

- PDPI., 2018. Pedoman Diagnosis & Penatalaksanaan di Indonesia. Jakarta : Balai Penerbit PDPI.
- Sardjoko., 1993. Rancangan Obat, UGM Press, Yogyakarta
- Siswandono.,2015. *Kimia Medisinal*. Surabaya: Universitas Airlangga.
- Siswandono, Soekardjo, B. (1995). Kimia Medisinal. Surabaya: Airlangga University Press.
- WHO., 2018. *Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2018*.

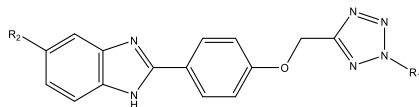
Lampiran 1 Validasi Leave One Out (LOO)

Kode senyawa	log IC ₅₀	konstan	Koef	LogP	Koef	EGibbs	koef	Balaban Index	koef	CAA
9a	1,727	19,859	1,103	4,807	36,951	0,322	0,000002	1193665	-0,014	659,190
9e	-0,076	18,283	1,108	5,726	34,413	0,320	0,000002	2155075	0,013	719,086
9f	0,976	19,185	1,134	4,942	37,122	0,348	0,000002	1414040	-0,001	689,111
10b	0,923	18,990	1,306	5,985	43,435	0,405	0,000002	2145850	0,008	750,974
10d	-1,097	18,659	1,123	6,888	37,581	0,397	0,000002	2145850	-0,014	791,240
10e	1,933	13,802	0,976	6,742	31,922	0,413	0,000002	3203068	0,028	796,440
11c	-1,222	18,365	1,100	5,205	36,477	0,355	0,000002	1633275	0,004	733,077
11e	-0,229	19,133	1,208	5,502	38,791	0,365	0,000002	2461800	0,002	757,571
12c	0,901	17,489	1,302	5,475	37,227	0,289	0,000002	875819	0,026	639,646
13c	0,464	18,381	0,853	6,477	41,370	0,248	0,000002	848881	0,009	642,203
19a	1,433	18,227	1,139	4,366	36,551	0,301	0,000002	664215	0,008	613,419
19b	0,587	22,945	0,946	3,603	36,372	0,254	0,000002	471206	-0,026	576,425
20a	1,523	20,595	1,109	4,792	34,520	0,352	0,000002	997556	-0,010	673,118

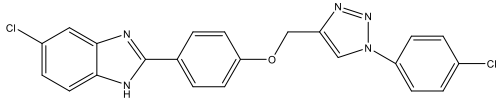
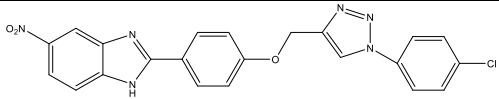
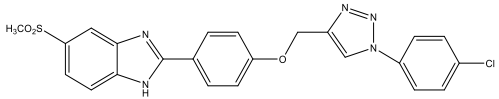
Lanjutan.....

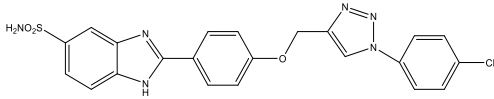
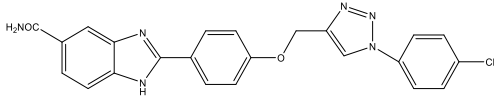
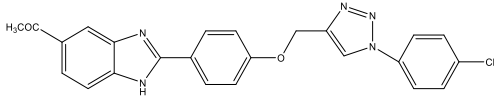
koef	CSEV	$\bar{Y}$	$y-\bar{y}$	$(y-\bar{y})^2$	$\sum(y-y')^2$	y rata	(y-y rata)	$(y-y \text{ rata})^2$	$\sum(y-y \text{ rata})^2$	q^2
-0,108	270,916	1,213	0,514	0,264	5,746	0,603	1,123	1,262	12,291	0,533
-0,164	301,164	0,318	-0,394	0,155		0,603	-0,679	0,461		
-0,139	285,501	0,871	0,105	0,011		0,603	0,373	0,139		
-0,170	315,831	1,908	-0,985	0,970		0,603	0,320	0,102		
-0,103	338,727	-0,605	-0,492	0,242		0,603	-1,700	2,890		
-0,176	339,972	0,927	1,006	1,013		0,603	1,330	1,770		
-0,145	307,537	-1,095	-0,127	0,016		0,603	-1,825	3,330		
-0,148	320,201	-0,511	0,282	0,079		0,603	-0,832	0,692		
-0,199	262,417	1,605	-0,704	0,495		0,603	0,298	0,089		
-0,158	267,532	-0,688	1,152	1,327		0,603	-0,139	0,019		
-0,155	252,940	1,327	0,106	0,011		0,603	0,830	0,689		
-0,088	234,549	1,369	-0,782	0,612		0,603	-0,016	0,000		
-0,118	277,786	0,782	0,741	0,550		0,603	0,920	0,847		

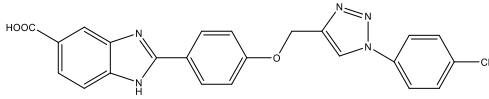
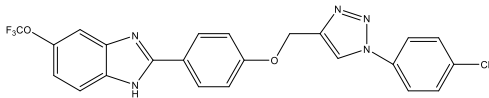
Lampiran 2 Struktur Desain Senyawa Baru dan Data Nilai Aktivitas



No	Senyawa	Struktur	IC ₅₀
1	B1 5-bromo-2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-1 <i>H</i> -benzo[<i>d</i>]imidazole		0,07
2	B2 2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-5-(trifluoromethyl)-1 <i>H</i> -benzo[<i>d</i>]imidazole		0,5

3	B3 5-chloro-2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-1 <i>H</i> -benzo[<i>d</i>]imidazole		0,3
4	B4 2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-5-nitro-1 <i>H</i> -benzo[<i>d</i>]imidazole		0,001
5	B5 2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-5-(methylsulfonyl)-1 <i>H</i> -benzo[<i>d</i>]imidazole		0,009

6	B6 2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-1 <i>H</i> -benzo[<i>d</i>]imidazole-5-sulfonamide		0,009
7	B7 2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-1 <i>H</i> -benzo[<i>d</i>]imidazole-5-carboxamide		0,02
8	B8 1-(2-(4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-5-yl)ethan-1-one		0,2

9	B9		0,09
10	B10		0,2

Lampiran 3 Nilai RMSD hasil *re-docking*

Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	76	-9.11	0.00	1.70	RANKING
1	2	56	-9.02	0.18	1.72	RANKING
1	3	41	-8.94	1.64	1.25	RANKING
1	4	62	-8.92	1.68	1.25	RANKING
1	5	68	-8.88	1.62	1.18	RANKING
1	6	78	-8.88	1.69	1.11	RANKING
1	7	91	-8.81	1.69	0.89	RANKING
1	8	47	-8.77	1.95	1.55	RANKING
1	9	44	-8.74	1.85	1.26	RANKING
1	10	51	-8.73	1.86	1.27	RANKING
1	11	92	-8.72	1.76	0.93	RANKING
1	12	16	-8.70	1.78	0.87	RANKING
1	13	82	-8.68	1.97	1.18	RANKING
1	14	93	-8.67	1.90	1.14	RANKING
1	15	31	-8.66	1.91	1.23	RANKING
1	16	72	-8.65	1.75	1.22	RANKING
1	17	69	-8.65	1.99	1.50	RANKING
1	18	48	-8.64	1.73	1.09	RANKING
1	19	67	-8.63	1.97	1.14	RANKING
1	20	80	-8.63	1.98	1.35	RANKING
1	21	12	-8.62	1.98	1.41	RANKING
1	22	96	-8.61	1.99	1.66	RANKING
1	23	34	-8.60	2.00	1.46	RANKING
1	24	74	-8.58	1.87	1.18	RANKING
1	25	33	-8.56	0.80	1.70	RANKING
1	26	97	-8.54	1.98	1.27	RANKING
1	27	70	-8.52	1.91	0.98	RANKING
1	28	23	-8.48	1.82	1.33	RANKING
1	29	7	-8.32	1.76	1.18	RANKING
1	30	24	-8.24	1.25	2.12	RANKING
1	31	32	-8.23	1.22	2.08	RANKING
1	32	29	-8.04	1.96	2.01	RANKING

Lampiran 4 Interaksi asam amino ligan alami sebelum dan sesudah
re-docking

Ligan Alami	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
5UG9- 8AM9001 (Struktur Kristal)	Hidrogen	Donor :	Akseptor :	
		A:MET793:O	A:8AM9001:N14	3,0
		A:8AM9001:N18	A:MET793:O	3,0
	Hidrofobik π Sigma	A:LEU844:CD1	A:8AM9001	3,6
	Hidrofobik alkil	A:ALA743	A:8AM9001:C16	4,0
		A:8AM9001:C17	A:CYS775	3,7
		A:8AM9001:C17	A:MET790	3,9
		A:8AM9001:C17	A:LEU844	5,2
		A:8AM9001:C16	A:VAL726	4,2
		A:8AM9001:C16	A:MET790	4,3
	Hidrofobik π - alkil	A:8AM9001	A:LEU718	5,0
		A:8AM9001	A:VAL726	4,6
		A:8AM9001	A:ALA743	5,1
		A:8AM9001	A:LEU844	4,6
		A:8AM9001	A:VAL726	5,3
		A:8AM9001	A:ALA743	3,7
	Carbon Hidrogen	A:8AM9001:C13	A:GLN791:O	3,2
	Halogen	A:GLY719:C	A:8AM9001:F27	3,1
Ligan Alami	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)

5UG9-8AM9001 (Hasil <i>Re-docking</i>)	Hidrogen	Donor : A:MET793:F A:CYS797:N	Akseptor : A:8AM9001:N14 A:8AM9001:F27	3,0 3,2
	Hidrofobik π Sigma	A:LEU844:CD1 A:LEU844:CD1	A:8AM9001 A:8AM9001	3,8 3,6
	Hidrofobik alkil	A:ALA743 A:8AM9001:C17 A:8AM9001:C17 A:8AM9001:C17 A:8AM9001:C16 A:8AM9001:C16 A:8AM9001:C16	A:8AM9001:C16 A:CYS775 A:MET790 A:LEU844 A:VAL726 A:LYS745 A:MET790	4,4 3,7 4,0 5,0 4,1 4,5 4,5
	Hidrofobik π -alkil	A:8AM9001 A:8AM9001 A:8AM9001 A:8AM9001 A:8AM9001 A:8AM9001	A:LEU718 A:VAL726 A:ALA743 A:VAL726 A:ALA743 A:MET793	5,0 5,0 5,1 5,3 3,6 5,2
	Carbon Hidrogen	A:8AM9001:C13	A:8AM9001:O	3,1

Lampiran 5 Interaksi asam amino dengan senyawa uji

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
1	Hidrogen	Donor : Br:H	Akseptor : A:CYS797:O	2,7
	Electrostatic	A:GLU804:O	Br	4,3
	Hidrofobik π	A:VAL726:C	Br	3,9
	Sigma	A:GLY796:C	Br	3,3
	Hidrofobik	Br:Cl	A:CYS775	3,5
	alkil	Br:Cl	A:MET790	3,4
	Hidrofobik π - alkil	A:HIS805	Br:Br	5,0
		Br	A:CYS797	4,4
		Br	A:LEU718	5,2
		Br	A:VAL726	4,7
		Br	A:ALA743	4,4
		Br	A:LEU844	4,6
	Carbon Hidrogen	A:GLY719:C	Br:Cl	3,3
	Pi-Lone Pair	A:PHE795:O	Br	2,6
	Pi-Sulfur	A:PHE797:SG	Br	4,6

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
2	Hidrogen	Donor :	Akseptor :	
		A:CYS797:N	CF3:O	2,9
		A:THR854:O	CF3:F	2,9
	Electrostatic	A:ASP800:O	CF3	3,3
		A:GLU804:O	CF3	3,7
		A:GLU804:O	CF3	4,0
	Hidrofobik π	A:LEU844:C	CF3	3,6
	Sigma	A:LEU844:C	CF3	3,2
		A:LEU844:C	CF3	3,9
	Hidrofobik alkil	A:ALA743	CF3:C	4,2
		CF3:C	A:MET790	3,6
	Hidrofobik π -alkil	A:PHE795	CF3:Cl	5,0
		A:TYR801	CF3:Cl	5,0
		A:HIS805	CF3:Cl	4,3
		CF3	A:CYS797	4,4
		CF3	A:VAL726	5,0
		CF3	A:VAL726	5,0
		CF3	A:ALA743	4,0
		CF3	A:CYS797	4,5
	Carbon	A:HIS805:CE1	CF3:Cl	3,2
	Hidrogen			
	Halogen	A:GLN791:O	CF3:F	2,8
	Pi-Lone Pair	A:PHE795:O	CF3	2,9

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
3	Hidrogen	Donor : Cl:H	Akseptor : A:ASP800:O	2,0
	Electrostatic	A:GLU804:OE1:B	Cl	4,2
	Hidrofobik π	A:LEU718:CD1	Cl	3,8
	Sigma	A:LEU844:CD1	Cl	3,4
	Hidrofobik	Cl:Cl	A:CYS775	3,2
	alkil	Cl:Cl	A:MET790	3,4
	Hidrofobik π -alkil	A:PHE795	Cl:Cl	4,8
		A:TYR801	Cl:Cl	4,7
		A:HIS805	Cl:Cl	4,3
		Cl	A:VAL726	5,5
		Cl	A:CYS797	4,9
		Cl	A:VAL726	4,6
		Cl	A:ALA743	4,4
		Cl	A:VAL726	5,4
		Cl	A:ALA743	4,3
		Cl	A:CYS775	4,8
		Cl	A:MET790	5,0
		Cl	A:LEU844	4,7
	Carbon	A:HIS805:C	Cl:Cl	3,2
	Hidogen			
	Pi:Donor	A:CYS797:N	Cl	4,2
	Hidrogen			
	Pi-Lone Pair	A:PHE795:O	Cl	2,7

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
4	Hidrogen	Donor :	Akseptor :	
		A:MET793:N	NO2:H	3,0
		NO2:H	A:LEU718:O	2,1
		NO2:H	A:GLN791:O	1,8
		NO2:H	A:THR854:O	2,0
	Pi-Sulfur	A:CYS775:SG	NO2	5,3
		A:MET790:SD	NO2	5,4
	Hidrofobik π Sigma	A:LEU718:C	Cl	3,5
	Hidrofobik alkil	NO2:Cl	A:VAL717	4,7
	Hidrofobik π - alkil	NO2	A:LEU718	5,3
		NO2	A:VAL726	5,2
		NO2	A:ALA743	3,7
		NO2	A:LEU792	5,4
		NO2	A:LEU844	5,0
		NO2	A:VAL726	5,0
		NO2	A:ALA743	3,4
		NO2	A:LEU844	5,1
		NO2	A:LEU792	5,4
		NO2	A:LEU718	4,6
	Pi-Lone Pair	A:VAL717:O	NO2	2,8

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
5	Hidrogen	Donor :	Akseptor :	
		A:CYS797:N	SO2CH3:H	2,9
		A:CYS797:H	SO2CH3:N	3,3
	Electrostatic	A:ASP800:O	SO2CH3	3,3
		A:GLU804:O	SO2CH3	3,7
		A:GLU804:O	SO2CH3	4,0
	Hidrofobik π	A:LEU844:C	SO2CH3	4,0
	Sigma	A:LEU844:C	SO2CH3	3,4
	Hidrofobik π -alkil	A:PHE795	SO2CH3	4,8
		A:TYR801	SO2CH3	4,7
		A:HIS805	SO2CH3	4,3
		SO2CH3	A:VAL726	5,1
		SO2CH3	A:CYS797	4,7
		SO2CH3	A:VAL726	4,9
		SO2CH3	A:ALA743	4,0
		SO2CH3	A:VAL726	4,6
		SO2CH3	A:ALA743	4,5
	Carbon	A:HIS805:CE1	SO2CH3:Cl	3,2
	Hidogen			
	Pi-Lone Pair	A:PHE795:O	SO2CH3	2,8

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
6	Hidrogen	Donor :	Akseptor :	
		A:CYS797:N	SO2NH2:H	2,9
		A:CYS797:H	SO2NH2:N	3,2
		SO2NH2:H	A:THR854:O	2,1
	Electrostatic	A:ASP800:O	SO2NH2	3,3
		A:GLU804:O	SO2NH2	3,7
		A:GLU804:O	SO2NH2	4,0
	Hidrofobik π	A:LEU844:C	SO2NH2	3,6
	Sigma	A:LEU844:C	SO2NH2	3,1
		A:LEU844:C	SO2NH2	3,9
	Hidrofobik π -alkil	A:PHE795	CF3:Cl	4,8
		A:TYR801	CF3:Cl	4,9
		A:HIS805	CF3:Cl	4,3
		SO2NH2	A:CYS797	4,9
		SO2NH2	A:VAL726	5,0
		SO2NH2	A:VAL726	4,2
		SO2NH2	A:ALA743	4,3
		SO2NH2	A:CYS797	4,5
	Pi-Lone Pair	A:PHE795:O	SO2NH2	2,9

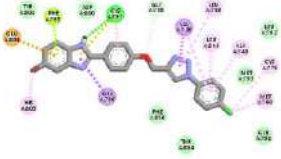
No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
7	Hidrogen	Donor :	Akseptor :	
		CONH2:H	A:CYS797:O	2,7
		CONH2:H	A:ASP800:O	2,1
		CONH2:H	A:GLU804:O	1,9
	Hidrofobik π	A:VAL726:C	CONH2	3,4
	Sigma	A:VAL726:C	CONH2	3,7
		A:GLY796:C	CONH2	3,4
	Hidrofobik alkil	CONH2:Cl	A:CYS775	3,5
		CONH2:Cl	A:MET790	3,5
	Hidrofobik π -alkil	CONH2	A:LEU718	5,0
		CONH2	A:VAL726	4,5
		CONH2	A:ALA743	4,3
		CONH2	A:LEU844	4,7
		CONH2	A:CYS797	4,6
	Pi-Lone Pair	A:CYS797:SG	CONH2	5,9

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
8	Hidrogen	Donor :	Akseptor :	
		COCH3:H	A:MET793:O	2,8
		COCH3:H	A:GLU804:O	2,0
		COCH3:H	A:ASP800:O	2,2
	Electrostatic	A:GLU804:O	COCH3	3,4
		A:GLU804:O	COCH3	3,7
	Hidrofobik π Sigma	A:LEU718:C	COCH3	3,6
		A:LEU844:C	COCH3	3,9
		A:LEU844:C	COCH3	3,1
	Hidrofobik π - alkil	A:PHE795	COCH3:Cl	4,5
		A:TYR801	COCH3:Cl	4,4
		A:HIS805	COCH3:Cl	4,3
		COCH3	A:LEU718	5,1
		COCH3	A:VAL726	4,8
		COCH3	A:ALA743	5,0
		COCH3	A:VAL726	5,2
		COCH3	A:ALA743	4,0
		COCH3	A:MET793	5,4
	Carbon	A:HIS805:C	COCH3:Cl	3,2
	Hidrogen			

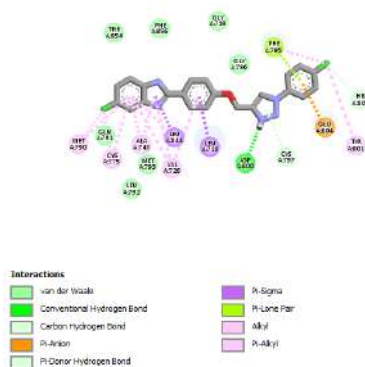
No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
9	Hidrogen	Donor :	Akseptor :	
		A:LYS716:N	COOH:O	2,7
		A:LYS728:N	COOH:O	2,7
		COOH:H	A:MET793:O	2,6
	Hidrofobik π	A:LEU718:C	COOH	3,7
	Sigma	A:LEU718:C	COOH	3,5
		A:LEU718:C	COOH	3,8
	Hidrofobik alkil	COOH:Cl	A:CYS775	3,4
		COOH:Cl	A:MET790	3,5
	Hidrofobik π - alkil	COOH	A:LYS728	5,0
		COOH	A:LEU792	5,0
		COOH	A:LEU718	5,1
		COOH	A:CYS797	5,0
		COOH	A:VAL726	4,2
		COOH	A:LEU844	5,2
		COOH	A:VAL726	5,1
		COOH	A:ALA743	4,7
		COOH	A:CYS775	5,3
		COOH	A:LEU844	4,3

No Senyawa	Jenis ikatan	Interaksi	Interaksi	Jarak (Å)
10	Hidrogen	Donor :	Akseptor :	
		A:GLN791:N	OCF3:F	3,1
		A:CYS797:H	OCF3:O	3,6
		A:THR854:O	OCF3:F	2,9
		OCF3:H	A:LEU718:O	2,7
		OCF3:H	A:LEU718:O	2,0
	Hidrofobik π Sigma	A:LEU718:C	OCF3	3,4
		A:VAL726:C	OCF3	3,8
		A:VAL726:C	OCF3	3,9
		A:LEU844:C	OCF3	3,8
		A:LEU844:C	OCF3	3,9
	Hidrofobik alkil	OCF3:Cl	A:LYS728	4,3
		OCF3:Cl	A:LEU792	3,9
		OCF3:Cl	A:PRO794	4,6
	Hidrofobik π -alkil	OCF3	A:ALA743	4,3
		OCF3	A:LEU718	4,9
	Carbon Hidrogen	OCF3:C	A:ASP800:O	3,2
	Halogen	A:ARG776:O	OCF3:F	3,6
		A:MET790:C:B	OCF3:F	3,7
		A:GLN791:O	OCF3:F	2,8
		A:GLN791:O	OCF3:F	2,7
	Pi-Sulfur	A:MET790:SD	OCF3	5,2
		A:CYS797:SG	OCF3	4,9

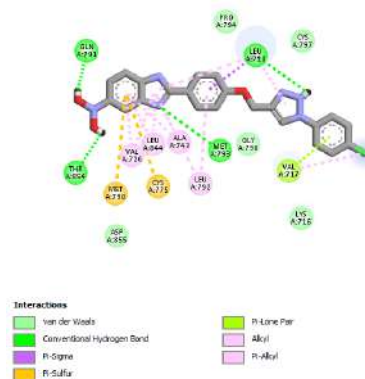
Lampiran 6 Visualisasi Senyawa Uji

No	Visualisasi
1	 Interactions - van der Waals - Conventional Hydrogen Bond - Carbon Hydrogen Bond - Pi-Alkyl - Pi-Sigma - Pi-Sulfur - Pi-Lone Pair - Alkyl - Pi-Alkyl
2	 Interactions - van der Waals - Conventional Hydrogen Bond - Carbon Hydrogen Bond - Hydrogen - Pi-Alkyl - Pi-Sigma - Pi-Lone Pair - Alkyl - Pi-Alkyl

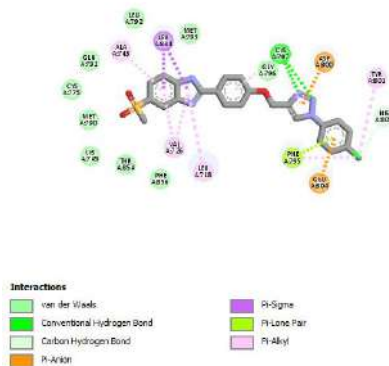
3



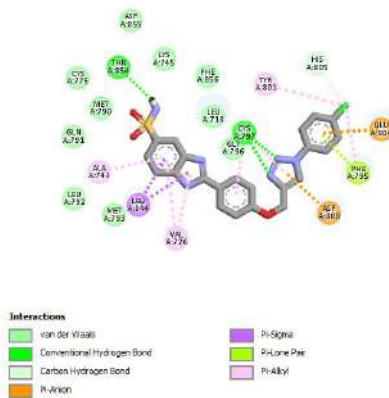
4



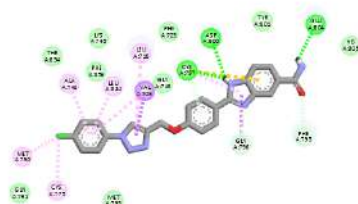
5



6



7

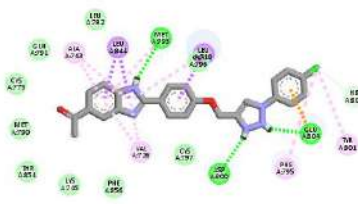


Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon-Hydrogen Bond
- Pi-Dimer Hydrogen Bond

- Pi-Sigma
- Pi-Sulfur
- Alkyl
- Pi-Alkyl

8

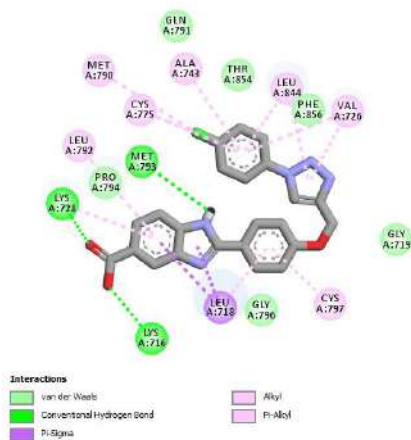


Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon-Hydrogen Bond

- Pi-Arene
- Pi-Sigma
- Pi-Alkyl

9



10

