



SUPPLEMENTARY MATERIAL TO
Monte Carlo optimization-based QSAR modeling of *Staphylococcus aureus* inhibitory activity of coumarin-1,2,3-triazole hybrids

KRISHNA N. MISHRA, HARISH C. UPADHYAY* AND POONAM VERMA

Laboratory of Chemistry, Department of Applied Sciences, Rajkiya Engineering College
(Affiliated with Dr. A.P.J. Abdul Kalam Technical University, Lucknow), Churk, Sonbhadra-
231206, India.

Table SI. List of Compounds with SMILES along with their antibacterial activity against *S. aureus* expressed in pMIC (-log MIC in µg/mL)

ID	SMILES	PMIC
1	<chem>Cc3ccc2c(Cn1nnc(N)c1C#N)cc(=O)oc2c3</chem>	0.39794
2	<chem>Cc3cc(C)c2c(Cn1nnc(N)c1C#N)cc(=O)oc2c3</chem>	0.09691
3	<chem>COc3ccc2oc(=O)cc(Cn1nnc(N)c1C#N)c2c3</chem>	-0.79588
4	<chem>N#Cc1c(N)nnn1Cc2cc(=O)oc4c2ccc3ccccc34</chem>	0.39794
5	<chem>Cc3ccc2oc(=O)cc(Cn1nnc(N)c1C#N)c2c3</chem>	0.39794
6	<chem>N#Cc1c(N)nnn1Cc3cc(=O)oc4ccc2ccccc2c34</chem>	-0.79588
7	<chem>CCOC(=O)c1c(C)nnn1Cc2cc(=O)oc3cc(C)ccc23</chem>	-0.49415
8	<chem>CCOC(=O)c1c(C)nnn1Cc2cc(=O)oc3cc(C)cc(C)c23</chem>	-1.39794
9	<chem>CCOC(=O)c1c(C)nnn1Cc2cc(=O)oc3ccc(OC)cc23</chem>	-0.79588
10	<chem>CCOC(=O)c1c(C)nnn1Cc2cc(=O)oc4c2ccc3ccccc34</chem>	0.09691
11	<chem>CCOC(=O)c1c(C)nnn1Cc2cc(=O)oc3ccc(C)cc23</chem>	0.09691
12	<chem>CCOC(=O)c1c(C)nnn1Cc3cc(=O)oc4ccc2ccccc2c34</chem>	0.39794
13	<chem>Cc3ccc2c(Cn1nnc(C)c1C(=O)O)cc(=O)oc2c3</chem>	-0.79588
14	<chem>Cc3cc(C)c2c(Cn1nnc(C)c1C(=O)O)cc(=O)oc2c3</chem>	-0.79588
15	<chem>COc3ccc2oc(=O)cc(Cn1nnc(C)c1C(=O)O)c2c3</chem>	-0.49415
16	<chem>Cc4nnn(Cc1cc(=O)oc3c1ccc2ccccc23)c4C(=O)O</chem>	0.69897
17	<chem>Cc3ccc2oc(=O)cc(Cn1nnc(C)c1C(=O)O)c2c3</chem>	0.09691
18	<chem>Cc4nnn(Cc2cc(=O)oc3ccc1ccccc1c23)c4C(=O)O</chem>	0.39794
19	<chem>CC[N+](CC)(CC)CCCCCCCCCOc4cn(Cc2cc(=O)oc3cc1OC(C)(C)CCc1cc23)nn4</chem>	-1.07918
20	<chem>Cc3cc(=O)oc4cc(OCC(O)Cn2nnc1ccccc12)ccc34</chem>	-1.20412
21	<chem>O=c4cc(OCc2cn(Cc1ccc(N(=O)=O)cc1)nn2)c3ccccc3o4</chem>	-0.90309
22	<chem>O=c4cc(OCc2cn(Cc1ccc(N(=O)=O)c1)nn2)c3ccccc3o4</chem>	-0.90309

* Corresponding author. E-mail: harishcu@recsonbhadra.ac.in

23	<chem>O=c4cc(OCc2cn(Cc1ccc(Cl)cc1)nn2)c3ccccc3o4</chem>	-1.20412
24	<chem>O=c4cc(OCc2cn(Cc1cccc(Cl)c1)nn2)c3ccccc3o4</chem>	-0.90309
25	<chem>O=c4cc(OCc2cn(Cc1ccc(Br)cc1)nn2)c3ccccc3o4</chem>	-1.20412
26	<chem>COc4ccc3oc(=O)cc(Cn2cc(C(O)c1cccc1)nn2)c3c4</chem>	-1.57403
27	<chem>Cc4ccc3oc(=O)cc(Cn2cc(C(O)c1cccc1)nn2)c3c4</chem>	-1.273
28	<chem>CC(C)(C)c4ccc3oc(=O)cc(Cn2cc(C(O)c1cccc1)nn2)c3c4</chem>	-0.96848
29	<chem>O=c5cc(Cn2cc(C(O)c1cccc1)nn2)c4cc(Cc3ccccc3)ccc4o5</chem>	-1.273
30	<chem>O=c5cc(Cn2cc(C(O)c1cccc1)nn2)c4cc3ccccc3cc4o5</chem>	-1.273
31	<chem>Cc3cc(OCc2cn(Cc1ccc(N(=O)=O)cc1)nn2)cc4oc(=O)ccc34</chem>	-0.90309
32	<chem>Cc3cc(OCc2cn(Cc1ccc(N(=O)=O)c1)nn2)cc4oc(=O)ccc34</chem>	-0.90309
33	<chem>Cc3cc(OCc2cn(Cc1ccc(Cl)cc1)nn2)cc4oc(=O)ccc34</chem>	-0.90309
34	<chem>Cc3cc(OCc2cn(Cc1cccc(Cl)c1)nn2)cc4oc(=O)ccc34</chem>	-1.20412
35	<chem>Cc3cc(OCc2cn(Cc1ccc(Br)cc1)nn2)cc4oc(=O)ccc34</chem>	-1.20412
36	<chem>Cc3cc(OCc2cn(Cc1cccc1)nn2)cc4oc(=O)ccc34</chem>	-0.90309
37	<chem>Cc5ccc4oc(=O)cc(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)c4c5</chem>	-1.20412
38	<chem>Cc5ccc4c(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)cc(=O)oc4c5</chem>	-1.49485
39	<chem>O=c5cc(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)c4cc(Cl)ccc4o5</chem>	-0.60206
40	<chem>O=c5cc(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)c4ccc(Cl)cc4o5</chem>	-0.60206
41	<chem>COc5ccc4oc(=O)cc(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)c4c5</chem>	-0.90309
42	<chem>COc5ccc4c(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)cc(=O)oc4c5</chem>	-1.20412
43	<chem>O=c5cc(COC(Cn2cc(c1cccc1)nn2)c3ccc(Cl)cc3Cl)c4ccc(Br)cc4o5</chem>	-1.20412
44	<chem>O=C(O)c4ccc(n3cc(CNC(=O)c2cc1ccc(=O)oc1cc2O)nn3)cc4</chem>	0.18709
45	<chem>COC(=O)c6cc5cc(C#CCCCC)C4cn(C3(C(C)C)O)c2cc1oc(=O)ccc1cc2C3=O)nn4)c(=O)oc5cc6O</chem>	-1.83727
46	<chem>COC(=O)c2cc1ccc(=O)oc1cc2c4cn(c3ccc(C(=O)O)cc3)nn4</chem>	-0.79796
47	<chem>Cc4cc(=O)oc5cc(OCc3cn(C1CCCC1O)c2ccnc2Cl)nn3)ccc45</chem>	-1
48	<chem>Cc4cc(=O)oc5cc(OCc3cn(C1CCCC1O)c2ccnc2Cl)nn3)ccc45</chem>	-1
49	<chem>Cc3cc(=O)oc4cc(OCc2cn(Cc1ccc(F)cc1)nn2)ccc34</chem>	-0.69897
50	<chem>Cc3cc(=O)oc4cc(OCc2cn(Cc1ccc(C#N)cc1)nn2)ccc34</chem>	-1.87506
51	<chem>CC[N+](CC)(CC)CCCCCCCCCOCc4cn(Cc2cc(=O)oc3c(OC)c1OC(C)C)CCc1cc23)nn4</chem>	-1.74036

Table SII. Distribution of compounds in Training, Invisible training, Calibration, and Validation set in three random splits.

Split number	Training	Invisible training	Calibration	Validation
Split 1	3, 6, 8, 12, 17, 20, 21, 24, 26, 34, 36, 40, 46, 48, 50, 51	1, 9, 10, 11, 14, 16, 25, 29, 30, 33, 37, 41, 45, 47	2, 4, 7, 13, 15, 28, 31, 35, 38, 43, 49	5, 18, 19, 22, 23, 27, 32, 39, 42, 44
Split 2	2, 4, 8, 13, 16, 26, 31, 34, 37, 42, 43, 44, 46, 47, 50	1, 6, 10, 11, 15, 17, 23, 25, 28, 29, 32, 39, 41, 48	3, 5, 7, 9, 14, 24, 27, 38, 40, 45, 49	12, 18, 19, 20, 21, 22, 30, 33, 35, 36, 51
Split 3	5, 6, 7, 13, 15, 23, 24, 28, 38, 39, 40	3, 9, 14, 19, 22, 25, 27, 29, 30, 35, 45, 46, 48, 49, 50	16, 17, 20, 31, 33, 34, 42, 43, 44, 51, 2, 10, 11, 12	1, 4, 8, 18, 21, 26, 32, 36, 37, 41, 47

Table SIII. Structural attributes (Good and bad fingerprints) of activity against *S. aureus* in three runs of Monte Carlo optimization

SAk	CWs P1	CWs P2	CWs P3	Defect [SAk]
Promoters of activity (M4)				
EC0-O...1...	1.3803	1.0059	0.3405	0.0000
c...3...c...	1.8324	1.1794	6.1565	0.0036
[xyyx0]....	0.4606	0.4647	4.9302	0.0000
c...2.....	0.9736	0.0192	1.9032	0.0031
[xyzyx0]....	0.9314	1.0758	1.0885	0.0066
n...n.....	1.3189	0.9413	2.9101	0.0031
O...=...(...	0.2947	0.1729	1.8528	0.0071
c...c...c...	1.4163	0.9521	2.0173	0.0029
BOND10000000	1.6066	1.9218	3.1289	0.0026
HALO00000000	1.3248	1.3766	0.0045	0.0081
NOSP01000000	1.5227	1.2056	2.2937	0.0151
c...c...2...	1.7570	2.1183	1.5168	0.0115
n...(C...	1.3563	0.2484	2.0366	0.0198
o...(O...	0.5513	0.2877	0.5311	0.0065
c...1...(...	0.0755	0.0070	0.8339	0.0123
C...1.....	1.2124	1.3100	0.3349	0.0094
c...3...4...	1.4420	0.9888	0.9371	0.0387
c...C...(...	1.6156	0.5518	1.6063	0.0157
[xyx4].....	0.7896	1.1156	0.9742	0.0120
n...1.....	0.5169	0.6534	1.4766	0.0189
n...C...(...	0.5010	1.1322	1.6241	0.0274
3...c...2...	1.6260	1.2054	0.9456	0.0289
C...(=...	1.3359	1.4561	1.2091	0.0275
N...(.....	1.1769	1.1051	0.2718	0.0503
c...(N...	1.1440	1.1733	0.9345	0.0503
Promoters of activity (M10)				
EC1-C...6...	0.9202	0.9533	0.8767	0.0000
EC1-C...9...	0.9054	1.3435	1.0562	0.0000
EC1-N...5...	0.4271	2.8375	1.4485	0.0000
[xyyx0]....	1.5770	1.8835	2.5635	0.0000
c...(=...	0.1594	1.0513	1.1669	0.0133
BOND10000000	1.4929	2.5504	1.1049	0.0081
c...c...2...	1.2138	1.5640	0.8367	0.0039
[xyzyx0]....	0.4841	1.0311	0.4801	0.0077
1...c...(...	0.8316	1.3412	0.9746	0.0150
n...C...(...	1.3817	0.1151	0.6553	0.0153
3...c...(...	0.2742	0.9664	1.3977	0.0043
4...c...(...	0.4650	1.7684	1.4240	0.0275
C...1.....	0.0756	1.1968	0.8009	0.0196
C...c...2...	0.4792	3.0906	1.6450	0.0043
EC1-Cl...6...	0.6074	1.6550	0.8792	0.0101

NOSP11000000	0.0556	1.2363	1.2616	0.0303
3...(.....	0.2700	1.2395	0.5709	0.0502
C...O...(...	1.1106	0.8134	1.1900	0.0035
EC1-O...4...	0.2074	1.1468	1.4376	0.0310
N...(.....	0.9440	0.2287	2.3996	0.0189
c...(Cl...	0.3360	1.7833	1.2956	0.0117
c...(N...	1.1713	1.6040	0.5362	0.0189
c...C...(...	0.1849	2.4469	1.5329	0.0208
n...1.....	1.3319	1.3245	0.1696	0.0251
n...c...2...	0.4277	0.4810	0.3850	0.0208
n...n...1...	1.0808	0.9214	1.1837	0.0251
(...N...(...	0.7168	1.0285	0.2306	0.0081
EC1-N...2...	0.4635	0.2711	0.5377	0.0163
O...(O...	0.4204	0.6575	1.1037	0.0364
c...(3...	0.1966	2.1458	1.3361	1.0000
c...o...4...	1.1627	1.5654	0.2008	1.0000
[xyx5].....	0.8728	0.9104	1.4503	1.0000
(...N...#...	0.0323	1.5227	0.7897	0.0442
3...2.....	0.7651	1.6091	1.2781	0.0442
4...c...2...	1.9553	1.8426	3.3051	1.0000
C...c...4...	1.0932	1.2439	0.8365	0.0442
C...n...1...	0.7667	1.3442	0.9407	0.0348
EC1-N...8...	1.5275	1.1218	1.2967	1.0000
c...1...C...	0.2776	1.1237	1.9595	0.0348
c...2...3...	1.0613	1.1736	1.1102	0.0442
Promoters of activity (M11)				
c...(.....	1.1802	0.5233	1.0124	0.0000
c...1.....	2.1678	1.1924	1.1989	0.0034
c...2.....	0.8964	1.8132	0.4523	0.0037
c...c...3...	0.2430	0.3123	1.3495	0.0079
[xyyx0]....	11.8616	9.4184	6.5641	0.0000
n...n.....	2.9301	1.8750	4.2672	0.0000
1...c...(...	1.1262	3.4869	2.3150	0.0340
BOND10000000	7.3038	7.3199	6.9298	0.0076
c...1...c...	4.0590	5.3725	4.8629	0.0081
[xyzyx0]....	4.1982	5.7704	3.7127	0.0160
n...n...(...	2.2563	1.6402	1.6530	0.0087
=...O...(...	0.2761	0.3821	0.1549	0.0183
O...=...(...	0.8956	0.6069	0.9192	0.0183
c...(O...	1.5929	0.5332	1.3473	0.0192
n...C...(...	1.8772	1.5804	2.7283	0.0357
n...C.....	1.4897	3.5828	0.3799	0.0357
n...(1...	2.1957	2.1046	0.6110	0.0198
Adversaries of activity (M4)				
EC0-C...3...	-0.0063	-0.0650	-0.7341	0.0000
EC0-C...4...	-0.0496	-0.1014	-0.8191	0.0000

EC0-H...1...	-0.1827	-0.4861	-0.0113	0.0000
EC0-N...2...	-2.1326	-0.3570	-2.7170	0.0000
C...(.....	-0.0407	-0.3134	-0.7258	0.0047
O...(.....	-0.0597	-0.2022	-0.8645	0.0047
c...1.....	-0.3059	-0.2583	-0.7519	0.0037
n...(.....	-0.4778	-0.2105	-0.8867	0.0079
n...n...(...	-0.6126	-0.0923	-1.5594	0.0081
c...4...c...	-0.4408	-0.7683	-1.1420	0.0194
c...c...4...	-1.5229	-0.4043	-0.7252	0.0156
c...(..C...	-0.4640	-0.2863	-0.8204	0.0117
C...c...2...	-0.2957	-0.2947	-0.1831	0.0115
c...C...O...	-0.2511	-0.4756	-0.6577	0.0343
n...n...2...	-0.2690	-0.4488	-0.9846	0.0123
C...C.....	-0.4162	-0.0034	-0.0894	0.0292
NOSP11000000	-0.4989	-1.0109	-0.0582	0.0536
o...c...4...	-0.6194	-0.5333	-0.2237	0.0503
Adversaries of activity (M10)				
EC1-C...7...	-0.3739	-0.2071	-0.3508	0.0000
EC1-H...4...	-0.3191	-0.1586	-0.2877	0.0000
c...c...(...	-0.4745	-0.2398	-0.3352	0.0000
=...(.....	-0.0985	-0.2175	-0.0736	0.0133
=...O...(...	-0.5946	-0.3410	-0.9036	0.0133
c...c...1...	-0.0411	-0.1527	-0.0192	0.0145
EC1-O...7...	-0.6302	-0.5737	-0.0433	0.0035
n...(..1...	-0.4972	-0.2252	-0.1054	0.0048
C...c...3...	-0.2623	-0.3367	-0.5491	0.0208
(..C...(...	-0.3545	-0.2937	-0.1888	0.0152
(...O...(...	-0.2777	-0.8833	-0.0415	0.0208
C...n...2...	-0.1559	-0.7780	-0.3644	0.0035
c...5...c...	-0.5686	-0.6239	-0.4424	0.0035
c...c...5...	-0.8525	-0.2827	-0.3115	0.0035
C...(..C...	-0.3105	-0.9544	-0.8406	0.0162
N...#...C...	-0.1494	-1.6585	-1.4759	0.0163
c...O.....	-0.8582	-2.3522	-1.0626	0.0081
o...c...1...	-0.4978	-0.4420	-0.4747	1.0000
Adversaries of activity (M11)				
O...=.....	-0.8329	-1.3695	-1.4543	0.0000
c...3...c...	-2.3114	-0.1758	-1.6712	0.0038
c...c.....	-1.0851	-0.3990	-1.1745	0.0000
c...c...c...	-0.0236	-1.4852	-0.1720	0.0079
C...(.....	-0.6451	-1.2806	-0.6066	0.0047
O...(.....	-0.8947	-0.7138	-0.6053	0.0098
NOSP01000000	-0.2907	-0.1564	-0.9909	0.0069
c...(..C...	-1.6102	-1.2066	-1.3291	0.0098
O...C.....	-1.9894	-2.4534	-2.7427	0.0069
c...(..=...	-1.0120	-1.1744	-2.8074	0.0189

c...C.....	-0.9450	-0.9782	-0.4993	0.0109
HALO00000000	-1.0185	-1.3042	-0.7699	0.0139
n...n...2...	-2.7940	-0.4582	-0.4058	0.0117

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