NMR spectra of compound **3l**

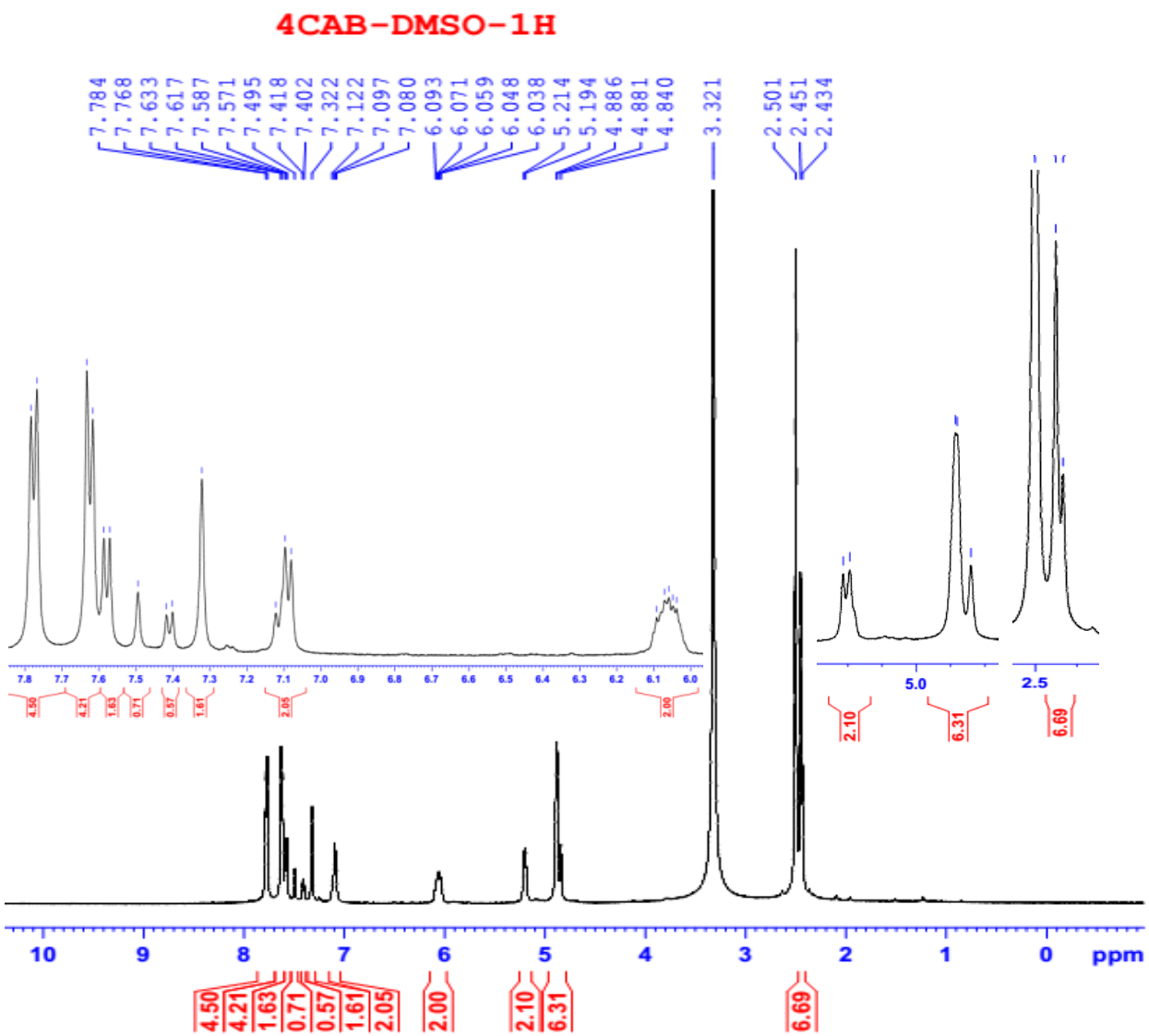


Figure S158. ^{1}H NMR spectra of compound **4a**

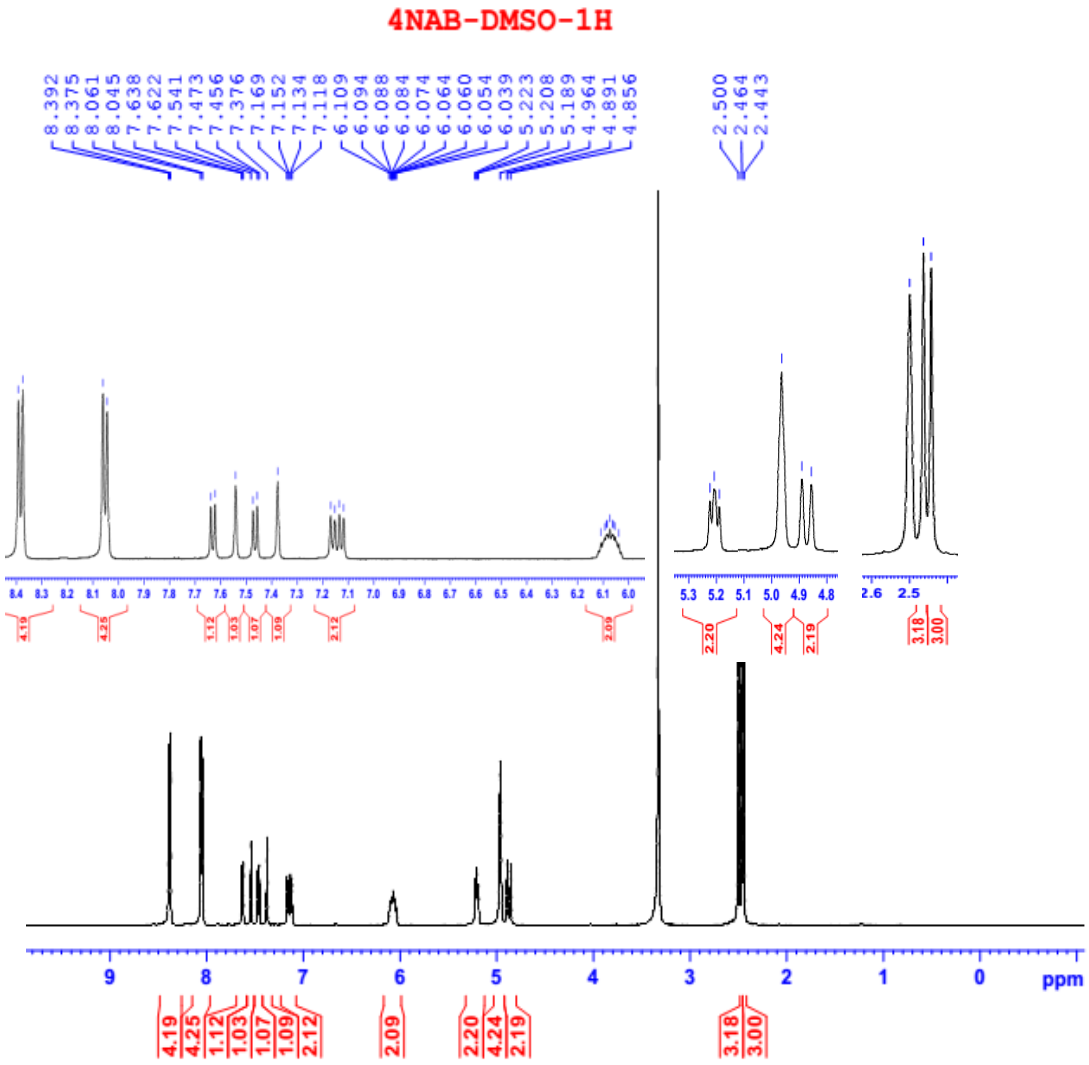


Figure S159. ^{1}H NMR spectra of compound **4b**

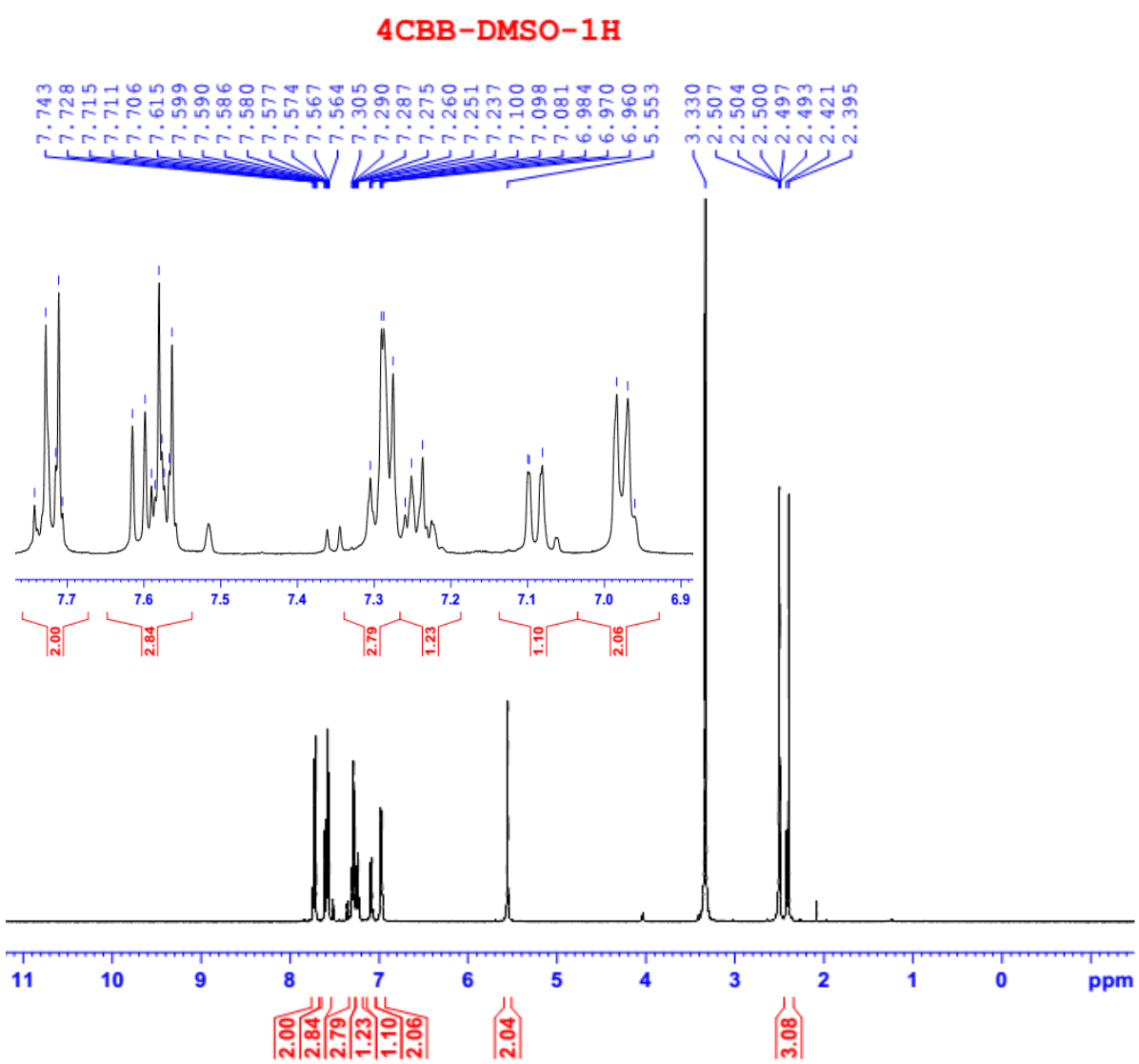


Figure S160. ^{1}H NMR spectra of compound **4c**

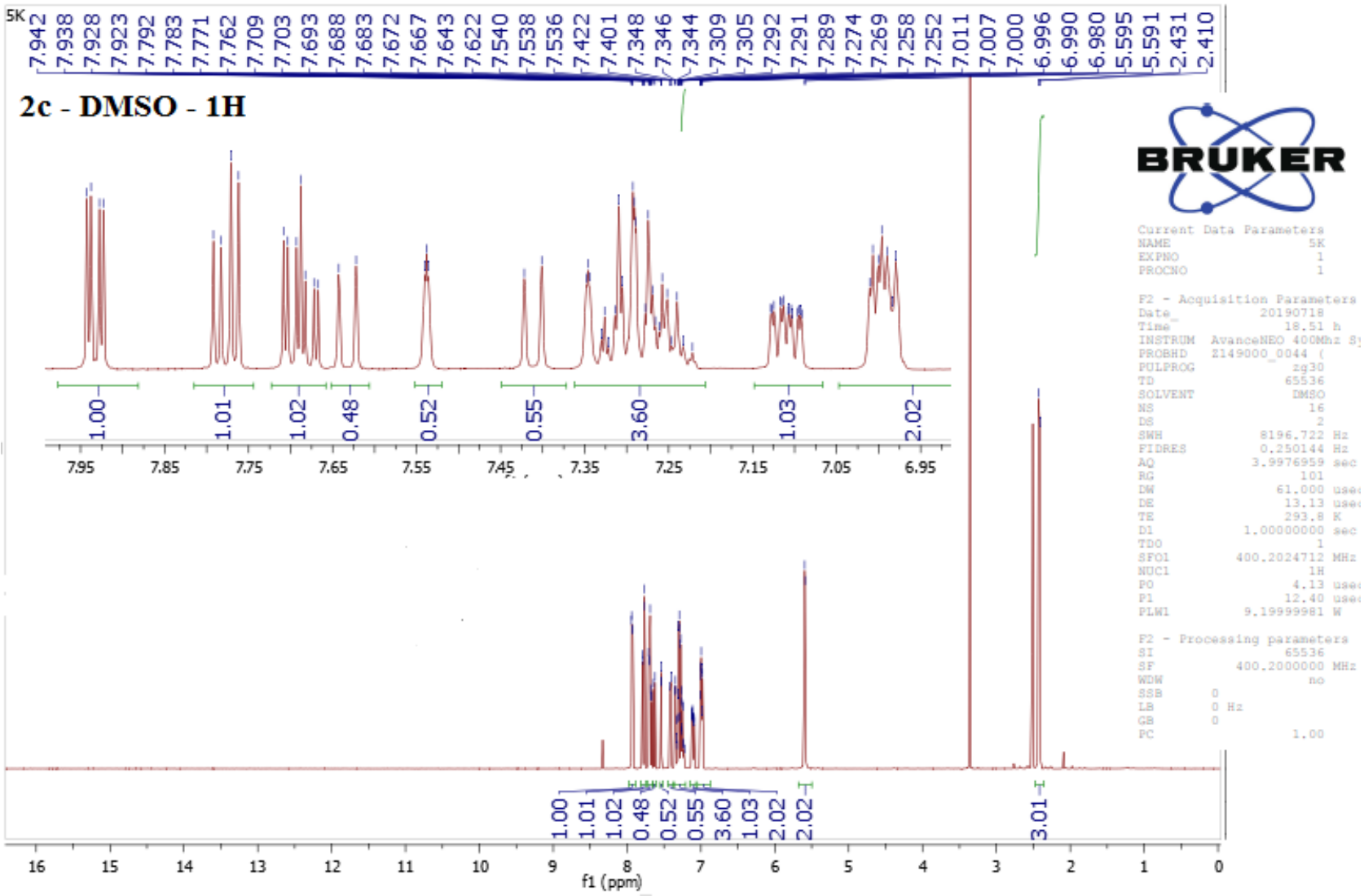


Figure S161. ^{1}H NMR spectra of compound **4d**

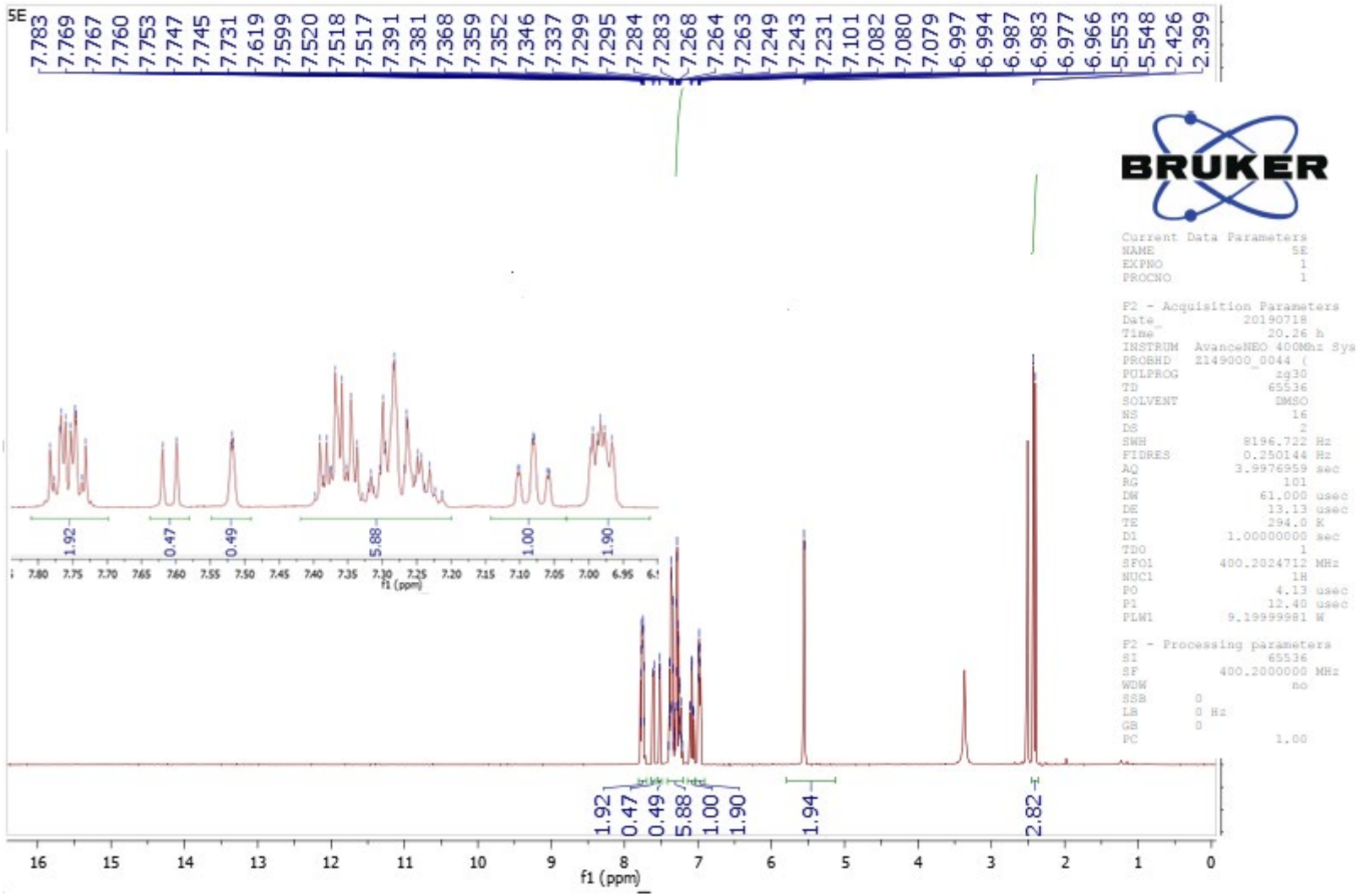


Figure S162. ^{1}H NMR spectra of compound **4e**

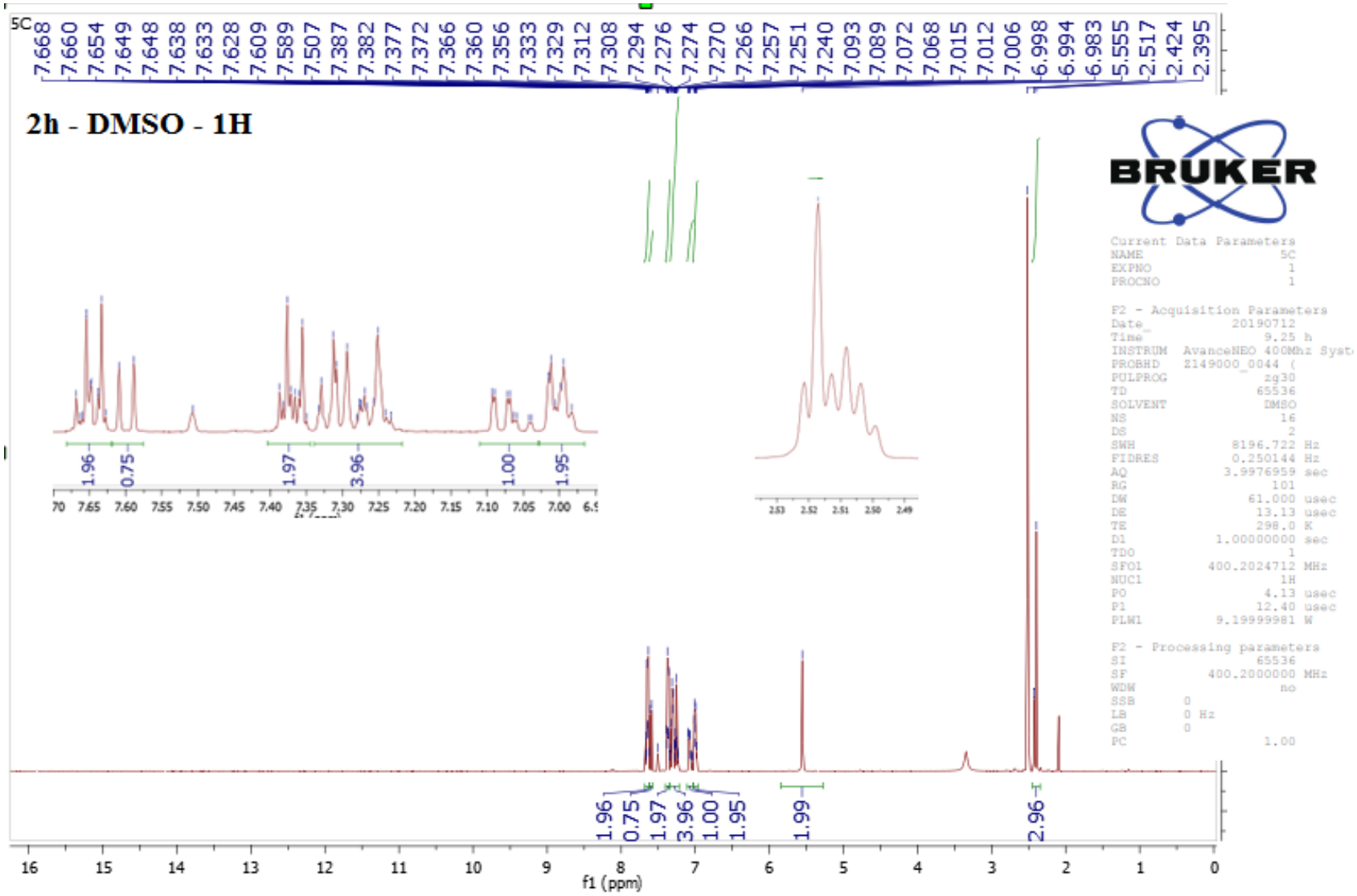


Figure S163. ^{1}H NMR spectra of compound **4f**

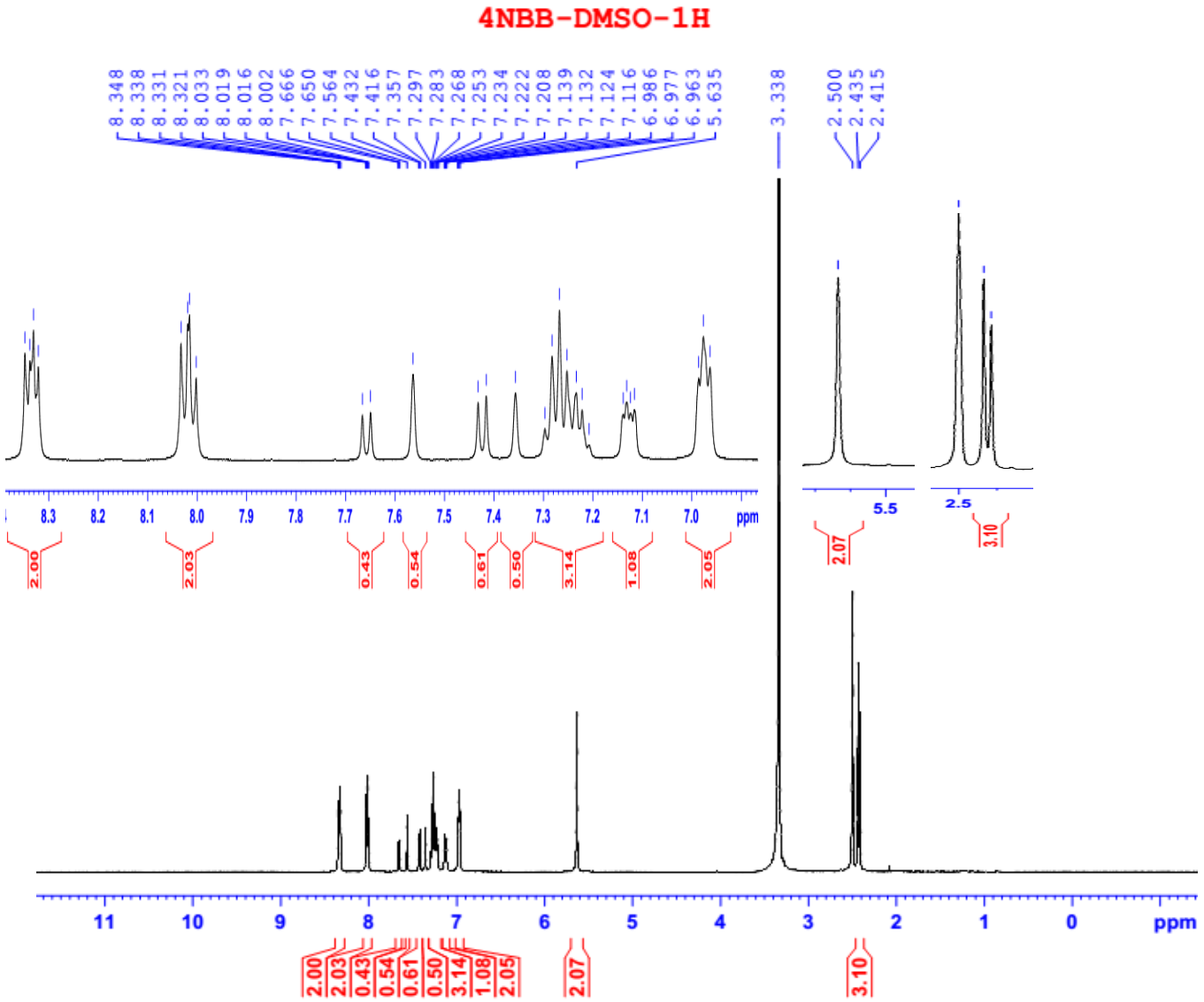


Figure S164. ^{1}H NMR spectra of compound **4g**

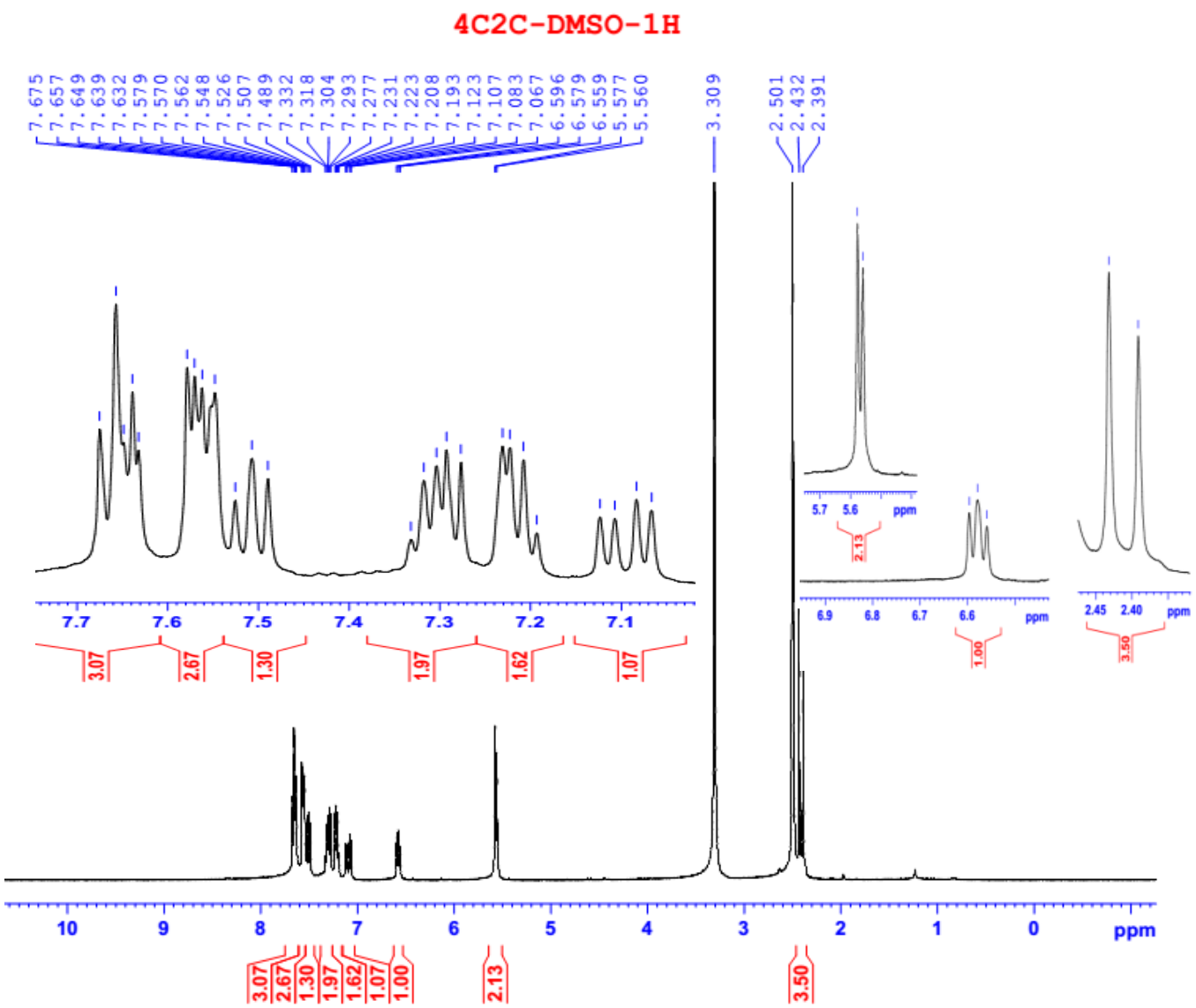


Figure S165. ^{1}H NMR spectra of compound **4h**

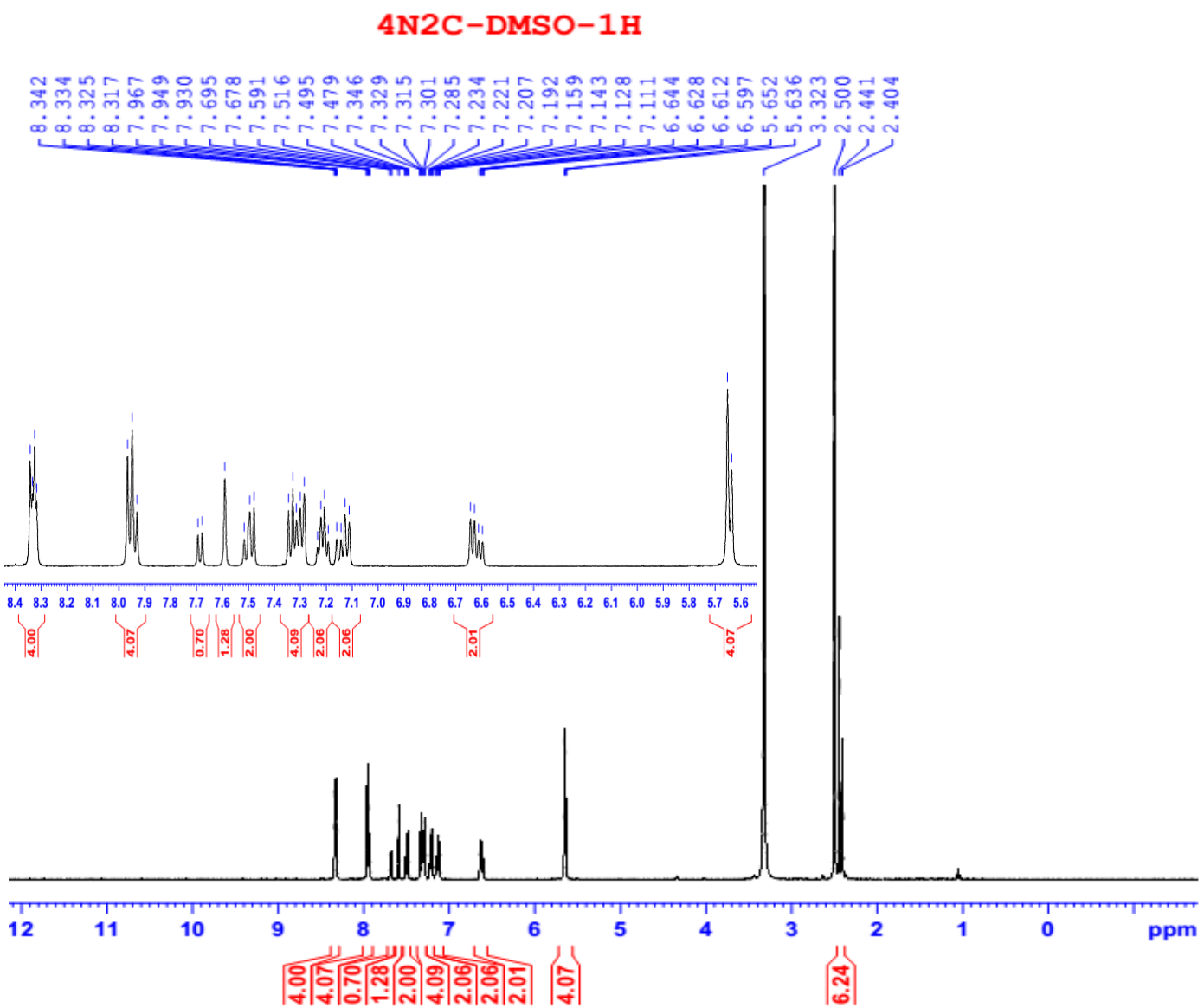


Figure S166. ^{1}H NMR spectra of compound **4i**

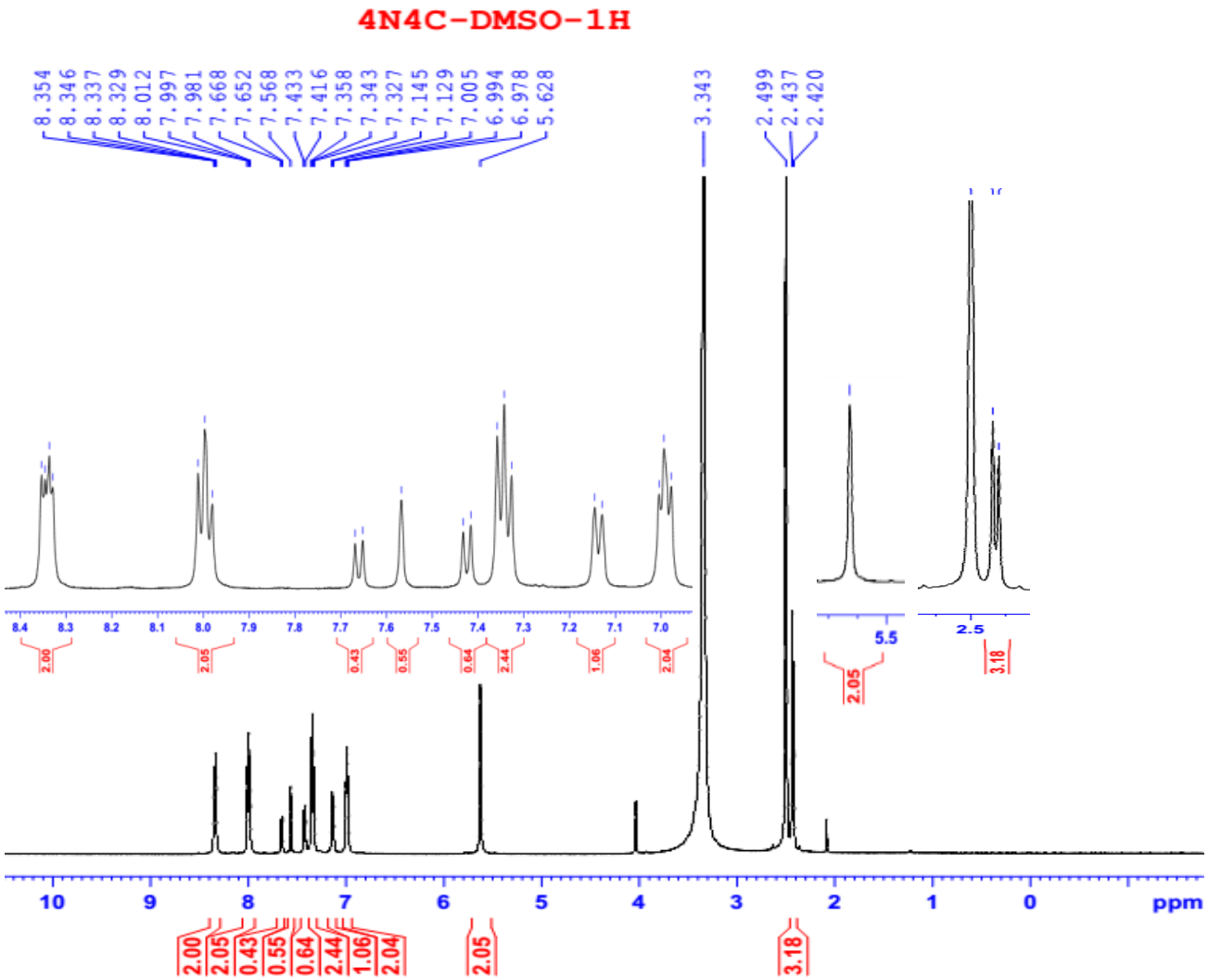


Figure S167. ^{1}H NMR spectra of compound **4j**

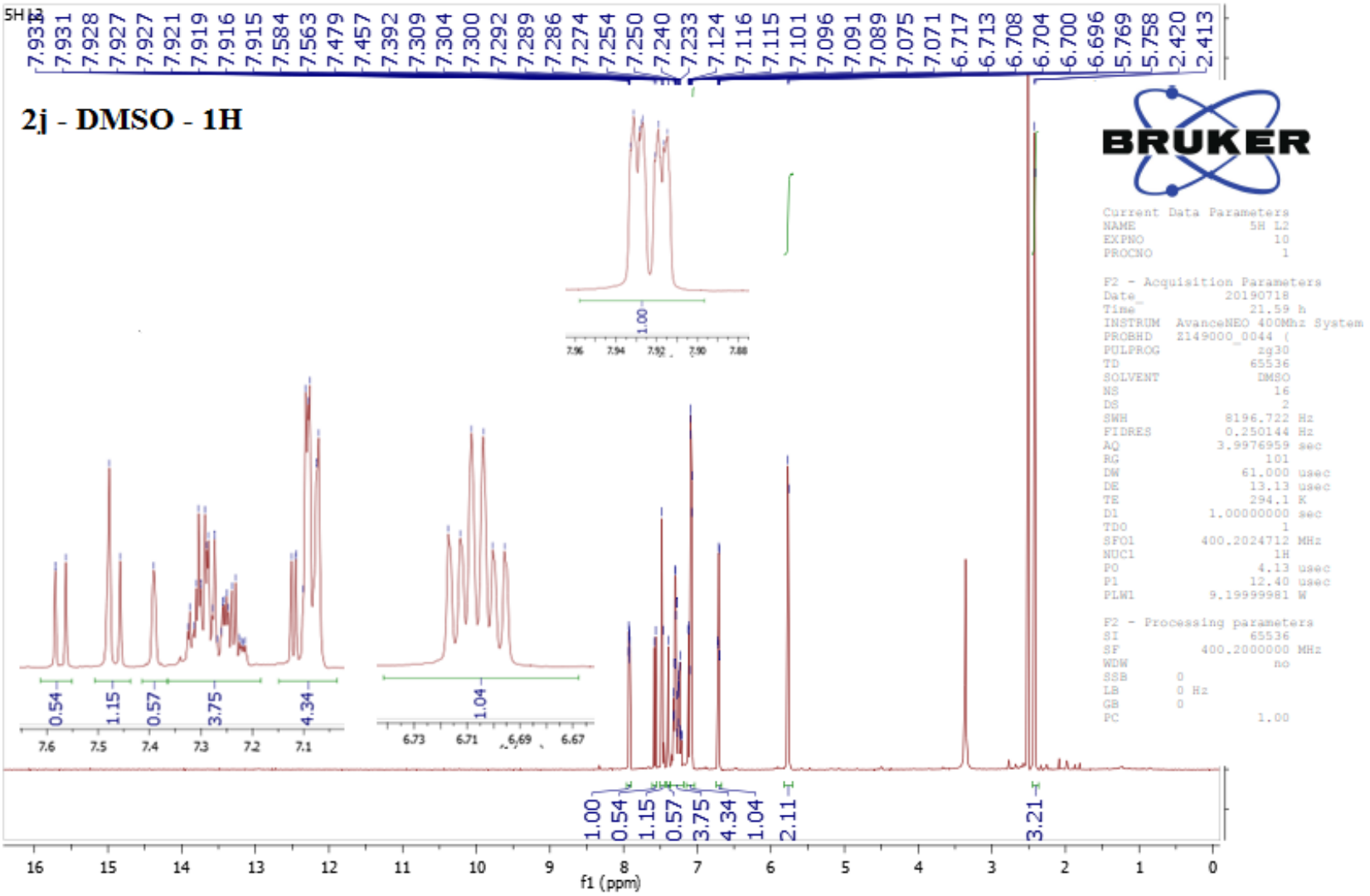


Figure S168. ^{1}H NMR spectra of compound **4k**

^{13}C NMR SPECTRA

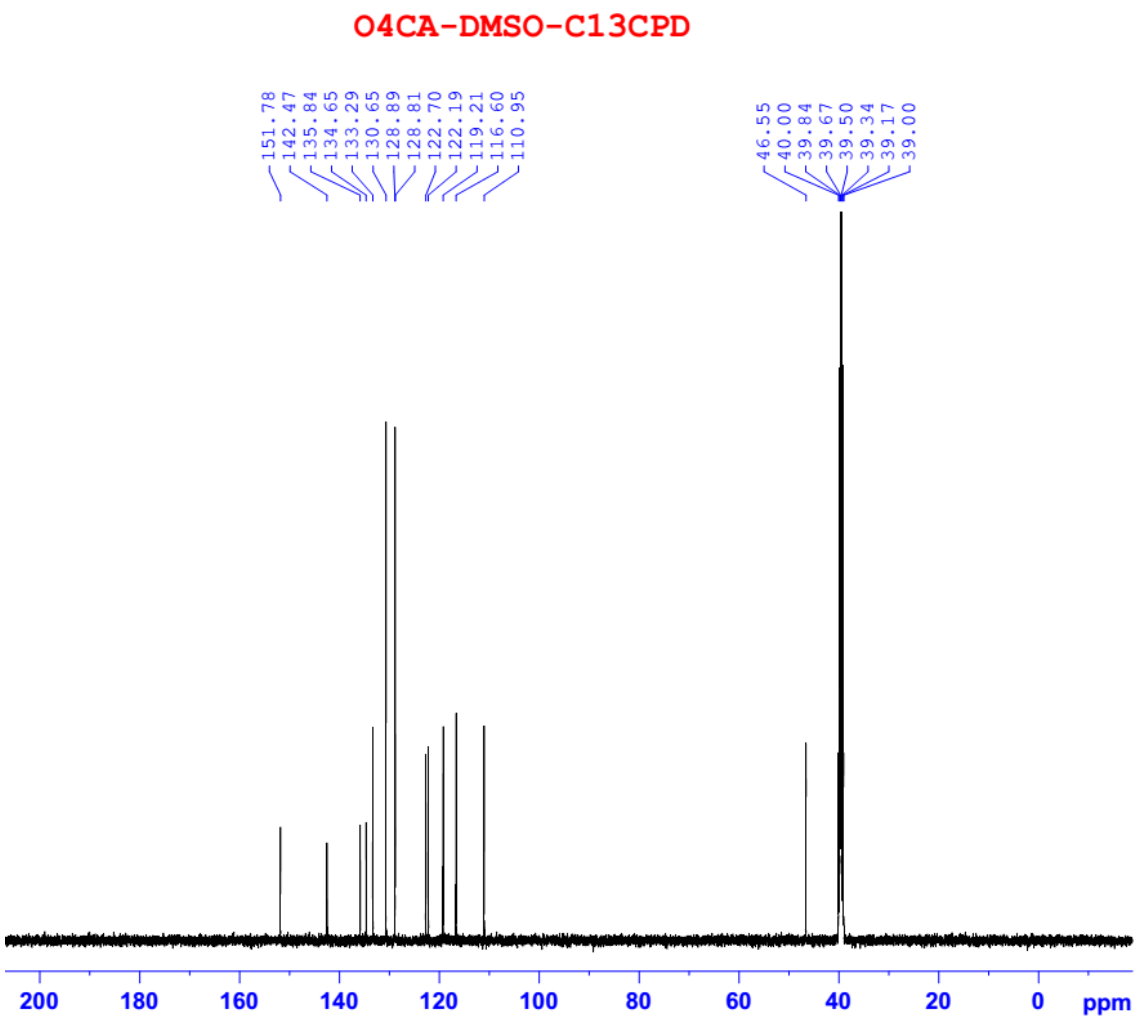


Figure S169. ^{13}C NMR spectra of compound **3a**

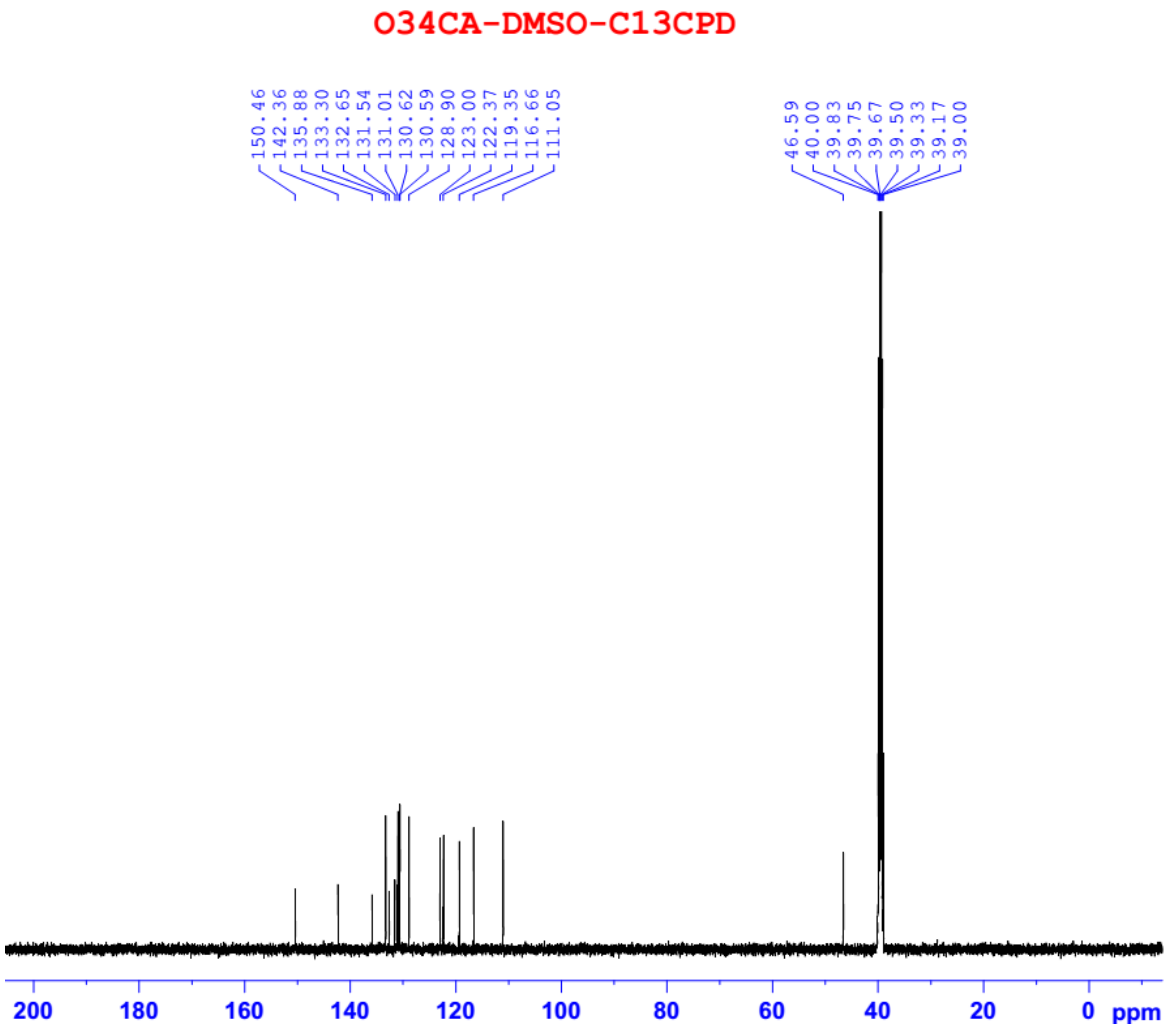


Figure S170. ^{13}C NMR spectra of compound **3b**

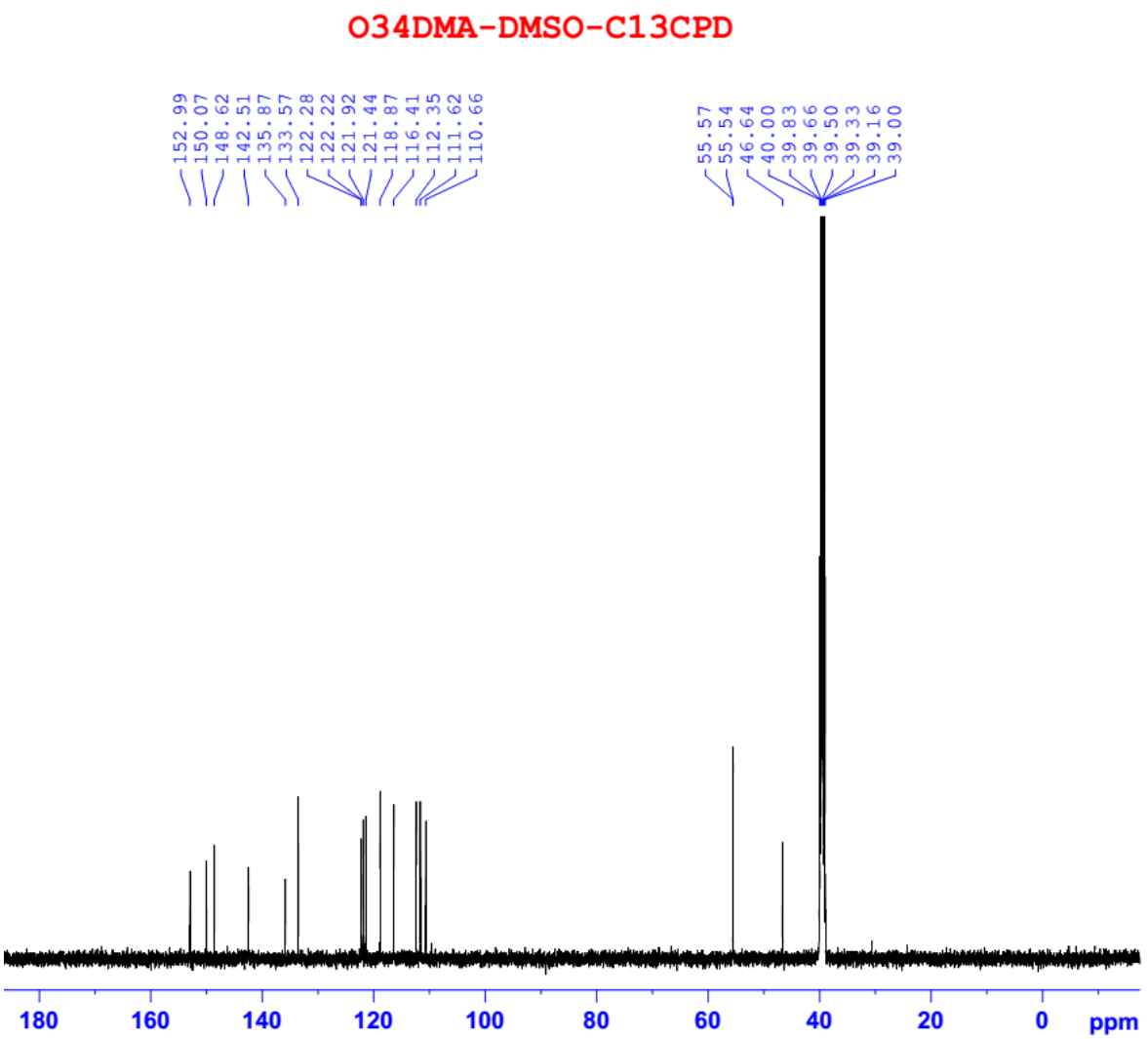


Figure S171. ^{13}C NMR spectra of compound **3c**

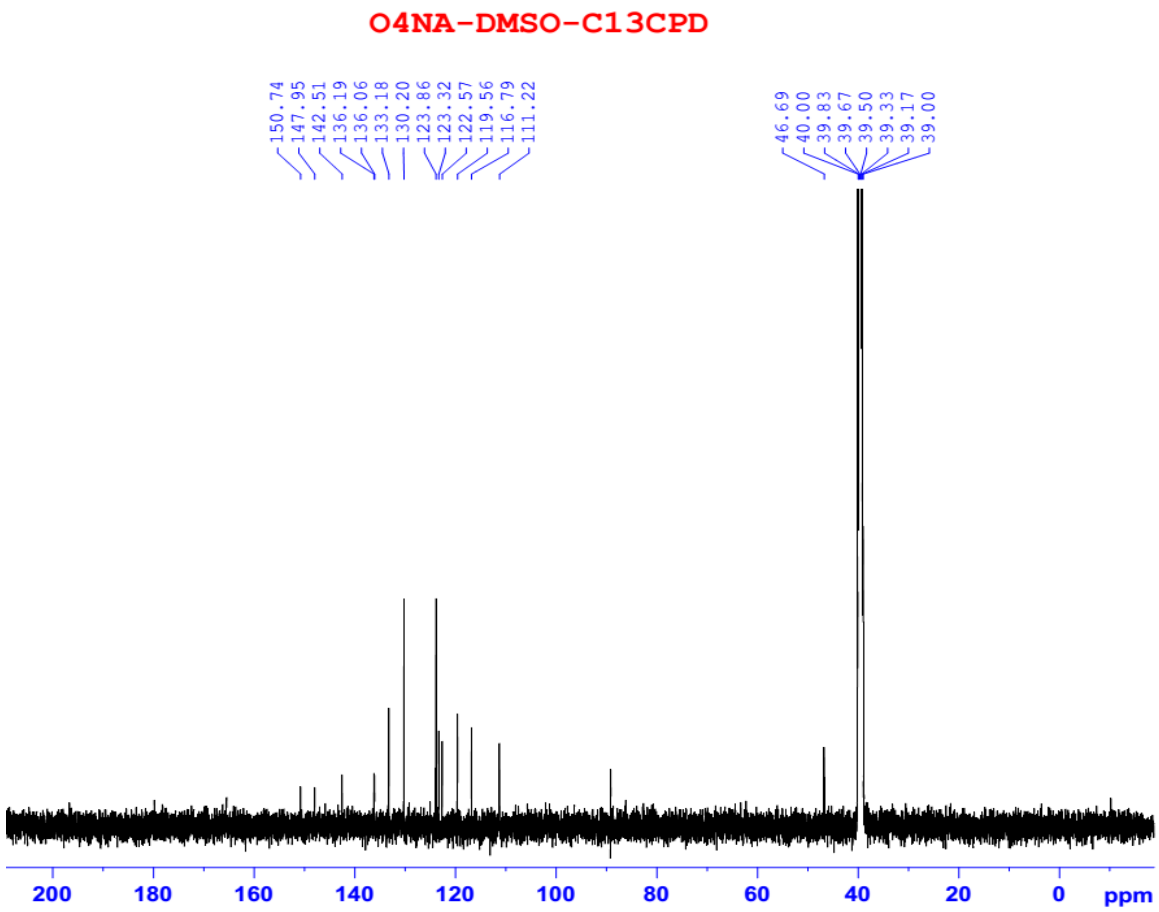


Figure S172. ^{13}C NMR spectra of compound **3d**

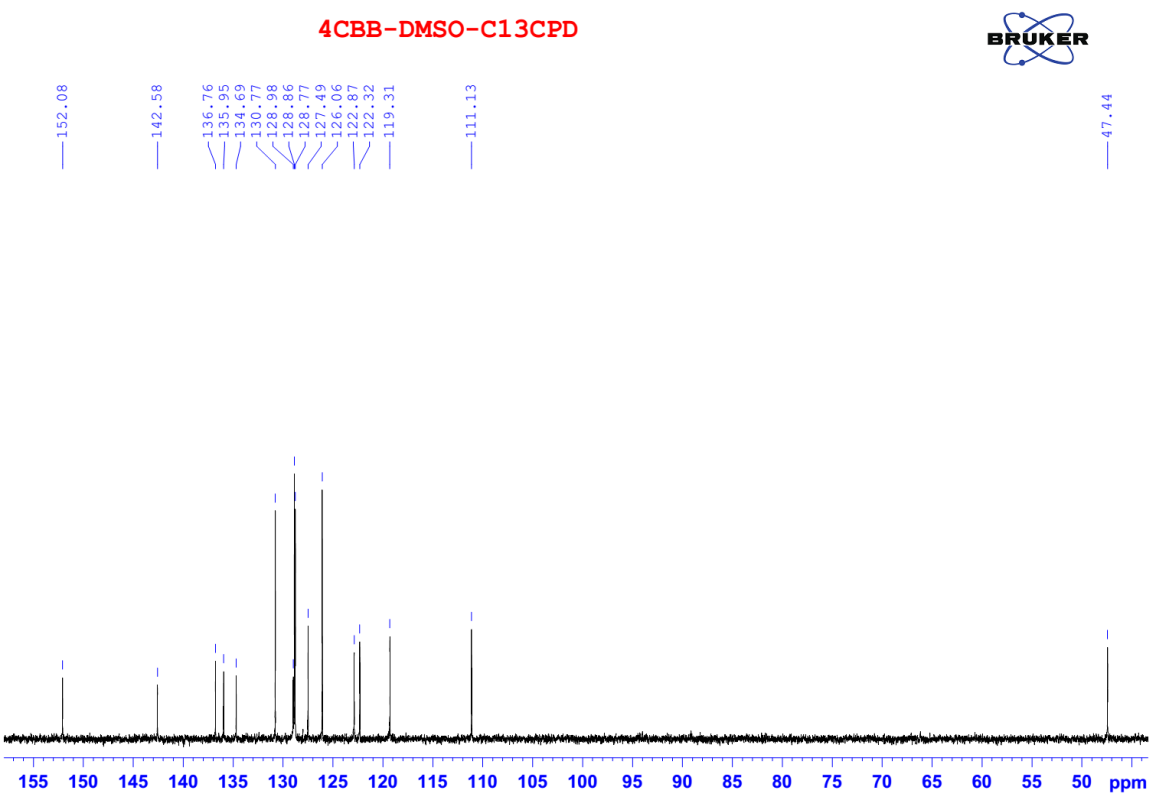


Figure S173. ^{13}C NMR spectra of compound **3e**

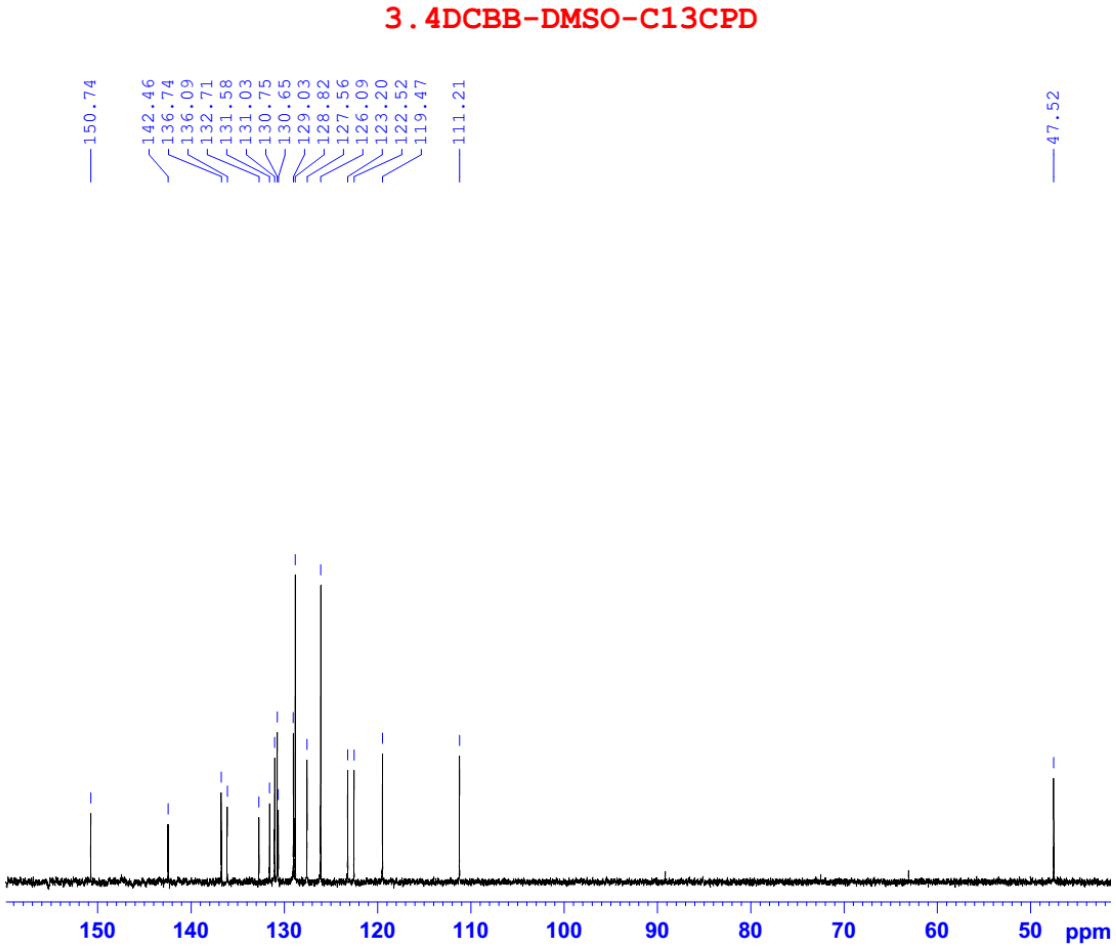


Figure S174. ^{13}C NMR spectra of compound **3f**

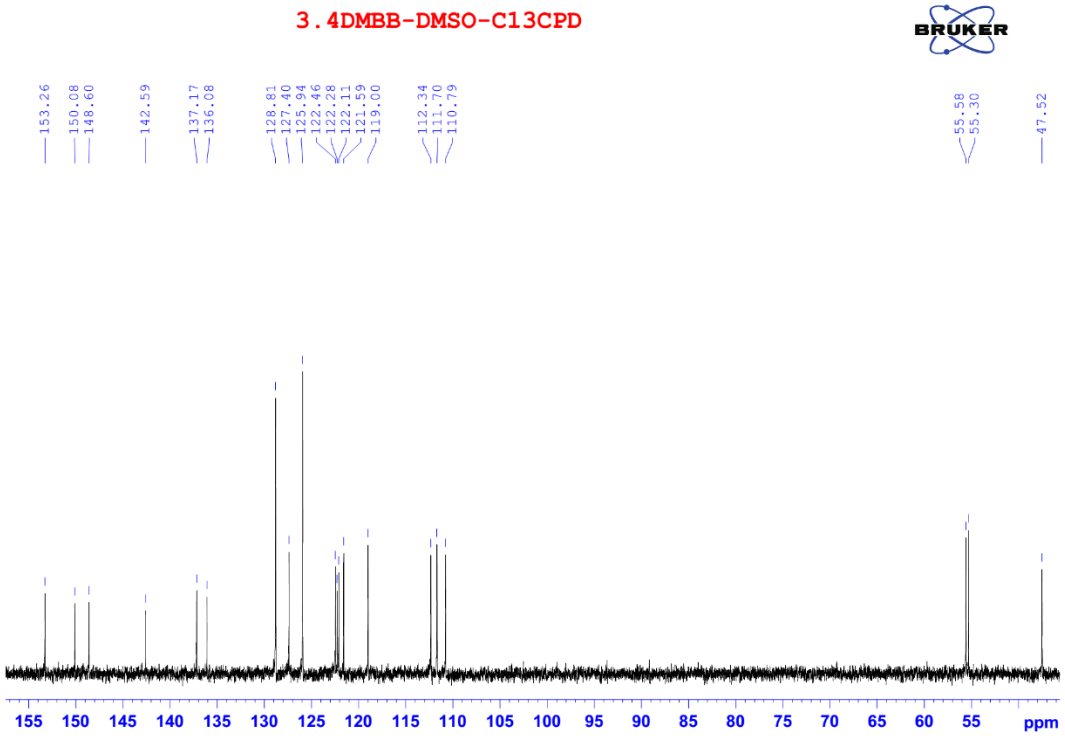


Figure S175. ^{13}C NMR spectra of compound **3g**

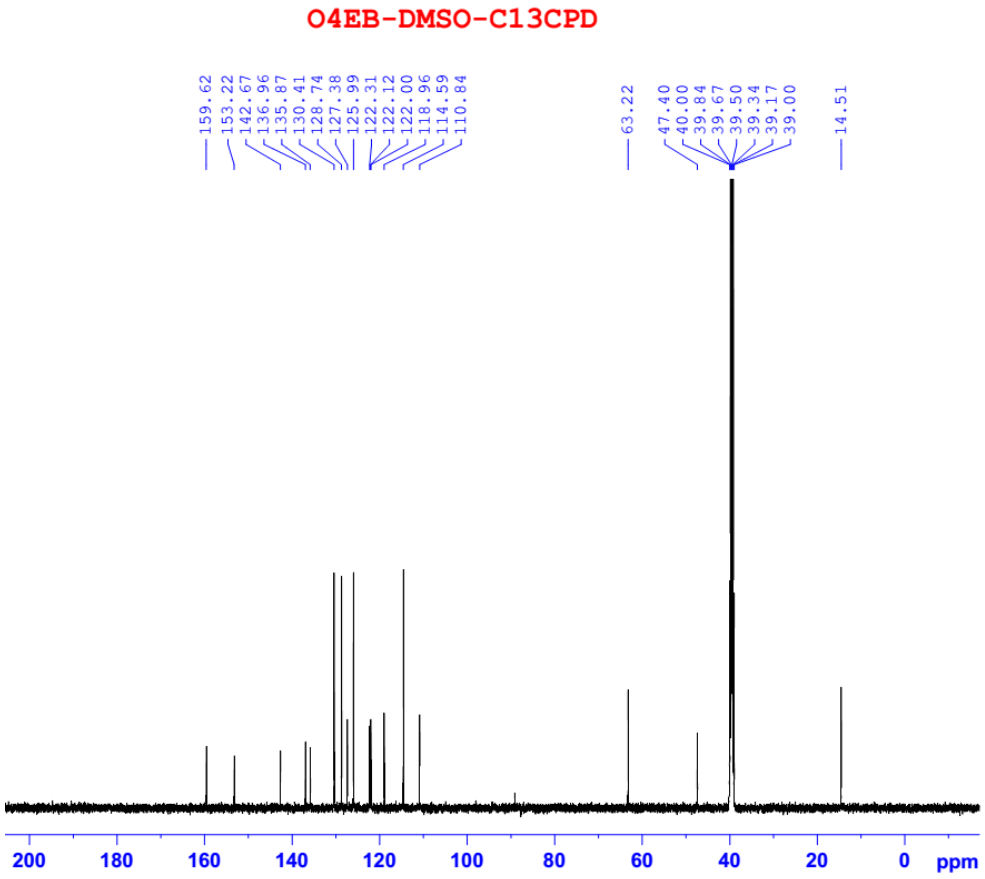


Figure S176. ^{13}C NMR spectra of compound **3h**

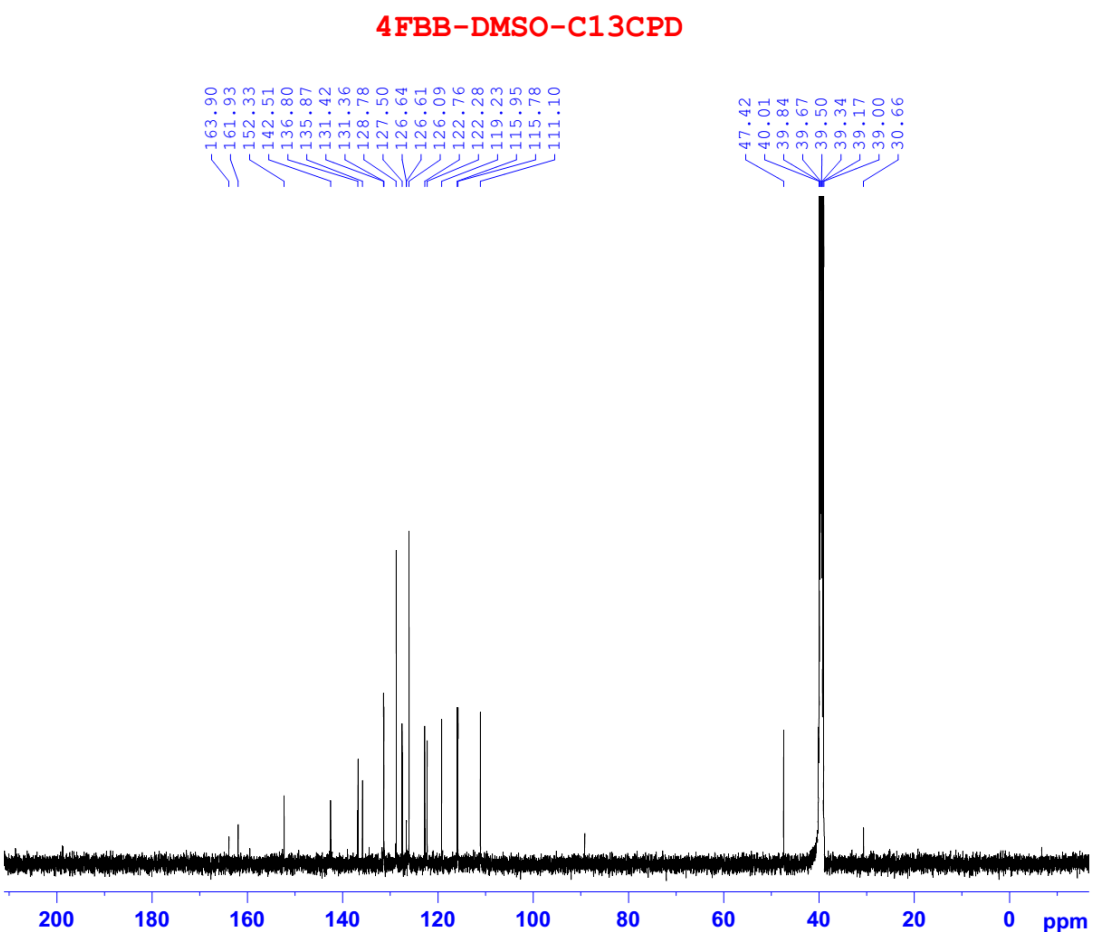


Figure S177. ^{13}C NMR spectra of compound **3i**

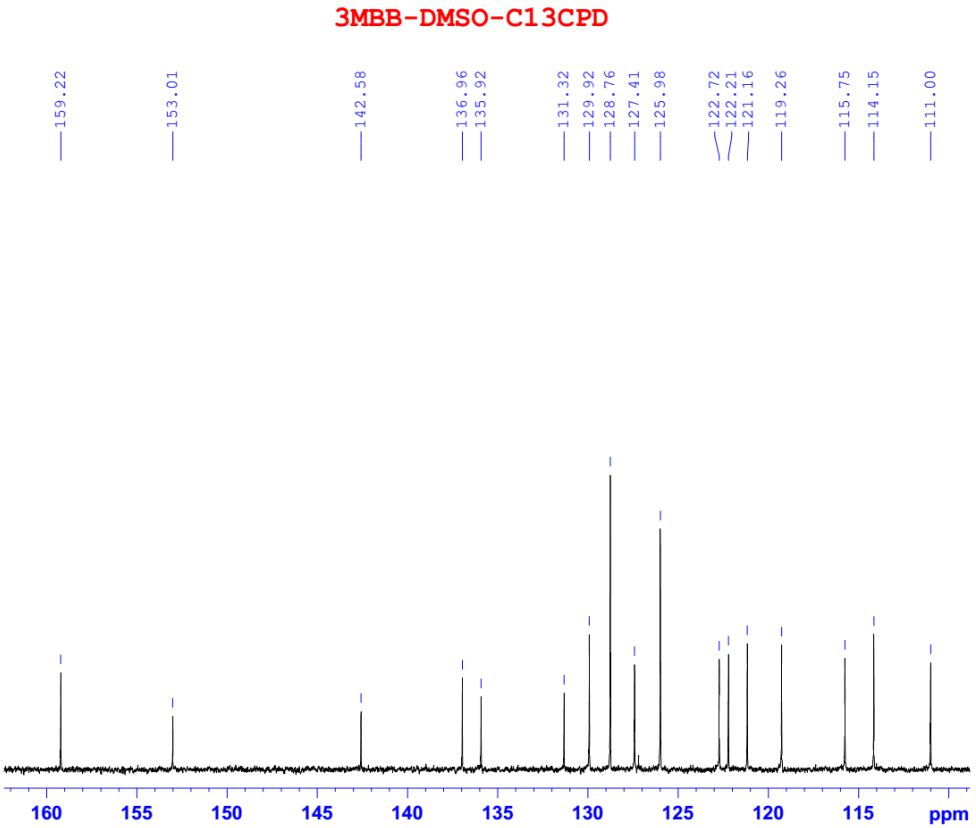


Figure S178. ^{13}C NMR spectra of compound **3j**

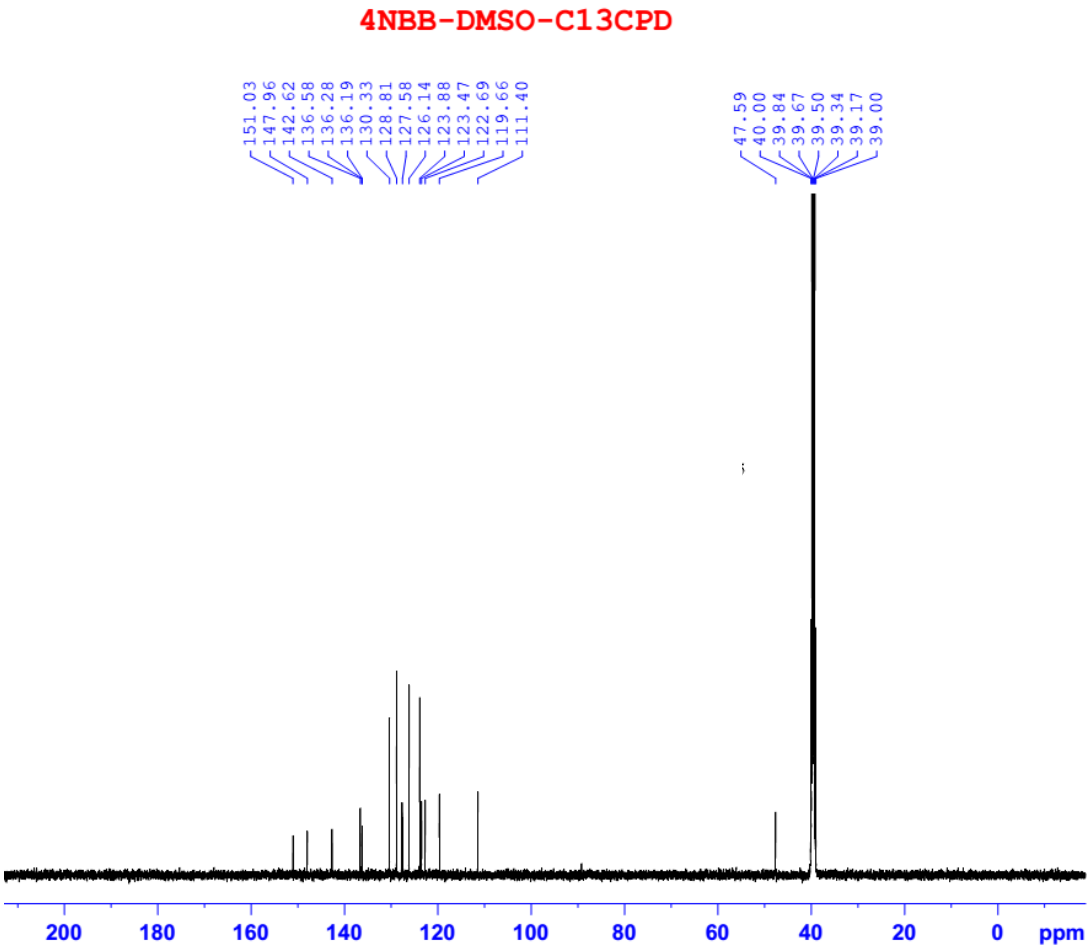


Figure S179. ^{13}C NMR spectra of compound **3k**

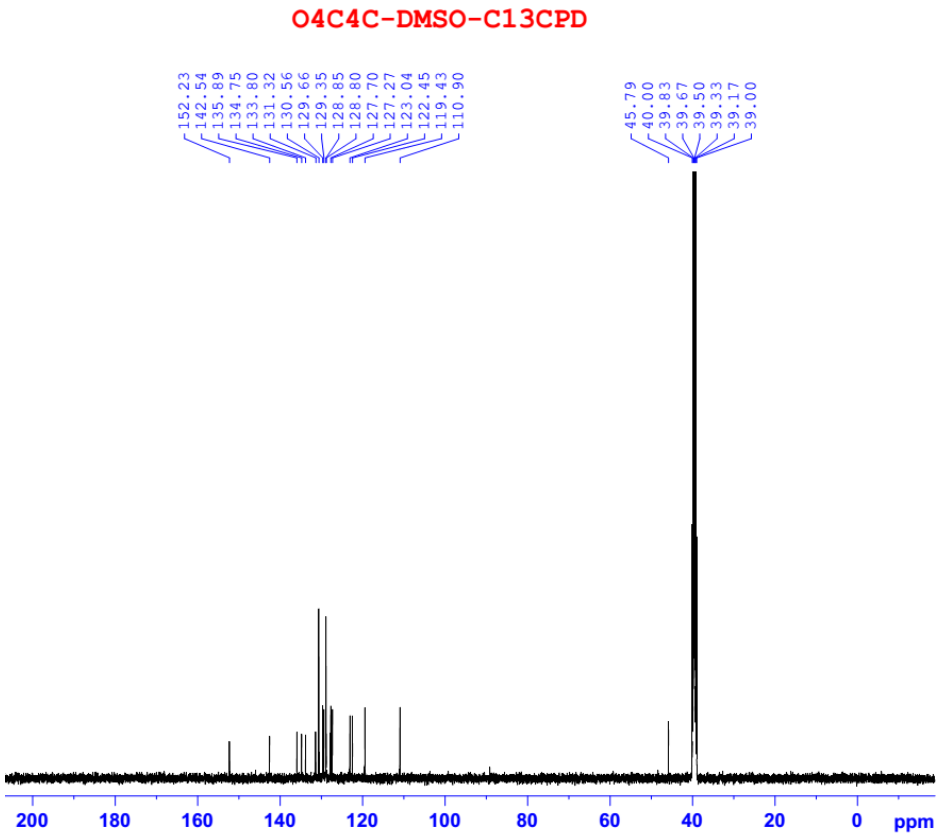


Figure S180. ^{13}C NMR spectra of compound **3l**

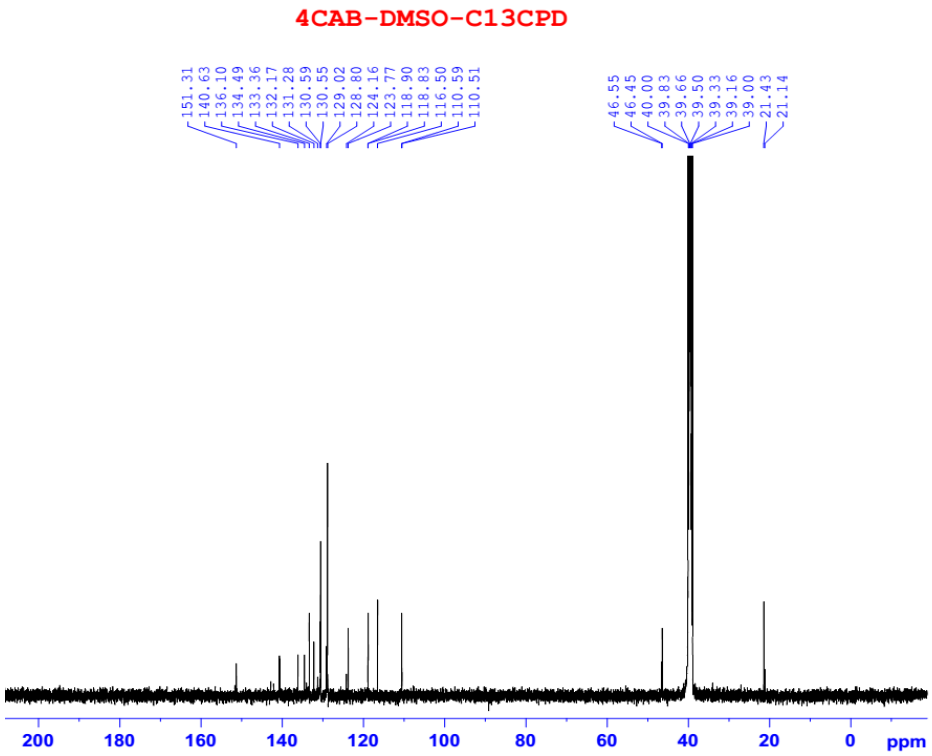


Figure S181. ^{13}C NMR spectra of compound **4a**

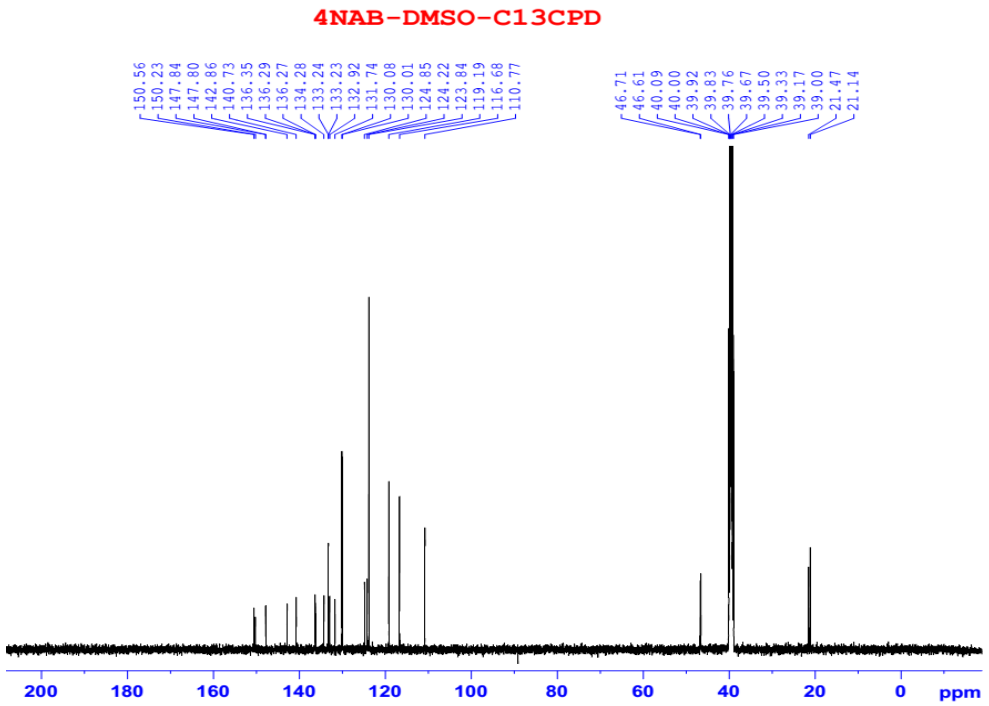


Figure S182. ^{13}C NMR spectra of compound **4b**

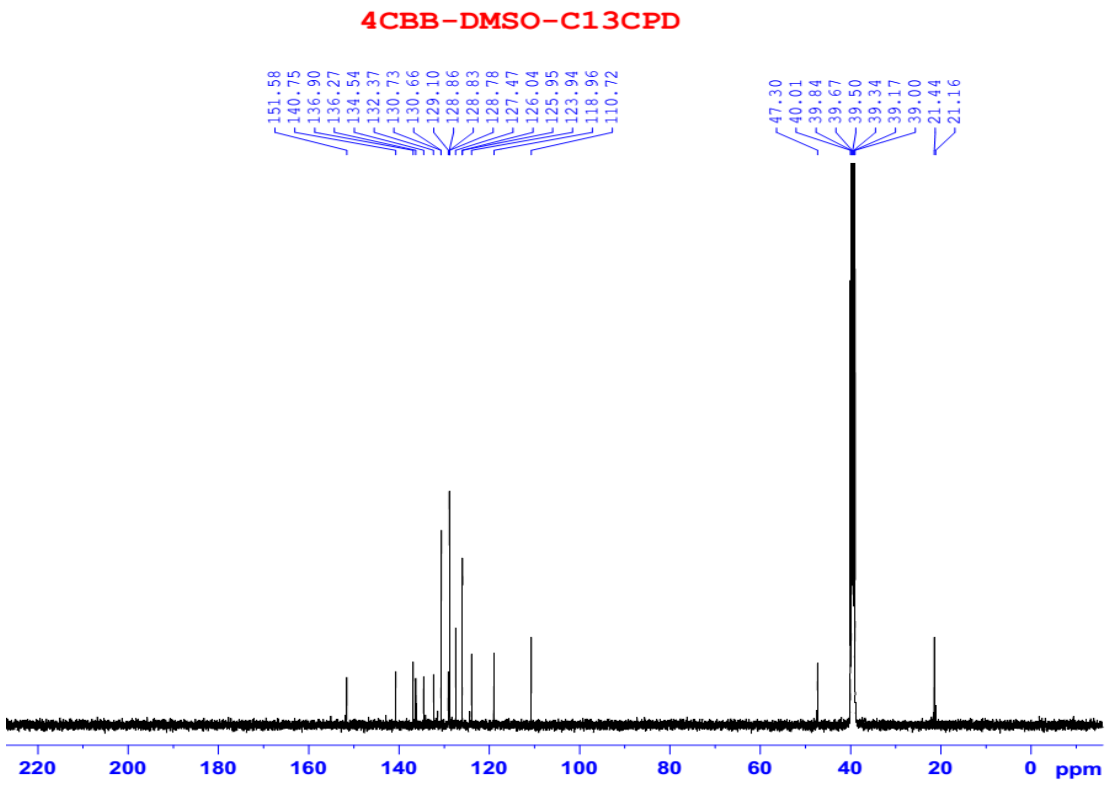
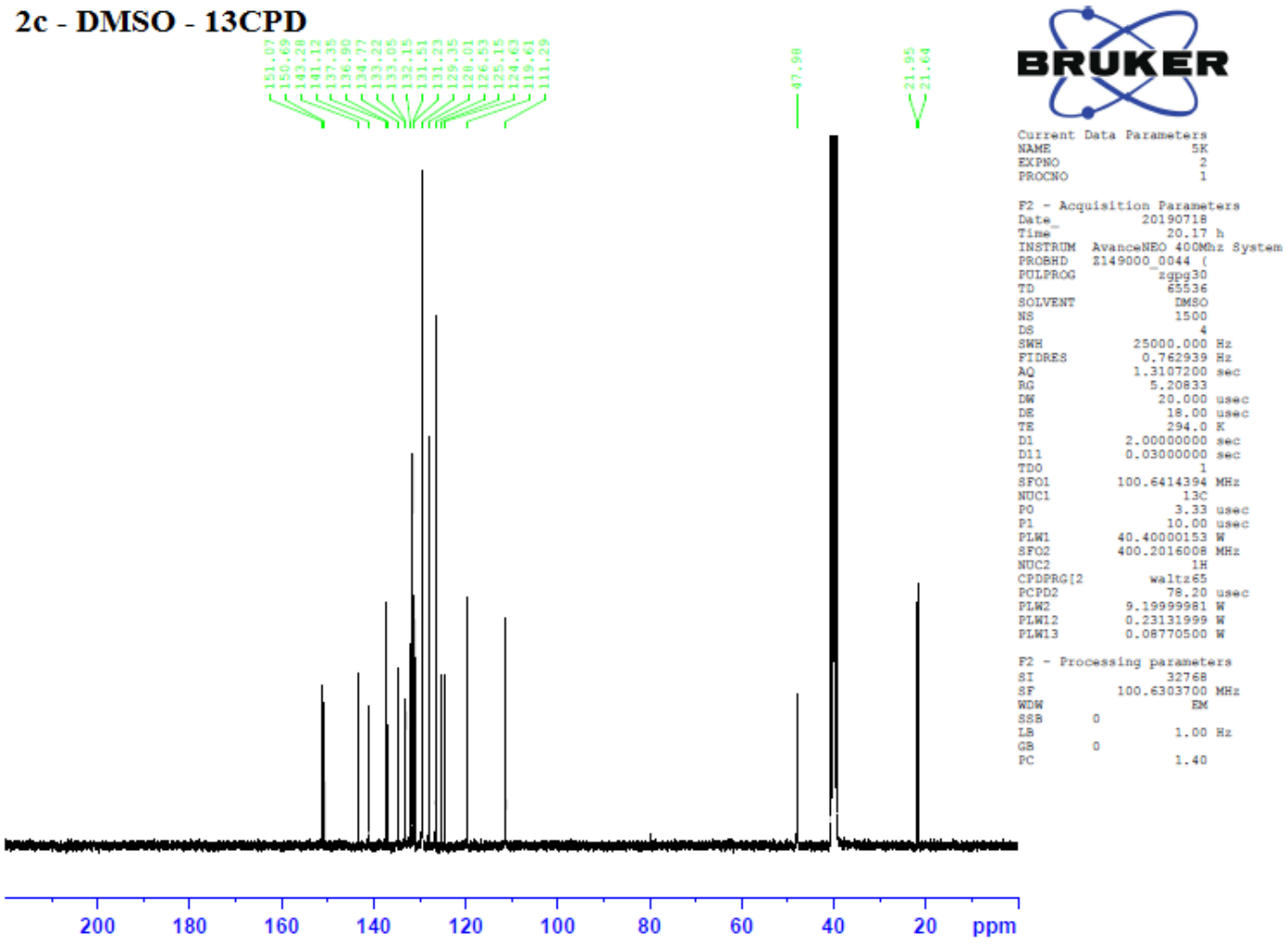


Figure S183. ^{13}C NMR spectra of compound **4c**



BRUKER

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Figure S184. ^{13}C NMR spectra of compound **4d**

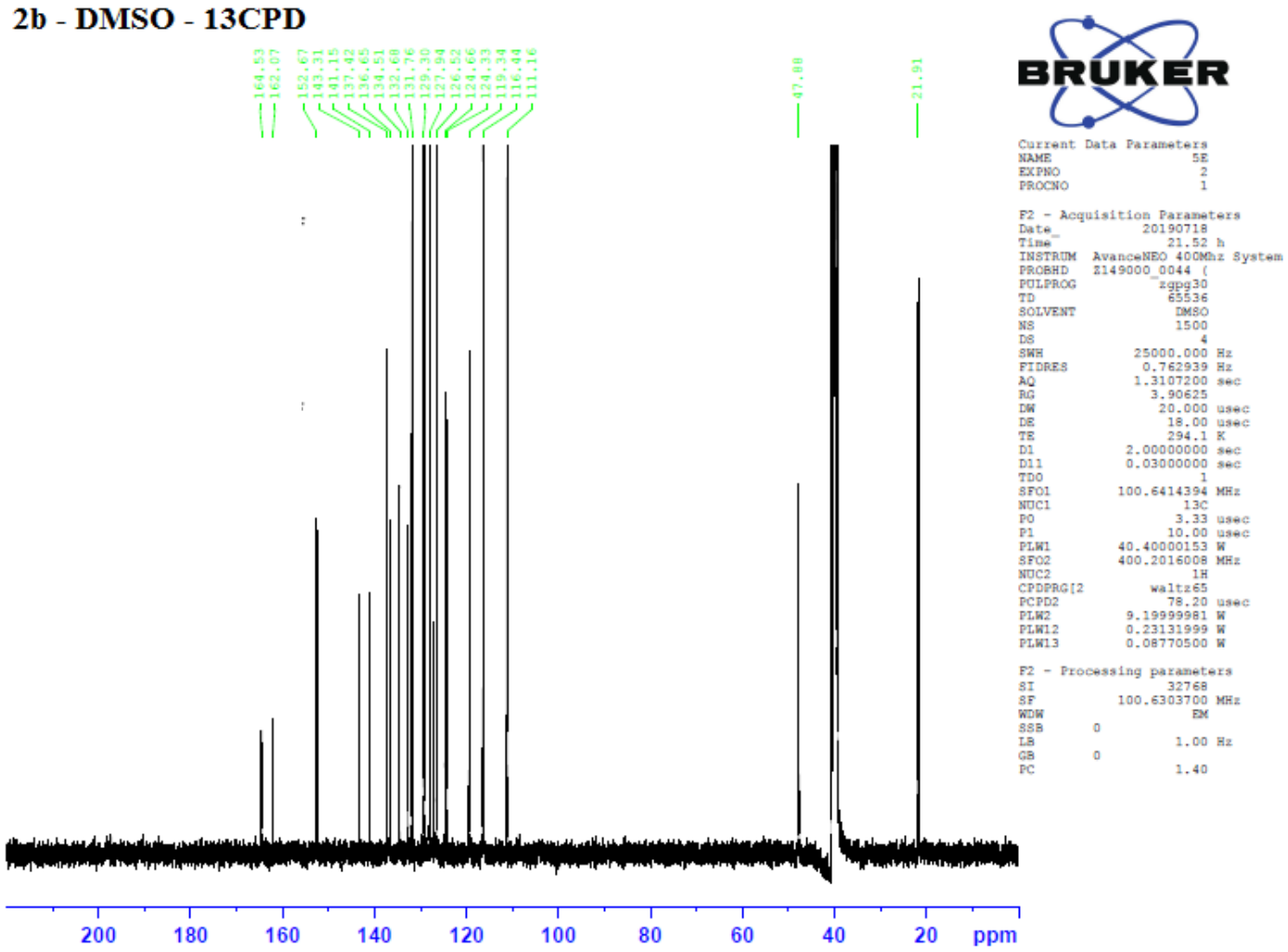

Figure S185. ^{13}C NMR spectra of compound **4e**

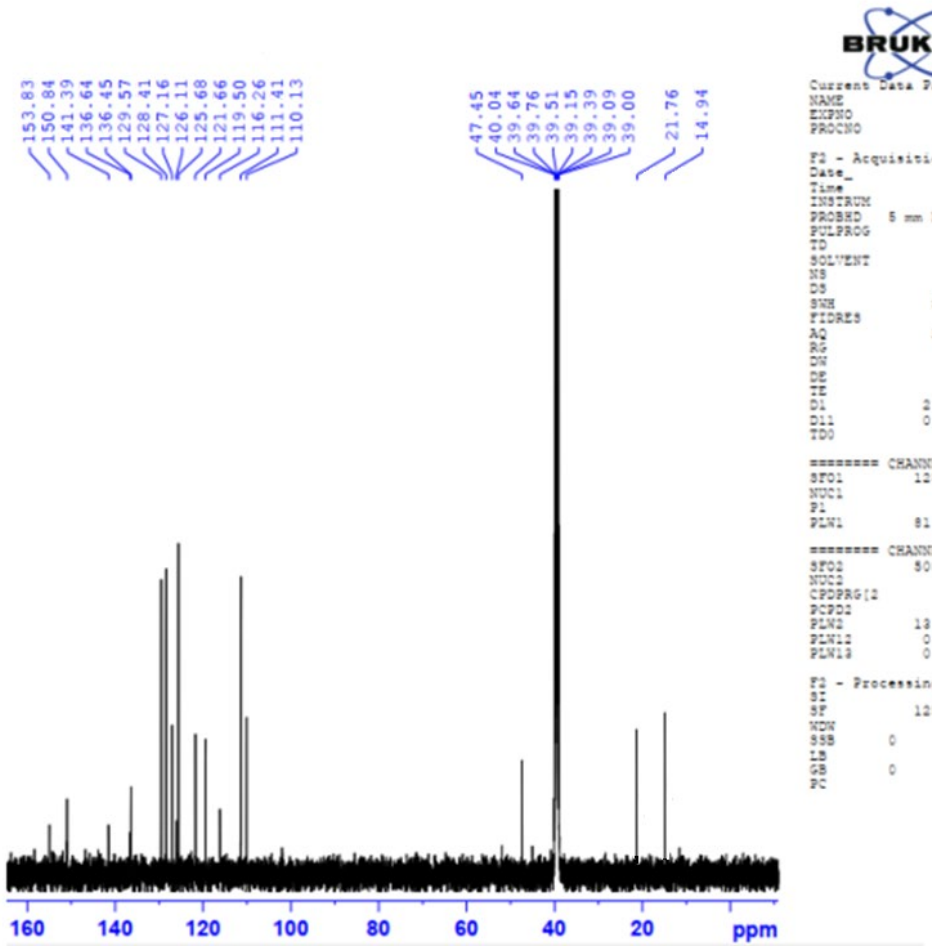

Figure S186. ^{13}C NMR spectra of compound **4f**

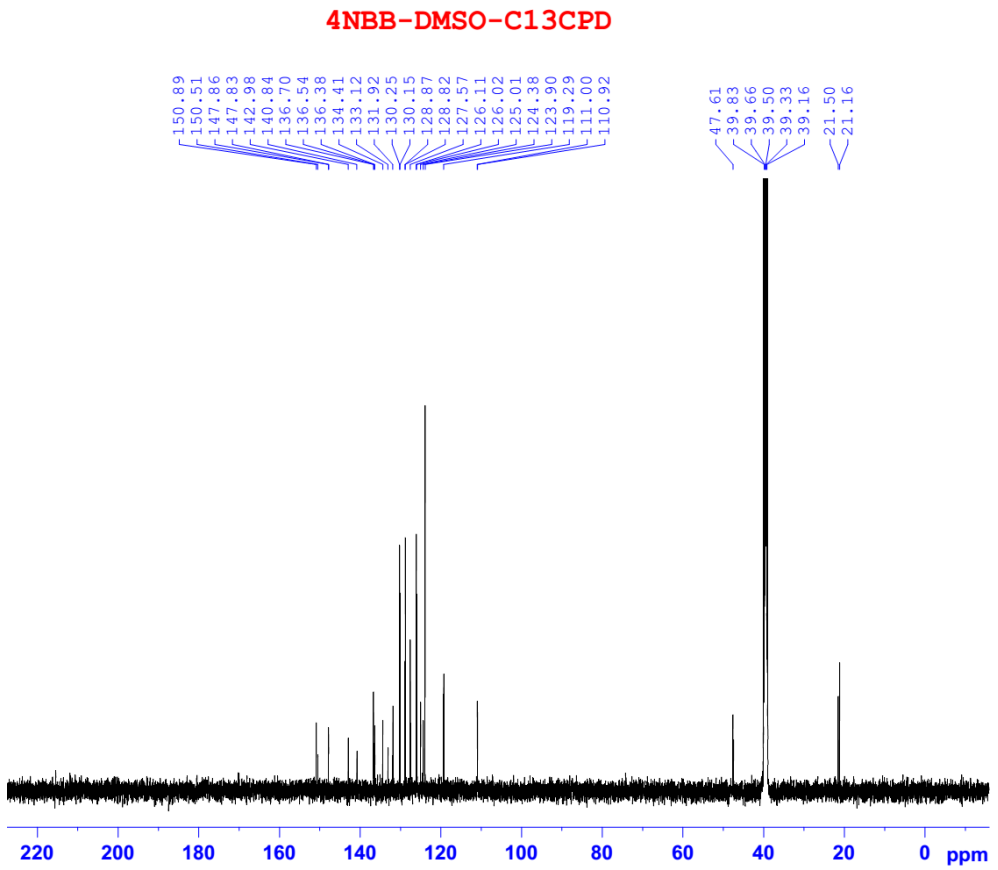

Figure S187. ^{13}C NMR spectra of compound **4g**

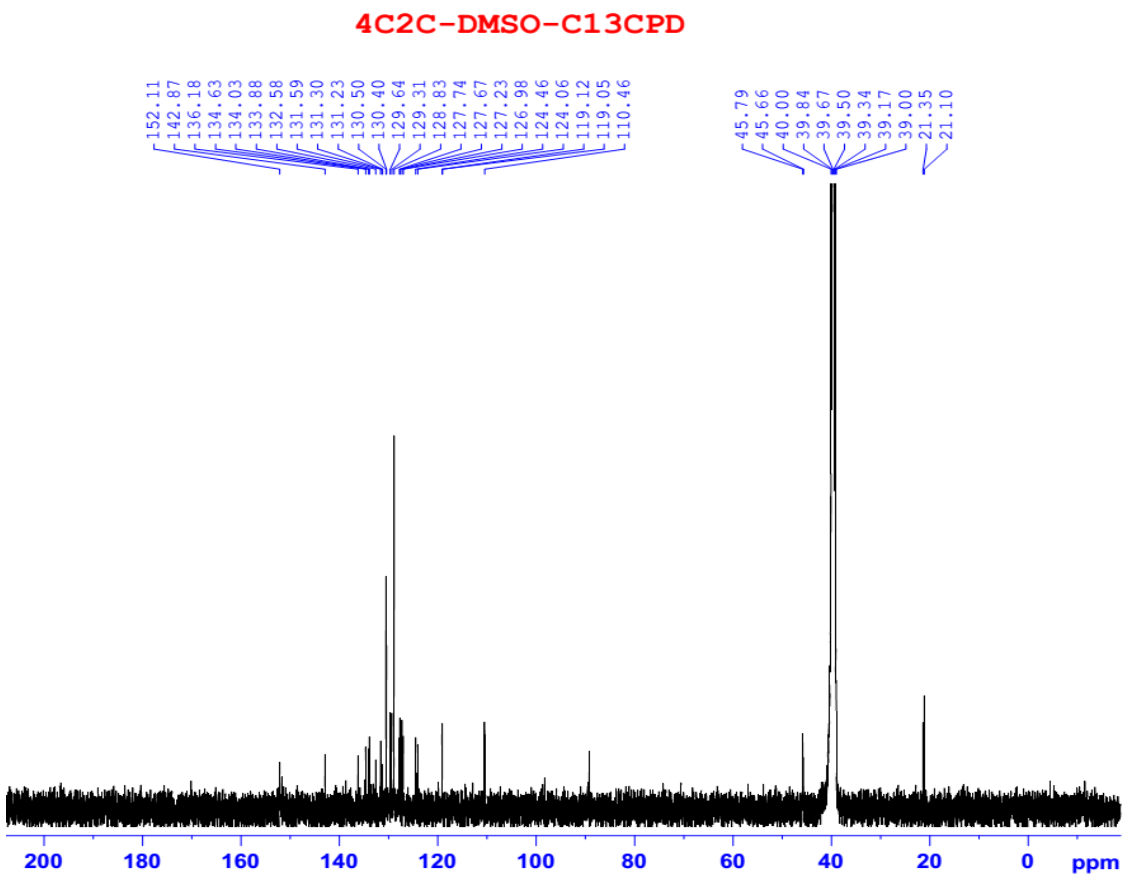

Figure S188. ^{13}C NMR spectra of compound **4h**

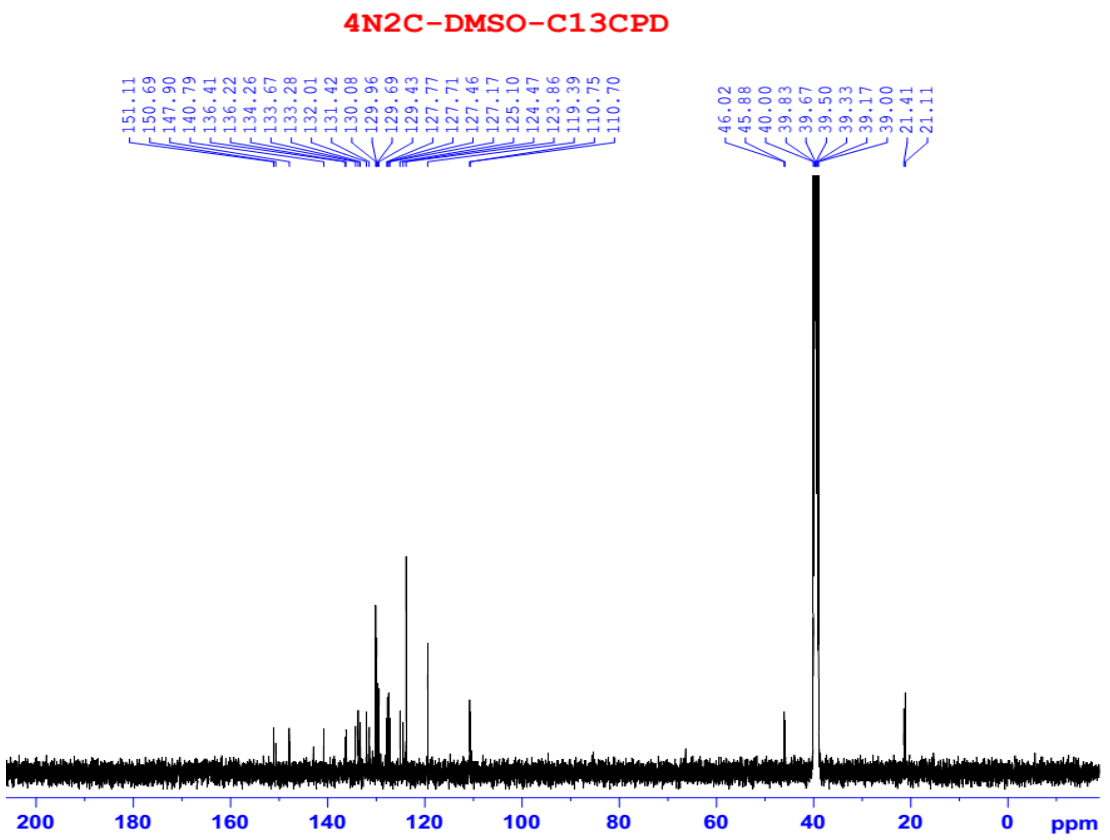

Figure S189. ^{13}C NMR spectra of compound **4i**

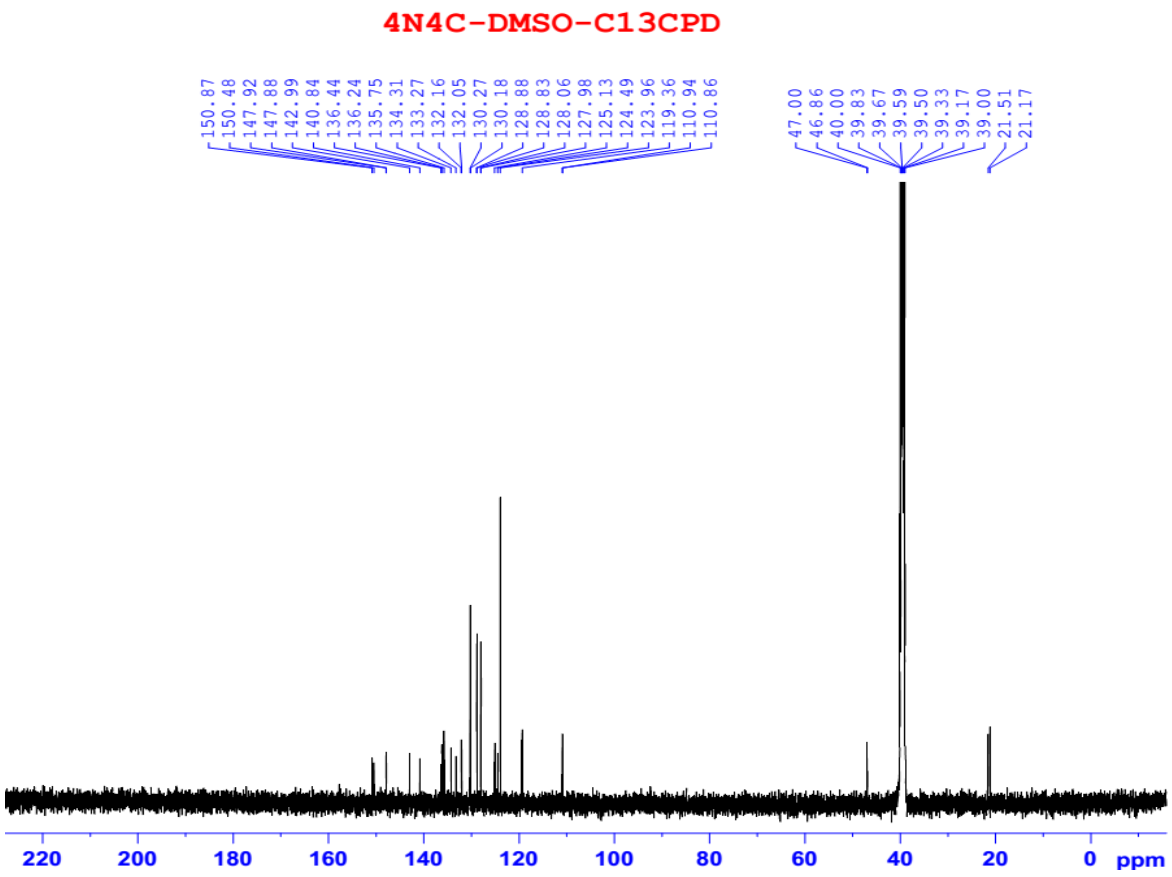

Figure S190. ^{13}C NMR spectra of compound **4j**

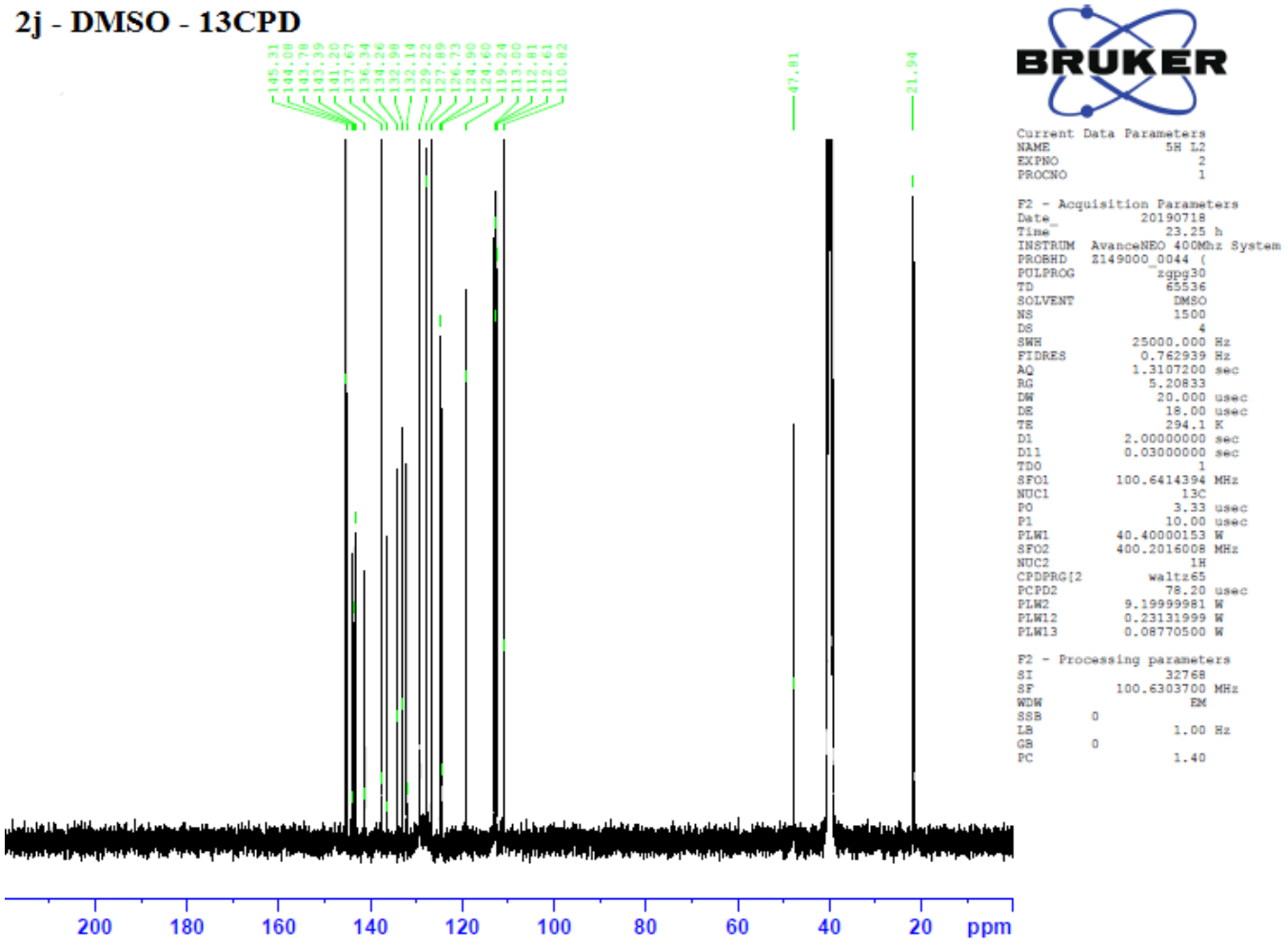

Figure S191. ^{13}C NMR spectra of compound **4k**

MS SPECTRA

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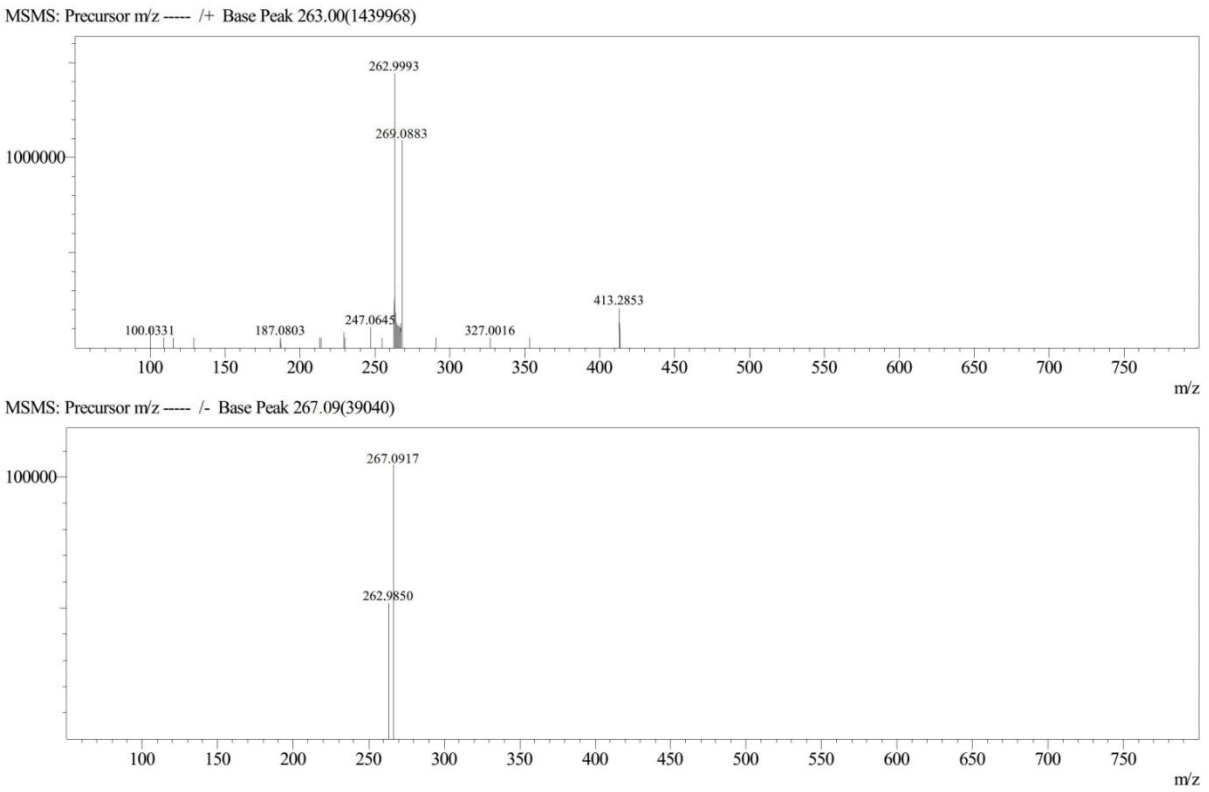

Figure S192. MS spectra of compound **3a**

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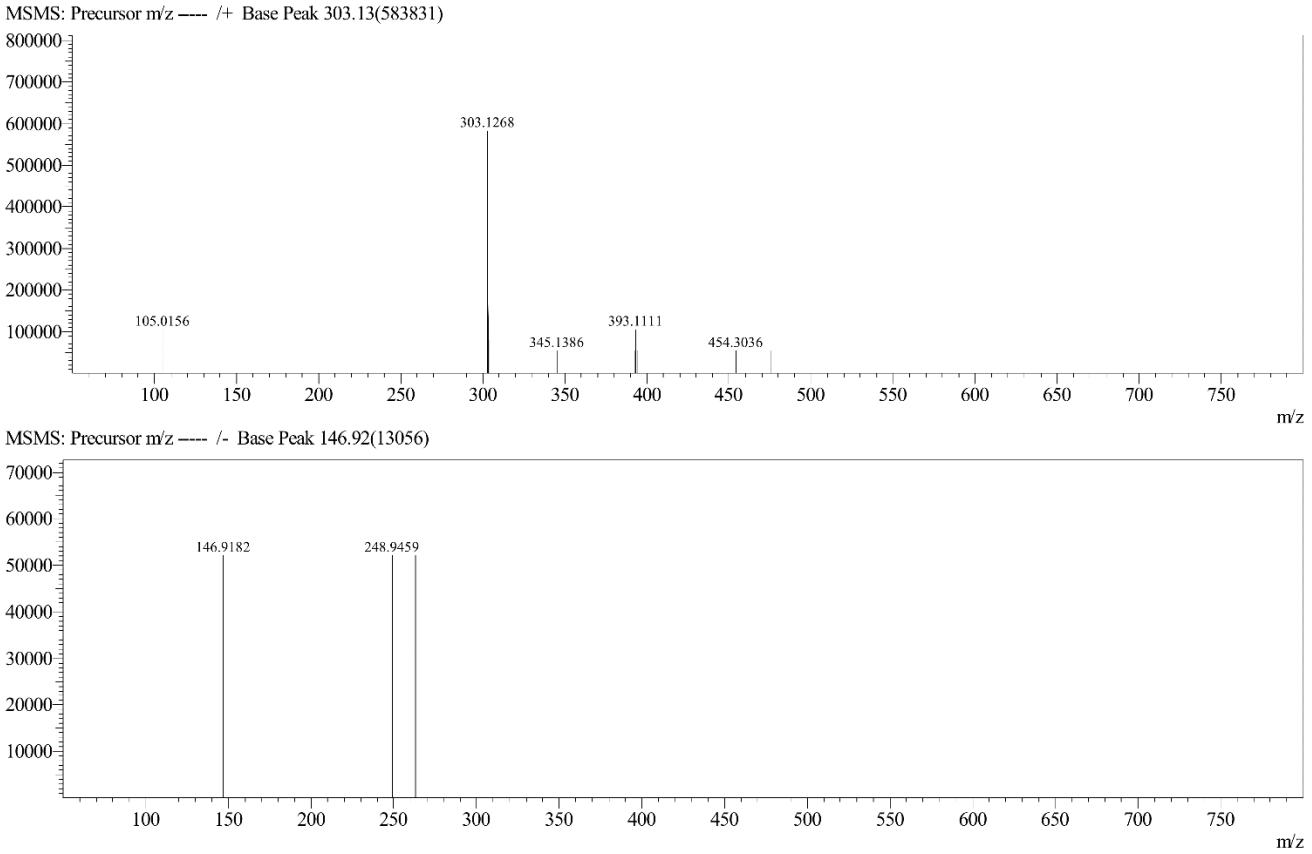

Figure S193. MS spectra of compound **3b**

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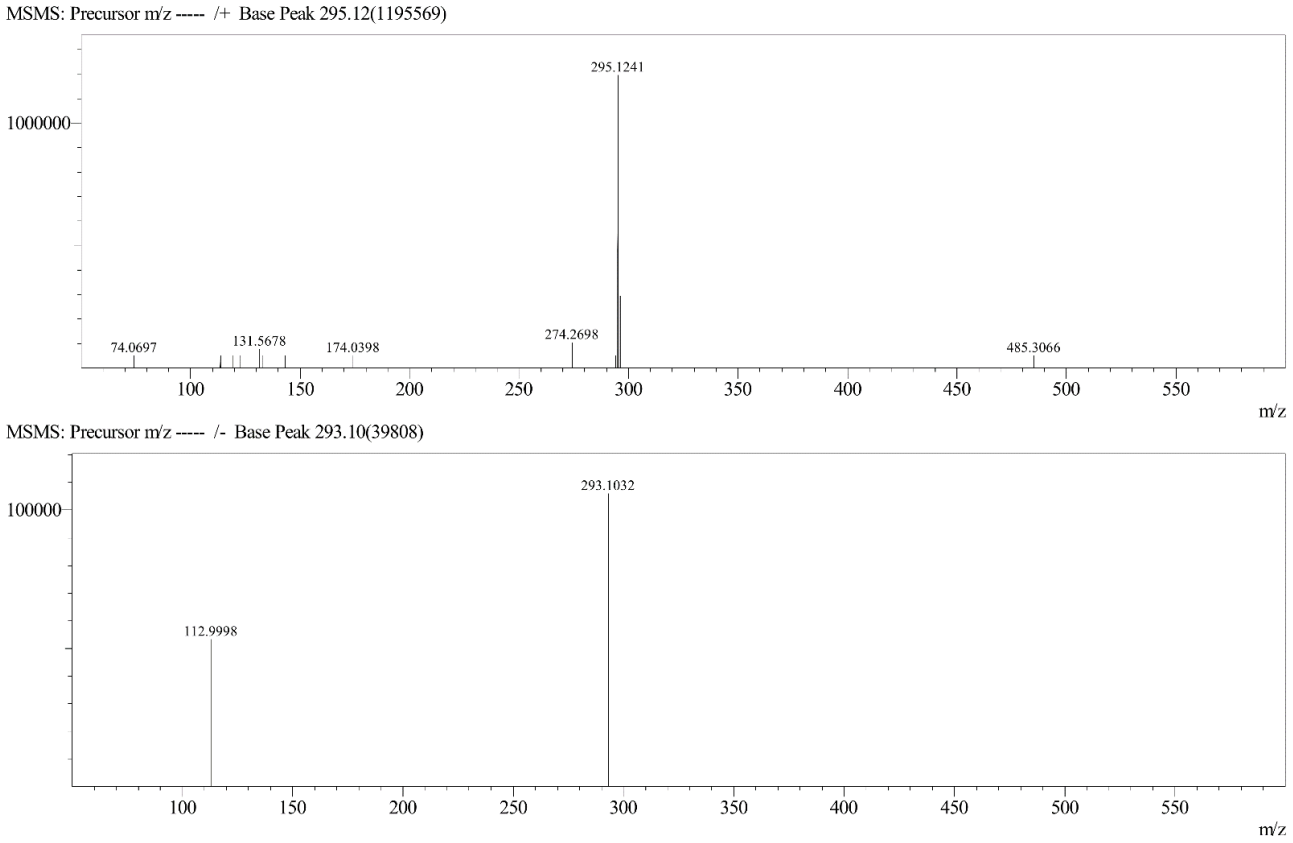

Figure S194. MS spectra of compound **3c**

<Spectrum>

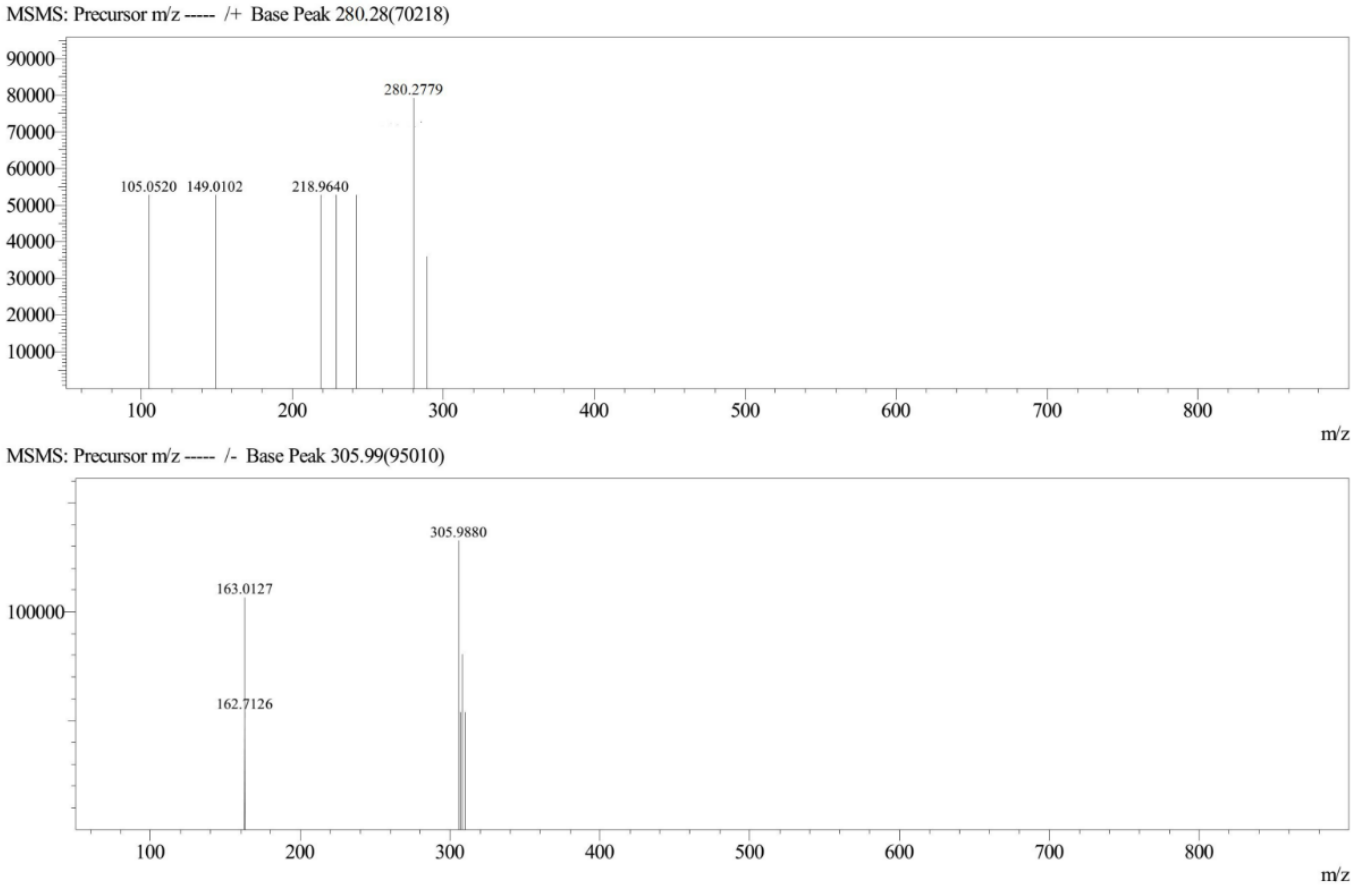

Figure S195. MS spectra of compound **3d**

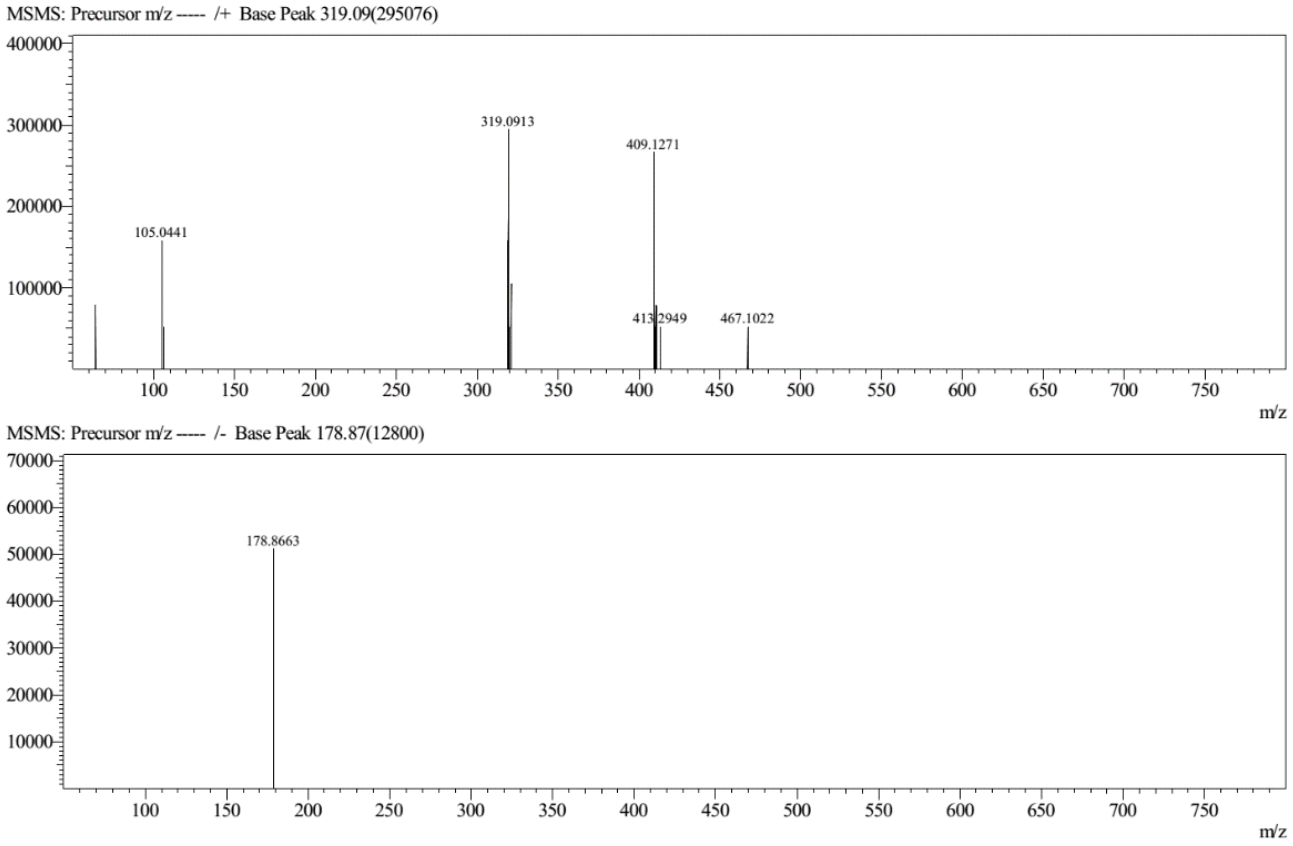

Figure S196. MS spectra of compound **3e**

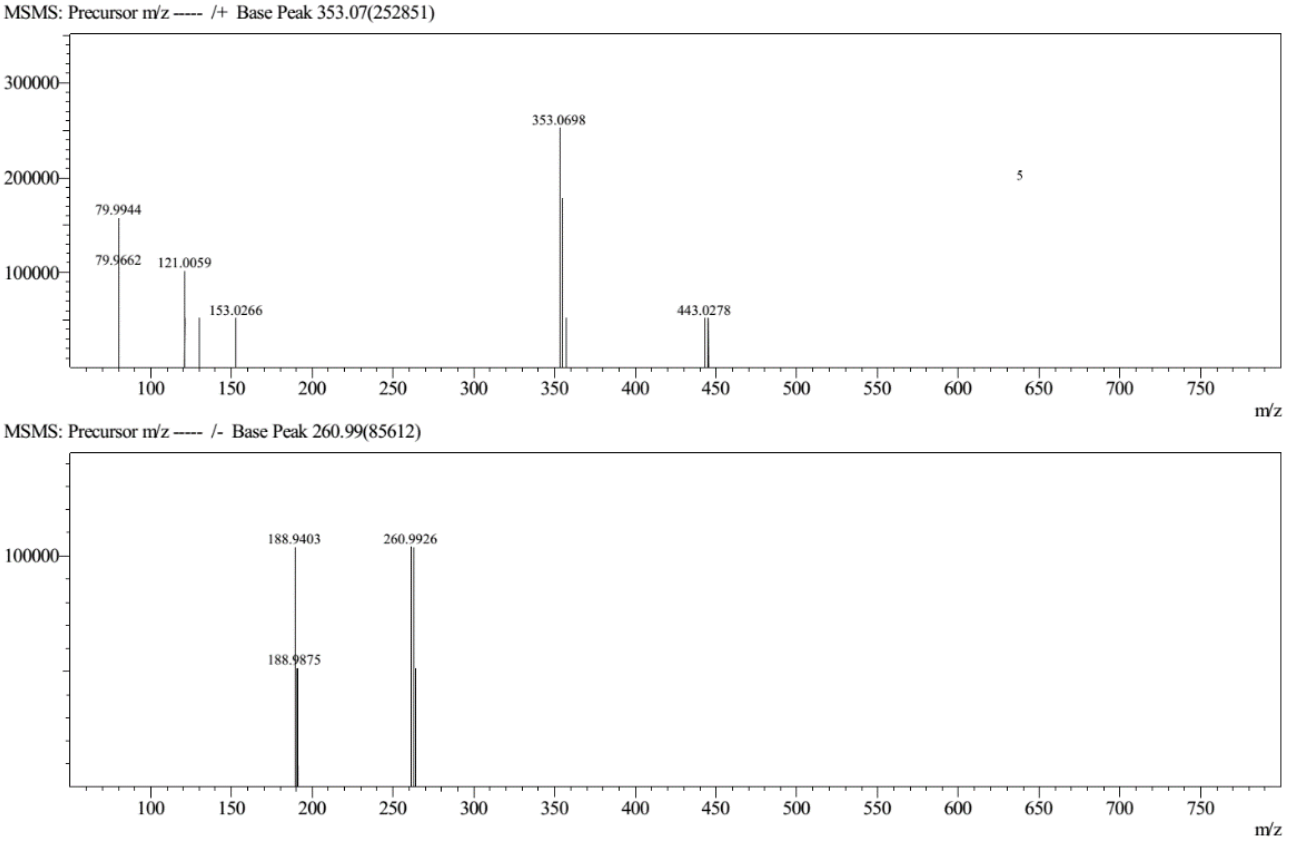

Figure S197. MS spectra of compound **3f**

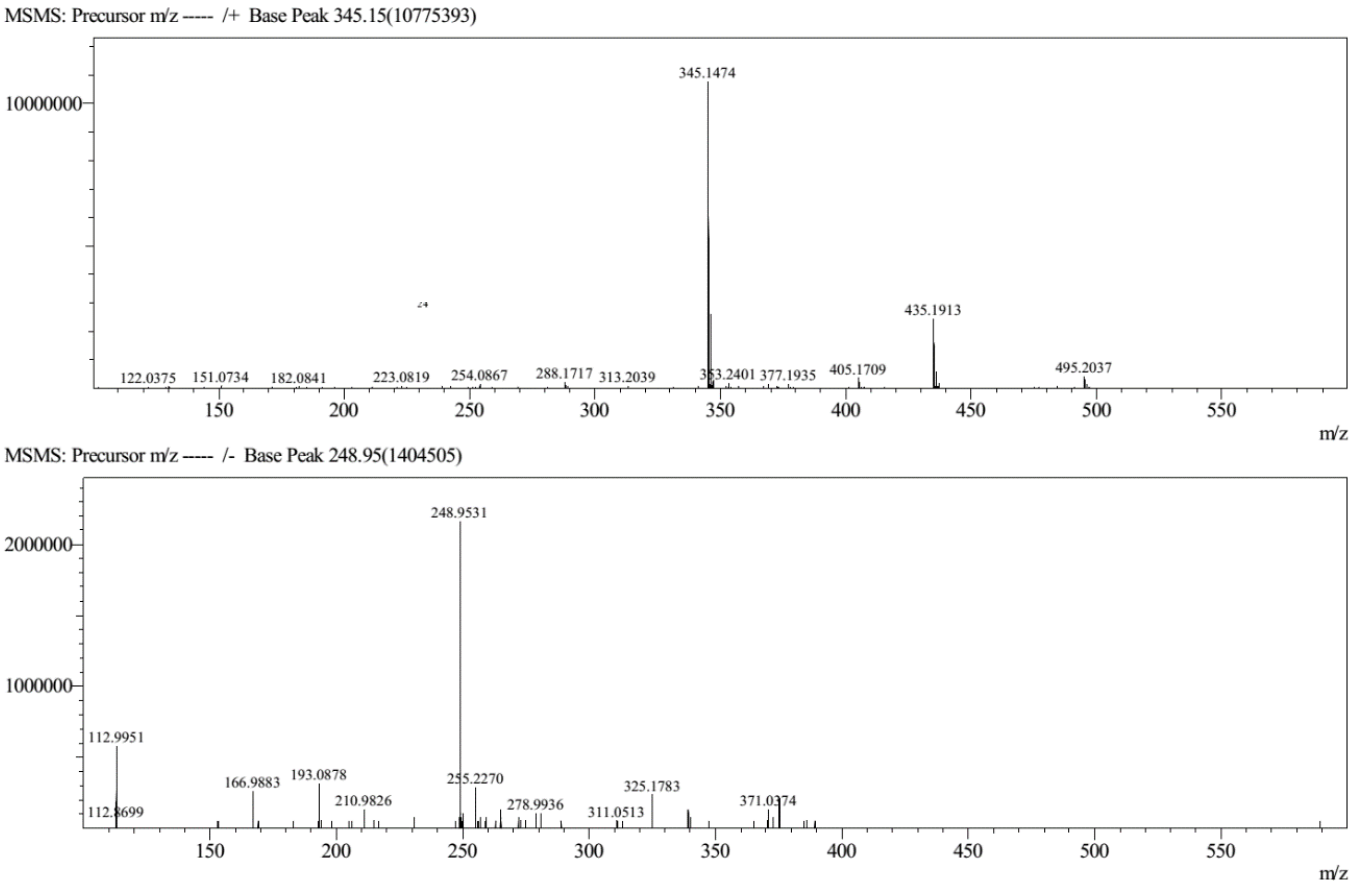

Figure S198. MS spectra of compound **3g**

<Spectrum>

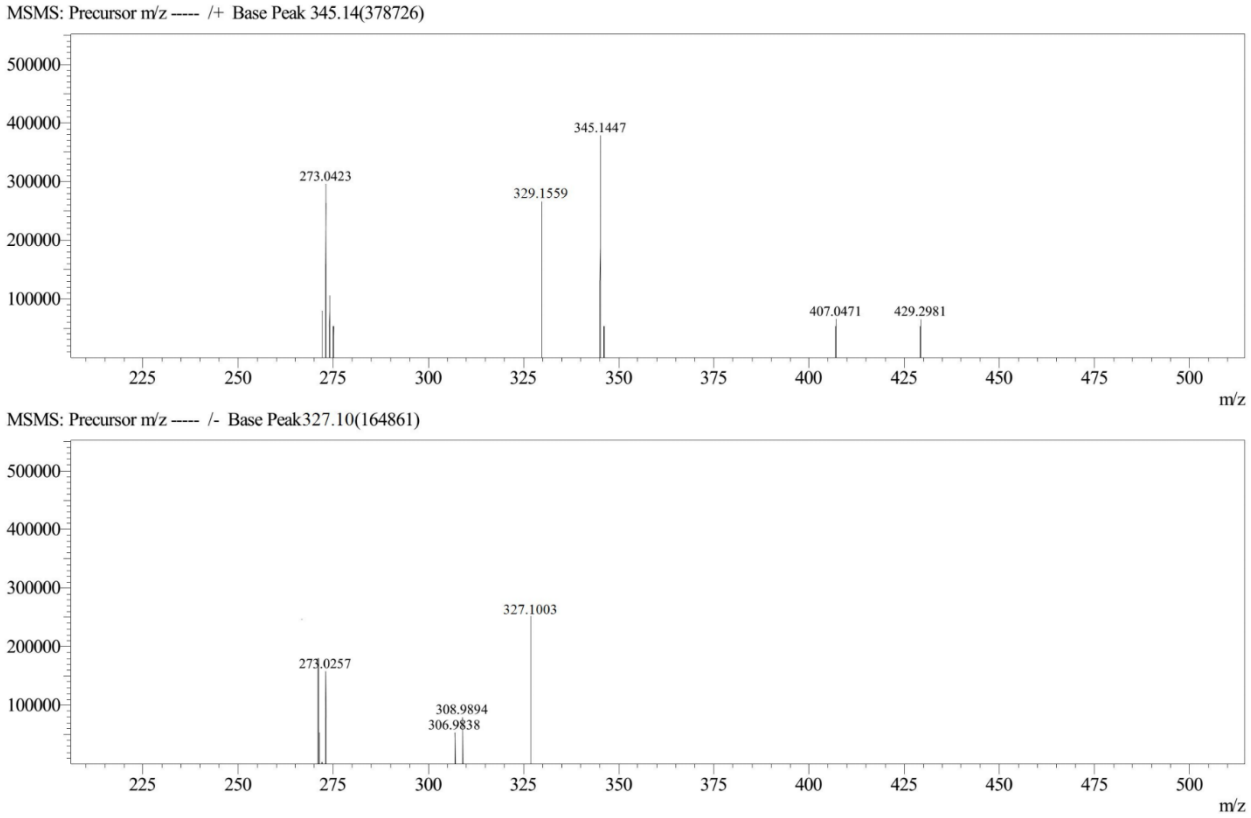

Figure S199. MS spectra of compound **3h**

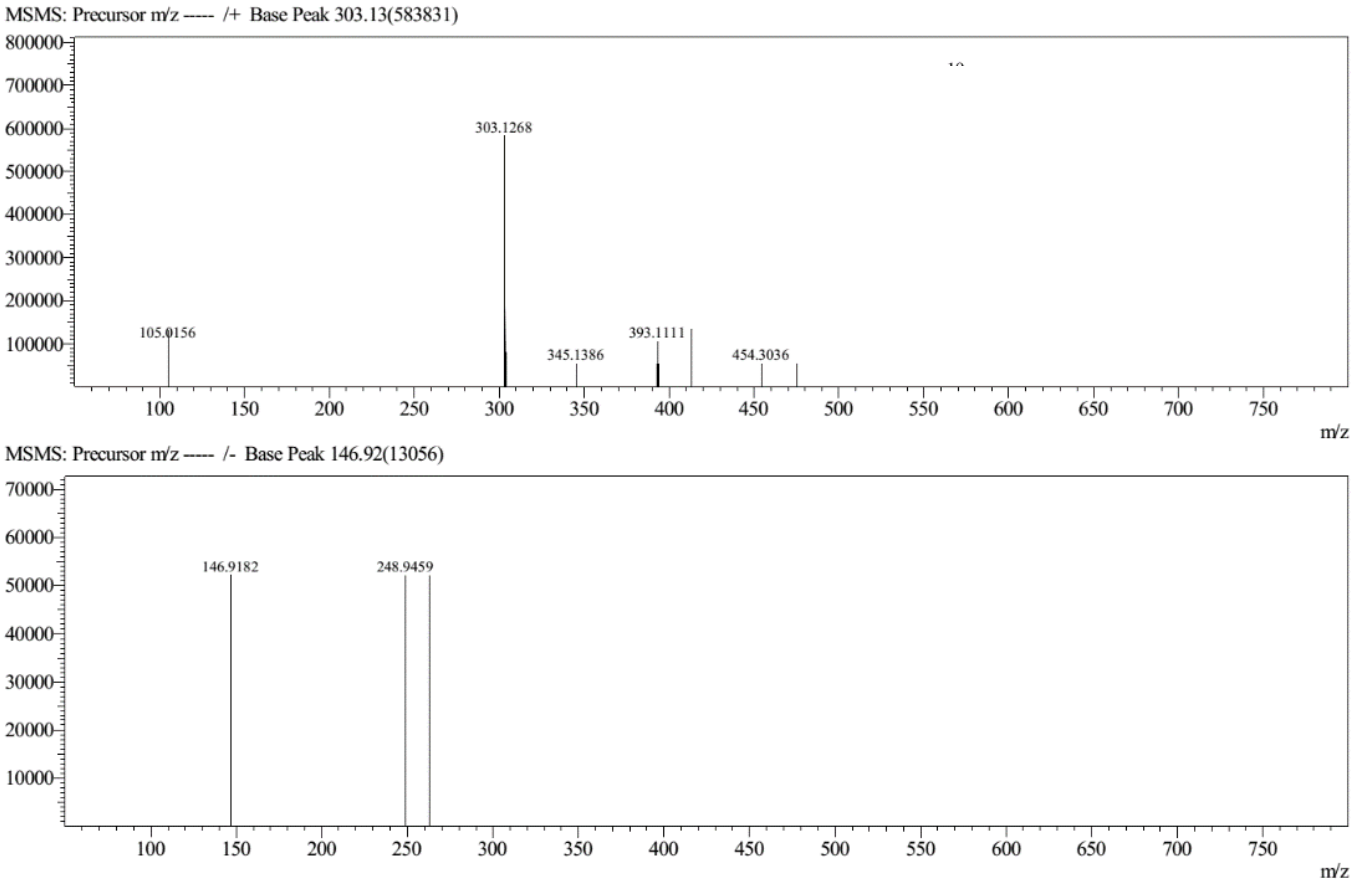

Figure S200. MS spectra of compound **3i**

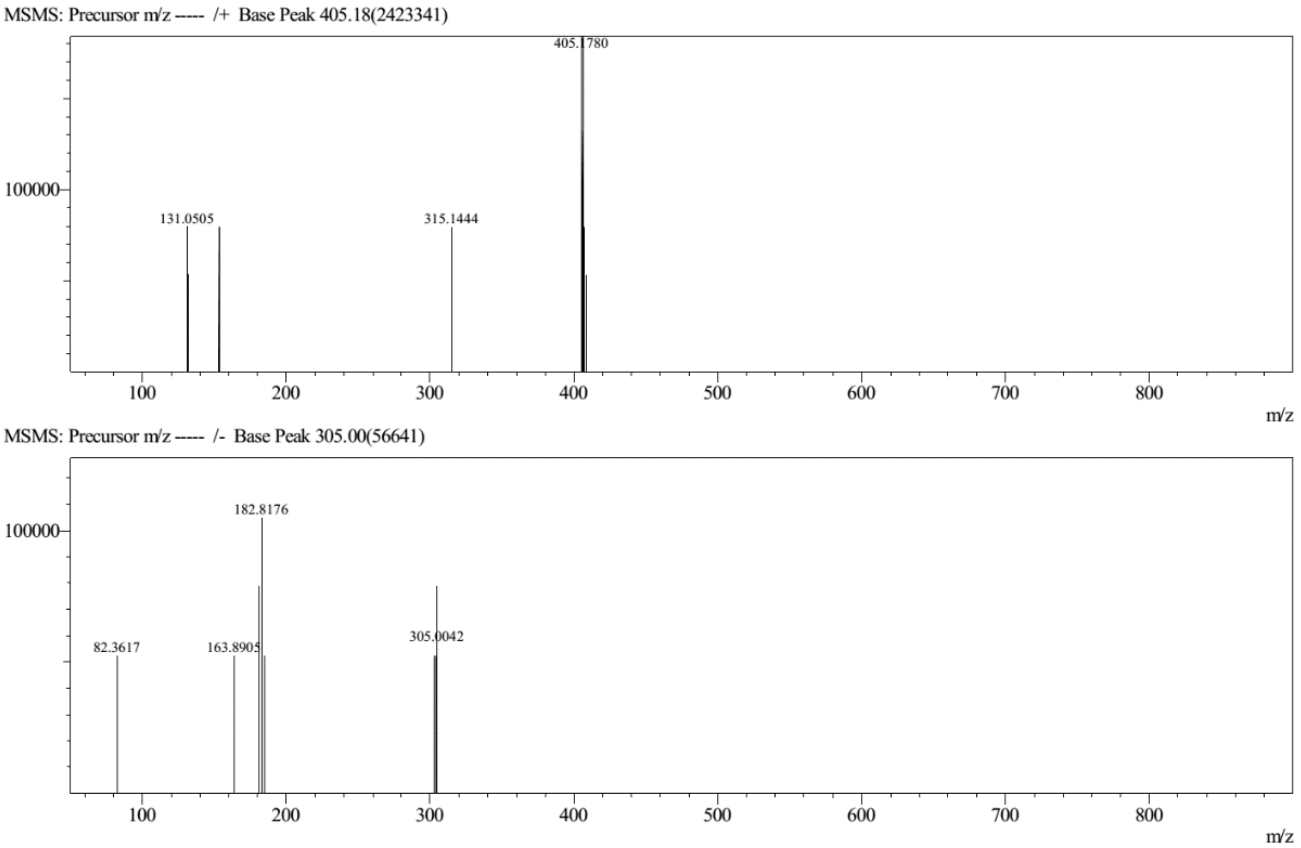

Figure S201. MS spectra of compound **3j**

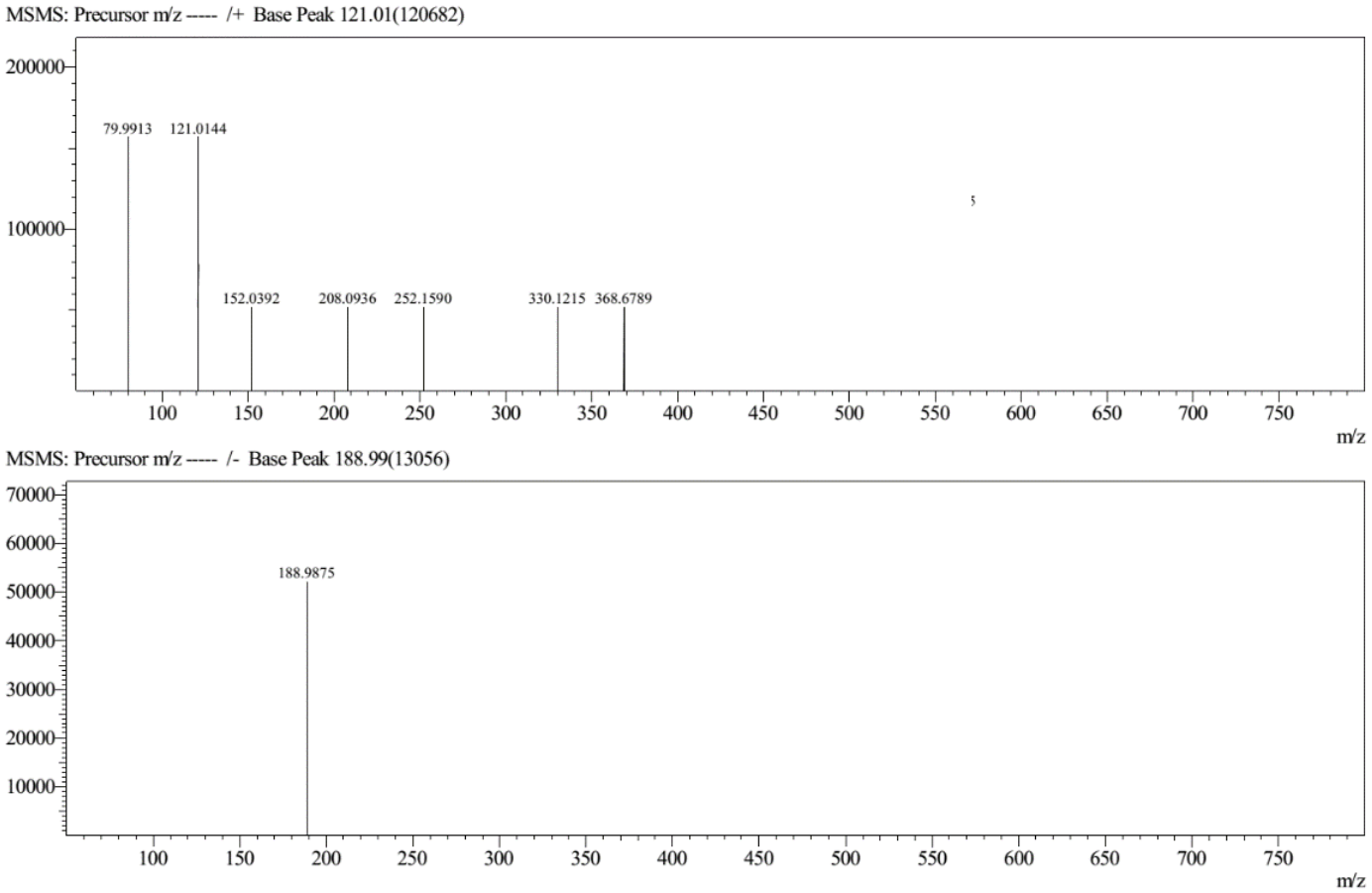

Figure S202. MS spectra of compound **3k**

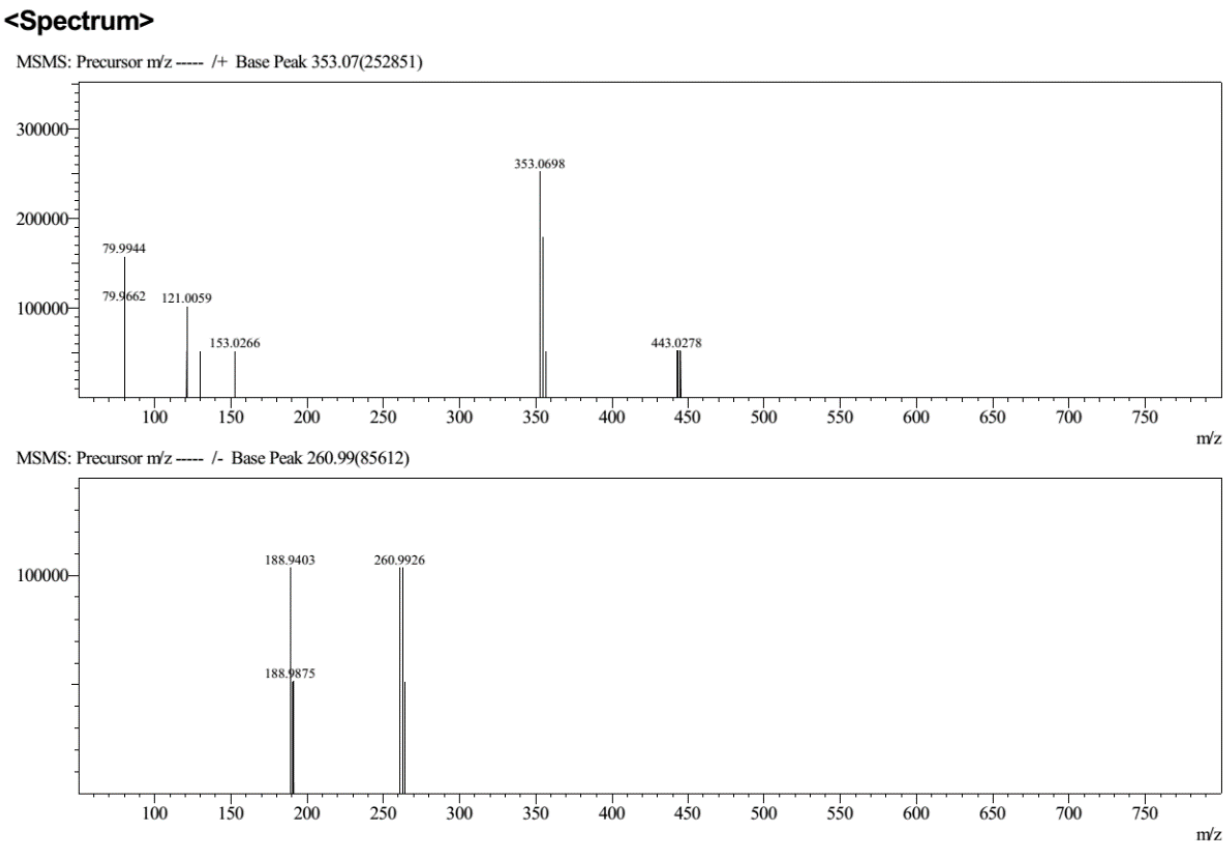

Figure S203. MS spectra of compound **3l**

<Spectrum>

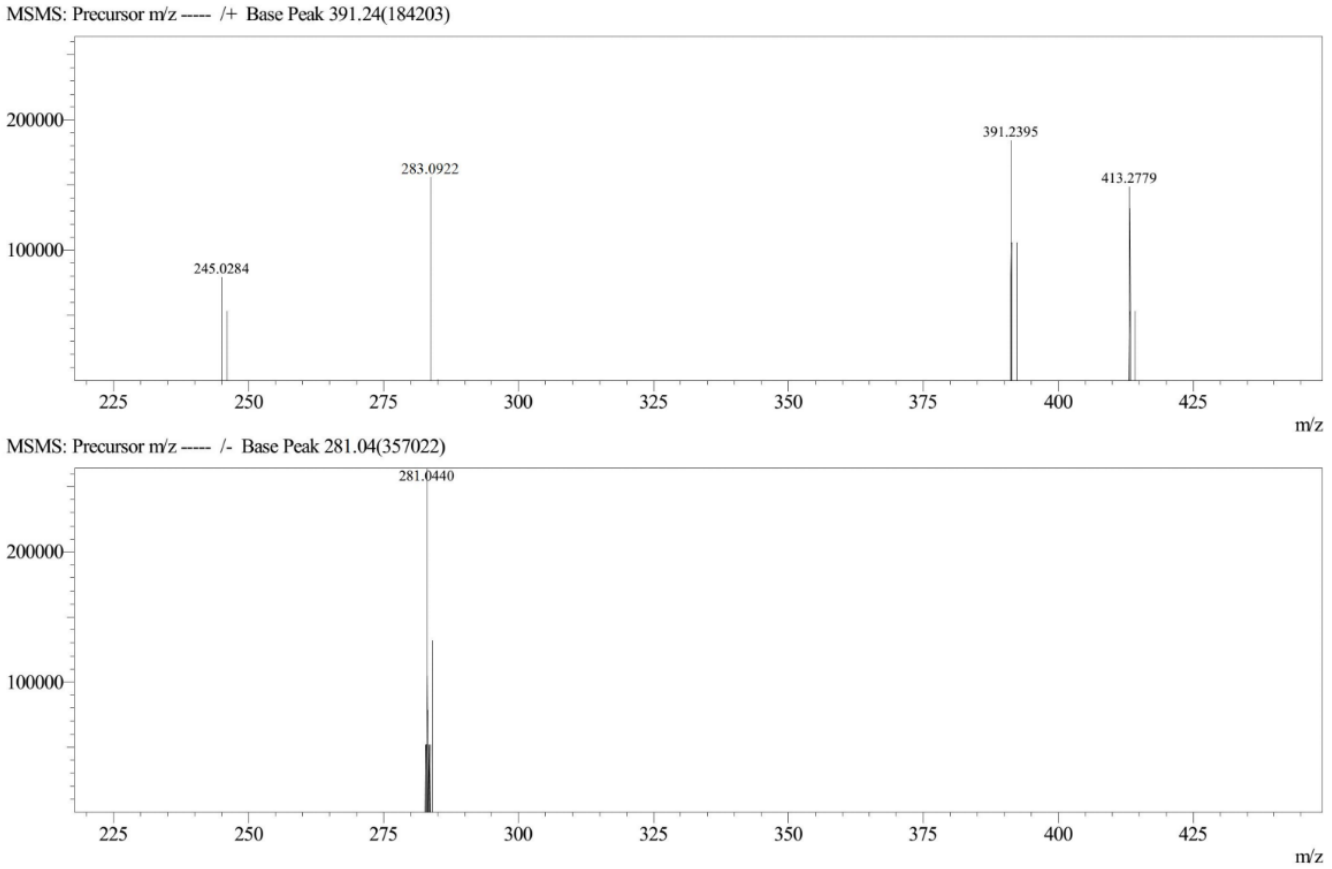

Figure S204. MS spectra of compound **4a**

<Spectrum>

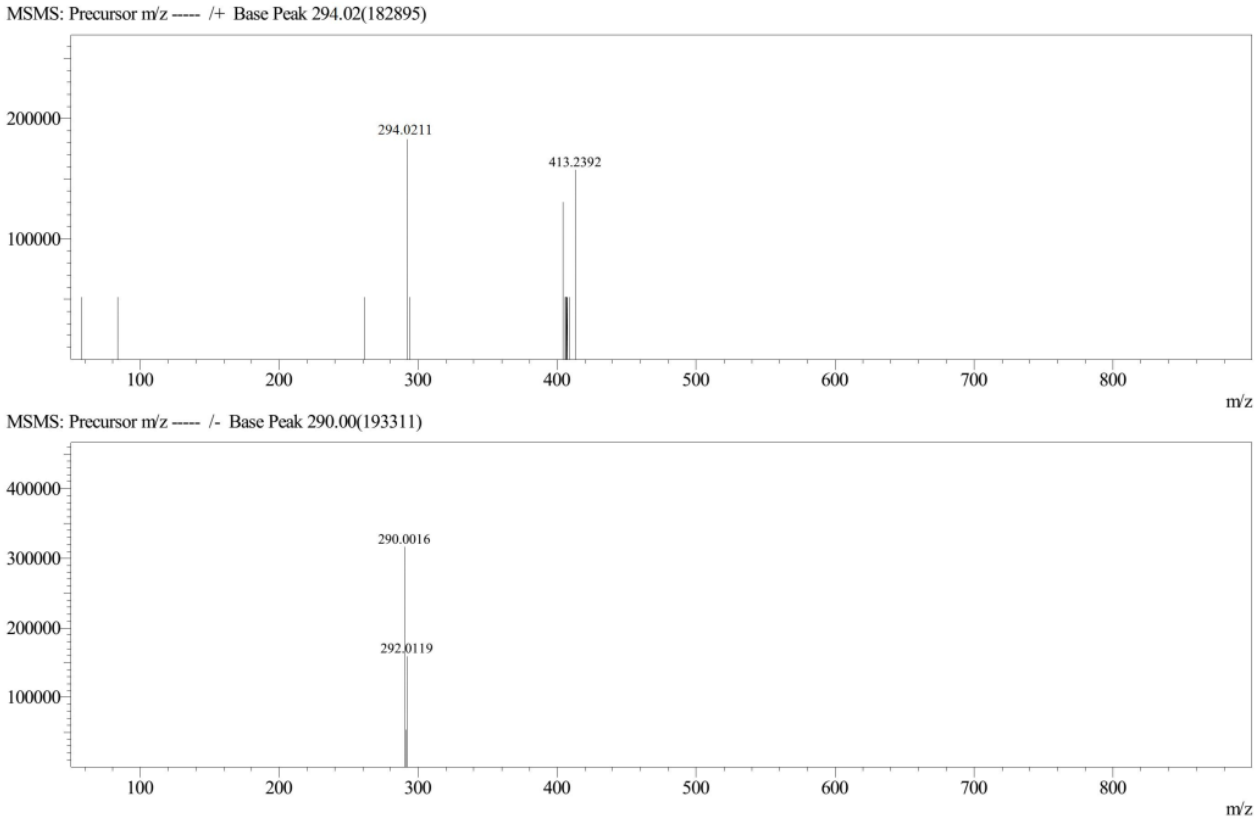

Figure S205. MS spectra of compound **4b**

<Spectrum>

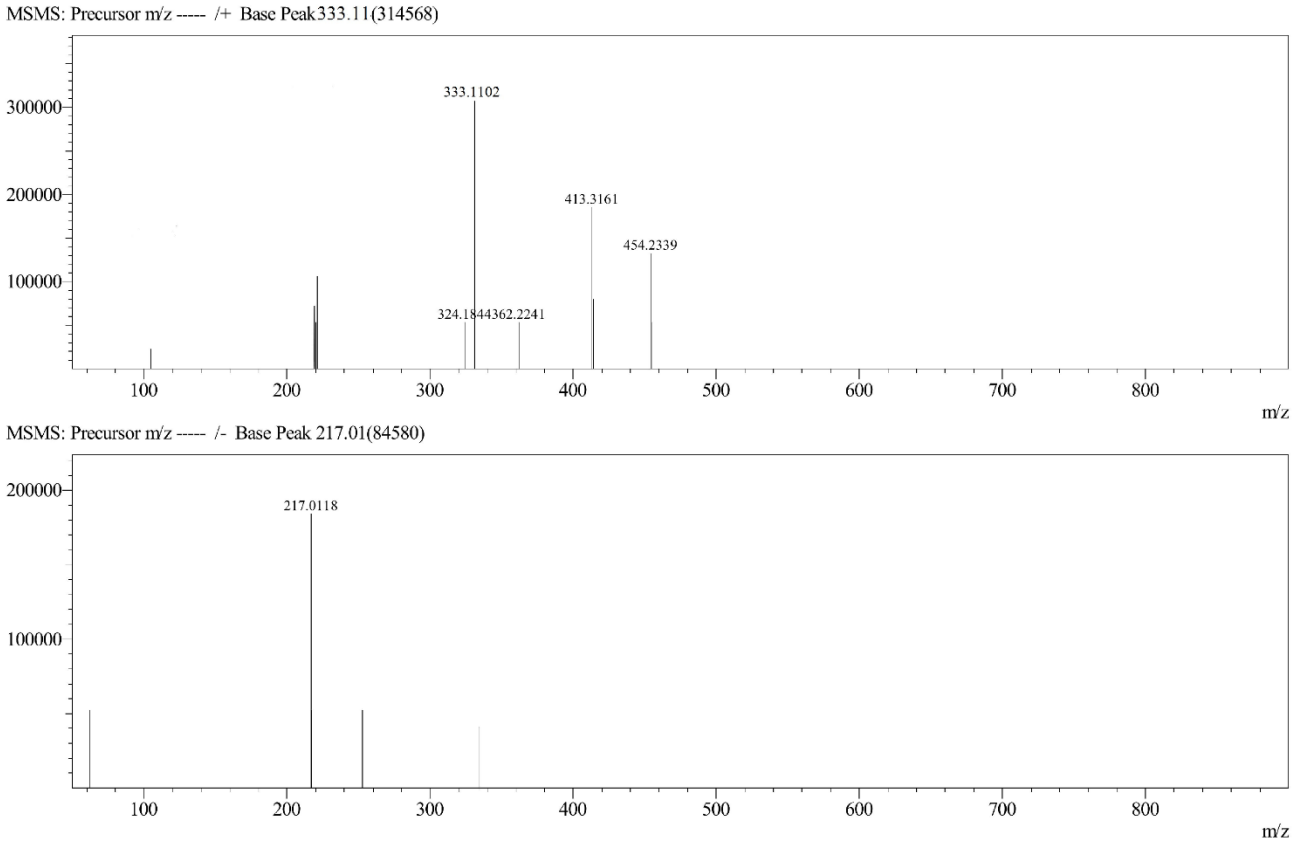

Figure S206. MS spectra of compound **4c**

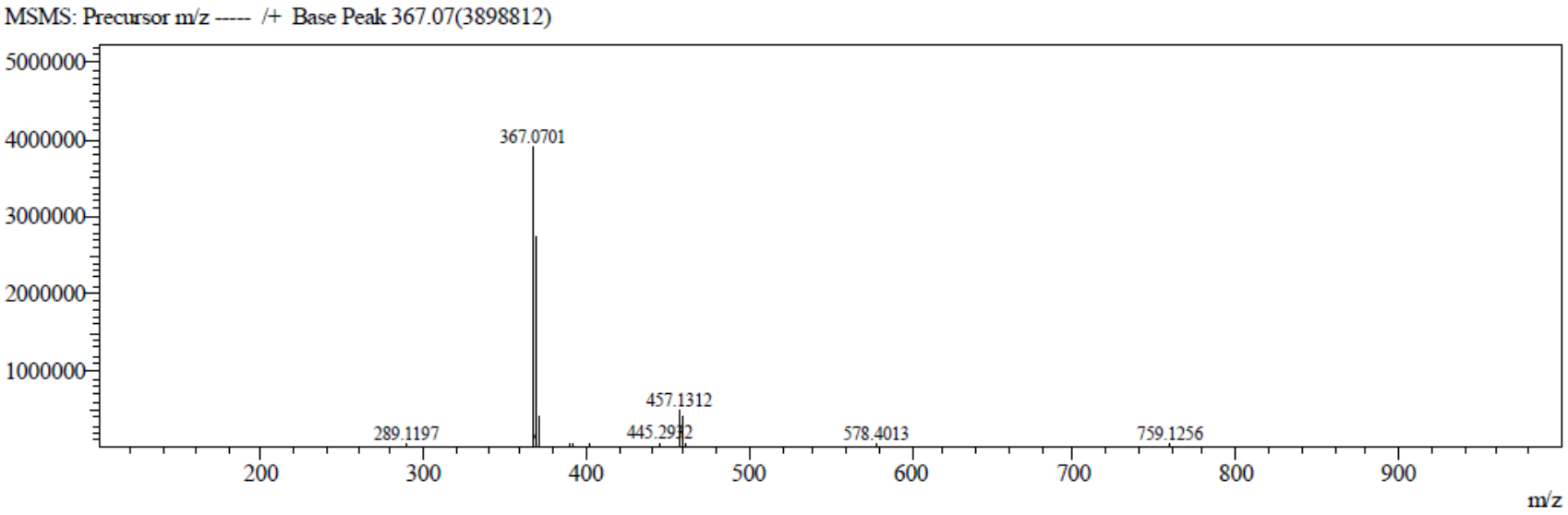

Figure S207. MS spectra of compound **4d**

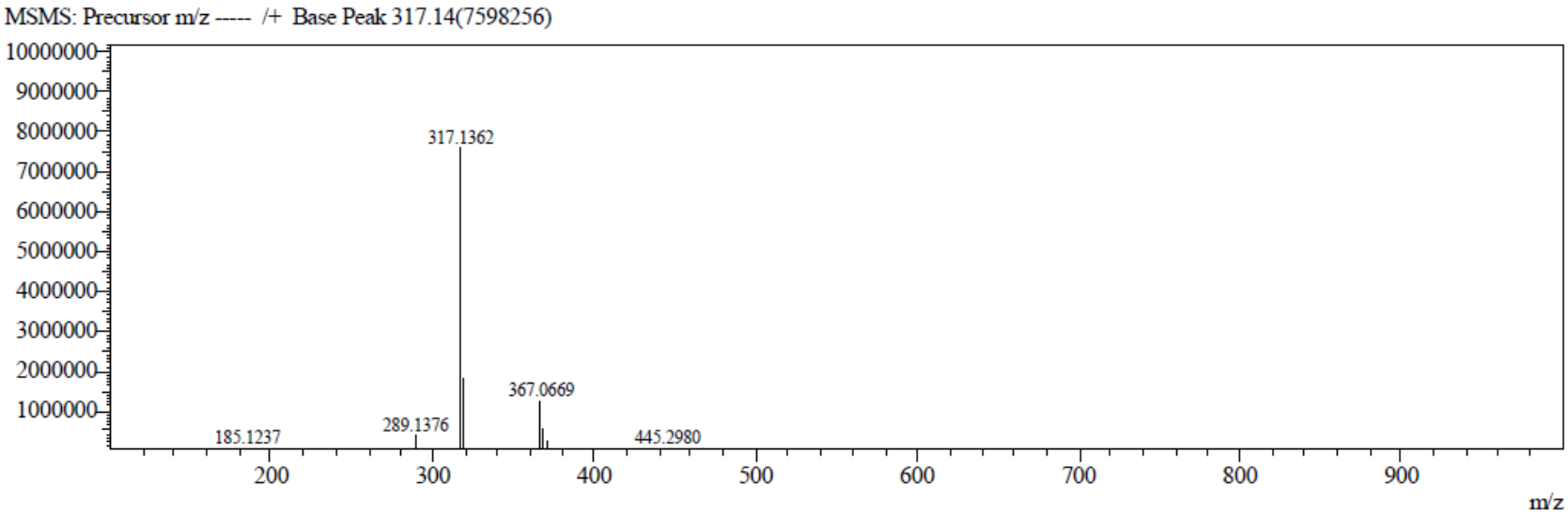

Figure S208. MS spectra of compound **4e**

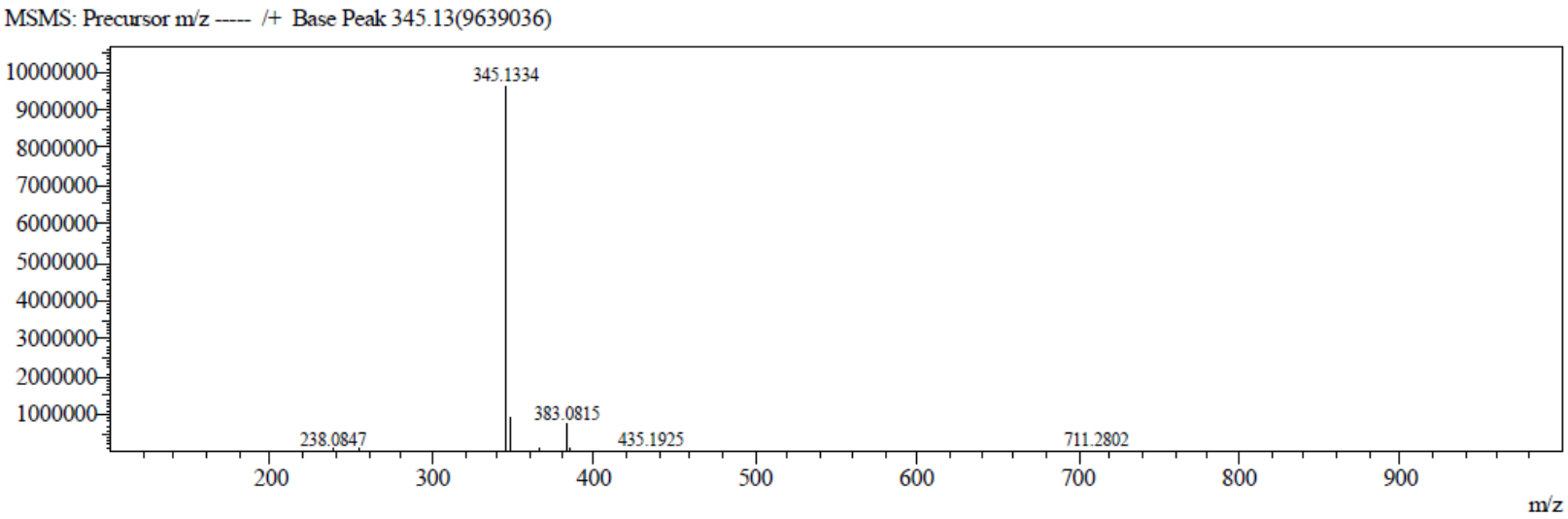

Figure S209. MS spectra of compound **4f**

<Spectrum>

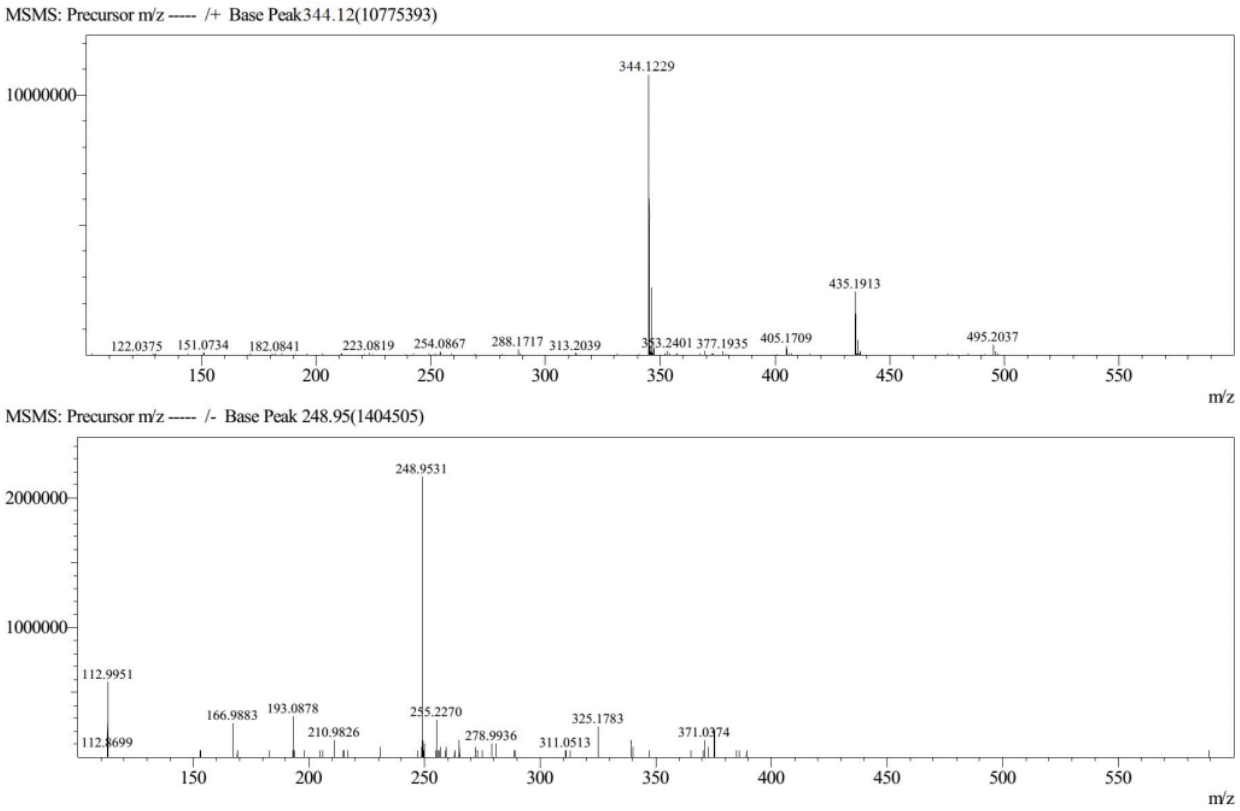

Figure S210. MS spectra of compound **4g**

<Spectrum>

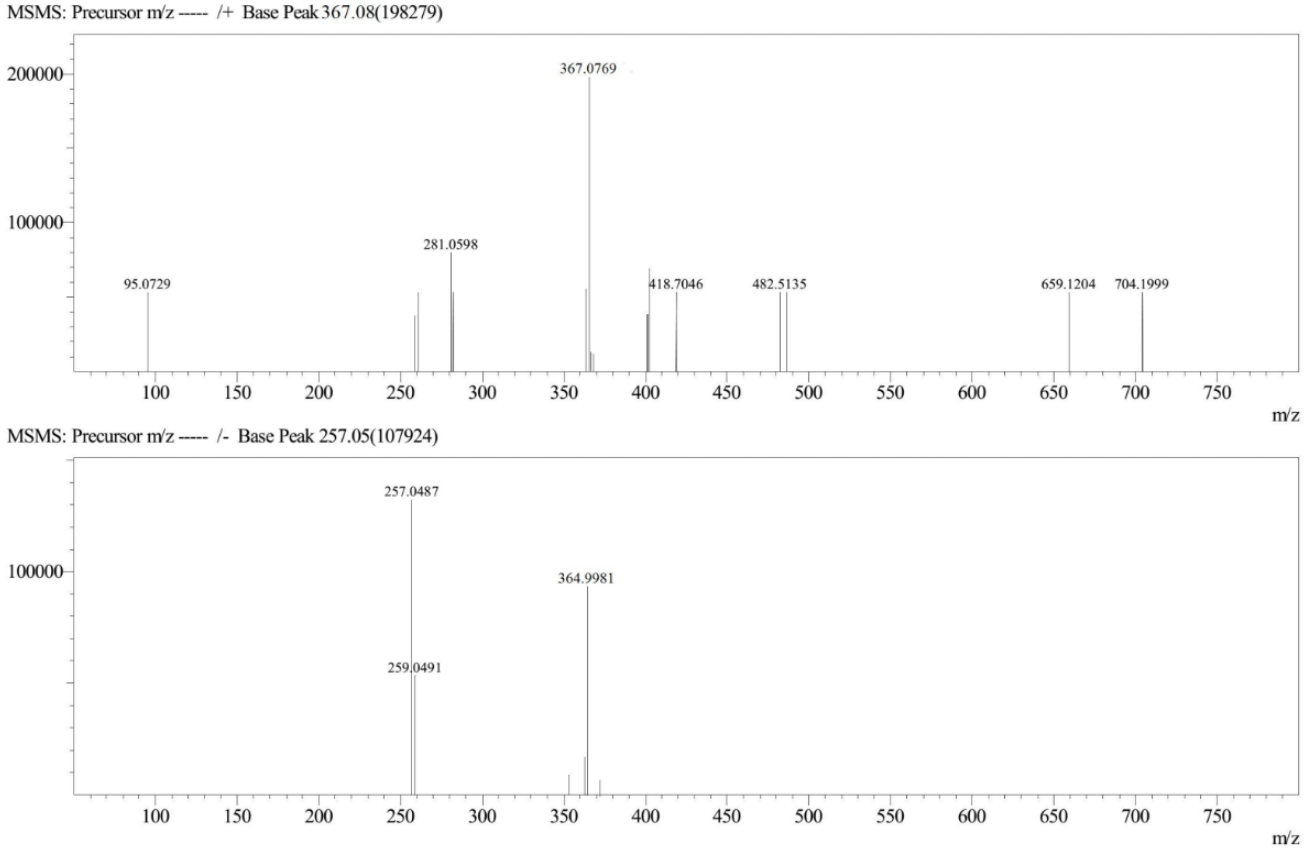

Figure S211. MS spectra of compound **4h**

<Spectrum>

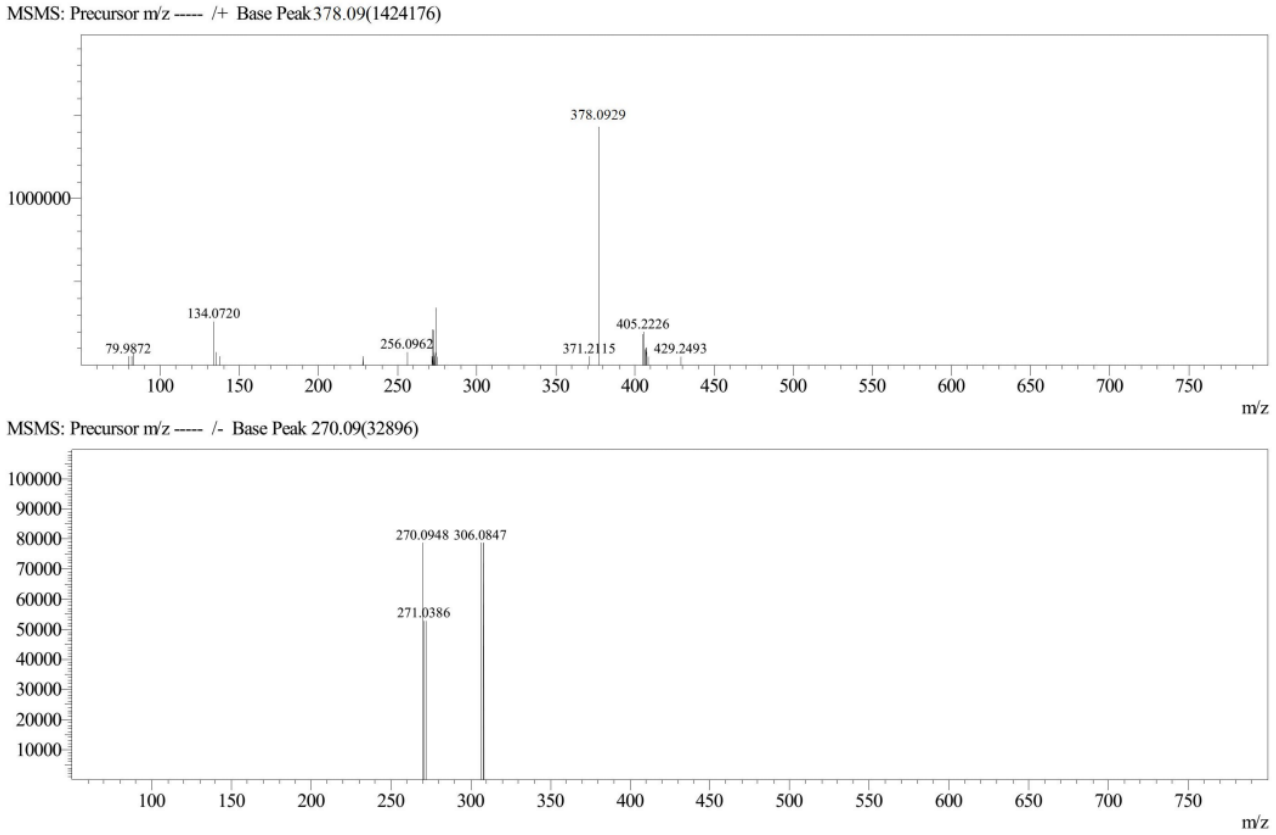

Figure S212. MS spectra of compound **4i**

<Spectrum>

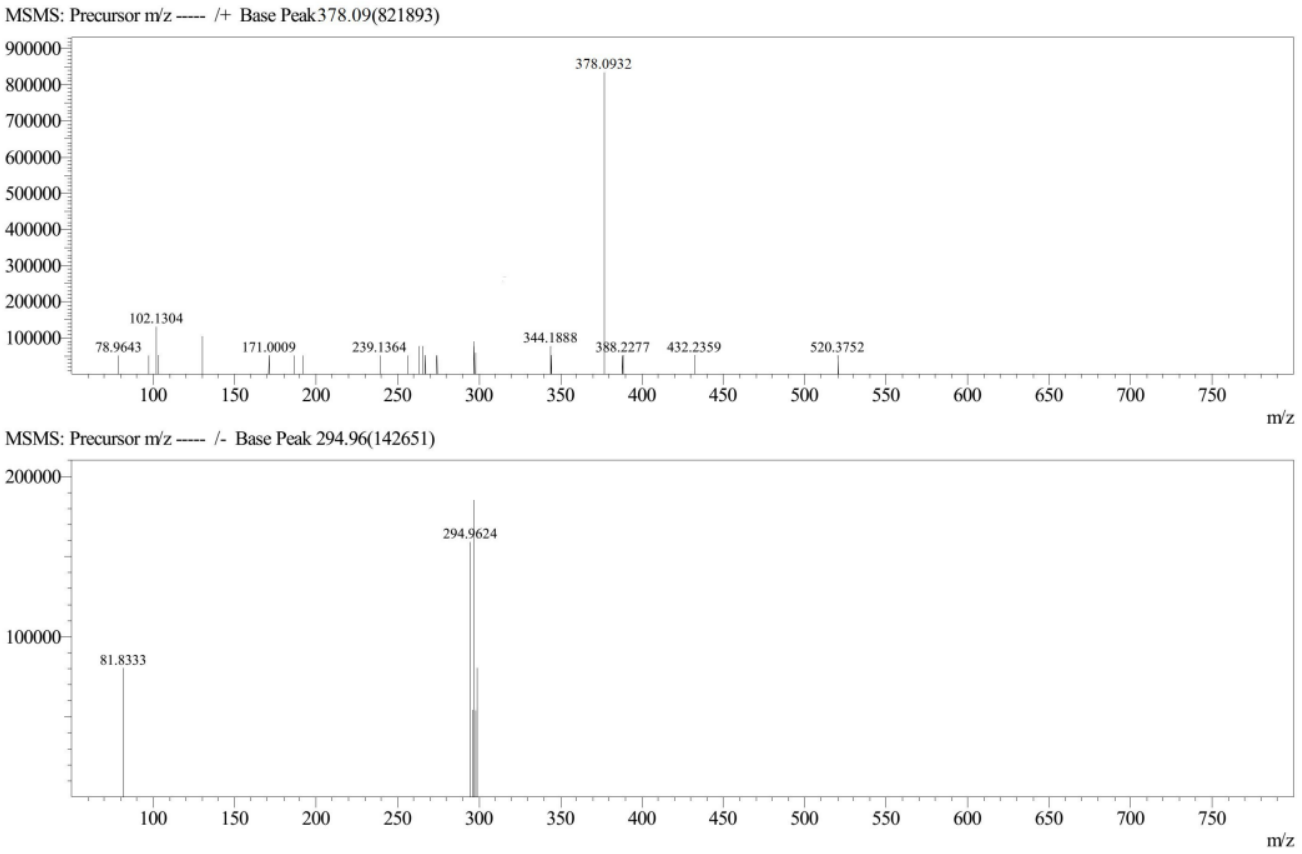

Figure S213. MS spectra of compound **4j**

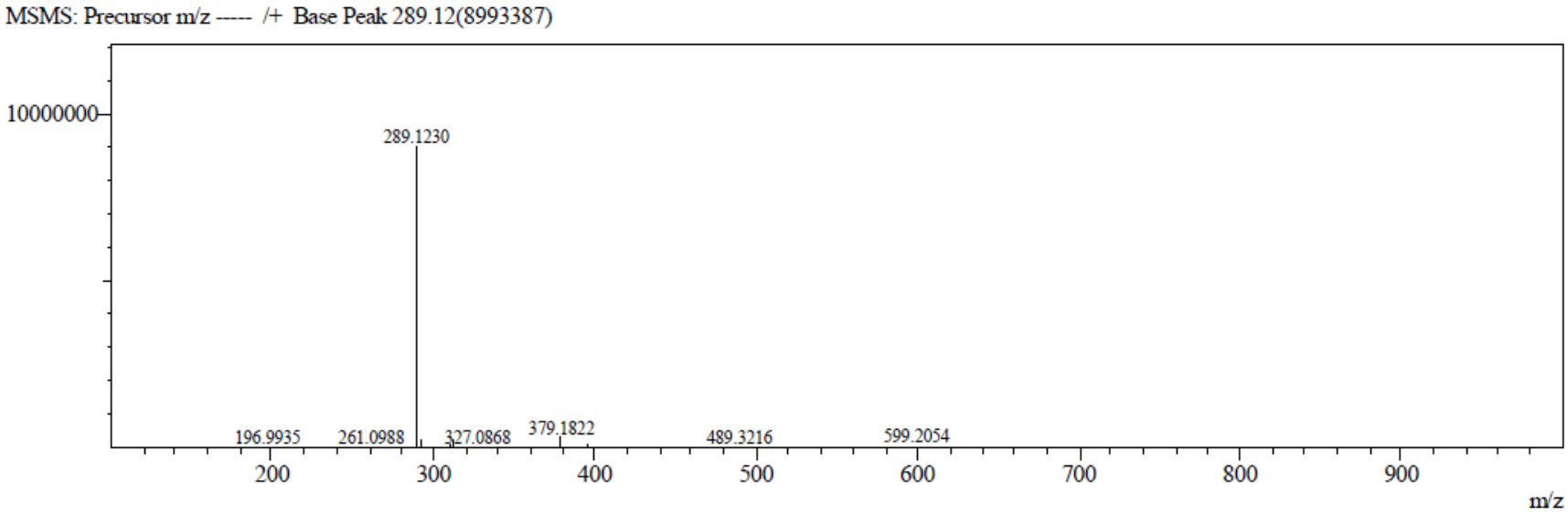

Figure S214. MS spectra of compound **4k**