

## Supplementary File

**Table S1.** The binding interactions of the molecules with the target enzyme

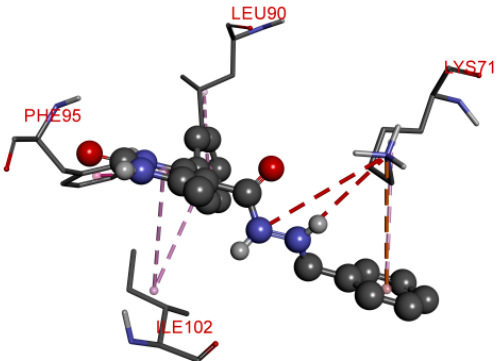
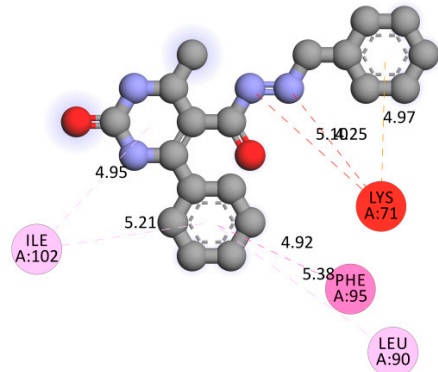
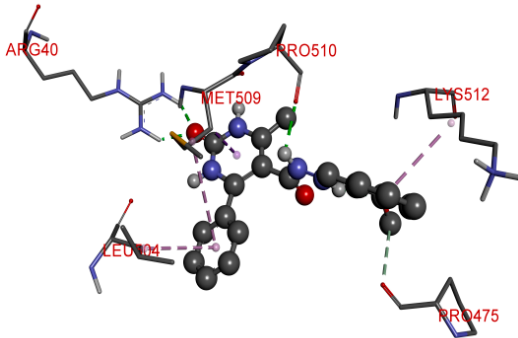
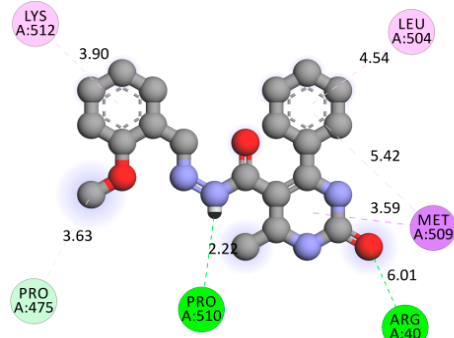
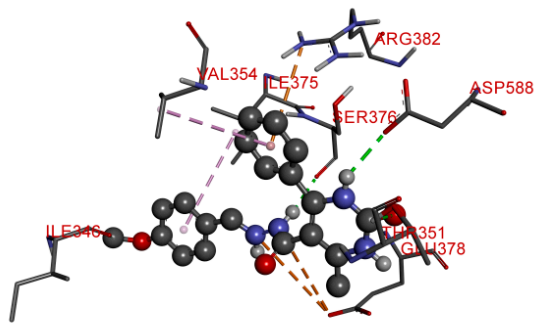
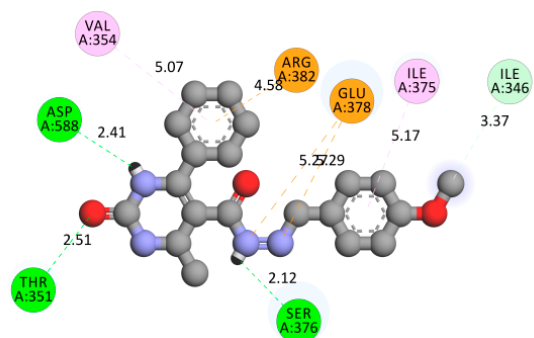
Active amino acid residues	Atom from ligand	Bond length (Å)	Bond type	Bond category	Ligand energy	Docking scores
					(kcal/mol)	
1a						
LYS71	Pi-Orbitals	4.96902	Electrostatic	Pi-Cation	288.14	−8.9
PHE95		Hydrophobic	4.92287	Pi-Pi T-shaped		
ILE102			4.94969			
LYS71			5.35011	Pi-Alkyl		
LEU90			5.37861			
ILE102			5.21468			
1c						
PRO510	H	2.22317	Hydrogen Bond	Conventional Hydrogen Bond	335.05	−8.8
ARG40	O	2.03718				
ARG40	O	2.57182				
PRO475	C	3.62995	Carbon Hydrogen Bond			
MET509	Pi-Orbitals	3.59319	Hydrophobic	Pi-Sigma		
LYS512		3.89571		Pi-Alkyl		
LEU504		4.54261				
MET509		5.42387				
1d						
GLU378	N	5.27299	Electrostatic	Attractive Charge	311.65	−8.9
GLU378	N	5.29489				
ASP588	H	2.41364	Hydrogen Bond	Conventional Hydrogen Bond		
SER376	H	2.12146				
ATHR351	O	2.50761	Hydrogen Bond	Carbon Hydrogen Bond		
ILE346	C	3.37113				
ARG382	Pi-Orbitals	4.58332	Electrostatic	Pi-Cation		
ILE375		5.17097	Hydrophobic	Pi-Alkyl		
VAL354		5.07038				
2a						
PHE95	Pi-Orbitals	4.98113	Hydrophobic	Pi-Pi T-shaped	339.38	−8.7
ILE102	Cl	3.49641		Alkyl		
ILE102	Pi-Orbitals	4.88951		Pi-Alkyl		
LEU90		5.11987				
2c						
ILE107	H	2.28309	Hydrogen Bond	Conventional Hydrogen Bond	378.97	−8.8
TRP157	NH	2.96701				

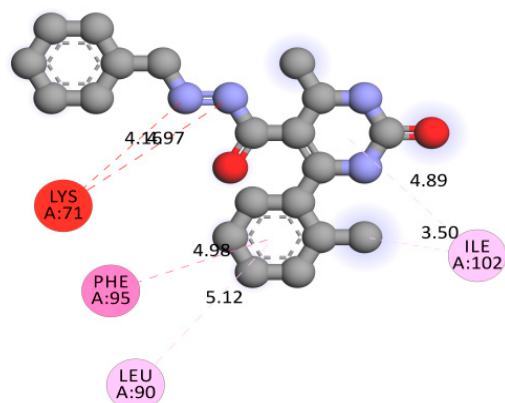
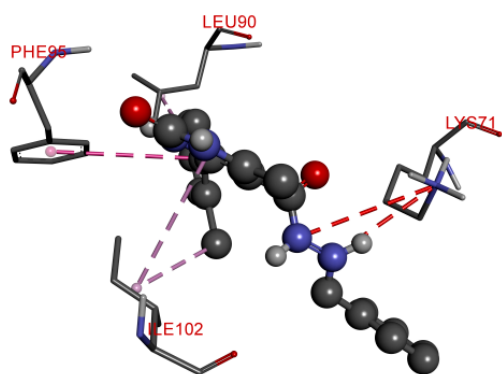
ARG61	O	2.40749				
ILE107	O	2.64522				
TRP157	O	2.06362				
SER212	C	3.77751				
LEU214	C	3.77116		Carbon Hydrogen Bond		
SER106	O	3.55398				
SER106		2.88245	Other	Pi-Lone Pair		
TRP216	Pi-Orbitals	5.49345	Hydrophobic	Pi-Pi T-shaped		
PRO159		5.20949		Pi-Alkyl		
2d						
ASN92	H	3.0358	Hydrogen Bond	Conventional Hydrogen Bond		
LYS71	Pi-Orbitals	4.93727	Electrostatic	Pi-Cation		
PHE95		5.01659		Pi-Pi T-shaped		
ILE102	Cl	3.47487		Alkyl	355.28	-8.8
ILE102		4.99551	Hydrophobic			
LYS71	Pi-Orbitals	5.32536		Pi-Alkyl		
LEU90		5.21993				
3a						
GLU206	H	2.41891	Hydrogen Bond	Conventional Hydrogen Bond		
PHE357	C	3.70779				
PHE357	C	3.95473		Pi-Sigma		
PHE357	Pi-Orbitals	3.99501				
TYR547		4.09098	Hydrophobic	Pi-Pi Stacked	337.99	-8.8
PHE357	Cl	4.71473				
TYR547	Cl	5.32992		Pi-Alkyl		
TYR662	Cl	4.47507				
TYR666	Cl	4.98485				
3c						
ILE107	H	2.17441				
THR156	NH	2.0726				
ARG61	O	2.46899	Hydrogen Bond	Conventional Hydrogen Bond		
ILE107	O	2.51808				
TRP157	O	2.13552			374.16	-8.9
SER106		2.89668	Other	Pi-Lone Pair		
TRP216	Pi-Orbitals	5.44173		Pi-Pi T-shaped		
PRO159		5.1031	Hydrophobic			
TRP154	Cl	4.98516		Pi-Alkyl		
3d						
ASP545	N	5.34106	Electrostatic	Attractive Charge	353.66	-8.8

TYR752	O	2.12135	Hydrogen Bond	Conventional Hydrogen Bond		
TRP629	Cl	3.8172				
TRP629	Cl	3.98947		Pi-Sigma		
TYR547		3.87254				
TRP629	Pi-Orbitals	4.19414	Hydrophobic	Pi-Pi Stacked		
TRP629		4.42556				
LYS554		5.44561				
TRP629	Cl	5.02642		Pi-Alkyl		
4b						
ASN103	H	3.07942				
ILE102	H	2.67703	Hydrogen Bond	Conventional Hydrogen Bond		
HIS100	H	2.06913				
ILE102	O	2.26069				
ASN74	F	3.08835	Halogen	Halogen (Fluorine)	318.42	-8.9
LYS71		4.96134	Electrostatic	Pi-Cation		
TYR105	Pi-Orbitals	5.0545	Hydrophobic	Pi-Pi T-shaped		
ILE76		5.40444				
ILE102		5.07332		Pi-Alkyl		
4c						
ASN103	C	3.57787	Hydrogen Bond	Carbon Hydrogen Bond		
PHE95		5.00945		Pi-Pi T-shaped		
ILE102		4.94343			353.37	-8.8
LYS71	Pi-Orbitals	5.38863	Hydrophobic	Pi-Alkyl		
LEU90		5.35004				
ILE102		5.31852				
4d						
ASN92	H	3.03667	Hydrogen Bond	Conventional Hydrogen Bond		
PHE95		4.96081		Pi-Pi T-shaped		
ILE102		4.99511			330.06	-8.9
LYS71	Pi-Orbitals	5.42747	Hydrophobic	Pi-Alkyl		
LEU90		5.30662				
ILE102		5.38307				
5a						
PRO510	H	2.08203				
ARG40	O	2.32727	Hydrogen Bond	Conventional Hydrogen Bond		
ARG40	O	2.4405				
ASP501	F	3.40107	Hydrogen Bond;Halogen	Carbon Hydrogen Bond;Halogen (Fluorine)	314.94	-8.8
ASP501	F	3.05778	Halogen	Halogen (Fluorine)		

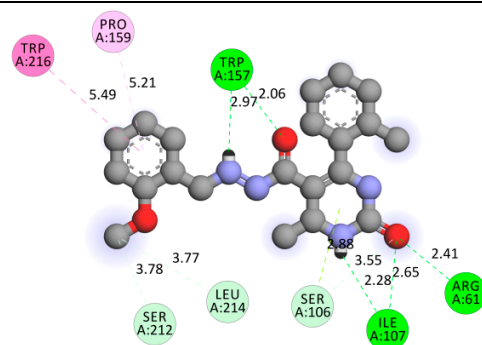
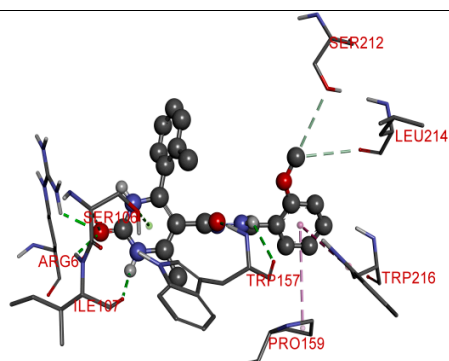
<b>MET509</b>		3.63018		Pi-Sigma		
<b>PHE559</b>		5.66091		Pi-Pi Stacked		
<b>LEU504; GLN505</b>	Pi-Orbitals	4.85965	Hydrophobic	Amide-Pi Stacked		
<b>LYS512</b>		3.84082				
<b>LEU504</b>		4.6698		Pi-Alkyl		
<b>MET509</b>		5.10781				
5c						
<b>ASN103</b>	H	3.00917		Conventional		
<b>ILE102</b>	H	2.29053	Hydrogen Bond	Hydrogen Bond		
<b>ASN92</b>	C	3.73613		Carbon Hydrogen Bond		
<b>ASN74</b>	F	3.09031	Halogen	Halogen (Fluorine)	352.31	-8.8
<b>TYR105</b>		5.14358		Pi-Pi T-shaped		
<b>ILE76</b>	Pi-Orbitals	5.49595	Hydrophobic			
<b>ILE102</b>		5.01132		Pi-Alkyl		
5d						
<b>GLU378</b>	N	5.1091				
<b>GLU378</b>	N	5.11935	Electrostatic	Attractive Charge		
<b>ASP588</b>	H	2.40892				
<b>SER376</b>	H	2.35939	Hydrogen Bond	Conventional Hydrogen Bond		
<b>THR351</b>	O	2.48898				
<b>GLY355</b>	F	1.95875	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	330.02	-8.9
<b>ILE346</b>	C	3.3198		Carbon Hydrogen Bond		
<b>HIS592</b>	F	3.15587	Hydrogen Bond			
<b>GLU347</b>	F	2.7357				
<b>TRP353</b>	F	3.68392				
<b>VAL354</b>	F	3.56747	Halogen	Halogen (Fluorine)		
<b>ASP588</b>	F	3.06595				
<b>ILE375</b>	Pi-Orbitals	5.27418				
<b>VAL354</b>		5.26117	Hydrophobic	Pi-Alkyl		

**Table S2.** 2D- and 3D-binding postures of the molecules

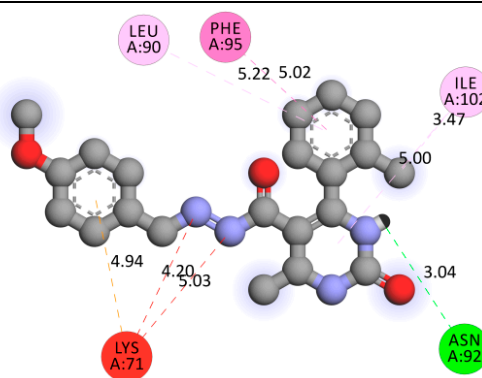
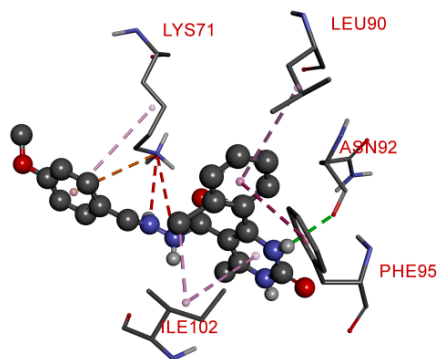
3D Docking Pose	2D Docking Pose
Compound 1a	
	
Compound 1c	
	
Compound 1d	
	
Compound 2a	



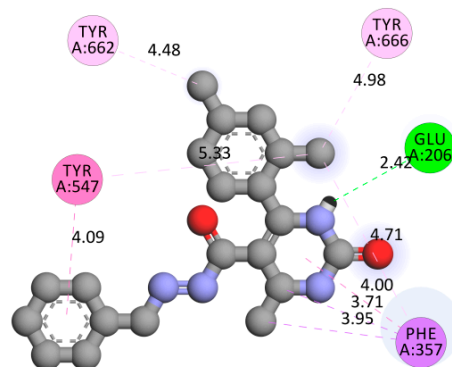
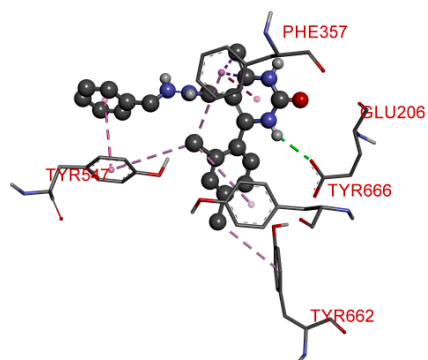
Compound 2c



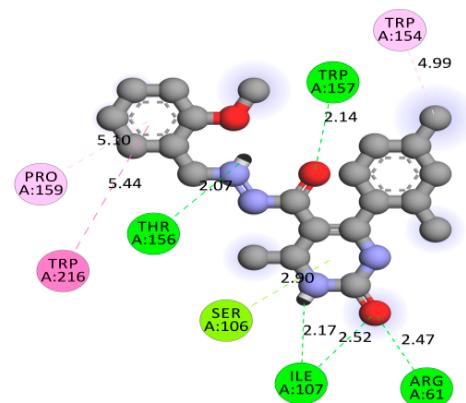
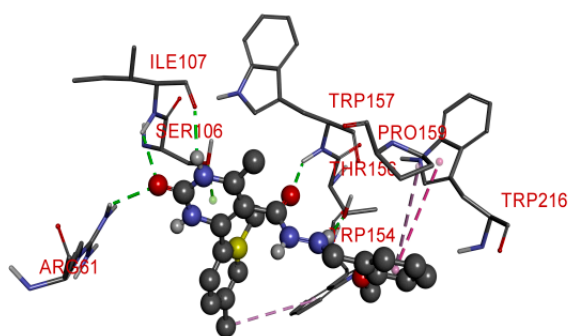
Compound 2d



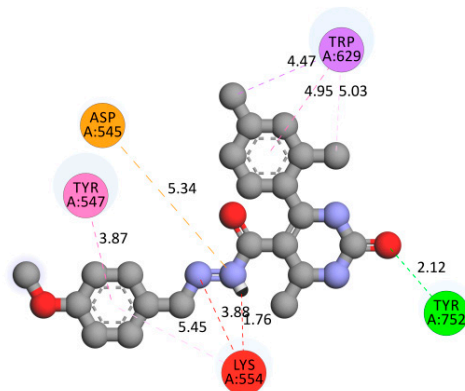
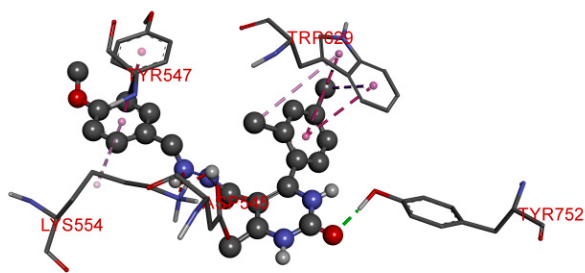
Compound 3a



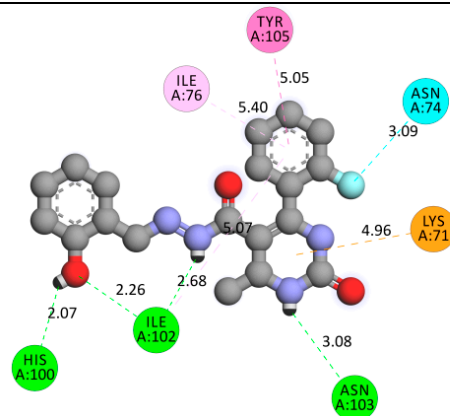
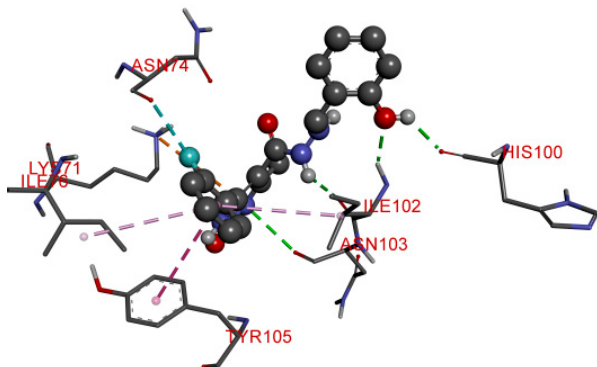
Compound 3c



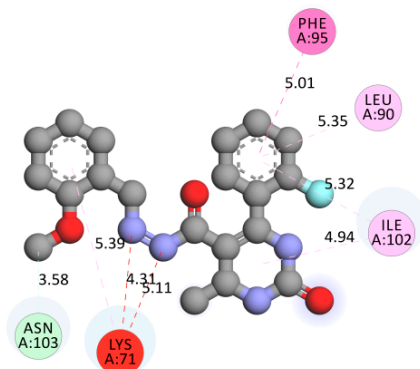
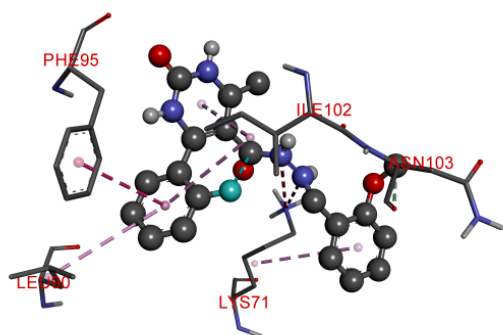
Compound 3d



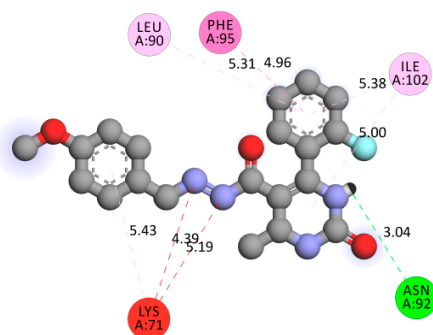
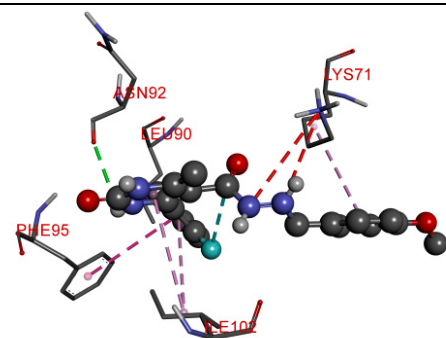
Compound 4b



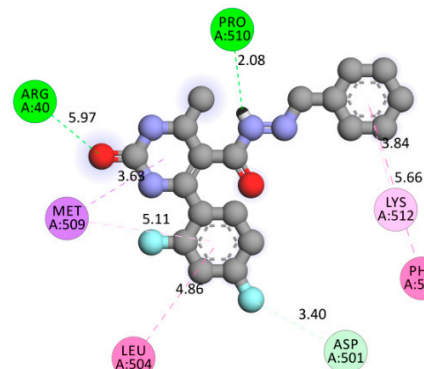
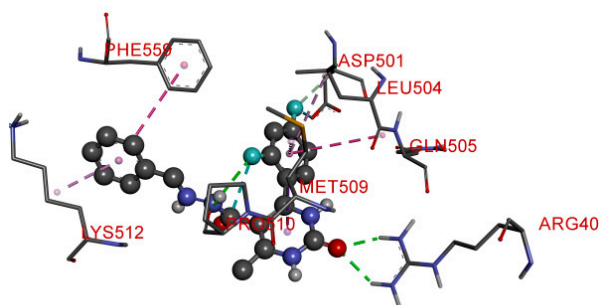
Compound 4c



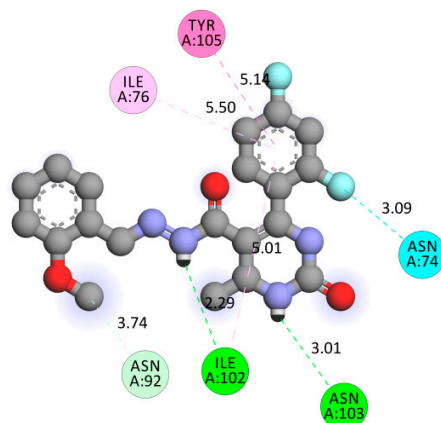
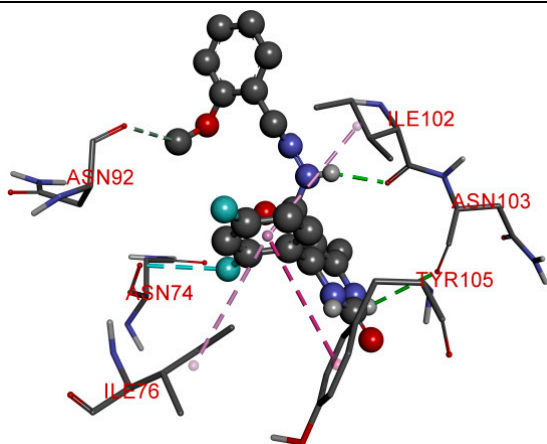
Compound 4d



Compound 5a



Compound 5c





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Compound **5d**

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