Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supplementary material

Quantitative Structural Assessments of Potential Meprin β Inhibitors by Non-linear QSAR Approaches and Validation by Binding Mode of Interaction Analysis

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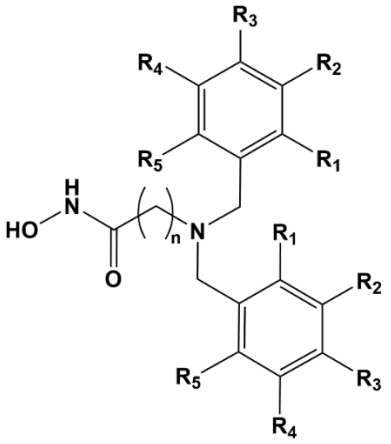
Supplementary Table S1. The structure and substitutions of the 107 dataset meprin β inhibitors with their inhibitory IC_{50} (in nM)



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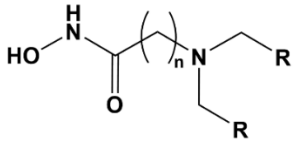

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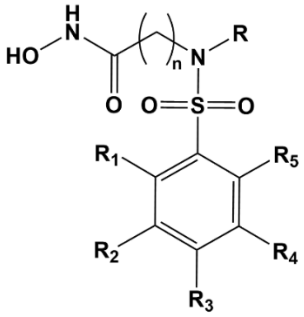
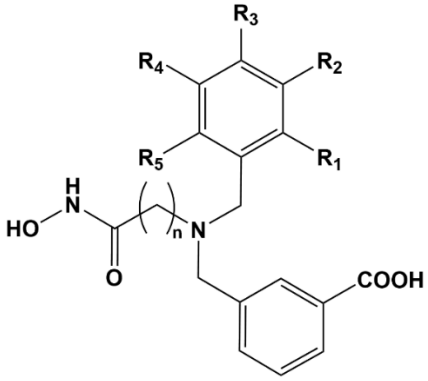


(05-06, 11-12, 15-16, 18, 23-25, 30, 32, 35-36, 38, 43, 45, 49, 52, 54, 56-58, 60-61, 63-64, 72-73, 77-78, 81-82, 87-88, 90-91, 94-99)



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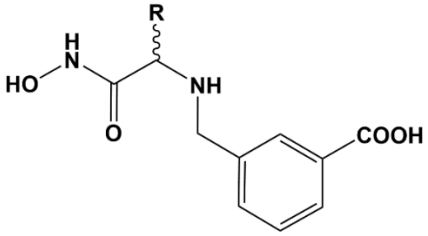
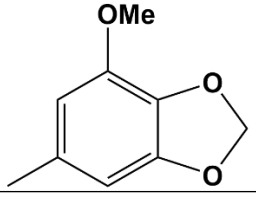
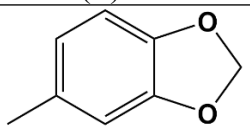
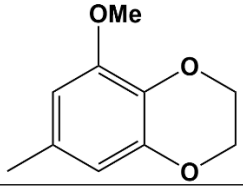
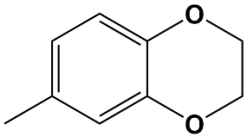
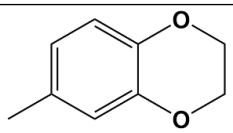


(21, 27, 31, 34, 41, 47, 50-51, 65-66, 68, 74-75)

Cpd No	*n*	*R*	R_1	R_2	R_3	R_4	R_5	IC_{50} *(nM)*
01	1	-	F	OH	F	H	H	23
02	1	-	F	OH	Cl	H	H	24
03	2	-2-F, 3-OH, 4-Cl-Ph	-	-	-	-	-	30
04*	1	-	H	COOH	H	H	H	49

05	1	-CH_2Ph(*m*-COOH)	H	H	-OCH_3	H	H	60
06	1	-CH_2Ph(*m*-COOH)	H	COOH	H	H	H	60
07	1	-	H	H	Cl	H	H	76
08*	1	-	H	H	-OCH_3	H	H	77
09	1	-	H	H	F	H	H	177
10	1	-	H	H	COOH	H	H	207
11	2	H	H	COOH	H	H	H	220
12	1	-CH_2Ph(*m*-COOH)	H	-OCH_2O-		H	H	270
13*	1	-	H	F	OH	F	H	272
14	1	-	H	-OCH_2O-		H	H	
15	1	H	H	COOH	H	H	H	310
16	1	-CH_2Ph(*m*-COOH)	H	H	COOH	H	H	320
17*	1	-	H	H	CN	H	H	320
18	2	H	H	H	COOH	H	H	340
19	1	-	F	H	-OCH_3	H	F	347
20*	1	-	H	F	-OCH_3	H	H	375
21	-	H	-	-	-	-	-	377
22*	1	-	H	H	CH_3	H	H	386
23	2	H	H	Cl	OH	Cl	H	400
24*	1	H	H	H	COOH	H	H	410
25	1	H	H	Cl	OH	Cl	H	430
26	1	-	H	H	COOH	H	H	524
27	-	(*R*)-CH_2COOH	-	-	-	-	-	548
28	1	-	H	-OCH_3	H	H	H	559
29	2	-	H	H	-OCH_3	H	H	643
30	1	-CH_2Ph(*m*-COOH)	H	F	-OCH_3	H	H	650
31	-	(*S*)-CH_2CH_2COOH	-	-	-	-	-	654
32	1	-CH_2Ph(*m*-COOH)	H	H	-OCF_3	H	H	700
33	3	-	H	H	-OCH_3	H	H	742
34	-	(*R*)-CH_2CH_2COOH	-	-	-	-	-	768
35	1	-CH_2Ph(*p*-COOH)	H	H	-OCH_3	H	H	980
36	1	-CH_2Ph(*m*-COOH)	H	H	F	H	H	1060
37	1	-	H	OH	F	H	H	1060
38	1	-CH_2Ph(*m*-COOH)	H	H	Ph	H	H	1080
39	1	-	H	H	Ph	H	H	1280
40*	1	-	H	H	H	H	H	1285
41	-	(*S*)-CH_2COOH	-	-	-	-	-	1325
42	2		-	-	-	-	-	1890
43*	1	-CH_2Ph(3,4OCH_2O)	H	H	-OCH_3	H	H	1930
44	1	-	H	O-*n*-Pr	H	H	H	2250
45	1	-CH_2CH_2COOH	H	H	-OCH_3	H	H	2550

46*	1	-	F	OH	H	H	H	2905
47	-	(*R*)-Bn	-	-	-	-	-	2910
48	2		-	-	-	-	-	2950
49*	1	H	H	H	Ph	H	H	3850
50	-	(*S*)-CH_3	-	-	-	-	-	4200
51	-	(*R*)-CH_3	-	-	-	-	-	4255
52*	1	H	H	H	Ph(*p*-OCH_3)	H	H	4420
53	1		-	-	-	-	-	4580
54	1	H	H	H	CH_2COOH	H	H	5030
55	1	-	F	OH	H	H	F	5515
56*	1	H	H	H	Ph(*p*-Cl)	H	H	5650
57	1	-CH_2COOH	H	H	-OCH_3	H	H	5980
58	1	H	H	F	-OCH_3	H	H	6190
59	1	-	H	-OCH_2O-		H	H	
60	1	H	H	H	Ph(*p*-F)	H	H	7310
61	1	H	H	-OCH_2CH_2O-		H	H	
62	2		-	-	-	-	-	7590
63*	1	H	H	H	-OCH_3	H	H	9020
64*	1	H	H	CF_3	Cl	H	H	10260
65	-	(*R*)-Ph	-	-	-	-	-	11650
66*	-	(*R*)-*i*-Pr	-	-	-	-	-	11850
67	1	-	H	CN	H	H	H	12000
68	-	(*S*)-Ph	-	-	-	-	-	12150
69*	1	-	F	-OCH_3	Cl	H	H	12800
70	1	-	H	$CONH_2$	H	H	H	13100
71	1	-2F, 4Cl-Ph	-	-	-	-	-	13800
72*	1	H	H	H	F	H	H	14320
73*	1	H	-CH_3	H	CH_3	H	H	14770
74	-	(*S*)-Bn	-	-	-	-	-	15500
75	-	(*S*)-*i*-Pr	-	-	-	-	-	15800
76	1	-$CH_2CH(CH_3)_2$	H	H	-OCH_3	H	H	17100
77	1	H	H	H	Cl	H	H	17170
78	1	H	H	F	H	H	CH_3	17970
79	1	-	F	-OCH_3	F	H	H	18200
80	2	-2,4 diF, 3OMe-Ph	-	-	-	-	-	18700
81	1	H	H	H	OPh	H	H	18800

82*	1	H	H	$-OCH_3$	H	H	H	18850
83	2	-2F, 4Cl-Ph	-	-	-	-	-	19200
84	2	-2F, 3OMe, 4Cl-Ph	-	-	-	-	-	19550
85	1	-3,4,5 triOMePh	-	-	-	-	-	20150
86*	1	-3Pyridine	-	-	-	-	-	21000
87*	1	H	$-OCH_3$	H	CH_3	H	H	25700
88	1	H	H	$-OCH_3$	$-OCH_3$	H	H	26900
89	1		-	-	-	-	-	30600
90	1	$-CH_2CH_3$	H	H	$-OCH_3$	H	H	31200
91*	1	$-CH_3$	H	H	$-OCH_3$	H	H	32530
92	1	*p*-CNPh	-	-	-	-	-	33050
93	2	-3-CNPh	-	-	-	-	-	33050
94	1	$-CH_2Ph(p\text{-}OCH_3)$	H	H	$-OCH_3$	H	H	34950
95	1	$-(CH_2)_3CH_3$	H	H	$-OCH_3$	H	H	37500
96	1	$-CH_2CH_2CH(CH_3)_2$	H	H	$-OCH_3$	H	H	38800
97*	1	$-CH_2Ph$	H	H	$-OCH_3$	H	H	40470
98	1	$-CH_2CH_2Ph$	H	H	$-OCH_3$	H	H	42900
99	1	$-CH_2$-(2-Norbornyl)	H	H	$-OCH_3$	H	H	43870
100*	2	-3Pyridine	-	-	-	-	-	53900
101	1	-	H	$-OCHF_2$	H	H	H	65950
102	2	-4-CNPh	-	-	-	-	-	68250
103	2	Pyridine	-	-	-	-	-	72400
104	2	Ph	-	-	-	-	-	75000
105	2	-3,4,5 triOMePh	-	-	-	-	-	89950
106	1	-	H	COOEt	H	H	H	94850
107	1	Pyridine	-	-	-	-	-	132500
** marked compounds are considered as the test set*								

Supplementary Table S2. The SMILES notation and InChI of the 107 dataset meprin β inhibitors with their inhibitory IC_{50} (in nM)

Cpd No	SMILES	InChI	Meprin β IC_{50} (nM)
1	c1c(c(c(c(c1)F)O)F)CN(CC(=O)NO)Cc1ccc(c(c1F)O)F	InChI=1S/C16H14F4N2O4/c17-10-3-1-8(13(19)15(10)24)5-22(7-12(23)21-26)6-9-2-4-11(18)16(25)14(9)20/h1-4,24-26H,5-7H2,(H,21,23)	23
2	c1c(c(c(c(c1)Cl)O)F)CN(CC(=O)NO)Cc1ccc(c(c1F)O)Cl	InChI=1S/C16H14Cl2F2N2O4/c17-10-3-1-8(13(19)15(10)24)5-22(7-12(23)21-26)6-9-2-4-11(18)16(25)14(9)20/h1-4,24-26H,5-7H2,(H,21,23)	24
3	ONC(=O)CCN(Cc1c(c(c(cc1)Cl)O)F)Cc1c(c(c(cc1)Cl)O)F	InChI=1S/C17H16Cl2F2N2O4/c18-11-3-1-9(14(20)16(11)25)7-23(6-5-13(24)22-27)8-10-2-4-12(19)17(26)15(10)21/h1-4,25-27H,5-8H2,(H,22,24)	30
4	c1c(cc(cc1)C(=O)O)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H18N2O6/c21-16(19-26)11-20(9-12-3-1-5-14(7-12)17(22)23)10-13-4-2-6-15(8-13)18(24)25/h1-8,26H,9-11H2,(H,19,21)(H,22,23)(H,24,25)	49
5	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C17H18N2O7S/c1-26-14-5-7-15(8-6-14)27(24,25)19(11-16(20)18-23)10-12-3-2-4-13(9-12)17(21)22/h2-9,23H,10-11H2,1H3,(H,18,20)(H,21,22)	60
6	O=S(=O)(c1cc(ccc1)C(=O)O)N(CC(=O)NO)Cc1cc(ccc1)C(=O)O	InChI=1S/C17H16N2O8S/c20-15(18-25)10-19(9-11-3-1-4-12(7-11)16(21)22)28(26,27)14-6-2-5-13(8-14)17(23)24/h1-8,25H,9-10H2,(H,18,20)(H,21,22)(H,23,24)	60
7	c1c(ccc(c1)Cl)CN(CC(=O)NO)Cc1ccc(c1)C(=O)O	InChI=1S/C17H17ClN2O4/c18-15-6-4-12(5-7-15)9-20(11-16(21)19-24)10-13-2-1-3-14(8-13)17(22)23/h1-8,24H,9-11H2,(H,19,21)(H,22,23)	76
8	c1c(ccc(c1)OC)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H20N2O5/c1-25-16-7-5-13(6-8-16)10-20(12-17(21)19-24)11-14-3-2-4-15(9-14)18(22)23/h2-9,24H,10-12H2,1H3,(H,19,21)(H,22,23)	77
9	c1c(ccc(c1)F)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C17H17FN2O4/c18-15-6-4-12(5-7-15)9-20(11-16(21)19-24)10-13-2-1-3-14(8-13)17(22)23/h1-8,24H,9-11H2,(H,19,21)(H,22,23)	177
10	c1c(ccc(c1)C(=O)O)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H18N2O6/c21-16(19-26)11-20(9-12-4-6-14(7-5-12)17(22)23)10-13-2-1-3-15(8-13)18(24)25/h1-8,26H,9-11H2,(H,19,21)(H,22,23)(H,24,25)	207
11	O=S(=O)(c1cc(ccc1)C(=O)O)NCCC(=O)NO	InChI=1S/C10H12N2O6S/c13-9(12-16)4-5-11-19(17,18)8-3-1-2-7(6-8)10(14)15/h1-3,6,11,16H,4-5H2,(H,12,13)(H,14,15)	220
12	O=S(=O)(c1cc2c(cc1)OCO2)N(CC(=O)NO)Cc1cc(ccc1)C(=O)O	InChI=1S/C17H16N2O8S/c20-16(18-23)9-19(8-11-2-1-3-12(6-11)17(21)22)28(24,25)13-4-5-14-15(7-13)27-10-26-14/h1-7,23H,8-10H2,(H,18,20)(H,21,22)	270
13	c1c(cc(c(c1F)O)F)CN(CC(=O)NO)Cc1cc(c(c(c1)F)O)F	InChI=1S/C16H14F4N2O4/c17-10-1-8(2-11(18)15(10)24)5-22(7-14(23)21-26)6-9-3-12(19)16(25)13(20)4-9/h1-4,24-26H,5-7H2,(H,21,23)	272
14	c1c(cc2c(c1)OCO2)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H18N2O6/c21-17(19-24)10-20(8-12-2-1-3-14(6-12)18(22)23)9-13-4-5-15-16(7-13)26-11-25-15/h1-7,24H,8-11H2,(H,19,21)(H,22,23)	285
15	O=S(=O)(c1cc(ccc1)C(=O)O)NCC(=O)NO	InChI=1S/C9H10N2O6S/c12-8(11-15)5-10-18(16,17)7-3-1-2-6(4-7)9(13)14/h1-4,10,15H,5H2,(H,11,12)(H,13,14)	310
16	O=S(=O)(c1ccc(cc1)C(=O)O)N(CC(=O)NO)Cc1cc(ccc1)C(=O)O	InChI=1S/C17H16N2O8S/c20-15(18-25)10-19(9-11-2-1-3-13(8-11)17(23)24)28(26,27)14-6-4-12(5-7-14)16(21)22/h1-8,25H,9-10H2,(H,18,20)(H,21,22)(H,23,24)	320
17	c1c(ccc(c1)C#N)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H17N3O4/c19-9-13-4-6-14(7-5-13)10-21(12-17(22)20-25)11-15-2-1-3-16(8-15)18(23)24/h1-8,25H,10-12H2,(H,20,22)(H,23,24)	320
18	O=S(=O)(c1ccc(cc1)C(=O)O)NCCC(=O)NO	InChI=1S/C10H12N2O6S/c13-9(12-16)5-6-11-19(17,18)8-3-1-7(2-4-8)10(14)15/h1-4,11,16H,5-6H2,(H,12,13)(H,14,15)	340
19	c1(c(c(cc(c1)OC)F)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O)F	InChI=1S/C18H18F2N2O5/c1-27-13-6-15(19)14(16(20)7-13)9-22(10-17(23)21-26)8-11-3-2-4-12(5-11)18(24)25/h2-7,26H,8-10H2,1H3,(H,21,23)(H,24,25)	347
20	c1c(cc(c(c1)OC)F)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H19FN2O5/c1-26-16-6-5-13(8-15(16)19)10-21(11-17(22)20-25)9-12-3-2-4-14(7-12)18(23)24/h2-8,25H,9-11H2,1H3,(H,20,22)(H,23,24)	375
21	c1ccc(cc1CNCC(=O)NO)C(=O)O	InChI=1S/C10H12N2O4/c13-9(12-16)6-11-5-7-2-1-3-8(4-7)10(14)15/h1-4,11,16H,5-6H2,(H,12,13)(H,14,15)	377
22	c1c(ccc(c1)C)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H20N2O4/c1-13-5-7-14(8-6-13)10-20(12-17(21)19-24)11-15-3-2-4-16(9-15)18(22)23/h2-9,24H,10-12H2,1H3,(H,19,21)(H,22,23)	386
23	O=S(=O)(c1cc(c(c(c1Cl)O)Cl)NCCC(=O)NO	InChI=1S/C9H10Cl2N2O5S/c10-6-3-5(4-7(11)9(6)15)19(17,18)12-2-1-8(14)13-16/h3-4,12,15-16H,1-2H2,(H,13,14)	400
24	O=S(=O)(c1ccc(cc1)C(=O)O)NCC(=O)NO	InChI=1S/C9H10N2O6S/c12-8(11-15)5-10-18(16,17)7-3-1-6(2-4-7)9(13)14/h1-4,10,15H,5H2,(H,11,12)(H,13,14)	410
25	O=S(=O)(c1cc(c(c(c1)Cl)O)Cl)NCC(=O)NO	InChI=1S/C8H8Cl2N2O5S/c9-5-1-4(2-6(10)8(5)14)18(16,17)11-3-7(13)12-15/h1-2,11,14-15H,3H2,(H,12,13)	430
26	c1c(ccc(c1)C(=O)O)CN(CC(=O)NO)Cc1ccc(cc1)C(=O)O	InChI=1S/C18H18N2O6/c21-16(19-26)11-20(9-12-1-5-14(6-2-12)17(22)23)10-13-3-7-15(8-4-13)18(24)25/h1-8,26H,9-11H2,(H,19,21)(H,22,23)(H,24,25)	524
27	c1ccc(cc1CN[C@@H](C(=O)NO)CC(=O)O)C(=O)O	InChI=1S/C12H14N2O6/c15-10(16)5-9(11(17)14-20)13-6-7-2-1-3-8(4-7)12(18)19/h1-4,9,13,20H,5-6H2,(H,14,17)(H,15,16)(H,18,19)/t9-/m1/s1	548
28	c1c(cc(cc1)OC)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C18H20N2O5/c1-25-16-7-3-5-14(9-16)11-20(12-17(21)19-24)10-13-4-2-6-15(8-13)18(22)23/h2-9,24H,10-12H2,1H3,(H,19,21)(H,22,23)	559
29	c1c(ccc(c1)OC)CN(CCC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C19H22N2O5/c1-26-17-7-5-14(6-8-17)12-21(10-9-18(22)20-25)13-15-3-2-4-16(11-15)19(23)24/h2-8,11,25H,9-10,12-13H2,1H3,(H,20,22)(H,23,24)	643
30	O=S(=O)(c1cc(c(cc1)OC)F)N(CC(=O	InChI=1S/C17H17FN2O7S/c1-27-15-6-5-13(8-14(15)18)28(25,26)20(10-	650

	)NO)Cc1cc(ccc1)C(=O)O	16(21)19-24)9-11-3-2-4-12(7-11)17(22)23/h2-8,24H,9-10H2,1H3,(H,19,21)(H,22,23)	
31	c1ccc(cc1CN[C@H](C(=O)NO)CCC(=O)O)C(=O)O	InChI=1S/C13H16N2O6/c16-11(17)5-4-10(12(18)15-21)14-7-8-2-1-3-9(6-8)13(19)20/h1-3,6,10,14,21H,4-5,7H2,(H,15,18)(H,16,17)(H,19,20)/t10-/m0/s1	654
32	O=S(=O)(c1ccc(cc1)OC(F)(F)F)N(CC(=O)NO)Cc1cc(ccc1)C(=O)O	InChI=1S/C17H15F3N2O7S/c18-17(19,20)29-13-4-6-14(7-5-13)30(27,28)22(10-15(23)21-26)9-11-2-1-3-12(8-11)16(24)25/h1-8,26H,9-10H2,(H,21,23)(H,24,25)	700
33	c1c(ccc(c1)OC)CN(CCCC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C20H24N2O5/c1-27-18-9-7-15(8-10-18)13-22(11-3-6-19(23)21-26)14-16-4-2-5-17(12-16)20(24)25/h2,4-5,7-10,12,26H,3,6,11,13-14H2,1H3,(H,21,23)(H,24,25)	742
34	c1ccc(cc1CN[C@@H](C(=O)NO)CCC(=O)O)C(=O)O	InChI=1S/C13H16N2O6/c16-11(17)5-4-10(12(18)15-21)14-7-8-2-1-3-9(6-8)13(19)20/h1-3,6,10,14,21H,4-5,7H2,(H,15,18)(H,16,17)(H,19,20)/t10-/m1/s1	768
35	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)Cc1ccc(cc1)C(=O)O	InChI=1S/C17H18N2O7S/c1-26-14-6-8-15(9-7-14)27(24,25)19(11-16(20)18-23)10-12-2-4-13(5-3-12)17(21)22/h2-9,23H,10-11H2,1H3,(H,18,20)(H,21,22)	980
36	O=S(=O)(c1ccc(cc1)F)N(CC(=O)NO)Cc1cc(ccc1)C(=O)O	InChI=1S/C16H15FN2O6S/c17-13-4-6-14(7-5-13)26(24,25)19(10-15(20)18-23)9-11-2-1-3-12(8-11)16(21)22/h1-8,23H,9-10H2,(H,18,20)(H,21,22)	1,060
37	c1c(cc(c(c1)F)O)CN(CC(=O)NO)Cc1ccc(c(c1)O)F	InChI=1S/C16H16F2N2O4/c17-12-3-1-10(5-14(12)21)7-20(9-16(23)19-24)8-11-2-4-13(18)15(22)6-11/h1-6,21-22,24H,7-9H2,(H,19,23)	1,060
38	O=S(=O)(c1ccc(cc1)c1ccccc1)N(CC(=O)NO)Cc1cc(ccc1)C(=O)O	InChI=1S/C22H20N2O6S/c25-21(23-28)15-24(14-16-5-4-8-19(13-16)22(26)27)31(29,30)20-11-9-18(10-12-20)17-6-2-1-3-7-17/h1-13,28H,14-15H2,(H,23,25)(H,26,27)	1,080
39	c1c(ccc(c1)c1ccccc1)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C23H22N2O4/c26-22(24-29)16-25(15-18-5-4-8-21(13-18)23(27)28)14-17-9-11-20(12-10-17)19-6-2-1-3-7-19/h1-13,29H,14-16H2,(H,24,26)(H,27,28)	1,280
40	c1c(cccc1)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C17H18N2O4/c20-16(18-23)12-19(10-13-5-2-1-3-6-13)11-14-7-4-8-15(9-14)17(21)22/h1-9,23H,10-12H2,(H,18,20)(H,21,22)	1,285
41	c1ccc(cc1CN[C@H](C(=O)NO)CC(=O)O)C(=O)O	InChI=1S/C12H14N2O6/c15-10(16)5-9(11(17)14-20)13-6-7-2-1-3-8(4-7)12(18)19/h1-4,9,13,20H,5-6H2,(H,14,17)(H,15,16)(H,18,19)/t9-/m0/s1	1,325
42	ONC(=O)CCN(Cc1cc(c2c(c1)OCO2)OC)Cc1cc2c(c(c1)OC)OCO2	InChI=1S/C21H24N2O8/c1-26-15-5-13(7-17-20(15)30-11-28-17)9-23(4-3-19(24)22-25)10-14-6-16(27-2)21-18(8-14)29-12-31-21/h5-8,25H,3-4,9-12H2,1-2H3,(H,22,24)	1,890
43	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)Cc1ccc2c(c1)OCO2	InChI=1S/C17H18N2O7S/c1-24-13-3-5-14(6-4-13)27(22,23)19(10-17(20)18-21)9-12-2-7-15-16(8-12)26-11-25-15/h2-8,21H,9-11H2,1H3,(H,18,20)	1,930
44	c1c(cc(cc1)OCCC)CN(CC(=O)NO)Cc1cccc(c1)C(=O)O	InChI=1S/C20H24N2O5/c1-2-9-27-18-8-4-6-16(11-18)13-22(14-19(23)21-26)12-15-5-3-7-17(10-15)20(24)25/h3-8,10-11,26H,2,9,12-14H2,1H3,(H,21,23)(H,24,25)	2,250
45	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)CCC(=O)O	InChI=1S/C12H16N2O7S/c1-21-9-2-4-10(5-3-9)22(19,20)14(7-6-12(16)17)8-11(15)13-18/h2-5,18H,6-8H2,1H3,(H,13,15)(H,16,17)	2,550
46	c1c(c(c(cc1)O)F)CN(CC(=O)NO)Cc1cccc(c1F)O	InChI=1S/C16H16F2N2O4/c17-15-10(3-1-5-12(15)21)7-20(9-14(23)19-24)8-11-4-2-6-13(22)16(11)18/h1-6,21-22,24H,7-9H2,(H,19,23)	2,905
47	C(N[C@@H](C(=O)NO)Cc1ccccc1)c1cc(ccc1)C(=O)O	InChI=1S/C17H18N2O4/c20-16(19-23)15(10-12-5-2-1-3-6-12)18-11-13-7-4-8-14(9-13)17(21)22/h1-9,15,18,23H,10-11H2,(H,19,20)(H,21,22)/t15-/m1/s1	2,910
48	ONC(=O)CCN(Cc1ccc2c(c1)OCO2)Cc1cc2c(cc1)OCO2	InChI=1S/C19H20N2O6/c22-19(20-23)5-6-21(9-13-1-3-15-17(7-13)26-11-24-15)10-14-2-4-16-18(8-14)27-12-25-16/h1-4,7-8,23H,5-6,9-12H2,(H,20,22)	2,950
49	c1cc(ccc1S(=O)(=O)NCC(=O)NO)c1ccccc1	InChI=1S/C14H14N2O4S/c17-14(16-18)10-15-21(19,20)13-8-6-12(7-9-13)11-4-2-1-3-5-11/h1-9,15,18H,10H2,(H,16,17)	3,850
50	c1ccc(cc1CN[C@H](C(=O)NO)C)C(=O)O	InChI=1S/C11H14N2O4/c1-7(10(14)13-17)12-6-8-3-2-4-9(5-8)11(15)16/h2-5,7,12,17H,6H2,1H3,(H,13,14)(H,15,16)/t7-/m0/s1	4,200
51	c1ccc(cc1CN[C@@H](C(=O)NO)C)C(=O)O	InChI=1S/C11H14N2O4/c1-7(10(14)13-17)12-6-8-3-2-4-9(5-8)11(15)16/h2-5,7,12,17H,6H2,1H3,(H,13,14)(H,15,16)/t7-/m1/s1	4,255
52	O=S(=O)(c1ccc(cc1)c1ccc(cc1)OC)NCC(=O)NO	InChI=1S/C15H16N2O5S/c1-22-13-6-2-11(3-7-13)12-4-8-14(9-5-12)23(20,21)16-10-15(18)17-19/h2-9,16,19H,10H2,1H3,(H,17,18)	4,420
53	ONC(=O)CN(Cc1cc(c2c(c1)OCO2)OC)Cc1cc2c(c(c1)OC)OCO2	InChI=1S/C20H22N2O8/c1-25-14-3-12(5-16-19(14)29-10-27-16)7-22(9-18(23)21-24)8-13-4-15(26-2)20-17(6-13)28-11-30-20/h3-6,24H,7-11H2,1-2H3,(H,21,23)	4,580
54	O=S(=O)(c1ccc(cc1)CC(=O)O)NCC(=O)NO	InChI=1S/C10H12N2O6S/c13-9(12-16)6-11-19(17,18)8-3-1-7(2-4-8)5-10(14)15/h1-4,11,16H,5-6H2,(H,12,13)(H,14,15)	5,030
55	c1(c(c(c(cc1)O)F)CN(CC(=O)NO)Cc1c(ccc(c1F)O)F)F	InChI=1S/C16H14F4N2O4/c17-10-1-3-12(23)15(19)8(10)5-22(7-14(25)21-26)6-9-11(18)2-4-13(24)16(9)20/h1-4,23-24,26H,5-7H2,(H,21,25)	5,515
56	O=S(=O)(c1ccc(cc1)c1ccc(cc1)Cl)NCC(=O)NO	InChI=1S/C14H13ClN2O4S/c15-12-5-1-10(2-6-12)11-3-7-13(8-4-11)22(20,21)16-9-14(18)17-19/h1-8,16,19H,9H2,(H,17,18)	5,650
57	N(C(=O)CN(CC(=O)O)S(=O)(=O)c1ccc(cc1)OC)O	InChI=1S/C11H14N2O7S/c1-20-8-2-4-9(5-3-8)21(18,19)13(7-11(15)16)6-10(14)12-17/h2-5,17H,6-7H2,1H3,(H,12,14)(H,15,16)	5,980
58	O=S(=O)(c1cc(c(cc1)OC)F)NCC(=O)NO	InChI=1S/C9H11FN2O5S/c1-17-8-3-2-6(4-7(8)10)18(15,16)11-5-9(13)12-14/h2-4,11,14H,5H2,1H3,(H,12,13)	6,190
59	c1c(cc2c(c1)OCO2)CN(CC(=O)NO)Cc1ccc2c(c1)OCO2	InChI=1S/C18H18N2O6/c21-18(19-22)9-20(7-12-1-3-14-16(5-12)25-10-23-14)8-13-2-4-15-17(6-13)26-11-24-15/h1-6,22H,7-11H2,(H,19,21)	6,539
60	O=S(=O)(c1ccc(cc1)c1ccc(cc1)F)NCC(=O)NO	InChI=1S/C14H13FN2O4S/c15-12-5-1-10(2-6-12)11-3-7-13(8-4-11)22(20,21)16-9-14(18)17-19/h1-8,16,19H,9H2,(H,17,18)	7,310
61	O=S(=O)(c1cc2c(cc1)OCCO2)NCC(=O)NO	InChI=1S/C10H12N2O6S/c13-10(12-14)6-11-19(15,16)7-1-2-8-9(5-7)18-4-3-17-8/h1-2,5,11,14H,3-4,6H2,(H,12,13)	7,420
62	ONC(=O)CCN(Cc1ccc2c(c1)OCCO2)Cc1cc2c(cc1)OCCO2	InChI=1S/C21H24N2O6/c24-21(22-25)5-6-23(13-15-1-3-17-19(11-15)28-9-7-26-17)14-16-2-4-18-20(12-16)29-10-8-27-18/h1-4,11-12,25H,5-10,13-	7,590

		14H2,(H,22,24)	
63	C(=O)(NO)CNS(=O)(=O)c1ccc(cc1)OC	InChI=1S/C9H12N2O5S/c1-16-7-2-4-8(5-3-7)17(14,15)10-6-9(12)11-13/h2-5,10,13H,6H2,1H3,(H,11,12)	9,020
64	O=S(=O)(c1cc(c(cc1)Cl)C(F)(F)F)NCC(=O)NO	InChI=1S/C9H8ClF3N2O4S/c10-7-2-1-5(3-6(7)9(11,12)13)20(18,19)14-4-8(16)15-17/h1-3,14,17H,4H2,(H,15,16)	10,260
65	C(N[C@@H](C(=O)NO)c1ccccc1)c1cc(ccc1)C(=O)O	InChI=1S/C16H16N2O4/c19-15(18-22)14(12-6-2-1-3-7-12)17-10-11-5-4-8-13(9-11)16(20)21/h1-9,14,17,22H,10H2,(H,18,19)(H,20,21)/t14-/m1/s1	11,650
66	C(N[C@@H](C(=O)NO)C(C)C)c1cc(ccc1)C(=O)O	InChI=1S/C13H18N2O4/c1-8(2)11(12(16)15-19)14-7-9-4-3-5-10(6-9)13(17)18/h3-6,8,11,14,19H,7H2,1-2H3,(H,15,16)(H,17,18)/t11-/m1/s1	11,850
67	c1c(cc(cc1)C#N)CN(CC(=O)NO)Cc1ccccc(c1)C#N	InChI=1S/C18H16N4O2/c19-9-14-3-1-5-16(7-14)11-22(13-18(23)21-24)12-17-6-2-4-15(8-17)10-20/h1-8,24H,11-13H2,(H,21,23)	12,000
68	C(N[C@H](C(=O)NO)c1ccccc1)c1cc(ccc1)C(=O)O	InChI=1S/C16H16N2O4/c19-15(18-22)14(12-6-2-1-3-7-12)17-10-11-5-4-8-13(9-11)16(20)21/h1-9,14,17,22H,10H2,(H,18,19)(H,20,21)/t14-/m0/s1	12,150
69	c1c(c(c(c(c1Cl)Cl)OC)F)CN(CC(=O)NO)Cc1ccc(c(c1F)OC)Cl	InChI=1S/C18H18Cl2F2N2O4/c1-27-17-12(19)5-3-10(15(17)21)7-24(9-14(25)23-26)8-11-4-6-13(20)18(28-2)16(11)22/h3-6,26H,7-9H2,1-2H3,(H,23,25)	12,800
70	c1c(cc(cc1)C(=O)N)CN(CC(=O)NO)Cc1cccc(c1)C(=O)N	InChI=1S/C18H20N4O4/c19-17(24)14-5-1-3-12(7-14)9-22(11-16(23)21-26)10-13-4-2-6-15(8-13)18(20)25/h1-8,26H,9-11H2,(H2,19,24)(H2,20,25)(H,21,23)	13,100
71	ONC(=O)CN(Cc1c(cc(cc1)Cl)F)Cc1c(cc(cc1)Cl)F	InChI=1S/C16H14Cl2F2N2O2/c17-12-3-1-10(14(19)5-12)7-22(9-16(23)21-24)8-11-2-4-13(18)6-15(11)20/h1-6,24H,7-9H2,(H,21,23)	13,800
72	O=S(=O)(c1ccc(cc1)F)NCC(=O)NO	InChI=1S/C8H9FN2O4S/c9-6-1-3-7(4-2-6)16(14,15)10-5-8(12)11-13/h1-4,10,13H,5H2,(H,11,12)	14,320
73	O=S(=O)(c1c(cc(cc1)C)C)NCC(=O)NO	InChI=1S/C10H14N2O4S/c1-7-3-4-9(8(2)5-7)17(15,16)11-6-10(13)12-14/h3-5,11,14H,6H2,1-2H3,(H,12,13)	14,770
74	C(N[C@H](C(=O)NO)Cc1ccccc1)c1cc(ccc1)C(=O)O	InChI=1S/C17H18N2O4/c20-16(19-23)15(10-12-5-2-1-3-6-12)18-11-13-7-4-8-14(9-13)17(21)22/h1-9,15,18,23H,10-11H2,(H,19,20)(H,21,22)/t15-/m0/s1	15,500
75	C(N[C@H](C(=O)NO)C(C)C)c1cc(ccc1)C(=O)O	InChI=1S/C13H18N2O4/c1-8(2)11(12(16)15-19)14-7-9-4-3-5-10(6-9)13(17)18/h3-6,8,11,14,19H,7H2,1-2H3,(H,15,16)(H,17,18)/t11-/m0/s1	15,800
76	C(=O)(NO)CN(CC(C)C)S(=O)(=O)c1ccc(cc1)OC	InChI=1S/C13H20N2O5S/c1-10(2)8-15(9-13(16)14-17)21(18,19)12-6-4-11(20-3)5-7-12/h4-7,10,17H,8-9H2,1-3H3,(H,14,16)	17,100
77	O=S(=O)(c1ccc(cc1)Cl)NCC(=O)NO	InChI=1S/C8H9ClN2O4S/c9-6-1-3-7(4-2-6)16(14,15)10-5-8(12)11-13/h1-4,10,13H,5H2,(H,11,12)	17,170
78	O=S(=O)(c1cc(ccc1C)F)NCC(=O)NO	InChI=1S/C9H11FN2O4S/c1-6-2-3-7(10)4-8(6)17(15,16)11-5-9(13)12-14/h2-4,11,14H,5H2,1H3,(H,12,13)	17,970
79	c1c(c(c(c(c1)F)OC)F)CN(CC(=O)NO)Cc1ccc(c(c1F)OC)F	InChI=1S/C18H18F4N2O4/c1-27-17-12(19)5-3-10(15(17)21)7-24(9-14(25)23-26)8-11-4-6-13(20)18(28-2)16(11)22/h3-6,26H,7-9H2,1-2H3,(H,23,25)	18,200
80	ONC(=O)CCN(Cc1c(c(c(cc1)F)OC)F)Cc1c(c(c(cc1)F)OC)F	InChI=1S/C19H20F4N2O4/c1-28-18-13(20)5-3-11(16(18)22)9-25(8-7-15(26)24-27)10-12-4-6-14(21)19(29-2)17(12)23/h3-6,27H,7-10H2,1-2H3,(H,24,26)	18,700
81	S(=O)(=O)(NCC(=O)NO)c1ccc(Oc2ccccc2)cc1	InChI=1S/C14H14N2O5S/c17-14(16-18)10-15-22(19,20)13-8-6-12(7-9-13)21-11-4-2-1-3-5-11/h1-9,15,18H,10H2,(H,16,17)	18,800
82	O=S(=O)(c1cc(ccc1)OC)NCC(=O)NO	InChI=1S/C9H12N2O5S/c1-16-7-3-2-4-8(5-7)17(14,15)10-6-9(12)11-13/h2-5,10,13H,6H2,1H3,(H,11,12)	18,850
83	ONC(=O)CCN(Cc1c(cc(cc1)Cl)F)Cc1c(cc(cc1)Cl)F	InChI=1S/C17H16Cl2F2N2O2/c18-13-3-1-11(15(20)7-13)9-23(6-5-17(24)22-25)10-12-2-4-14(19)8-16(12)21/h1-4,7-8,25H,5-6,9-10H2,(H,22,24)	19,200
84	ONC(=O)CCN(Cc1c(c(c(cc1)Cl)OC)F)Cc1c(c(c(cc1)Cl)OC)F	InChI=1S/C19H20Cl2F2N2O4/c1-28-18-13(20)5-3-11(16(18)22)9-25(8-7-15(26)24-27)10-12-4-6-14(21)19(29-2)17(12)23/h3-6,27H,7-10H2,1-2H3,(H,24,26)	19,550
85	ONC(=O)CN(Cc1cc(c(c(c1)OC)OC)OC)Cc1cc(c(c(c1)OC)OC)OC	InChI=1S/C22H30N2O8/c1-27-16-7-14(8-17(28-2)21(16)31-5)11-24(13-20(25)23-26)12-15-9-18(29-3)22(32-6)19(10-15)30-4/h7-10,26H,11-13H2,1-6H3,(H,23,25)	20,150
86	ONC(=O)CN(Cc1cnccc1)Cc1cnccc1	InChI=1S/C14H16N4O2/c19-14(17-20)11-18(9-12-3-1-5-15-7-12)10-13-4-2-6-16-8-13/h1-8,20H,9-11H2,(H,17,19)	21,000
87	O=S(=O)(c1c(cc(cc1)C)OC)NCC(=O)NO	InChI=1S/C10H14N2O5S/c1-7-3-4-9(8(5-7)17-2)18(15,16)11-6-10(13)12-14/h3-5,11,14H,6H2,1-2H3,(H,12,13)	25,700
88	O=S(=O)(c1cc(c(cc1)OC)OC)NCC(=O)NO	InChI=1S/C10H14N2O6S/c1-17-8-4-3-7(5-9(8)18-2)19(15,16)11-6-10(13)12-14/h3-5,11,14H,6H2,1-2H3,(H,12,13)	26,900
89	ONC(=O)CN(Cc1ccc2c(c1)OCCO2)Cc1cc2c(cc1)OCCO2	InChI=1S/C20H22N2O6/c23-20(21-24)13-22(11-14-1-3-16-18(9-14)27-7-5-25-16)12-15-2-4-17-19(10-15)28-8-6-26-17/h1-4,9-10,24H,5-8,11-13H2,(H,21,23)	30,600
90	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)CC	InChI=1S/C11H16N2O5S/c1-3-13(8-11(14)12-15-19)10(16,17)10-6-4-9(18-2)5-7-10/h4-7,15H,3,8H2,1-2H3,(H,12,14)	31,200
91	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)C	InChI=1S/C10H14N2O5S/c1-12(7-10(13)11-14-18)6-9-5-3-8(17-2)4-6-9/h3-6,14H,7H2,1-2H3,(H,11,13)	32,530
92	ONC(=O)CN(Cc1ccc(cc1)C#N)Cc1ccc(cc1)C#N	InChI=1S/C18H16N4O2/c19-9-14-1-5-16(6-2-14)11-22(13-18(23)21-24)12-17-7-3-15(10-20)4-8-17/h1-8,24H,11-13H2,(H,21,23)	33,050
93	ONC(=O)CCN(Cc1cc(ccc1)C#N)Cc1cc(ccc1)C#N	InChI=1S/C19H18N4O2/c20-11-15-3-1-5-17(9-15)13-23(8-7-19(24)22-25)14-18-6-2-4-16(10-18)12-21/h1-6,9-10,25H,7-8,13-14H2,(H,22,24)	33,050
94	C(=O)(NO)CN(S(=O)(=O)c1ccc(cc1)OC)Cc1ccc(cc1)OC	InChI=1S/C17H20N2O6S/c1-24-14-5-3-13(4-6-14)11-19(12-17(20)18-21)26(22,23)16-9-7-15(25-2)8-10-16/h3,10,21H,11-12H2,1-2H3,(H,18,20)	34,950
95	O=S(=O)(c1ccc(cc1)OC)N(CC(=O)NO)CCCC	InChI=1S/C13H20N2O5S/c1-3-4-9-15(10-13(16)14-17)21(18,19)12-7-5-11(20-2)6-8-12/h5-8,17H,3-4,9-10H2,1-2H3,(H,14,16)	37,500

96	C(=O)(NO)CN(CCC(C)C)S(=O)(=O)c1ccc(cc1)OC	InChI=1S/C14H22N2O5S/c1-11(2)8-9-16(10-14(17)15-18)22(19,20)13-6-4-12(21-3)5-7-13/h4-7,11,18H,8-10H2,1-3H3,(H,15,17)	38,800
97	C(=O)(NO)CN(S(=O)(=O)c1ccc(cc1)OC)Cc1ccccc1	InChI=1S/C16H18N2O5S/c1-23-14-7-9-15(10-8-14)24(21,22)18(12-16(19)17-20)11-13-5-3-2-4-6-13/h2-10,20H,11-12H2,1H3,(H,17,19)	40,470
98	C(=O)(NO)CN(CCc1ccccc1)S(=O)(=O)c1ccc(cc1)OC	InChI=1S/C17H20N2O5S/c1-24-15-7-9-16(10-8-15)25(22,23)19(13-17(20)18-21)12-11-14-5-3-2-4-6-14/h2-10,21H,11-13H2,1H3,(H,18,20)	42,900
99	[C@H]1(C[C@H]2C[C@@H]1CC2)CN(S(=O)(=O)c1ccc(cc1)OC)CC(=O)NO	InChI=1S/C17H24N2O5S/c1-24-15-4-6-16(7-5-15)25(22,23)19(11-17(20)18-21)10-14-9-12-2-3-13(14)8-12/h4-7,12-14,21H,2-3,8-11H2,1H3,(H,18,20)/t12-,13+,14+/m1/s1	43,870
100	ONC(=O)CCN(Cc1cnccc1)Cc1cnccc1	InChI=1S/C15H18N4O2/c20-15(18-21)5-8-19(11-13-3-1-6-16-9-13)12-14-4-2-7-17-10-14/h1-4,6-7,9-10,21H,5,8,11-12H2,(H,18,20)	53,900
101	c1c(cc(cc1)OC(F)F)CN(CC(=O)NO)Cc1cccc(c1)OC(F)F	InChI=1S/C18H18F4N2O4/c19-17(20)27-14-5-1-3-12(7-14)9-24(11-16(25)23-26)10-13-4-2-6-15(8-13)28-18(21)22/h1-8,17-18,26H,9-11H2,(H,23,25)	56,950
102	ONC(=O)CCN(Cc1ccc(cc1)C#N)Cc1ccc(cc1)C#N	InChI=1S/C19H18N4O2/c20-11-15-1-5-17(6-2-15)13-23(10-9-19(24)22-25)14-18-7-3-16(12-21)4-8-18/h1-8,25H,9-10,13-14H2,(H,22,24)	68,250
103	ONC(=O)CCN(Cc1ccncc1)Cc1ccncc1	InChI=1S/C15H18N4O2/c20-15(18-21)5-10-19(11-13-1-6-16-7-2-13)12-14-3-8-17-9-4-14/h1-4,6-9,21H,5,10-12H2,(H,18,20)	72,400
104	ONC(=O)CCN(Cc1ccccc1)Cc1ccccc1	InChI=1S/C17H20N2O2/c20-17(18-21)11-12-19(13-15-7-3-1-4-8-15)14-16-9-5-2-6-10-16/h1-10,21H,11-14H2,(H,18,20)	75,000
105	ONC(=O)CCN(Cc1cc(c(c(c1)OC)OC)OC)Cc1cc(c(c(c1)OC)OC)OC	InChI=1S/C23H32N2O8/c1-28-17-9-15(10-18(29-2)22(17)32-5)13-25(8-7-21(26)24-27)14-16-11-19(30-3)23(33-6)20(12-16)31-4/h9-12,27H,7-8,13-14H2,1-6H3,(H,24,26)	89,950
106	c1c(cc(cc1)C(=O)OCC)CN(CC(=O)NO)Cc1cccc(c1)C(=O)OCC	InChI=1S/C22H26N2O6/c1-3-29-21(26)18-9-5-7-16(11-18)13-24(15-20(25)23-28)14-17-8-6-10-19(12-17)22(27)30-4-2/h5-12,28H,3-4,13-15H2,1-2H3,(H,23,25)	94,850
107	ONC(=O)CN(Cc1ccncc1)Cc1ccncc1	InChI=1S/C14H16N4O2/c19-14(17-20)11-18(9-12-1-5-15-6-2-12)10-13-3-7-16-8-4-13/h1-8,20H,9-11H2,(H,17,19)	132,500

Supplementary Table S3. Final selected features for the feature set A (PaDEL 2D descriptors)

Cpd No	*nHsOH*	*MIC2*	*SHCsatu*	*GATS8s*	*MDEO-22*	*VC-5*	*SpMax4_Bhv*	*pIC_{50}*
01	3	40.3297	0.924701	1.344462	0	0.084102	3.044706	7.638
02	3	45.6807	0.877054	1.050421	0	0.132897	3.057594	7.62
03	3	45.32981	0.742863	1.018306	0	0.132897	3.150775	7.523
04*	3	37.66587	0.834193	1.592027	0	0.030429	3.118595	7.31
05	2	45.49369	0.924657	1.357345	0	0.148133	3.228397	7.244
06	3	45.48989	0.949291	1.153416	0	0.163348	3.240194	7.222
07	2	40.78098	0.793549	1.674252	0	0.015215	3.105943	7.119
08*	2	38.13959	0.80956	1.634001	0	0.015215	3.106928	7.114
09	2	38.69409	0.817372	1.71012	0	0.015215	3.105046	6.752
10	3	37.25411	0.825619	1.350281	0	0.030429	3.135772	6.684
11	2	44.61068	0.721535	1.241749	0	0.073855	2.986122	6.658
12	2	47.9529	0.945065	0.998849	0.5	0.162022	3.243487	6.569
13*	3	37.9297	0.907375	1.088399	0	0.048795	3.050068	6.565
14	2	40.67433	0.829968	1.552346	0.5	0.029103	3.118931	6.545
15	2	45.54543	0.854416	1.276177	0	0.073855	2.978619	6.509
16	3	44.73855	0.940716	1.05474	0	0.163348	3.24933	6.495
17*	2	39.51846	0.814093	1.549689	0	0.015215	3.133332	6.495
18	2	43.06229	0.715437	1.303328	0	0.073855	2.910397	6.469
19	2	42.40988	0.892893	1.512403	0	0.05379	3.107029	6.46
20*	2	41.1672	0.840172	1.329242	0	0.028073	3.107521	6.426
21	2	37.89662	0.739319	1.8527	0	0.015215	2.866296	6.424
22*	2	35.44418	0.793935	1.658359	0	0.015215	3.111165	6.413
23	2	49.56177	0.701425	1.262307	0	0.131833	2.78953	6.398
24*	2	43.83114	0.845842	1.429157	0	0.073855	2.886952	6.387
25	2	50.83688	0.828775	1.31593	0	0.131833	2.78953	6.367
26	3	35.48405	0.817044	1.06879	0	0.030429	3.143844	6.281
27	3	41.79378	1.722613	1.43904	0	0.036048	3.033378	6.261
28	2	38.87422	0.814343	1.502344	0	0.015215	3.105469	6.253
29	2	38.12787	0.695028	1.402349	0	0.015215	3.174766	6.192
30	2	48.32001	0.95527	1.203363	0	0.160992	3.230839	6.187
31	3	41.25401	1.55573	1.129215	0	0.036048	3.094293	6.184
32	2	50.17951	0.969657	0.762309	0	0.148133	3.235271	6.155
33	2	38.01863	0.642376	1.148765	0	0.015215	3.229445	6.13
34	3	41.25401	1.55573	1.129215	0	0.036048	3.094293	6.115
35	2	44.42703	0.916083	1.317601	0	0.148133	3.229118	6.009
36	2	46.60207	0.93247	1.220321	0	0.148133	3.223207	5.975
37	3	38.20302	0.841368	1.398267	0	0.028172	3.044407	5.975
38	2	41.65898	0.926178	1.380666	0	0.175911	3.459362	5.967
39	2	34.99322	0.81108	1.626555	0	0.042992	3.386124	5.893

40*	2	35.06116	0.793935	1.657709	0	0.015215	3.10415	5.891
41	3	41.79378	1.722613	1.43904	0	0.036048	3.033378	5.878
42	1	36.04789	0.73819	1.313127	2.375452	0.048113	3.200266	5.724
43*	1	43.56744	0.920432	1.448297	0.467649	0.146807	3.228596	5.714
44	2	38.55796	0.814343	1.372453	0	0.015215	3.283171	5.648
45	2	43.25727	1.676555	1.499066	0	0.132919	3.222244	5.593
46*	3	38.20302	0.877826	1.033648	0	0.062973	3.028928	5.537
47	2	36.51481	0.825291	1.210872	0	0.036048	3.104488	5.536
48	1	35.38924	0.70694	1.369814	0.964155	0.027778	3.197425	5.53
49*	1	37.31685	0.831303	1.707652	0	0.086418	3.221748	5.415
50	2	37.57099	0.739319	1.436703	0	0.044677	2.866488	5.377
51	2	37.57099	0.739319	1.436703	0	0.044677	2.866488	5.371
52*	1	39.62364	0.838248	1.547511	0	0.086418	3.227525	5.355
53	1	35.85061	0.866559	1.116042	2.375452	0.048113	3.120026	5.339
54	2	43.06229	1.591337	0.74869	0	0.05864	3.091341	5.298
55	3	40.3297	0.961159	0.87172	0	0.096381	3.029418	5.258
56*	1	43.36883	0.831132	1.710699	0	0.086418	3.226923	5.248
57	2	43.72779	1.87165	1.70928	0	0.132919	3.157181	5.223
58	1	44.24518	0.860395	1.438499	0	0.071499	2.793614	5.208
59	1	35.17792	0.825743	1.437332	0.964155	0.027778	3.119319	5.184
60	1	41.02834	0.84172	1.711147	0	0.086418	3.224687	5.136
61	1	41.9408	0.850191	1.333767	0.333333	0.072529	3.069136	5.13
62	1	33.96664	0.70694	1.315665	0.842267	0.027778	3.246009	5.12
63*	1	40.29109	0.829783	1.868607	0	0.05864	2.793289	5.045
64*	1	52.38695	0.884085	1.538925	0	0.136815	2.989066	4.989
65	2	36.60879	0.898624	1.110092	0	0.054002	3.09882	4.934
66*	2	36.12608	0.739319	1.047424	0	0.115558	3.023019	4.926
67	1	36.09674	0.805334	1.611033	0	0	3.115257	4.921
68	2	36.60879	0.898624	1.110092	0	0.054002	3.09882	4.915
69*	1	44.05032	0.877054	1.140298	0.1	0.124679	3.06986	4.893
70	1	36.24632	0.818568	1.561127	0	0.039284	3.139632	4.883
71	1	42.3089	0.836238	1.372223	0	0.044544	3.051373	4.86
72*	1	42.46929	0.837596	1.574794	0	0.05864	2.645815	4.844
73*	1	38.71252	0.814158	1.337254	0	0.101783	2.949243	4.831
74	2	36.51481	0.825291	1.210872	0	0.036048	3.104488	4.81
75	2	36.12608	0.739319	1.047424	0	0.115558	3.023019	4.801
76	1	37.9772	0.829783	1.289903	0	0.132919	3.223643	4.767
77	1	45.43587	0.813772	1.185668	0	0.05864	2.645815	4.765
78	1	43.43361	0.84477	1.139142	0	0.101783	2.928822	4.745
79	1	39.25727	0.924701	1.39795	0.1	0.080136	3.059438	4.74
80	1	39.27995	0.78051	1.221449	0.1	0.080136	3.149874	4.728
81	1	38.92282	0.843738	1.148571	0	0.05864	3.22095	4.726
82*	1	41.94627	0.834566	0.780777	0	0.05864	2.858828	4.725
83	1	42.13095	0.711613	0.982441	0	0.044544	3.144565	4.717

84	1	43.83897	0.742863	0.969883	0.1	0.124679	3.15961	4.709
85	1	30.37171	0.866559	0.943047	2.25044	0.048113	3.087509	4.696
86*	1	33.41987	0.781454	1.478082	0	0	2.997614	4.678
87*	1	41.31031	0.841936	0.808696	0	0.071604	2.913275	4.59
88	1	40.26499	0.850191	1.499736	0.333333	0.072529	2.863319	4.57
89	1	33.67906	0.825743	1.355763	0.842267	0.027778	3.193644	4.514
90	1	39.3133	0.829783	1.480097	0	0.132919	3.033859	4.506
91*	1	39.70811	0.829783	1.894778	0	0.165507	2.819307	4.488
92	1	33.69674	0.793993	1.413313	0	0	3.141137	4.481
93	1	36.20606	0.691315	1.436391	0	0	3.18757	4.481
94	1	39.03626	0.900024	1.403097	0.083333	0.132919	3.227873	4.457
95	1	38.63028	0.829783	1.452341	0	0.132919	3.224101	4.426
96	1	37.813	0.829783	1.559493	0	0.132919	3.226528	4.411
97*	1	40.12286	0.884399	1.542692	0	0.132919	3.227571	4.393
98	1	39.97766	0.867782	1.64143	0	0.132919	3.2296	4.368
99	1	38.63565	0.829783	1.645164	0	0.216252	3.228171	4.358
100*	1	33.64501	0.671407	1.363622	0	0	3.093931	4.268
101	1	39.20271	0.868567	0.787453	0.1	0	3.071291	4.245
102	1	33.9735	0.683344	1.092048	0	0	3.215226	4.166
103	1	31.18347	0.666623	1.510813	0	0	3.066971	4.14
104	1	27.96759	0.650998	1.353662	0	0	3.118444	4.125
105	1	30.7951	0.73819	1.134304	2.25044	0.048113	3.173239	4.046
106	1	36.38915	0.834193	1.3539	0.083333	0.027778	3.221798	4.023
107	1	30.7532	0.774084	1.867051	0	0	2.961126	3.878

** marked compounds are considered as the test set*

Supplementary Table S4. Final selected features for the feature set B (PaDEL 2D descriptors and Pubchem fingerprint feature combination)

Cpd No	*PubchemFP667*	*PubchemFP338*	*ATSC1e*	*ATSC8m*	*LipoaffinityIndex*	*AATS7i*	*PubchemFP599*	*SHBint3*	*ATSC4m*	*pIC$_{50}$*
01	1	0	-0.8817	-108.778	6.469286	166.8231	1	43.7535	-111.64	7.638
02	1	0	-0.77216	-1182.22	5.58572	164.5934	1	24.80922	-142.875	7.62
03	1	0	-0.69533	-656.765	6.006587	163.3276	1	23.47392	-461.498	7.523
04*	1	0	-0.44173	-518.613	4.632986	158.9274	1	9.610608	319.1561	7.31
05	1	0	0.009944	-1050.99	4.187283	158.8328	1	9.16093	-554.694	7.244
06	1	0	-0.27723	-414.763	3.037126	158.5913	1	9.083932	-185.177	7.222
07	1	0	-0.16996	-1124.83	6.001636	159.6857	1	9.664663	187.9807	7.119
08*	1	0	-0.17557	-481.355	5.985063	159.5438	1	9.676942	33.32923	7.114
09	1	0	-0.21435	-745.614	6.190214	160.7531	1	9.692165	274.9221	6.752
10	1	0	-0.44173	-419.997	4.708672	161.0071	1	9.633999	198.0901	6.684
11	1	0	-0.17711	-254.333	1.561464	164.5719	1	8.735525	-1006.51	6.658
12	1	0	-0.24127	-510.946	3.073279	160.602	1	9.182543	-250.045	6.569
13*	1	0	-0.8817	346.5028	6.602901	175.5561	1	45.53492	783.7895	6.565
14	1	0	-0.36902	-553.778	4.855796	160.9329	1	9.703444	187.7962	6.545
15	1	0	-0.29275	-48.272	1.407589	167.4452	1	16.38904	-531.005	6.509
16	1	0	-0.27723	-565.267	3.063015	160.5518	1	9.109645	-526.842	6.495
17*	1	0	-0.14128	-555.28	5.274178	160.6034	1	9.668705	303.6272	6.495
18	1	0	-0.17711	-339.626	1.565721	165.6415	1	8.734122	-1348.17	6.469
19	1	0	-0.4477	-722.308	6.525473	163.4196	1	9.540383	328.0889	6.46
20*	1	0	-0.31261	-86.8614	6.287307	162.4852	1	9.641832	189.4635	6.426
21	1	0	-0.3562	-116.719	2.473596	167.4138	1	16.00444	-134.827	6.424
22*	1	0	-0.05952	-745.537	6.487082	161.8877	1	9.653394	314.0339	6.413
23	1	0	-0.34699	-1223.29	1.521472	164.6449	1	9.048103	388.7153	6.398
24*	1	0	-0.29275	-426.599	1.398432	168.8935	1	16.3535	-872.671	6.387
25	1	0	-0.49114	471.2177	1.3127	168.0362	1	16.37567	761.9112	6.367
26	1	0	-0.44173	-321.381	4.785217	163.1284	1	9.657245	77.02404	6.281
27	1	1	-0.70696	-140.8	1.693605	164.8494	1	15.71309	-215.404	6.261
28	1	0	-0.17557	-290.374	5.953642	162.3791	1	9.670364	198.2752	6.253
29	1	0	-0.13273	-173.343	6.507577	158.404	1	8.374909	-299.696	6.192
30	1	0	-0.14366	-730.206	4.64585	161.7743	1	9.111851	-191.618	6.187
31	1	1	-0.62427	111.0752	1.97067	165.4813	1	15.15992	-463.624	6.184
32	1	0	-0.44499	-63.4896	6.088728	160.0214	1	9.115335	-237.005	6.155
33	1	0	-0.09478	29.86376	7.089785	158.2812	1	8.352287	-296.135	6.13
34	1	1	-0.62427	111.0752	1.97067	165.4813	1	15.15992	-463.624	6.115
35	1	0	0.009944	-609.033	4.246198	161.2234	1	9.186131	-675.76	6.009
36	1	0	-0.01499	-678.828	4.514964	160.3827	1	9.166753	-428.196	5.975
37	1	0	-0.58482	-39.6329	5.689254	162.5166	1	25.2965	170.6508	5.975
38	1	0	0.256147	-828.319	6.88368	158.5299	1	9.02773	-365.812	5.967
39	1	0	-0.02152	-458.37	8.837939	159.2024	1	9.533629	176.2517	5.893
40*	1	0	-0.09457	-389.904	5.888352	159.8369	1	9.711627	363.3607	5.891

41	1	1	-0.70696	-140.8	1.693605	164.8494	1	15.71309	-215.404	5.878
42	0	0	-0.4436	-1221.68	5.645658	166.353	1	8.365535	61.69537	5.724
43*	0	0	0.065989	-1160.67	4.344598	161.023	1	9.257958	-692.755	5.714
44	1	0	-0.09478	-116.16	6.968935	161.433	1	9.581106	307.8574	5.648
45	0	0	-0.14153	-854.279	2.016073	165.8139	1	9.250376	-1076.44	5.593
46*	1	0	-0.58482	823.4099	5.534675	164.9091	1	26.216	-165.781	5.537
47	1	1	-0.16356	-84.7113	5.428139	162.9023	1	14.55025	-277.214	5.536
48	0	0	-0.22731	-691.022	5.675321	161.3577	1	8.409059	-285.216	5.53
49*	0	0	0.366143	-635.5	5.125488	161.3418	1	15.99213	-654.189	5.415
50	1	1	-0.28693	-40.7724	2.936939	165.9969	1	15.28721	-482.858	5.377
51	1	1	-0.28693	-40.7724	2.936939	165.9969	1	15.28721	-482.858	5.371
52*	0	0	0.267202	-988.161	5.251755	159.6237	1	16.00977	-1009.13	5.355
53	0	0	-0.52451	-417.5	5.109706	168.0513	1	9.705395	370.254	5.339
54	0	0	-0.17711	-91.7471	1.636533	167.6609	1	16.20271	-313.178	5.298
55	1	0	-0.8817	1401.574	6.203926	169.2156	0	26.60659	-244.754	5.258
56*	0	0	0.286416	-1177.8	5.246351	160.7018	1	15.93536	-1139.55	5.248
57	0	0	-0.2449	-1013.39	1.880054	166.6845	1	9.598273	-270.234	5.223
58	0	0	-0.15481	-532.613	2.952786	168.5506	1	16.55044	-544.051	5.208
59	0	0	-0.29631	-588.942	5.117823	162.9384	1	9.795144	56.43633	5.184
60	0	0	0.239617	-903.303	5.46927	165.2222	1	16.08065	-900.947	5.136
61	0	0	-0.15209	-367.85	1.733097	168.1022	1	16.39812	-648.805	5.13
62	0	0	-0.11091	-382.482	6.552673	161.6074	1	8.328469	-477.014	5.12
63*	0	0	0.051101	-756.182	2.420523	163.9545	1	16.28581	-859.254	5.045
64*	0	0	-0.34538	-894.957	4.437277	173.3375	1	16.51744	-596.233	4.989
65	1	1	-0.20389	74.52159	4.969268	161.2264	1	15.00598	-152.138	4.934
66*	1	1	-0.1821	148.64	3.868882	161.7241	1	14.35455	-25.9147	4.926
67	0	0	0.121558	-3.72972	5.841592	157.041	1	9.702081	526.1994	4.921
68	1	1	-0.20389	74.52159	4.969268	161.2264	1	15.00598	-152.138	4.915
69*	0	0	-0.34832	-1948.87	7.899184	168.6181	1	9.507087	385.53	4.893
70	0	0	-0.30431	-539.367	5.004961	161.424	1	9.584664	163.3593	4.883
71	0	0	-0.10918	-2128.69	7.786257	165.0919	1	9.592702	627.2504	4.86
72*	0	0	-0.00753	-301.012	2.758688	171.0823	1	16.4241	-780.72	4.844
73*	0	0	0.328958	-452.382	3.331155	170.5006	1	15.85027	-687.355	4.831
74	1	1	-0.16356	-84.7113	5.428139	162.9023	1	14.55025	-277.214	4.81
75	1	1	-0.1821	148.64	3.868882	161.7241	1	14.35455	-25.9147	4.801
76	0	0	0.410136	-671.186	4.30506	164.3003	1	9.286407	217.1052	4.767
77	0	0	0.06246	-556.861	2.365759	166.8227	1	16.10857	-1060.37	4.765
78	0	0	0.094937	-164.367	3.248985	171.5199	1	16.25474	-648.665	4.745
79	0	0	-0.4452	-885.715	8.553665	170.3783	1	9.5466	105.4884	4.74
80	0	0	-0.38038	-455.875	8.945983	168.6342	1	8.530645	-188.814	4.728
81	0	0	0.204816	-166.873	4.633567	161.1834	1	16.20019	-663.837	4.726
82*	0	0	0.051101	167.5768	2.400713	172.3131	1	16.3105	-393.754	4.725
83	0	0	-0.06898	-832.92	8.279936	163.6982	1	8.409979	281.7465	4.717
84	0	0	-0.2888	-1441.64	8.371316	167.0906	1	8.370061	104.1711	4.709

85	0	0	-0.264	717.077	7.434944	169.5138	1	9.561136	211.2635	4.696
86*	0	0	0.084697	6.935676	5.395234	163.2255	1	9.90016	428.1723	4.678
87*	0	0	0.144005	159.5428	2.90463	172.6018	1	16.2193	-186.539	4.59
88	0	0	-0.07971	-507.011	2.491003	171.8228	1	16.36794	-647.814	4.57
89	0	0	-0.1659	-261	5.982086	163.0318	1	9.692514	-155.789	4.514
90	0	0	0.289975	-413.453	3.322786	167.0188	1	9.436722	-1233.43	4.506
91*	0	0	0.212997	-893.328	3.057701	166.7802	1	9.458095	-753.706	4.488
92	0	0	0.121558	-591.859	5.932071	162.4616	1	9.72571	284.0674	4.481
93	0	0	0.145845	46.92086	6.374683	156.1716	1	8.385695	170.2197	4.481
94	0	0	0.292397	-758.396	5.468562	159.7108	1	9.235541	-688.47	4.457
95	0	0	0.410136	-1064.42	4.2434	165.9061	1	9.321751	-541.263	4.426
96	0	0	0.457927	-1568.92	4.843439	166.2202	1	9.240377	-26	4.411
97*	0	0	0.390043	-1174.73	5.375808	160.0213	1	9.271656	-343.998	4.393
98	0	0	0.436993	-1093.13	5.855621	160.5955	1	9.224966	-874.053	4.368
99	0	0	0.509974	-1621.54	5.725164	162.3901	1	9.070383	490.1792	4.358
100*	0	0	0.121336	303.8184	5.951654	161.8517	1	8.487367	75.98785	4.268
101	0	0	-0.4452	478.7832	8.150104	172.892	1	9.684278	939.5632	4.245
102	0	0	0.145845	-6.78323	6.478092	160.8052	1	8.385999	-71.9123	4.166
103	0	0	0.121336	37.68582	6.000847	164.7994	1	8.471459	4.490566	4.14
104	0	0	0.222275	206.9842	7.770411	159.4042	1	8.393731	20.62621	4.125
105	0	0	-0.20471	-120.381	7.973763	168.1756	1	8.271218	-72.4877	4.046
106	0	0	0.011002	-153.939	6.897787	158.239	1	9.517959	45.38031	4.023
107	0	0	0.084697	-431.754	5.433731	167.4372	1	9.889442	354.4465	3.878

** marked compounds are considered as the test set*

Supplementary Table S5. Final selected features for the feature set B (PaDEL 2D descriptors and Pubchem fingerprint feature combination)

Cpd No	*nHsOH*	*KRFP20*	*KRFP4734*	*SIC3*	*naasC*	*SpMax2_Bhs*	*KRFP588*	*KRFP1653*	*ATS5s*	*pIC_{50}*
1	3	0	0	0.830888	8	5.096018731	0	0	354.7777778	7.638
2	3	0	0	0.830888	8	5.046411987	0	0	334.8148148	7.62
3	3	0	0	0.83714	8	5.077284228	0	0	325.8148148	7.523
4	3	0	0	0.833482	4	4.782211501	0	0	361.3333333	7.31
5	2	0	0	0.92411	4	4.720400038	0	0	509.5725309	7.244
6	3	0	0	0.916741	4	4.753255885	0	0	547.9753086	7.222
7	2	0	0	0.887303	4	4.679289345	1	0	294.0185185	7.119
8	2	0	0	0.888685	4	4.659491766	0	0	322.5833333	7.114
9	2	0	0	0.887303	4	4.770010583	0	0	304	6.752
10	3	0	0	0.860501	4	4.782235017	0	0	348.1666667	6.684
11	2	0	0	0.960932	2	4.817318476	0	0	262.0601852	6.658
12	2	0	0	0.958371	5	4.804163033	0	0	539.058642	6.569
13	3	0	0	0.755728	8	5.096936637	0	0	384	6.565
14	2	0	0	0.925067	5	4.741564838	0	0	323.8333333	6.545
15	2	0	0	0.970284	2	4.765392787	0	0	320.3055556	6.509
16	3	0	0	0.896947	4	4.753256607	0	0	537.3117284	6.495
17	2	0	0	0.878532	4	4.612667232	0	0	317.75	6.495
18	2	0	0	0.908842	2	4.817753689	0	0	250.7299383	6.469
19	2	0	0	0.907925	6	4.869360523	0	0	399.6944444	6.46
20	2	0	0	0.916017	5	4.78224346	0	0	377.5833333	6.426
21	2	0	0	0.970284	2	4.728553568	0	0	175	6.424
22	2	0	0	0.845474	4	4.659491684	0	0	306	6.413
23	2	0	0	0.900626	4	4.846903767	0	0	212.566358	6.398
24	2	0	0	0.910851	2	4.765872829	0	0	308.9753086	6.387
25	2	0	0	0.90181	4	4.796714893	0	0	270.8117284	6.367
26	3	0	0	0.766875	4	4.782280291	0	0	335	6.281
27	3	1	0	0.976875	2	4.895643439	0	0	376.8333333	6.261
28	2	0	0	0.899832	4	4.659491761	0	0	332.3333333	6.253
29	2	0	0	0.889921	4	4.68714155	0	0	313.4722222	6.192
30	2	0	0	0.948389	5	4.844448709	0	0	648.5725309	6.187
31	3	1	0	0.968872	2	4.926194878	0	0	328.3888889	6.184
32	2	0	0	0.92411	4	5.021636101	0	0	632.8225309	6.155
33	2	0	0	0.89108	4	4.712779428	0	0	329.25	6.13
34	3	1	0	0.968872	2	4.926194878	0	0	328.3888889	6.115
35	2	0	0	0.891739	4	4.720462549	0	0	496.0138889	6.009
36	2	0	0	0.92716	4	4.829785444	0	0	485.6975309	5.975
37	3	0	0	0.830888	6	4.953047535	0	1	303.6666667	5.975
38	2	0	0	0.863082	5	4.67979967	0	0	553.9783951	5.967
39	2	0	0	0.832819	5	4.612664968	0	0	364.8333333	5.893
40	2	0	0	0.847447	3	4.64553695	0	0	294.8333333	5.891

41	3	1	0	0.976875	2	4.895643439	0	0	376.8333333	5.878
42	1	0	0	0.775109	8	4.179567591	0	0	391.2222222	5.724
43	1	0	0	0.896777	5	4.677658813	0	0	472.0725309	5.714
44	2	0	0	0.900603	4	4.713075314	0	0	353.9166667	5.648
45	2	0	0	0.895924	2	4.815247619	0	0	431.2546296	5.593
46	3	0	0	0.830888	6	4.950796192	0	0	336.4444444	5.537
47	2	1	0	0.896408	3	4.662833539	0	0	311.5	5.536
48	1	0	0	0.808477	6	4.170537373	0	0	277.2222222	5.53
49	1	0	0	0.839828	3	4.553185507	0	0	325.6419753	5.415
50	2	1	0	0.956017	2	4.717909553	0	0	211.0555556	5.377
51	2	1	0	0.956017	2	4.717909553	0	0	211.0555556	5.371
52	1	0	0	0.850799	4	4.574744317	0	0	353.808642	5.355
53	1	0	0	0.765505	8	4.160335358	0	0	400.3333333	5.339
54	2	0	0	0.908842	2	4.811109765	0	0	350.6990741	5.298
55	3	0	1	0.830888	8	5.088246597	0	0	456.8888889	5.258
56	1	0	0	0.855173	4	4.59148979	0	0	324.8847737	5.248
57	2	0	0	0.89553	2	4.771234834	0	0	588.0601852	5.223
58	1	0	0	0.92366	3	4.860924289	0	0	423.9027778	5.208
59	1	0	0	0.800179	6	4.148819443	0	0	286.3333333	5.184
60	1	0	0	0.855173	4	4.765771262	0	0	335.9753086	5.136
61	1	0	0	0.89582	3	4.820820462	0	0	328.6388889	5.13
62	1	0	0	0.76283	6	4.208529237	0	0	310.2222222	5.12
63	1	0	0	0.881071	2	4.611096193	0	0	281.2361111	5.045
64	1	0	0	0.934959	3	5.144919158	0	0	338.5240626	4.989
65	2	1	0	0.895924	3	4.63164261	0	0	316.0555556	4.934
66	2	1	0	0.898782	2	4.747114763	0	0	301.0555556	4.926
67	1	0	0	0.830888	4	4.44313958	0	0	295.3333333	4.921
68	2	1	0	0.895924	3	4.63164261	0	0	316.0555556	4.915
69	1	0	0	0.797273	8	4.966376376	0	0	396.8888889	4.893
70	1	0	0	0.818957	4	4.707849706	0	0	354.6666667	4.883
71	1	0	0	0.809449	6	4.943309922	0	0	277.8148148	4.86
72	1	0	0	0.896638	2	4.829846937	0	0	257.3611111	4.844
73	1	0	0	0.872967	3	4.639069724	0	0	336.1944444	4.831
74	2	1	0	0.896408	3	4.662833539	0	0	311.5	4.81
75	2	1	0	0.898782	2	4.747114763	0	0	301.0555556	4.801
76	1	0	0	0.834905	2	4.676333373	0	0	438.0138889	4.767
77	1	0	0	0.896638	2	4.646162018	0	0	255.2046182	4.765
78	1	0	0	0.920101	3	4.861414424	0	0	452.037037	4.745
79	1	0	0	0.797273	8	5.014444211	0	0	456.7777778	4.74
80	1	0	0	0.805504	8	5.043865213	0	0	447.7777778	4.728
81	1	0	0	0.845501	3	4.553184884	0	0	322.1805556	4.726
82	1	0	0	0.937856	2	4.611096192	0	0	327.1574074	4.725
83	1	0	0	0.8179	6	4.978366091	0	0	268.8148148	4.717
84	1	0	0	0.805504	8	4.996861139	0	0	387.8888889	4.709

85	1	0	0	0.619221	8	4.039799797	0	0	525.8333333	4.696
86	1	0	0	0.806574	2	3.997810828	0	0	224.3333333	4.678
87	1	0	0	0.915564	3	4.639070771	0	0	339.4166667	4.59
88	1	0	0	0.85877	3	4.639070966	0	0	366.8009259	4.57
89	1	0	0	0.751943	6	4.190364666	0	0	319.3333333	4.514
90	1	0	0	0.869044	2	4.636228131	0	0	397.4027778	4.506
91	1	0	0	0.865564	2	4.583482684	0	0	332.4027778	4.488
92	1	0	0	0.736937	4	4.443199503	0	0	274.1666667	4.481
93	1	0	0	0.83714	4	4.469477124	0	0	286.2222222	4.481
94	1	0	0	0.813015	4	4.594654475	0	0	470.4305556	4.457
95	1	0	0	0.874762	2	4.721932202	0	0	419.6157407	4.426
96	1	0	0	0.840707	2	4.713672676	0	0	430.2175926	4.411
97	1	0	0	0.869701	3	4.576711044	0	0	442.6805556	4.393
98	1	0	0	0.872499	3	4.610816984	0	0	452.337963	4.368
99	1	0	0	0.859135	2	4.962860028	0	0	452.8904321	4.358
100	1	0	0	0.815651	2	4.032346182	0	0	215.2222222	4.268
101	1	0	0	0.818957	4	5.196260521	0	0	456	4.245
102	1	0	0	0.751424	4	4.469530024	0	0	265.0555556	4.166
103	1	0	0	0.757435	2	4.032346099	0	0	224.2222222	4.14
104	1	0	0	0.738187	2	3.994448657	0	0	219.2222222	4.125
105	1	0	0	0.635798	8	4.061026533	0	0	516.7222222	4.046
106	1	0	0	0.798563	4	4.702338317	0	0	428.5	4.023
107	1	0	0	0.742098	2	3.997810175	0	0	233.3333333	3.878

** marked compounds are considered as the test set*

Supplementary Table S6. Statistical validation parameters for MLR models

MLR model	***MLR Feature set A***	***pIC_{50}*** *= -6.02436(+/-1.32154) +1.0932(+/-0.06563)* ***nHsOH*** *+0.14292(+/-0.01379)* ***MIC2*** *-1.19743(+/-0.17495)* ***SHCsatu*** *+1.12675(+/-0.18211)* ***GATS8s*** *+0.56502(+/-0.08575)* ***MDEO-22*** *-4.44019(+/-1.05368)* ***VC-5*** *+1.20802(+/-0.32352)* ***SpMax4_Bhv***	
	MLR Feature set B	***pIC_{50}*** *= 10.74258(+/-2.17295) +1.24791(+/-0.1025)* ***PubchemFP667*** *-1.0961(+/-0.11627)* ***PubchemFP338*** *-1.37093(+/-0.16721)* ***ATSC1e*** *-0.00038(+/-0.00007)* ***ATSC8m*** *-0.07941(+/-0.02115)* ***LipoaffinityIndex*** *-0.04411(+/-0.0126)* ***AATS7i*** *+1.21857(+/-0.3573)* ***PubchemFP599*** *+0.01865(+/-0.00776)* ***SHBint3*** *-0.00021(+/-0.00009)* ***ATSC4m***	
	MLR Feature set C	***pIC_{50}*** *= -0.15201(+/-0.6533) +1.04414(+/-0.06055)* ***nHsOH*** *-1.08587(+/-0.11256)* ***KRFP20*** *-1.99318(+/-0.3098)* ***KRFP4734*** *+7.4606(+/-0.78823)* ***SIC3*** *+0.20975(+/-0.02286)* ***naasC*** *-0.5998(+/-0.1653)* ***SpMax2_Bhs*** *+0.8872(+/-0.29437) KRFP588 -1.12364(+/-0.30825)* ***KRFP1653*** *-0.00121(+/-0.00034)* ***ATS5s***	
Parameter	***MLR (Feature set A)***	***MLR (Feature set B)***	***MLR (Feature set C)***
N_{Train}	82	82	82
SEE	0.354	0.307	0.289
R^2	0.875	0.908	0.919
R^2_A	0.863	0.897	0.909
PRESS	9.272	6.799	6.024
F	73.918 (*DF* :7, 74)	79.193 (*DF* :9, 72)	90.415(*DF* :9, 72)
p-value	<0.05	<0.05	<0.05
Q^2	0.844	0.842	0.867
Avg. rm^2_{LOO}	0.785	0.785	0.817
$_CR_p^2$	0.831	0.857	
N_{Test}	25	25	25
r^2	0.735	0.787	0.680
r_0^2	0.714	0.775	0.676
$RMSE_P$	0.479	0.422	0.495
R^2_{pred} (Q^2f_1)	0. .693	0.762	0.672
Q^2f_2	0.692	0.761	0.672
Average rm^2_{test}	0.649	0.715	0.581

Supplementary Table S7. Statistical validation parameters for MLR models

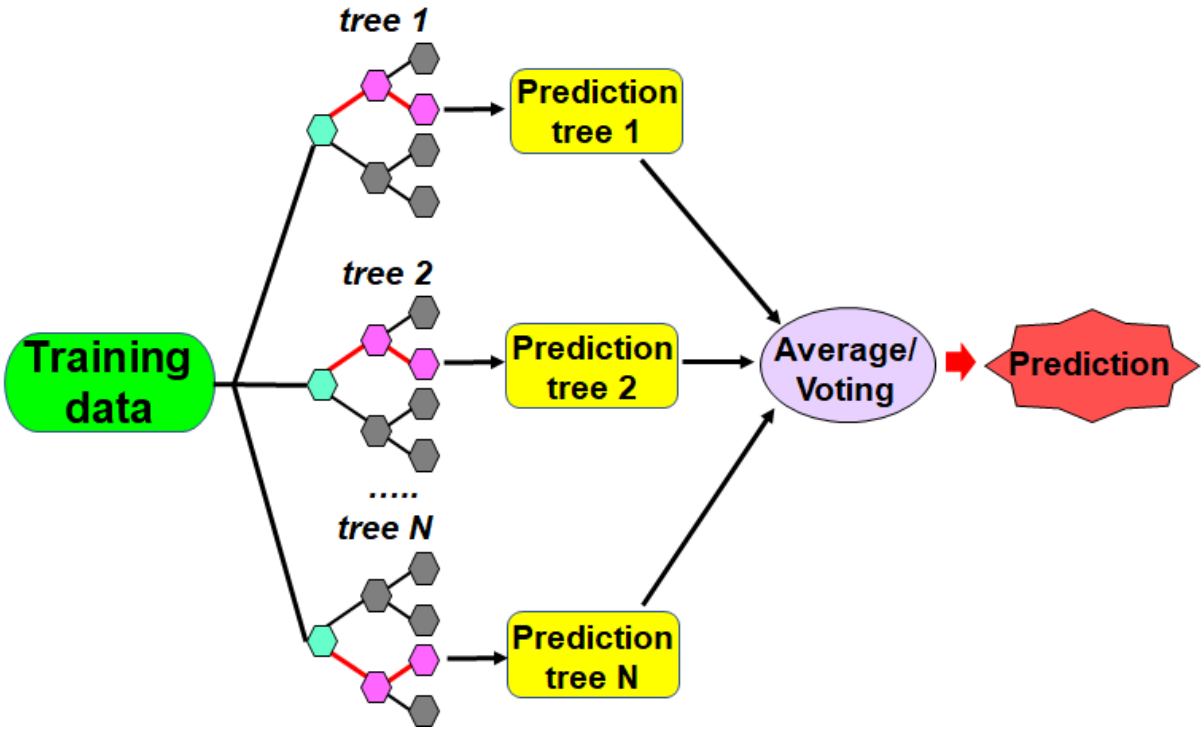
Training set					
Cpd No	actual	Predicted			
		k-NN	RF	ANN	SVM
1	7.638	7.638	7.146	6.738	7.634
2	7.62	7.62	7.234	6.976	7.517
3	7.523	7.523	7.287	7.112	7.284
5	7.244	7.244	6.891	6.354	6.465
6	7.222	7.222	6.94	7.035	6.627
7	7.119	7.119	6.884	6.647	6.459
9	6.752	6.752	6.572	6.361	6.319
10	6.684	6.684	6.366	6.767	6.588
11	6.658	6.658	6.54	6.396	6.432
12	6.569	6.569	6.532	6.514	6.547
14	6.545	6.545	6.559	6.683	6.539
15	6.509	6.509	6.484	6.393	6.524
16	6.495	6.495	6.539	6.882	6.657
18	6.469	6.469	6.29	6.149	6.476
19	6.46	6.46	6.265	6.405	6.465
21	6.424	6.424	6.289	6.224	6.487
23	6.398	6.398	6.451	6.667	6.749
25	6.367	6.367	6.363	6.742	6.365
26	6.281	6.281	6.146	6.216	6.487
27	6.261	6.069	6.022	6.249	6.029
28	6.253	6.253	6.223	6.136	6.079
29	6.192	6.192	6.19	6.147	6.155
30	6.187	6.187	6.175	6.493	6.344
31	6.184	6.149	6.139	6.082	5.827
32	6.155	6.155	6.198	6.287	6.482
33	6.13	6.13	6.064	5.949	6.006
34	6.115	6.149	6.139	6.082	5.827
35	6.009	6.009	6.172	6.154	6.238
36	5.975	5.975	6.234	6.339	6.268
37	5.975	5.975	6.011	6.831	6.929
38	5.967	5.967	6.037	5.943	5.891
39	5.893	5.893	5.864	5.909	5.887
41	5.878	6.069	6.022	6.249	6.029
42	5.724	5.724	5.434	5.821	5.319
44	5.648	5.648	5.807	6.149	5.871
45	5.593	5.593	5.66	5.195	5.288
47	5.536	5.173	5.238	5.265	5.135
48	5.53	5.53	5.331	5.043	5.114

50	5.377	5.374	5.471	5.49	5.376
51	5.371	5.374	5.471	5.49	5.376
53	5.339	5.339	5.308	5.252	5.108
54	5.298	5.298	5.538	4.625	5.086
55	5.258	5.258	5.851	6.065	5.262
57	5.223	5.223	5.538	5.181	5.323
58	5.208	5.208	5.088	4.983	5.132
59	5.184	5.184	5.183	4.857	5.123
60	5.136	5.136	5.014	5.306	4.767
61	5.13	5.13	4.991	5.052	5.185
62	5.12	5.12	5.05	4.78	4.826
65	4.934	4.925	5.063	4.978	5.215
67	4.921	4.921	4.74	4.786	4.501
68	4.915	4.925	5.063	4.978	5.215
70	4.883	4.883	4.838	4.622	5.158
71	4.86	4.86	4.889	5.077	5.05
74	4.81	5.173	5.238	5.265	5.135
75	4.801	4.801	5.037	4.708	5.178
76	4.767	4.767	4.665	4.348	4.231
77	4.765	4.765	5.116	4.816	5.045
78	4.745	4.745	4.815	4.615	4.578
79	4.74	4.74	4.774	4.541	4.891
80	4.728	4.728	4.734	4.607	4.728
81	4.726	4.726	4.766	4.535	4.732
83	4.717	4.717	4.797	4.875	4.611
84	4.709	4.709	4.807	4.798	4.985
85	4.696	4.696	4.665	4.329	4.218
88	4.57	4.57	4.717	4.78	4.953
89	4.514	4.514	4.632	4.608	4.82
90	4.506	4.506	4.524	4.472	4.5
92	4.481	4.481	4.477	4.386	4.525
93	4.481	4.481	4.504	4.825	4.475
94	4.457	4.457	4.524	4.512	4.649
95	4.426	4.426	4.445	4.538	4.431
96	4.411	4.411	4.443	4.545	4.404
98	4.368	4.368	4.421	4.844	4.553
99	4.358	4.358	4.4	4.441	4.356
101	4.245	4.245	4.522	4.354	4.241
102	4.166	4.166	4.294	4.322	4.349
103	4.14	4.14	4.173	4.282	4.236
104	4.125	4.125	4.243	4.031	4.136
105	4.046	4.046	4.405	4.721	4.45
106	4.023	4.023	4.377	4.587	4.647
107	3.878	3.878	4.144	4.334	4.357

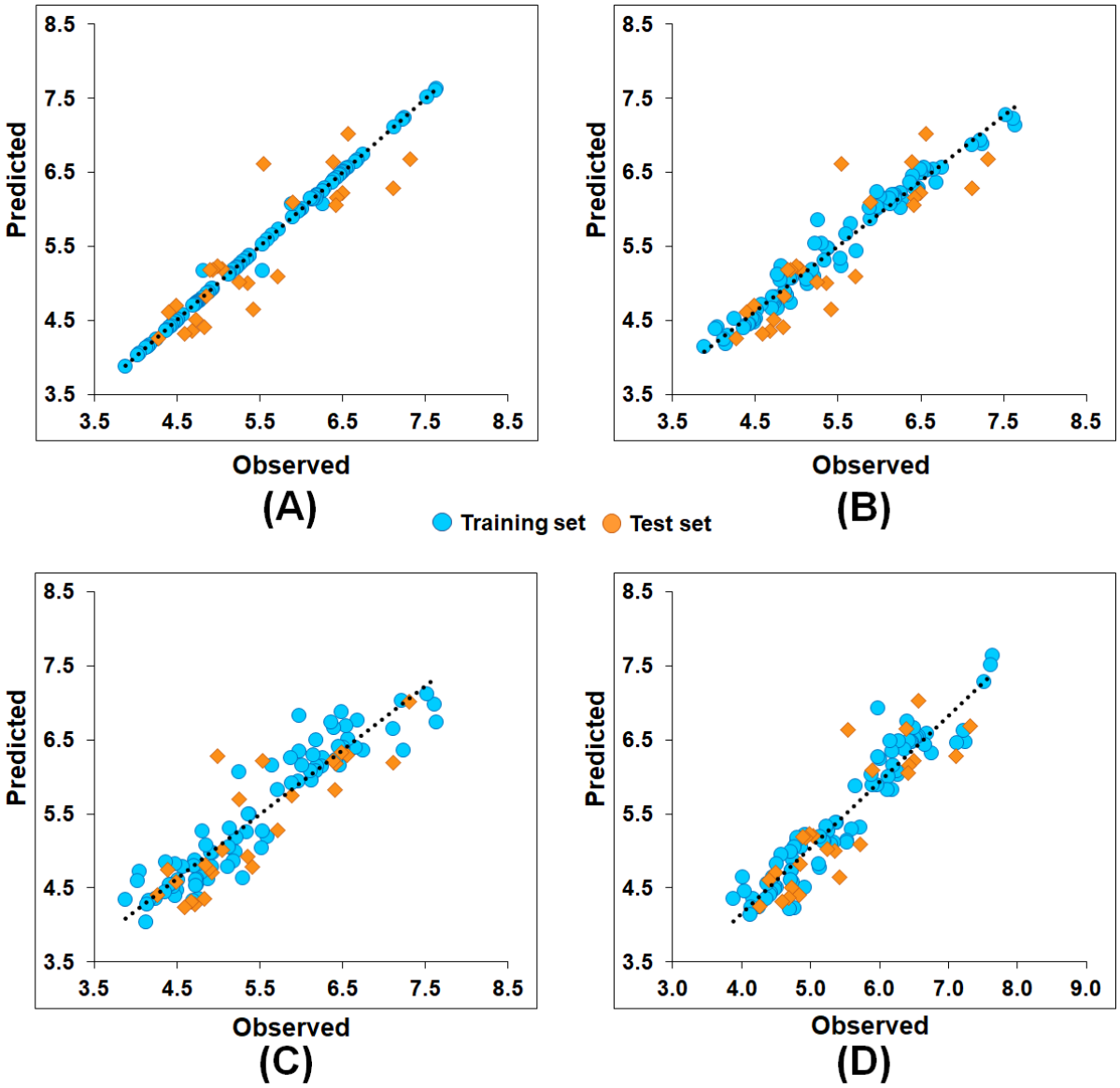
Test Set					
Cpd No	actual	Predicted			
		k-NN	RF	ANN	SVM
4	7.31	6.684	6.228	7.013	6.687
8	7.114	6.752	6.385	6.196	6.28
13	6.565	7.638	6.138	6.29	7.029
17	6.495	6.752	6.306	6.33	6.22
20	6.426	6.253	6.383	6.183	6.157
22	6.413	6.752	6.057	5.823	6.054
24	6.387	6.509	6.134	6.218	6.652
40	5.891	6.752	5.881	5.751	6.089
43	5.714	4.457	4.925	5.274	5.092
46	5.537	5.975	5.88	6.211	6.631
49	5.415	4.726	4.773	4.786	4.643
52	5.355	4.457	4.646	4.917	5.001
56	5.248	4.368	4.928	5.697	5.02
63	5.045	4.765	4.866	5.006	5.199
64	4.989	4.57	5.188	6.286	5.227
66	4.926	4.801	5.037	4.708	5.178
69	4.893	4.709	4.885	4.756	5.186
72	4.844	4.57	4.965	4.81	4.826
73	4.831	4.745	4.726	4.346	4.409
82	4.725	4.745	4.844	4.276	4.509
86	4.678	4.481	4.334	4.315	4.359
87	4.59	4.745	4.884	4.243	4.315
91	4.488	4.426	4.697	4.576	4.704
97	4.393	4.457	4.519	4.74	4.606
100	4.268	4.166	4.349	4.408	4.249

Supplementary Table S8. Binding energy calculation for the MD simulation study of the meprin β-compound **1** and meprin β-designed compound **P-1** complexes

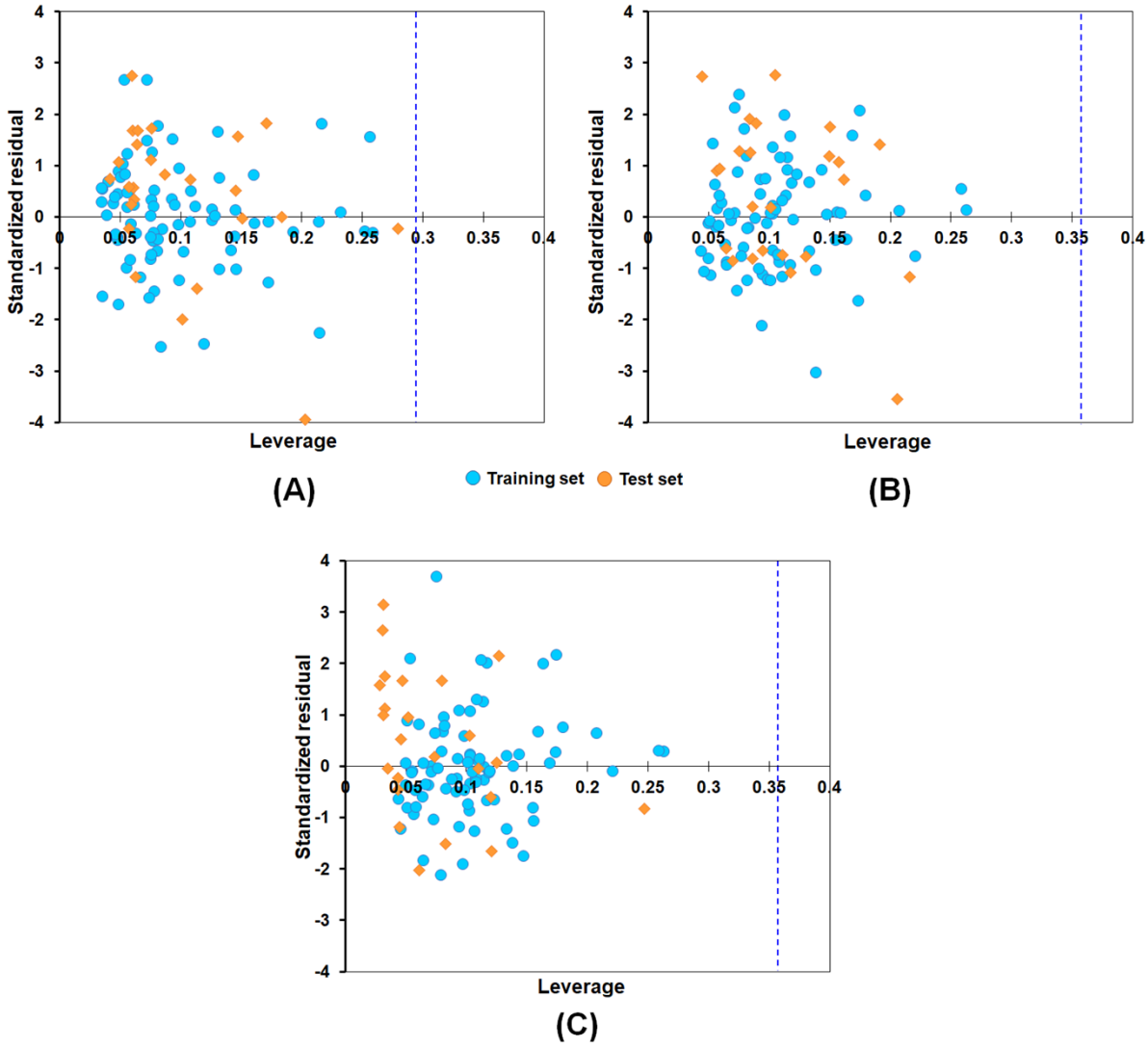
Complex	VDWAALS	EEL	EGB	ESURF	TΔS	ΔG (kCal/mol)
Meprin β-Compound 7 complex	8.79 ± 0.43	- 417.64 ± 2.95	432.91 ± 8.09	191.18 ± 2.18	29.93 ± 14.91	54.00 ± 15.33
Meprin β-designed compound P-1 complex	8.99 ± 0.54	- 421.20 ± 16.39	436.40 ± 11.05	187.64 ± 2.00	25.01 ± 9.92	49.20 ± 11.31



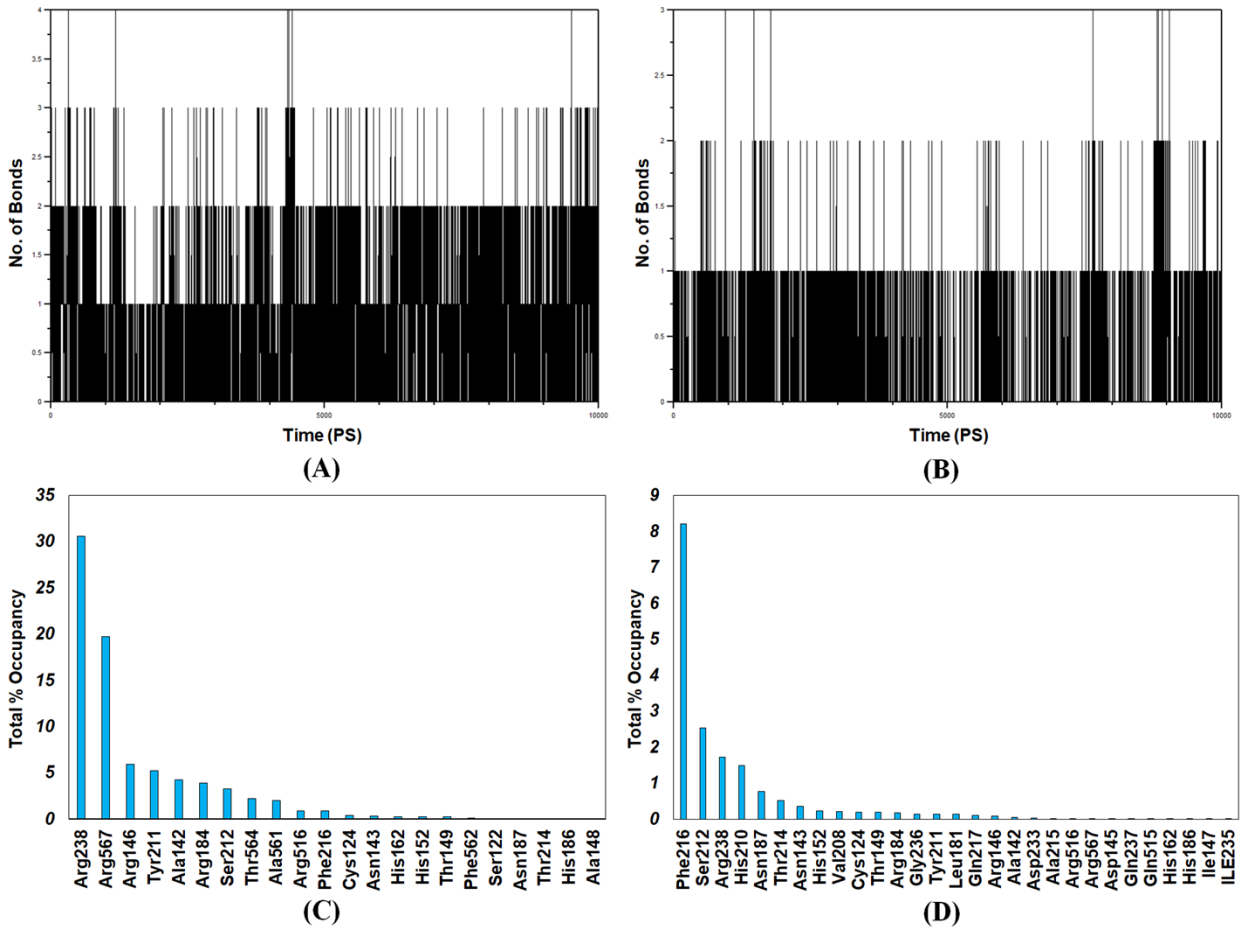
Supplementary Fig. S1. Generalized representation of the random forest (RF)-based ensemble method



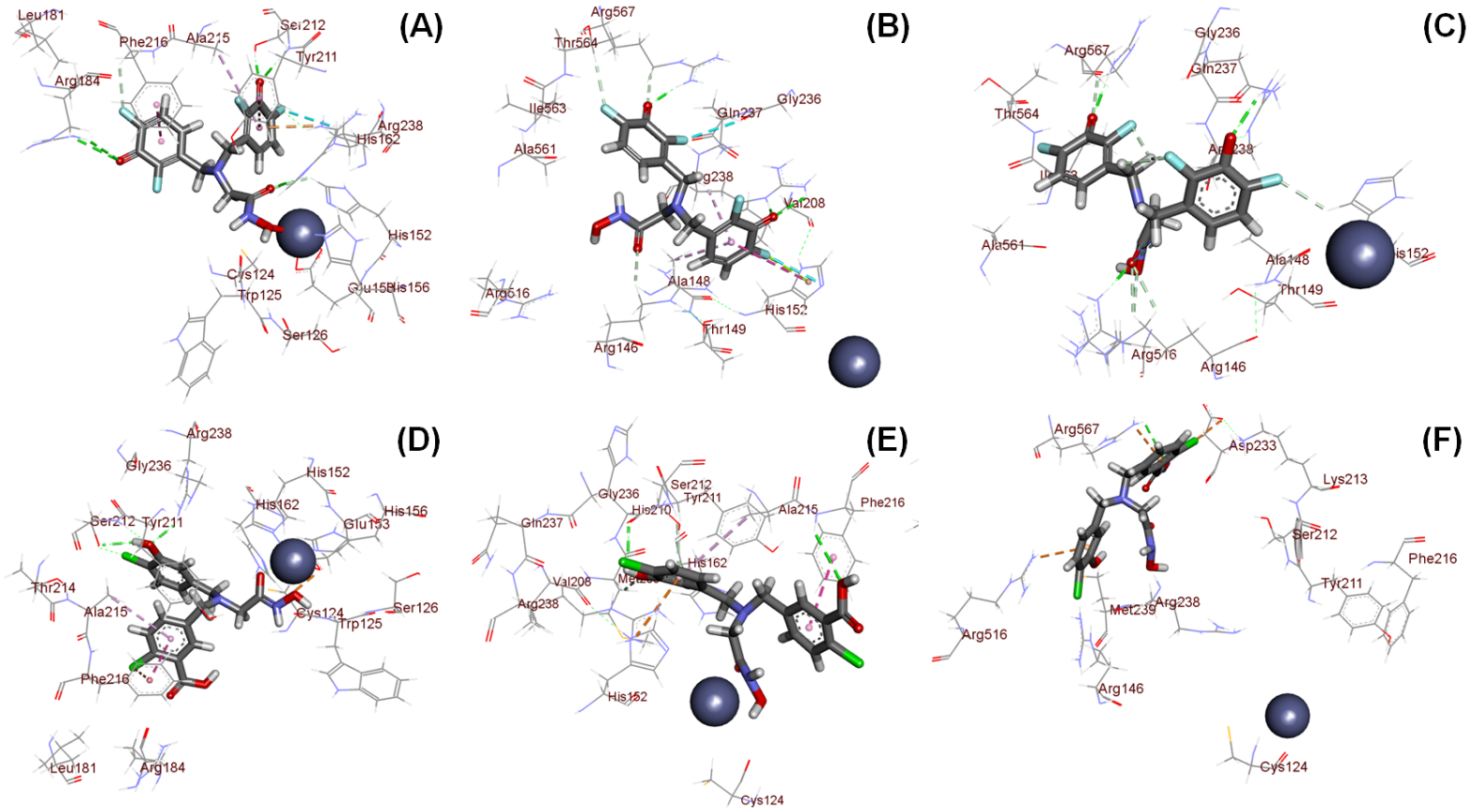
Supplementary Fig. S2. (A) The observed vs predicted activity of the training and test sets of the feature set-B based *k*-NN model; **(B)** The observed vs predicted activity of the training and test sets of the feature set-B based RF model; **(C)** The observed vs predicted activity of the training and test sets of the feature set-B based ANN model; **(D)** The observed vs predicted activity of the training and test sets of the feature set-B based SVM model.



Supplementary Fig. S3. MLR-based William's plot for the final set of descriptors of **(A)** feature set-A; **(B)** feature set-B; **(C)** feature set-C



Supplementary Figure S4. Frequency of hydrogen bond formation for **(A)** meprin β-compound **1** complex, **(B)** meprin β-compound **P-1** complex, **(C)** Hydrogen bond occupancy for meprin β-compound **1** complex, **(D)** Hydrogen bond occupancy for meprin β-compound **P-1** complex



Supplementary Figure S5. The interactions of compound **1** at the meprin β binding site at **(A)** 0 ns, **(B)** 50 ns, **(C)** 100 ns, the interactions of designed compound **P-1** at the meprin β binding site at **(D)** 0 ns, **(E)** 50 ns, **(F)** 100 ns