

Electronic Supplementary Information

Identification of 4-acrylamido-N-(pyridazin-3-yl)benzamide as anti-COVID-19 compound: A DFTB, molecular docking, and molecular dynamics study

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Fig. S1 QMEANDisCo Global scores of SARS-CoV-2 M^{pro} protein



Fig. S2 Overlay of the models of SARS-CoV-2 M^{pro} before (blue) and after (dark yellow) energy minimization

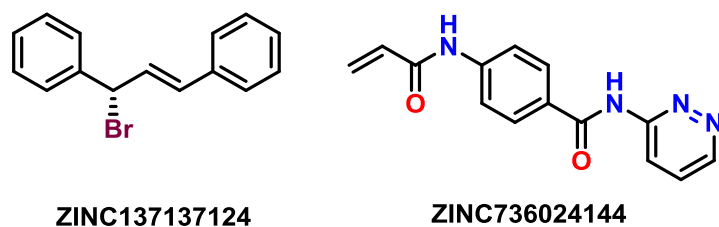


Fig. S3 The chemical structure of compounds showed the highest binding affinity toward SARS-CoV-2 M^{pro}

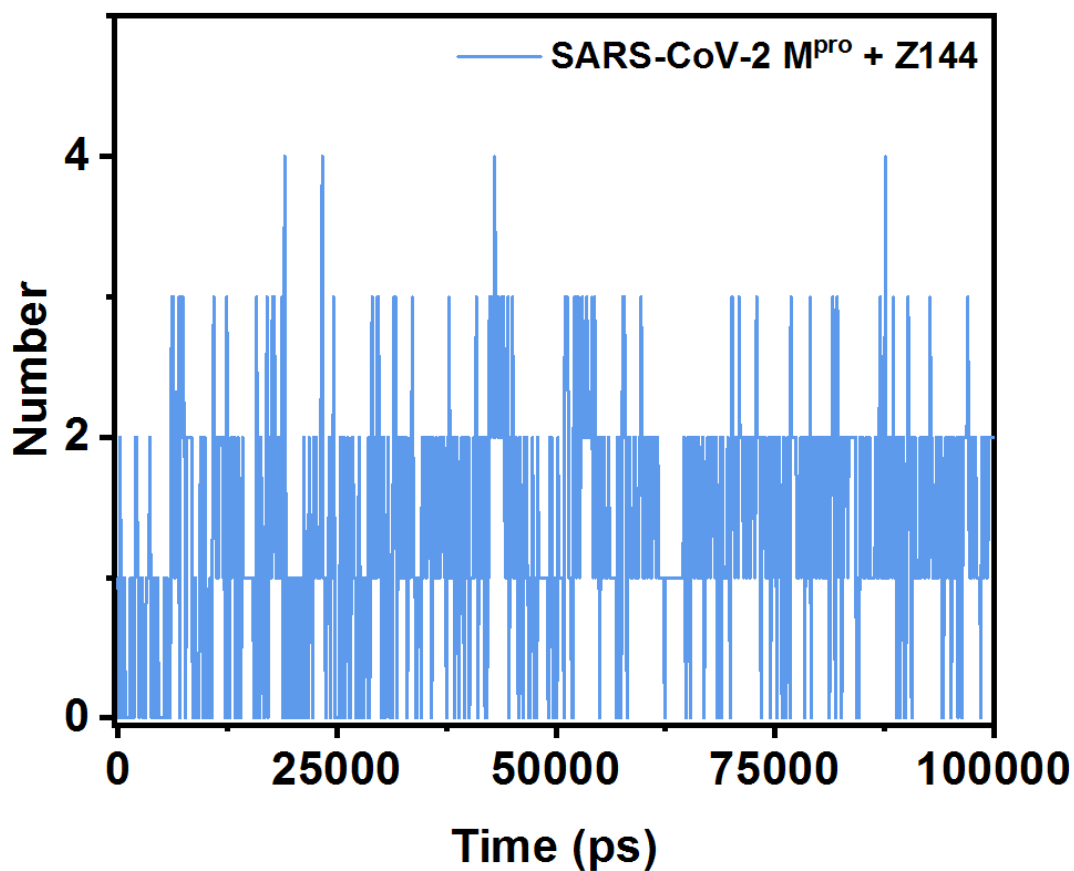


Fig. S4 The hydrogen bonding between **Z144** and SARS-CoV-2 M^{pro} during the trajectory obtained from MD.

Table S1 Binding energy from docking study with SARS-CoV-2 M^{PRO} and SMILES of compounds obtained from ZINC 15 database

S. No	Compounds	SMILES	Docking energy	K _i (M)
1	ZINC1532572628	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(Cl)c2)cc1</chem>	-5.6	7.82E-05
2	ZINC1532170012	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(C)c2)cc1</chem>	-5.4	1.10E-04
3	ZINC1130999491	<chem>CCC(=O)c1ccc(NC(=O)c2ccnc(Cl)c2)cc1</chem>	-5.6	7.82E-05
4	ZINC1131202558	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(F)c2)cc1</chem>	-5.6	7.82E-05
5	ZINC1147402683	<chem>Cc1cncc(C(=O)Nc2ccc(C(=O)CBr)cc2)c1</chem>	-5.8	5.58E-05
6	ZINC1437705401	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(I)c2)cc1</chem>	-5.7	6.60E-05
7	ZINC1461585059	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(Br)c2)cc1</chem>	-5.6	7.82E-05
8	ZINC1470123723	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(O)c2)cc1</chem>	-5.6	7.82E-05
9	ZINC1188621201	<chem>O=C(CBr)c1ccc(NC(=O)c2ccnc(Br)c2)cc1</chem>	-5.5	9.26E-05
10	ZINC1528834256	<chem>CCC(=O)c1ccc(NC(=O)c2ccnc(C)c2)cc1</chem>	-5.5	9.26E-05
11	ZINC1146907821	<chem>O=C(CBr)c1ccc(NC(=O)c2ccnc(O)c2)cc1</chem>	-5.8	5.58E-05
12	ZINC1188789692	<chem>Cc1cc(C(=O)Nc2ccc(C(=O)CBr)cc2)ccn1</chem>	-5.4	1.10E-04
13	ZINC1412345829	<chem>CCC(=O)c1ccc(NC(=O)c2ccnc(O)c2)cc1</chem>	-6.0	3.98E-05
14	ZINC1461582058	<chem>CCC(=O)c1ccc(NC(=O)c2ccnc(F)c2)cc1</chem>	-5.6	7.82E-05
15	ZINC1532161994	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(Cl)c2)cc1</chem>	-5.7	6.60E-05
16	ZINC1539123431	<chem>CCC(=O)c1ccc(NC(=O)c2ccnc(Br)c2)cc1</chem>	-5.6	7.82E-05
17	ZINC1131202548	<chem>CCC(=O)c1ccc(NC(=O)c2cc(Cl)ccn2)cc1</chem>	-5.7	6.60E-05
18	ZINC48546120	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(C)c2)cc1</chem>	-5.8	5.58E-05
19	ZINC1166741925	<chem>CCC(=O)c1ccc(NC(=O)c2cnnc(C)c2)cc1</chem>	-5.8	5.58E-05
20	ZINC1433526003	<chem>CCC(=O)c1ccc(NC(=O)c2cncc(Cl)n2)cc1</chem>	-5.7	6.60E-05
21	ZINC1437703406	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(Cl)n2)cc1</chem>	-5.7	6.60E-05
22	ZINC1186152205	<chem>O=C(CBr)c1ccc(NC(=O)c2cccc(S)c2)cc1</chem>	-5.5	9.26E-05
23	ZINC1191577661	<chem>O=C(CBr)c1ccc(NC(=O)c2cnnc(O)c2)cc1</chem>	-5.9	4.71E-05
24	ZINC1361320731	<chem>CNC(=O)c1ccc(NC(=O)c2cncc(Cl)c2)cc1</chem>	-5.8	5.58E-05
25	ZINC1363472418	<chem>CCC(=O)c1ccc(NC(=O)c2cnnc(O)c2)cc1</chem>	-6.0	3.98E-05
26	ZINC1587376815	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(F)c2)cc1</chem>	-5.7	6.60E-05
27	ZINC1587377849	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(Br)c2)cc1</chem>	-5.6	7.82E-05
28	ZINC1617718146	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(I)c2)cc1</chem>	-5.7	6.60E-05
29	ZINC1629363646	<chem>CCC(=O)c1ccc(NC(=O)c2cc(N)ccn2)cc1</chem>	-5.6	7.82E-05
30	ZINC79290900	<chem>CNC(=O)c1ccc(NC(=O)c2cncc(C)c2)cc1</chem>	-5.9	4.71E-05
31	ZINC1130999324	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(C)n2)cc1</chem>	-6.0	3.98E-05
32	ZINC1147870431	<chem>O=C(CBr)c1ccc(NC(=O)c2cncc(Br)n2)cc1</chem>	-5.5	9.26E-05
33	ZINC8424244	<chem>CNC(=O)c1ccc(NC(=O)c2cncc(Br)c2)cc1</chem>	-5.9	4.71E-05
34	ZINC109042869	<chem>CNC(=O)c1ccc(NC(=O)c2cncc(O)c2)cc1</chem>	-6.1	3.36E-05
35	ZINC155643179	<chem>CNC(=O)c1ccc(NC(=O)c2cncc(I)c2)cc1</chem>	-5.6	7.82E-05
36	ZINC164372679	<chem>CNC(=O)c1ccc(NC(=O)c2cncc(F)c2)cc1</chem>	-5.9	4.71E-05
37	ZINC307951867	<chem>COC(=O)c1ccc(NC(=O)c2cncc(Cl)c2)cc1</chem>	-5.5	9.26E-05
38	ZINC1147221214	<chem>Cc1cccc(C(=O)Nc2ccc(C(=O)CBr)cc2)n1</chem>	-5.7	6.60E-05
39	ZINC1147302366	<chem>O=C(CBr)c1ccc(NC(=O)c2cccc(O)n2)cc1</chem>	-5.8	5.58E-05
40	ZINC1188720210	<chem>O=C(CBr)c1ccc(NC(=O)c2cccc(F)n2)cc1</chem>	-5.6	7.82E-05
41	ZINC1434191219	<chem>CCC(=O)c1ccc(NC(=O)c2cccc(O)n2)cc1</chem>	-6.0	3.98E-05

42	ZINC1461585851	CCC(=O)c1ccc(NC(=O)c2cccc(Br)n2)cc1	-5.4	1.10E-04
43	ZINC1470120973	CCC(=O)c1ccc(NC(=O)c2ccc[n+][[O-]]c2)cc1	-5.4	1.10E-04
44	ZINC1532170010	CCC(=O)c1ccc(NC(=O)c2cccc(F)n2)cc1	-5.6	7.82E-05
45	ZINC307952759	CC(=NO)c1ccc(NC(=O)c2cncc(Cl)c2)cc1	-5.9	4.71E-05
46	ZINC307970035	NC(=NO)c1ccc(NC(=O)c2cncc(Cl)c2)cc1	-6.0	3.98E-05
47	ZINC121114	COC(=O)c1ccc(NC(=O)c2cncc(Br)c2)cc1	-5.6	7.82E-05
48	ZINC82334639	COC(=O)c1ccc(NC(=O)c2cncc(O)c2)cc1	-6.0	3.98E-05
49	ZINC88451750	COC(=O)c1ccc(NC(=O)c2cncc(C)c2)cc1	-5.7	6.60E-05
50	ZINC124806588	COC(=O)c1ccc(NC(=O)c2cncc(F)c2)cc1	-5.8	5.58E-05
51	ZINC154974090	COC(=O)c1ccc(NC(=O)c2cncc(I)c2)cc1	-5.4	1.10E-04
52	ZINC3562587	CNC(=O)c1ccc(NC(=O)c2cccc(Cl)c2)cc1	-5.8	5.58E-05
53	ZINC34925082	NNC(=O)c1ccc(NC(=O)c2cccc(Cl)c2)cc1	-5.8	5.58E-05
54	ZINC252665735	CC(=NO)c1ccc(NC(=O)c2cncc(C)c2)cc1	-6.0	3.98E-05
55	ZINC6618865	CC[C@@H](C)c1ccc(NC(=O)c2cncc(Br)c2)cc1	-5.5	9.26E-05
56	ZINC6619083	CC[C@H](C)c1ccc(NC(=O)c2cncc(Br)c2)cc1	-5.5	9.26E-05
57	ZINC20481016	C/C(=N\O)c1ccc(NC(=O)c2cncc(Br)c2)cc1	-6.1	3.36E-05
58	ZINC40367438	N/C(=N/O)c1ccc(NC(=O)c2cncc(Br)c2)cc1	-5.9	4.71E-05
59	ZINC88451862	Cc1cncc(C(=O)Nc2ccc(/C(N)=N/O)cc2)c1	-6.0	3.98E-05
60	ZINC111776195	CC[C@@H](C)c1ccc(NC(=O)c2cncc(O)c2)cc1	-5.6	7.82E-05
61	ZINC111776198	CC[C@H](C)c1ccc(NC(=O)c2cncc(O)c2)cc1	-5.6	7.82E-05
62	ZINC165251069	C/C(=N/O)c1ccc(NC(=O)c2cncc(F)c2)cc1	-5.9	4.71E-05
63	ZINC165318860	N/C(=N/O)c1ccc(NC(=O)c2cncc(F)c2)cc1	-6.1	3.36E-05
64	ZINC312107418	CC(=NO)c1ccc(NC(=O)c2cncc(Br)c2)cc1	-5.8	5.58E-05
65	ZINC379705214	CC(=NO)c1ccc(NC(=O)c2cncc(F)c2)cc1	-6.2	2.84E-05
66	ZINC1147391348	CC[C@@H](C)c1ccc(NC(=O)c2cncc(C)c2)cc1	-5.8	5.58E-05
67	ZINC1147391356	CC[C@H](C)c1ccc(NC(=O)c2cncc(C)c2)cc1	-5.9	4.71E-05
68	ZINC128857	COC(=O)c1ccc(NC(=O)c2cccc(Cl)c2)cc1	-5.8	5.58E-05
69	ZINC7597184	CNC(=O)c1ccc(NC(=O)c2cccc(C)c2)cc1	-5.8	5.58E-05
70	ZINC188980812	CNC(=O)c1ccc(NC(=O)c2cncc(Cl)n2)cc1	-5.6	7.82E-05
71	ZINC344730330	CNC(=O)c1ccc(NC(=O)c2cnnc(C)c2)cc1	-6.4	2.02E-05
72	ZINC3562639	CNC(=O)c1ccc(NC(=O)c2cccc(F)c2)cc1	-5.8	5.58E-05
73	ZINC4520332	Cc1cccc(C(=O)Nc2ccc(C(=O)NN)cc2)c1	-5.9	4.71E-05
74	ZINC6220431	NNC(=O)c1ccc(NC(=O)c2cccc(Br)c2)cc1	-6.0	3.98E-05
75	ZINC7597126	CNC(=O)c1ccc(NC(=O)c2cccc(Br)c2)cc1	-5.8	5.58E-05
76	ZINC7597138	CNC(=O)c1ccc(NC(=O)c2cccc(I)c2)cc1	-5.4	1.10E-04
77	ZINC37016168	CNC(=O)c1ccc(NC(=O)c2cccc(N)c2)cc1	-5.7	6.60E-05
78	ZINC913167829	CNC(=O)c1ccc(NC(=O)c2cccc(N)c2)cc1	-5.9	4.71E-05
79	ZINC918554367	O=C(NO)c1ccc(NC(=O)c2cccc(Br)c2)cc1	-6.0	3.98E-05
80	ZINC1361848411	CNC(=O)c1ccc(NC(=O)c2cnnc(O)c2)cc1	-6.7	1.22E-05
81	ZINC225320	COC(=O)c1ccc(NC(=O)c2cccc(C)c2)cc1	-5.7	6.60E-05
82	ZINC1412056070	CNC(=O)c1ccc(NC(=O)c2cncc(Cl)c2)nc1	-6.0	3.98E-05
83	ZINC232562964	C/C=C/C(=O)c1cncnc1	-6.4	2.02E-05
84	ZINC307902593	C/C=C\C(=O)c1cncnc1	-4.8	3.02E-04
85	ZINC575549302	C/C=C/C(=O)c1ncccn1	-4.9	2.55E-04
86	ZINC606243471	C/C=C\C(=O)c1ncccn1	-4.7	3.57E-04
87	ZINC5132781	C/C=C/C(=O)c1cccnc1	-4.9	2.55E-04

88	ZINC195764880	C/C=C\C(=O)c1cccnc1	-4.7	3.57E-04
89	ZINC5606416	C/C=C/C(=O)c1cccc1	-4.9	2.55E-04
90	ZINC100017506	C/C=C\C(=O)c1cccc1	-5.0	2.15E-04
91	ZINC39051361	C/C=C\C(=O)c1ccncc1	-4.6	4.23E-04
92	ZINC218741164	C/C=C/C(=O)c1ccncc1	-4.9	2.55E-04
93	ZINC104591177	N/C=C\C(=O)c1cccc1	-5.1	1.82E-04
94	ZINC104179608	C[C@@H]/(C=C\c1cccc1)c1cccc1	-6.3	2.40E-05
95	ZINC137137124	Br[C@@H]/(C=C/c1cccc1)c1cccc1	-7.0	7.35E-06
96	ZINC137137162	Br[C@H]/(C=C/c1cccc1)c1cccc1	-6.8	1.03E-05
97	ZINC211718554	Br[C@@H]/(C=C\c1cccc1)c1cccc1	-6.2	2.84E-05
98	ZINC211718627	Br[C@H]/(C=C\c1cccc1)c1cccc1	-6.5	1.71E-05
99	ZINC701667672	C=C(NNc1cccc1)c1cccc1	-6.1	3.36E-05
100	ZINC238005334	C=C(CNc1cccc1)c1cccc1	-6.3	2.40E-05
101	ZINC254292786	CC(=NNc1cccc1)c1cccc1	-6.2	2.84E-05
102	ZINC779809490	CC(=NN=c1cc[nH]cc1)c1cccc1	-6.1	3.36E-05
103	ZINC4114245	CC(=NNc1cccc1)c1cccc1	-6.2	2.84E-05
104	ZINC21986171	C=C(CNc1cccc1)c1cccc1	-6.3	2.40E-05
105	ZINC33966416	CN(/N=C/c1cccc1)c1cccc1	-6.3	2.40E-05
106	ZINC722673979	CC(=NNc1cccc1)c1cccc1	-6.4	2.02E-05
107	ZINC59153539	CN(/N=C/c1cccc1)c1cccc1	-6.1	3.36E-05
108	ZINC389704350	CN(N=Cc1cccc1)c1cccc1	-6.2	2.84E-05
109	ZINC4265707	C[C@@H](NCc1cccc1)c1cccc1	-5.9	4.71E-05
110	ZINC70799990	Br[C@H](CCc1cccc1)c1cccc1	-5.8	5.58E-05
111	ZINC70799995	Br[C@@H](CCc1cccc1)c1cccc1	-5.6	7.82E-05
112	ZINC97513772	C[C@@H](SCc1cccc1)c1cccc1	-5.6	7.82E-05
113	ZINC219843649	C=CC(=O)Nc1ccc(NC(=O)c2cccnc2)cc1	-5.7	6.60E-05
114	ZINC265458181	C=CC(=O)Nc1ccc(C(=O)N[C@@H]2CC=CCC2)cc1	-5.9	4.71E-05
115	ZINC265458183	C=CC(=O)Nc1ccc(C(=O)N[C@H]2CC=CCC2)cc1	-6.0	3.98E-05
116	ZINC490540657	C=CC(=O)Nc1ccc(C(=O)Nc2cccc2)cc1	-6.0	3.98E-05
117	ZINC490673695	C=CC(=O)Nc1ccc(C(=O)Nc2cncnc2)cc1	-5.8	5.58E-05
118	ZINC685944904	C=CC(=O)Nc1ccc(NC(=O)c2cccc2)cc1	-6.2	2.84E-05
119	ZINC736024144	C=CC(=O)Nc1ccc(C(=O)Nc2cccnc2)cc1	-7.3	4.43E-06
120	ZINC1129597078	C=CC(=O)Nc1ccc(C(=O)Nc2ccnnc2)cc1	-6.0	3.98E-05
121	ZINC1150006794	C=CC(=O)Nc1ccc(C(=O)N[C@@H]2C=CCCC2)cc1	-6.0	3.98E-05
122	ZINC1150006795	C=CC(=O)Nc1ccc(C(=O)N[C@H]2C=CCCC2)cc1	-6.3	2.40E-05
123	ZINC1336680773	C=CC(=O)Nc1ccc(C(=O)Nc2cccnc2)cc1	-6.0	3.98E-05
124	ZINC1337569058	C=CC(=O)Nc1ccc(C(=O)Nc2cccc2)cc1	-6.4	2.02E-05
125	ZINC1353366517	C=CC(=O)Nc1ccc(C(=O)Nc2cccc2)cc1	-6.5	1.71E-05