

## Article

# Blue Biotechnology: Computational Screening of *Sarcophyton* Cembranoid Diterpenes for SARS-CoV-2 Main Protease Inhibition

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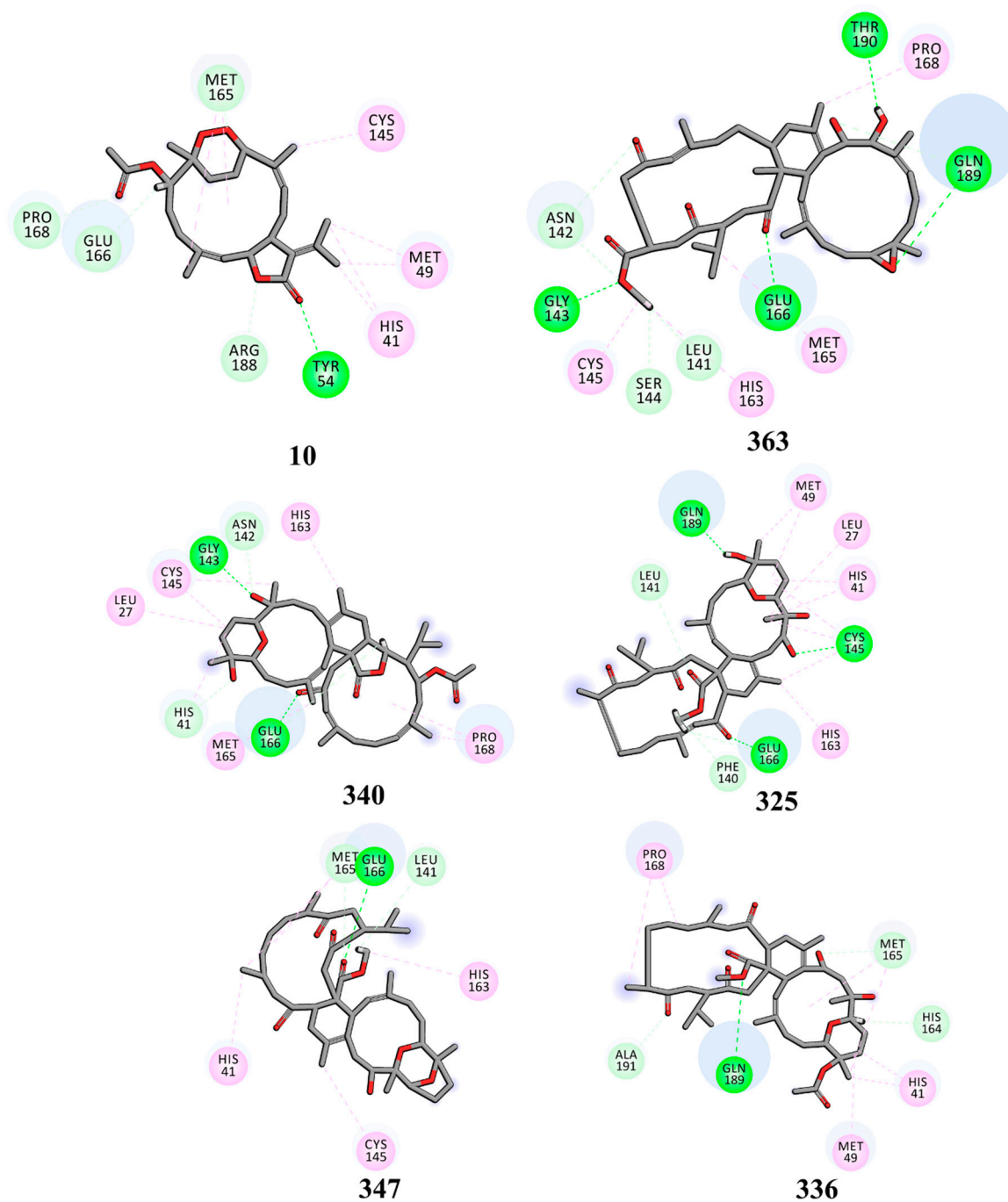
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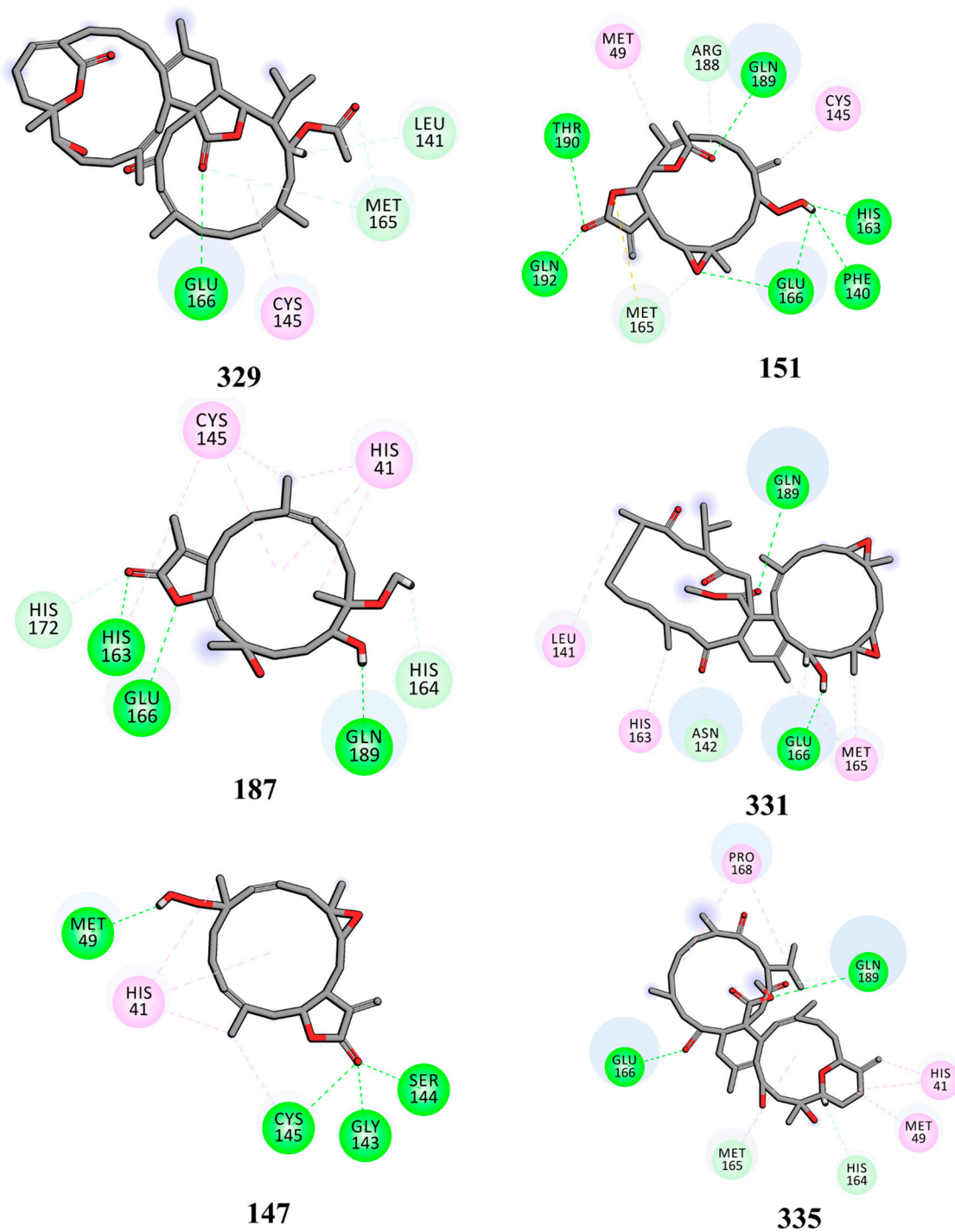
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<sup>15</sup> Pharmacognosy Group, Department of Pharmaceutical Biosciences, Uppsala University, Biomedical Centre, Box 574, 751 23 Uppsala, Sweden

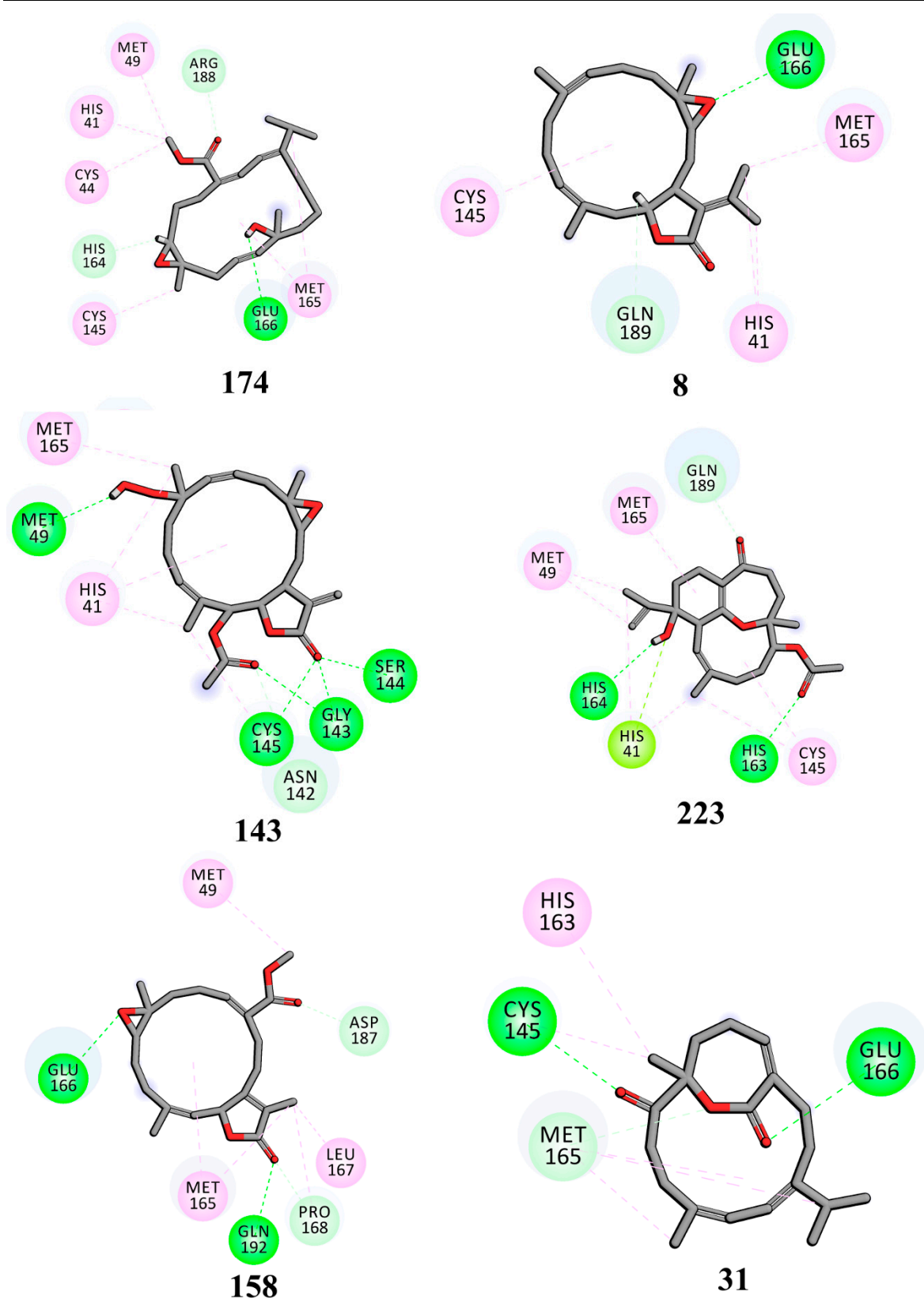
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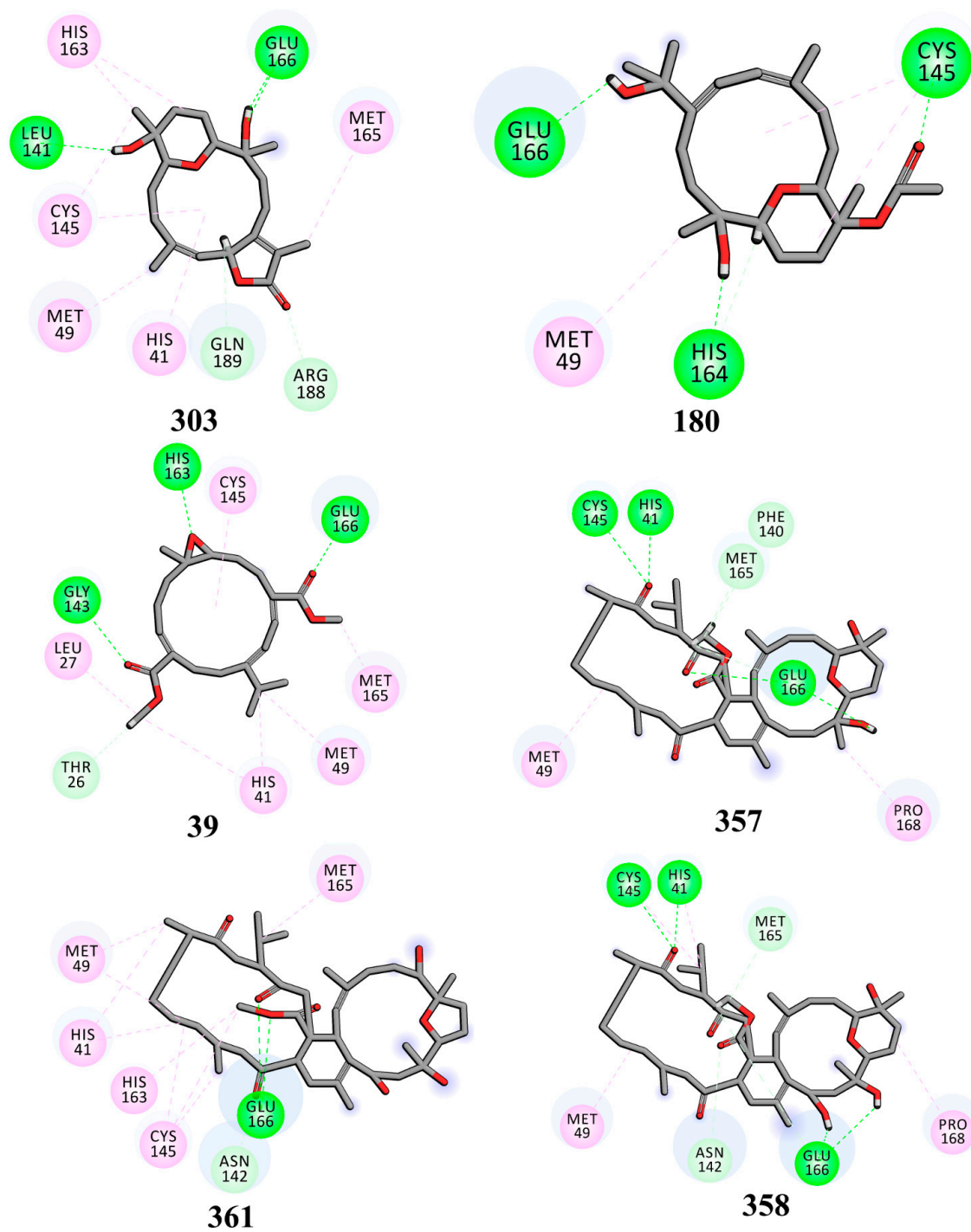
**Figure S1.** 2D representations of interactions of darunavir and the top 59 potent *Sarcophyton* cembranoid diterpenes metabolites with the proximal amino acid residues of SARS-CoV-2 main protease (M<sup>pro</sup>).



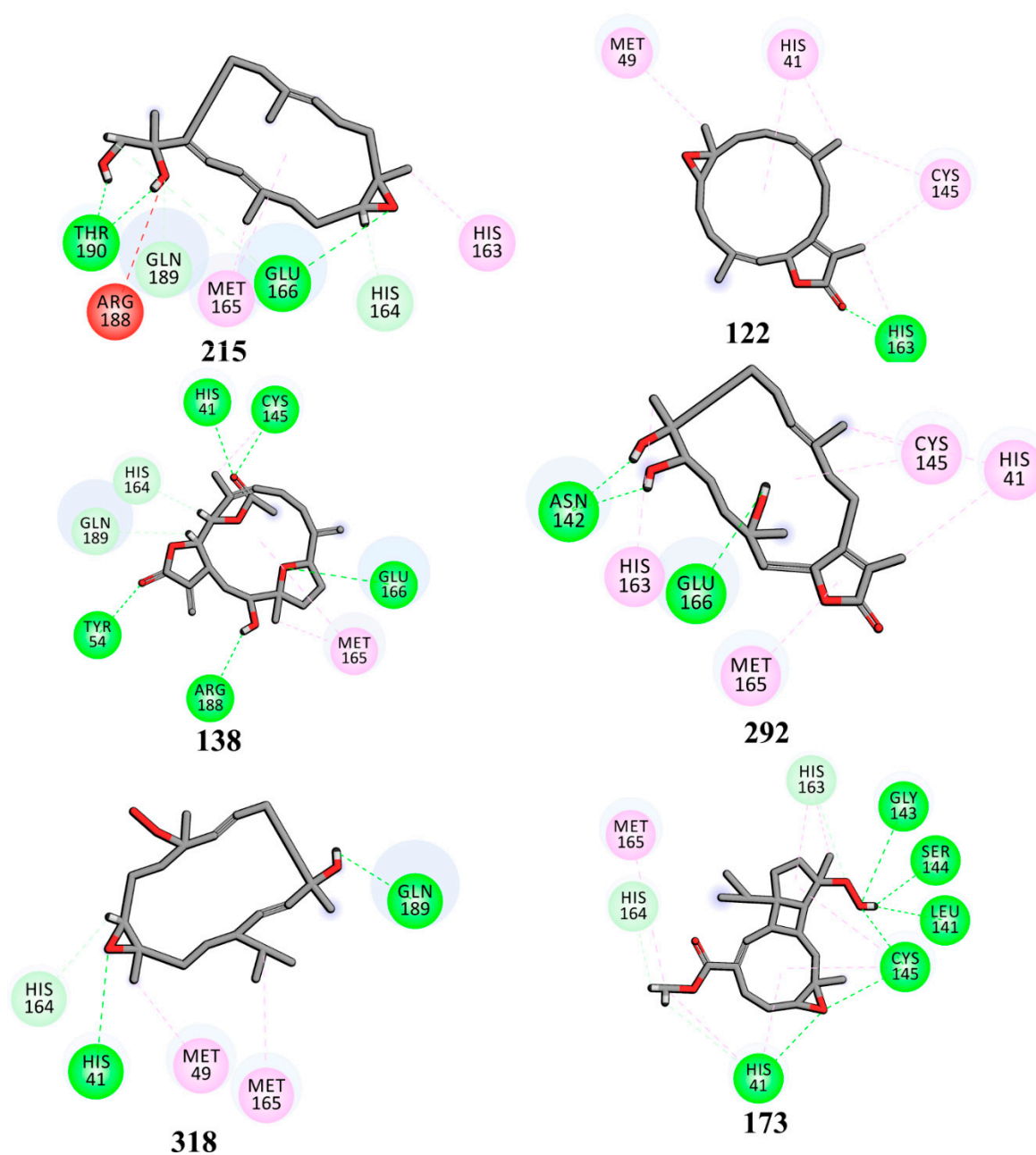
**Figure S1. Continued.**



**Figure S1.** *Continued.*



**Figure S1.** *Continued.*



**Figure S1.** *Continued.*

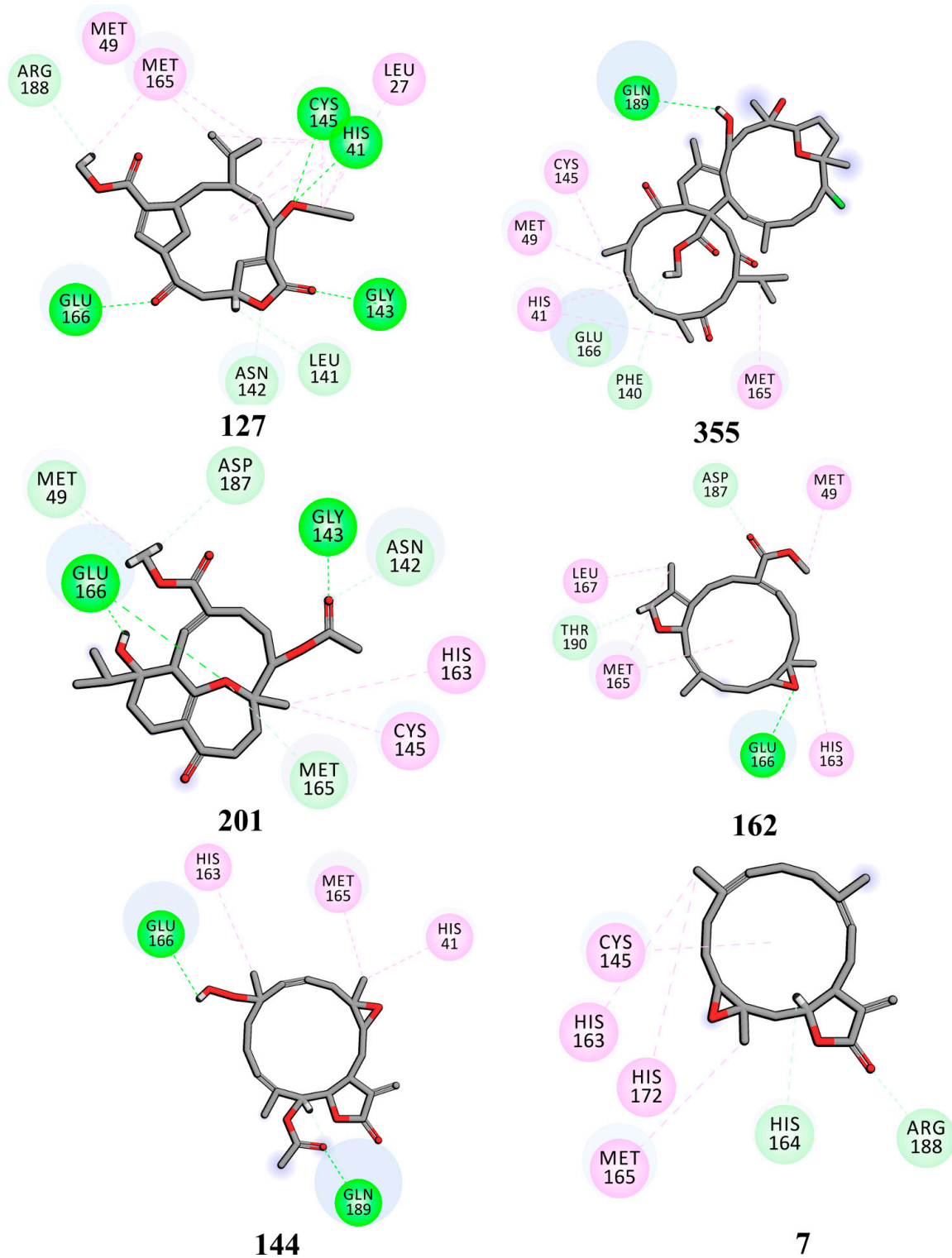
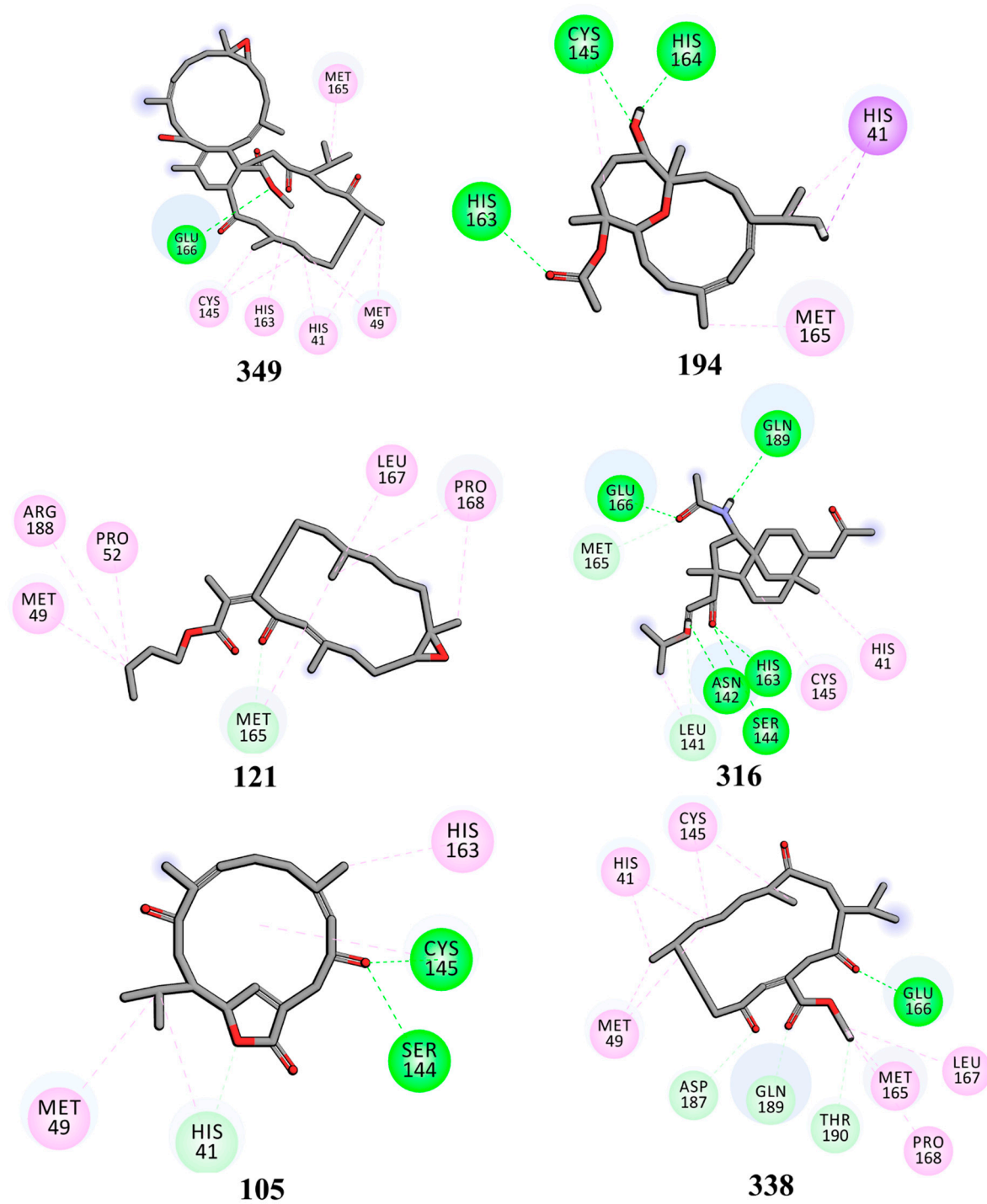
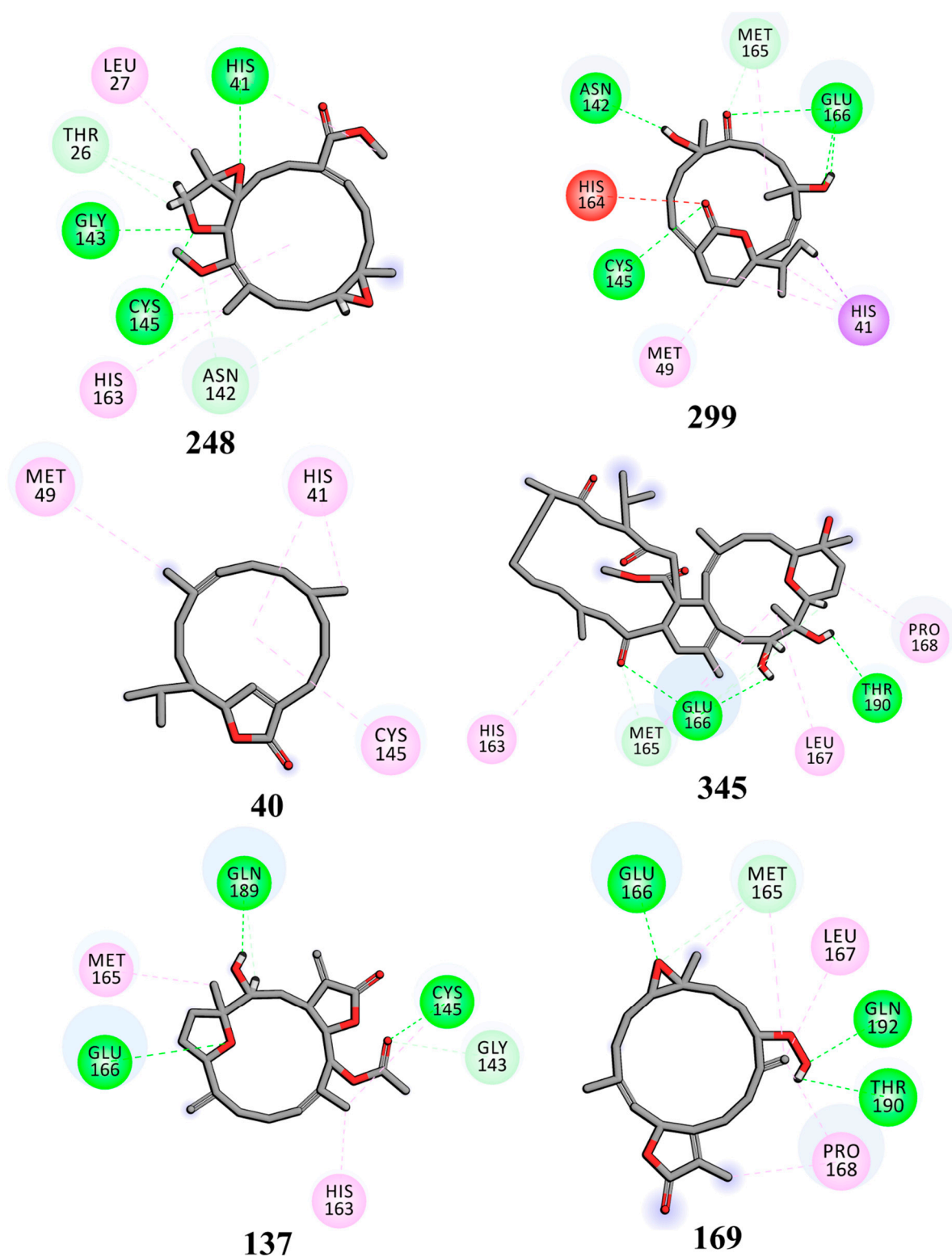


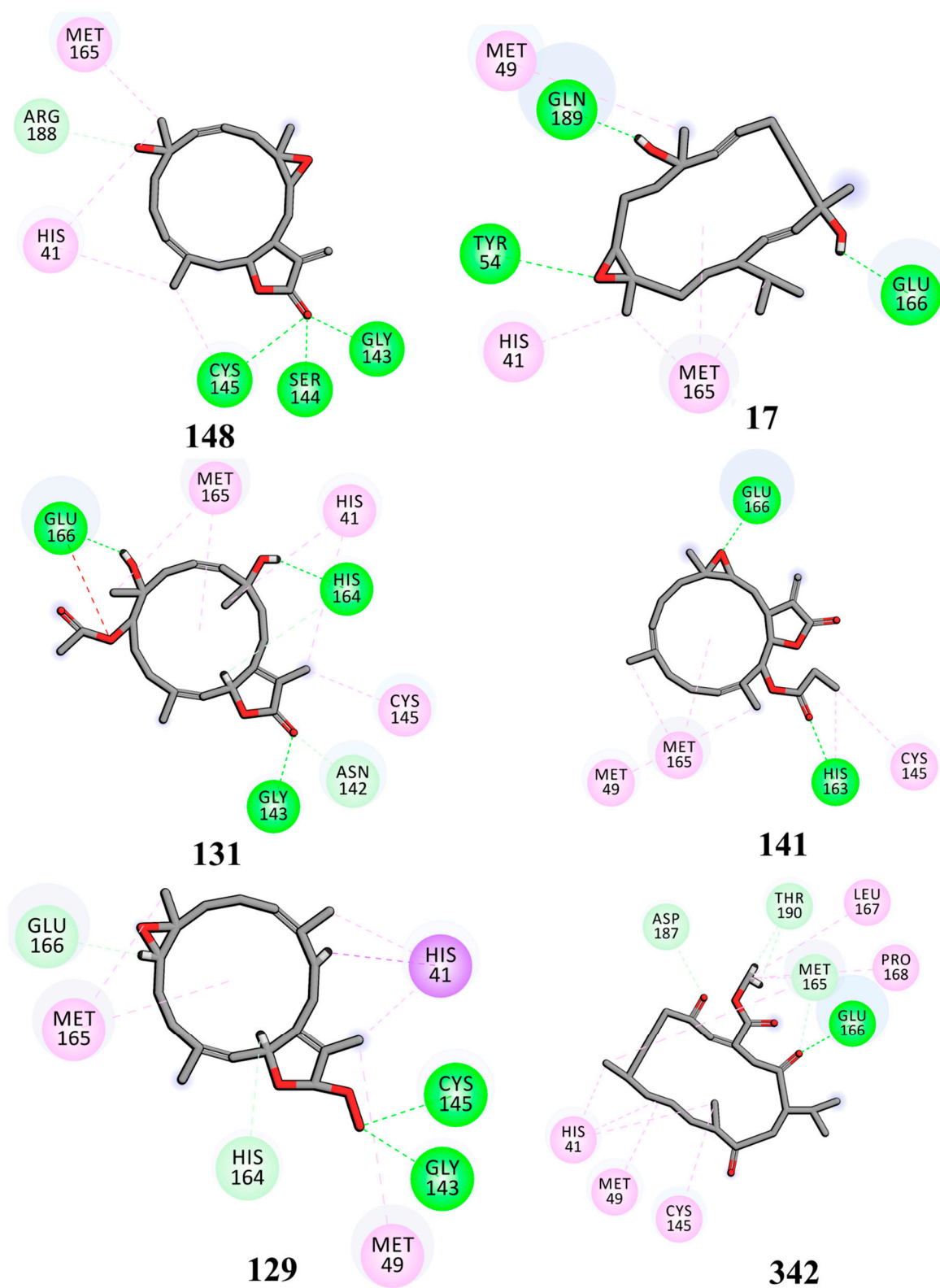
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**Figure S1.** *Continued.*



**Figure S1.** *Continued.*



**Figure S1. Continued.**

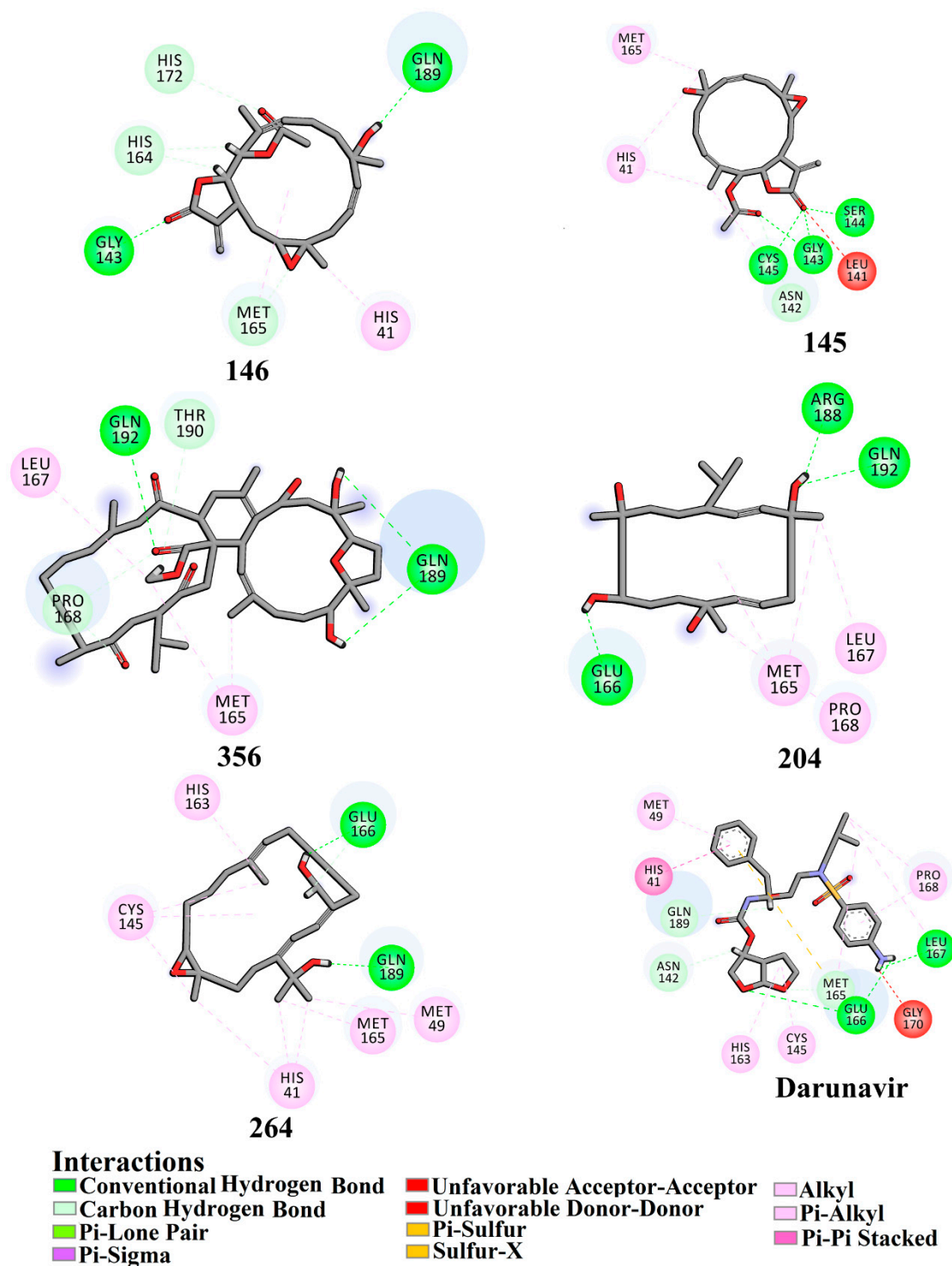
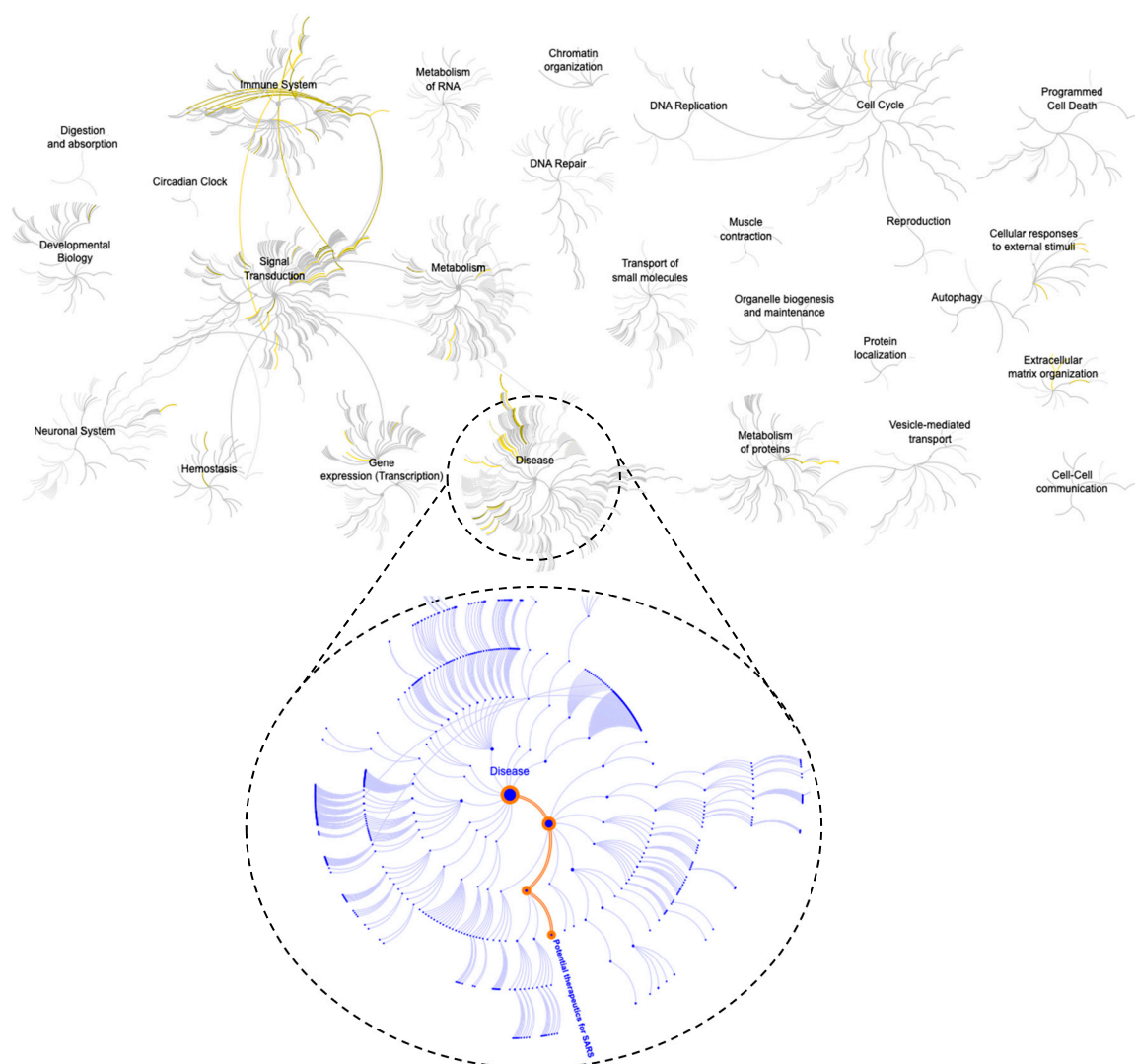
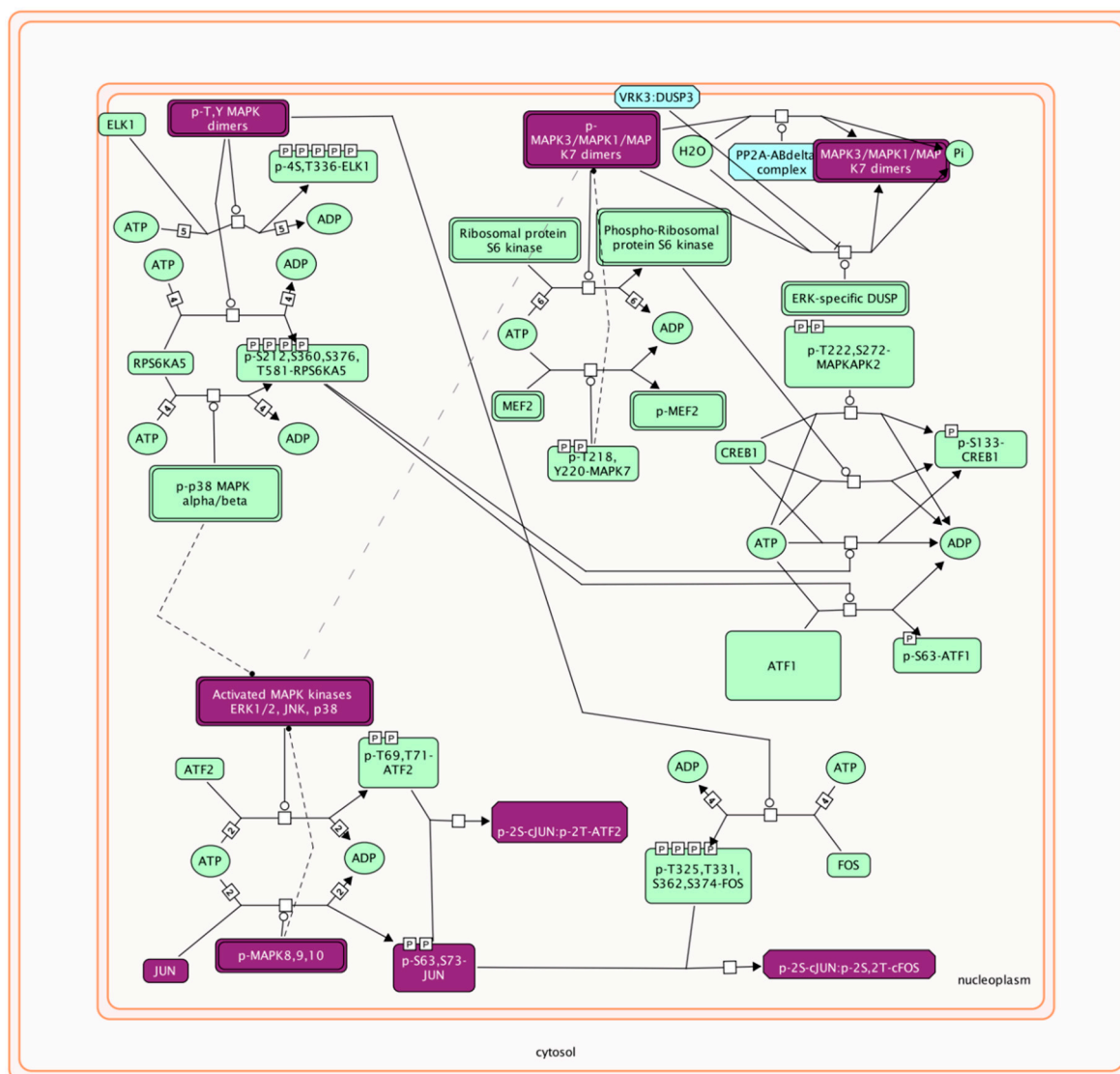


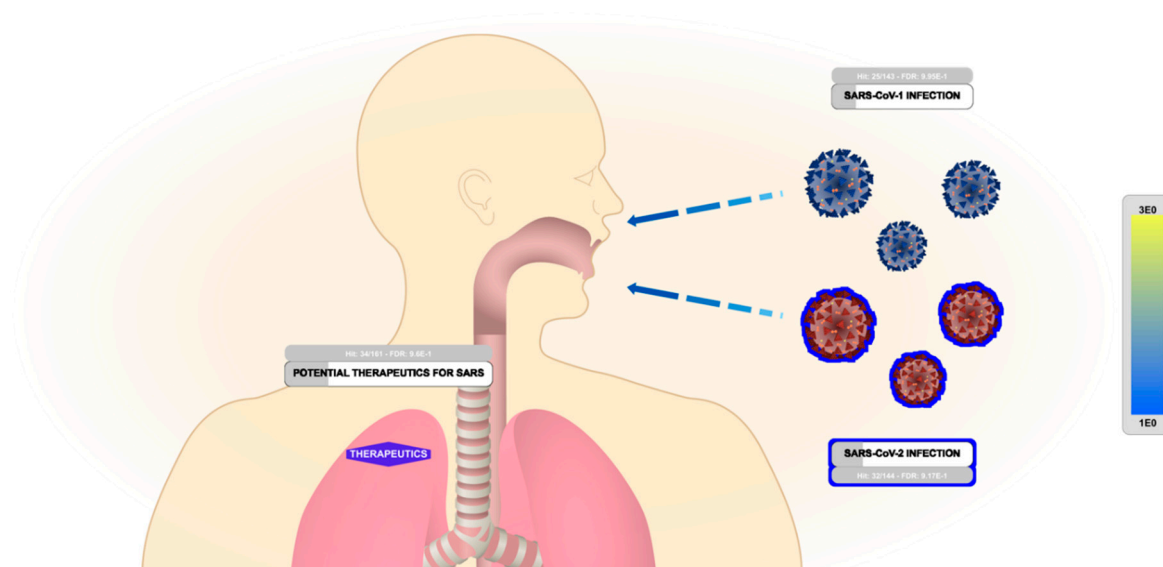
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**Figure S2.** A genome-wide overview of the Reactome Pathway Analysis (RPA) results for the top 20 genes targets stimulated by bislatumlide A (**340**) against SARS-CoV-2. Pathways are organized in a hierarchy form. The light grey color indicates that these pathways are not significantly over-represented. In comparison, light yellow color indicates that these pathways are significantly over-represented by the input gene dataset.

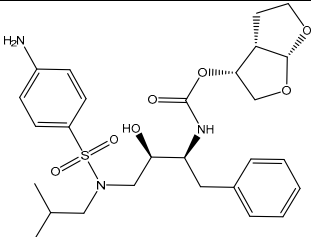
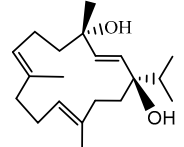
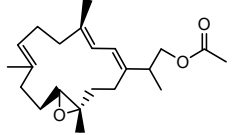
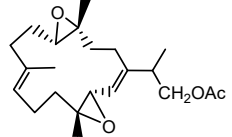
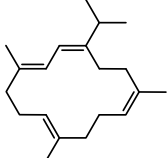
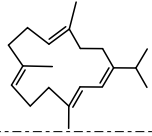
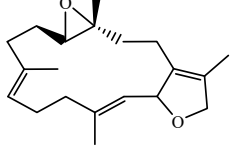
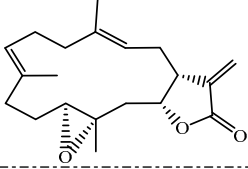
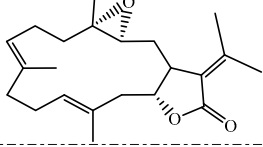
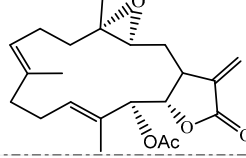


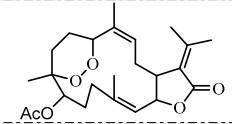
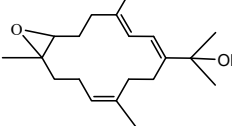
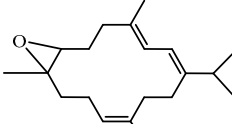
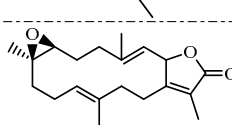
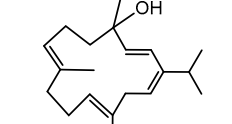
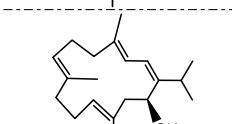
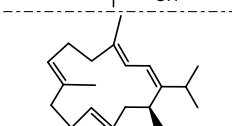
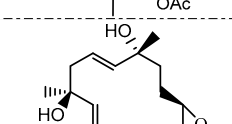
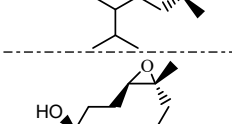
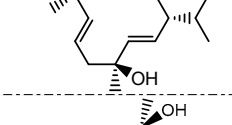
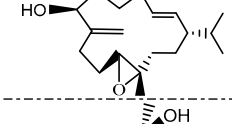
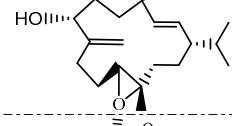
**Figure S3.** Pathway diagram analysis for enzymes/signals of the top 10 genes products/targets (highlighted in red) stimulated by bislatumlide A (340).

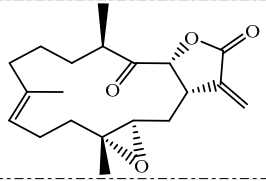
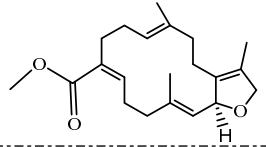
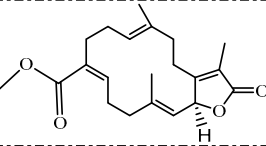
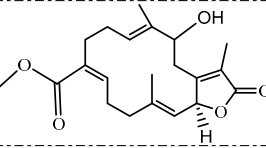
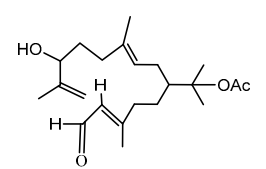
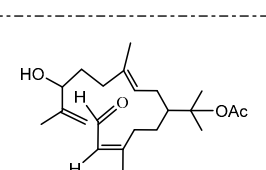
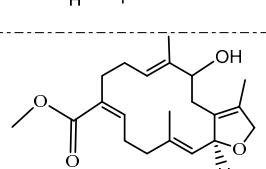
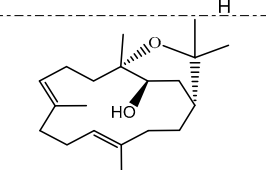
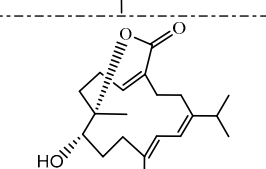
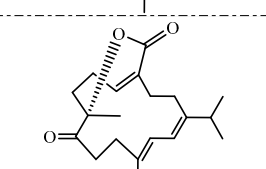
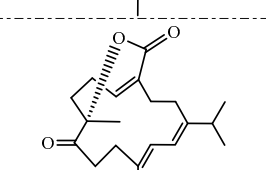


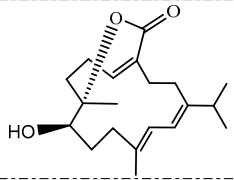
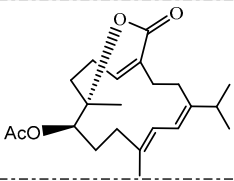
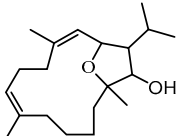
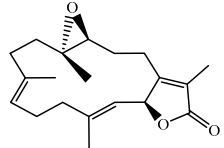
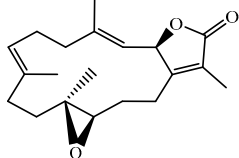
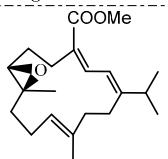
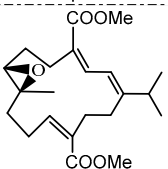
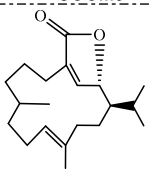
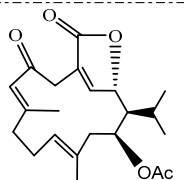
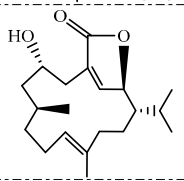
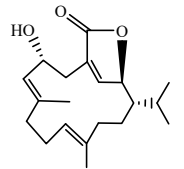
**Figure S4.** A diagrammatic model shows the potential therapeutic level of bislatumlide A (340) against SARS-CoV-2 viral infection.

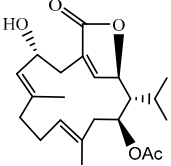
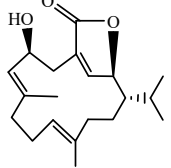
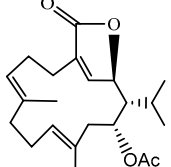
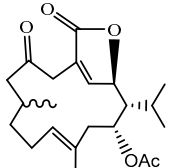
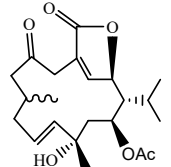
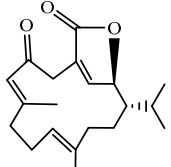
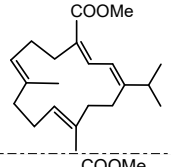
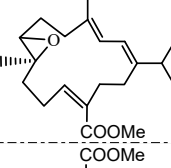
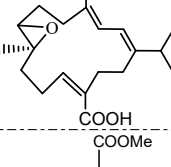
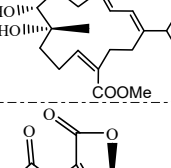
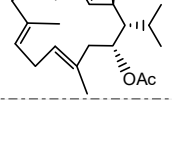
**Table S1.** Estimated docking score (in kcal/mol) for darunavir and the investigated *Sarcophyton* cembranoid diterpenes metabolites towards SARS-CoV-2 main protease (M<sup>pro</sup>)<sup>a</sup>.

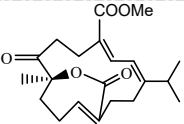
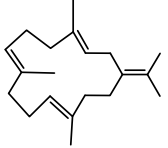
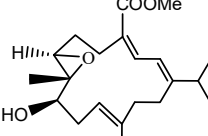
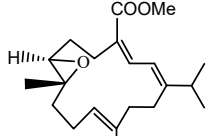
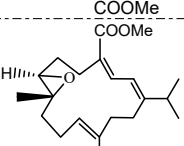
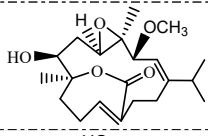
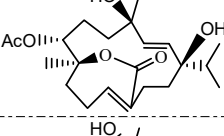
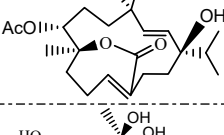
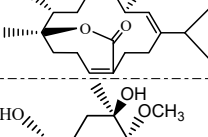
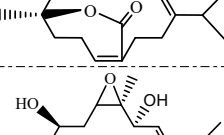
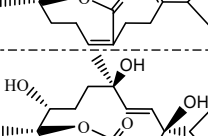
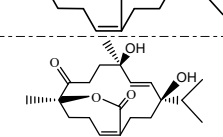

No.	Compound Name	Soft Coral	Chemical Structure	Docking Score (kcal/mol)
	Darunavir	-----		-8.2
1	Sarcophytol T	<i>Sarcophyton ehrenbergi</i>		-7.7
2	(1E,3E,7E,11R*12R*)-15-(acetoxymethyl)cembra-11,12-epoxy-1,3,7-triene	<i>Sarcophyton ehrenbergi</i>		-7.9
3	(11S*,12S*)-15-(acetoxymethyl) cembra-3,4:11,12-diepoxy-1,7-diene	<i>Sarcophyton ehrenbergi</i>		-7.6
4	Isonocembrene A	<i>Sarcophyton ehrenbergi</i>		-7.5
5	Neocembrane A	<i>Sarcophyton ehrenbergi</i>		-7.7
6	(2S*,11R*,12R*)-isosarcophytoxide	<i>Sarcophyton ehrenbergi</i>		-8.1
7	Crassolide	<i>S. crassocaule</i>		-8.5
8	Sarcocrassolide A	<i>S. crassocaule</i>		-9.0
9	13-acetoxysarcocrassolide	<i>S. crassocaule</i>		-7.4

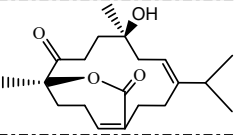
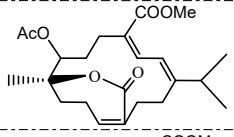
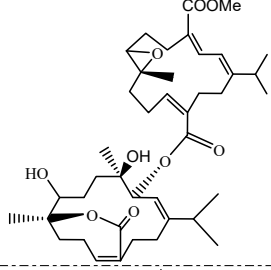
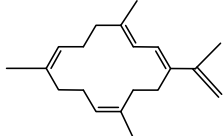
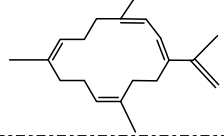
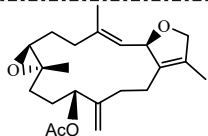
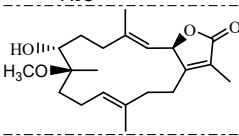
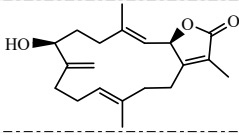
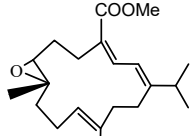
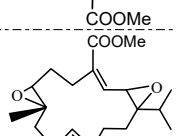
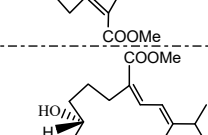
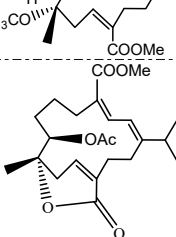
10	Denticulatolide	<i>S. crassocaule</i> <i>Sarcophyton</i> sp.		-9.9
11	7,8-epoxy-1(E),3(E),11(E)cembratrien-15-ol	<i>S. trocheliophorum</i>		-7.8
12	7,8-epoxy1(E),3(E),11(E)-cembratriene	<i>S. trocheliophorum</i>		-7.6
13	Sarcophin	<i>S. trocheliophorum</i>		-7.1
14	Acutanol	<i>S. acutangulum</i>		-7.8
15	Sarcophytol A	<i>S. acutangulum</i>		-7.5
16	Sarcophytol A acetate	<i>S. infundibuliforme</i>		-7.0
17	(1S,2E,4R,6E,8S,11S,12S)-11,12-Epoxy-2,6-cembrane-4,8-diol	<i>Sarcophyton</i> sp.		-8.3
18	(1S,2E,4R,6E,8R,11S,12S)-11,12-Epoxy-2,6-cembrane-4,8-diol	<i>Sarcophyton</i> sp.		-8.2
19	(1S,2E,4R,7S)-11,12-Epoxy-2,8(19)-cembradiene-4,7-diol	<i>Sarcophyton</i> sp.		-8.2
20	(1S,2E,4R,7R)-11,12-Epoxy-2,8(19)-cembradiene-4,7-diol	<i>Sarcophyton</i> sp.		-8.1
21	Sarcophycrassolide A	<i>S. crassocaule</i>		-7.9

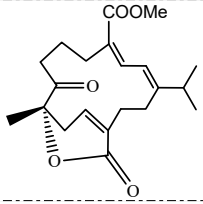
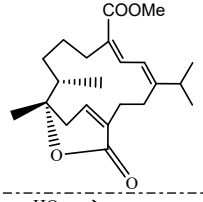
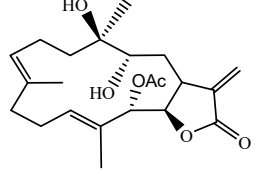
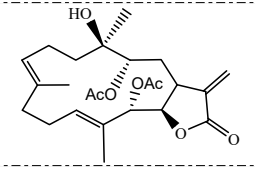
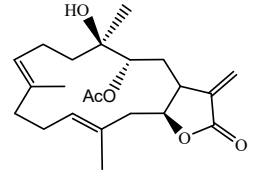
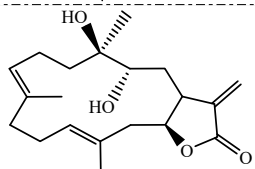
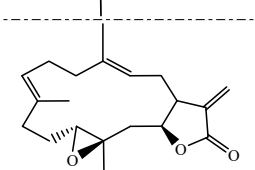
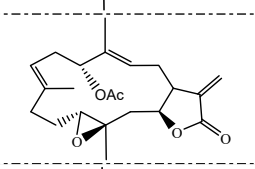
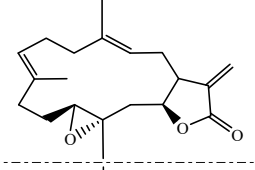
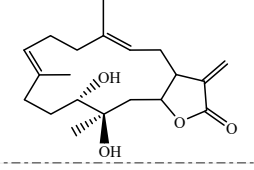
22	Sacophyocrassolide B	<i>S. crassocaule</i>		-7.8
23	13-dehydroxysarcoglaucol	<i>S. cherbonnieri</i>		-7.4
24	13-dehydroxysarcoglaucol-16-one	<i>S. cherbonnieri</i>		-8.1
25	Sarcoglaucol-16-one	<i>S. cherbonnieri</i> <i>S. ehrenbergi</i>		-7.8
26	(3E)-7-hydroxy-4,8,15,15-tetramethyl-1-[(E)-12-methyl-10-oxo-12-pentenyl]-3,8-decadienyl acetate	<i>S. cherbonnieri</i>		-7.4
27	(3E)-7-hydroxy-4,8,15,15-tetramethyl-1-[(Z)-12-methyl-10-oxo-12-pentenyl]-3,8-decadienyl acetate	<i>S. cherbonnieri</i>		-7.1
28	Sarcoglaucol	<i>S. cherbonnieri</i>		-7.5
29	Decaryiol	<i>S. cherbonnieri</i>		-6.8
30	(4Z,8S,9S,12Z,14E)-9-Hydroxy-1-isopropyl-8,12-dimethyl-oxabicyclo [9.3.2]-hexadeca-4,12,14-trien-18-one	<i>Sarcophyton</i> <i>new sp.</i>		-7.3
31	(4Z,12Z,14E)-sarcophytolide	<i>Sarcophyton</i> <i>new sp.</i>		-8.8
32	Sarcophytolide	<i>Sarcophyton</i> <i>new sp.</i>		-7.5

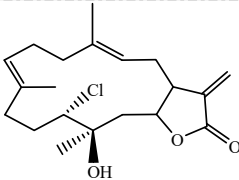
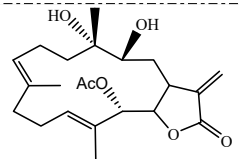
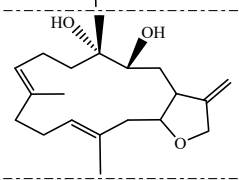
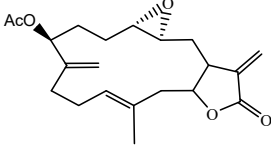
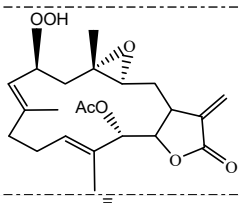
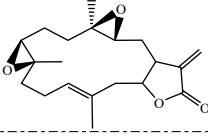
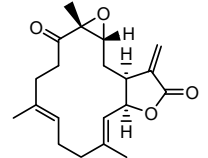
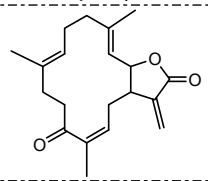
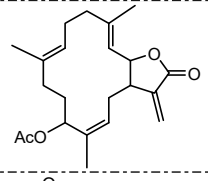
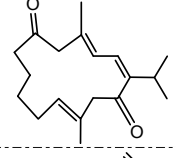
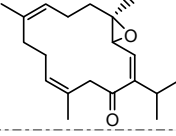
33	4Z,8S,9R,12E,14E)-9-Hydroxy-1-isopropyl-8,12-dimethyloxabicyclo[9.3.2]-hexadeca-4,12,14-trien-18-one	<i>Sarcophyton new sp.</i>		-7.8
34	(4Z,8S,9R,12E,14E)-1-Isopropyl-8,12-dimethyl-18-oxo-oxabicyclo[9.3.2]-hexadeca-4,12,14-trien-2-yl acetate	<i>Sarcophyton new sp.</i>		-8.0
35	Sarcophytolol	<i>S. glaucum</i>		-7.0
36	Sarcophytolide B	<i>S. glaucum</i>		-7.3
37	Sarcophytolide C	<i>S. glaucum</i>		-7.9
38	Sarcophytonolide A	<i>S. tortuosum</i>		-8.2
39	Sarcophytonolide B	<i>S. crassocaule</i>		-8.7
40	Sarcophytonolide C	<i>S. tortuosum</i>		-8.4
41	Sarcophytonolide D	<i>S. tortuosum</i>		-8.0
42	Sarcophytonolide E	<i>S. latum</i>		-7.7
43	Sarcophytonolide F	<i>S. latum</i>		-7.9

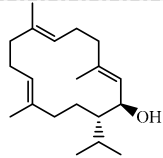
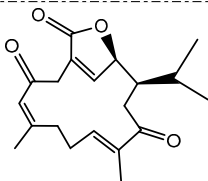
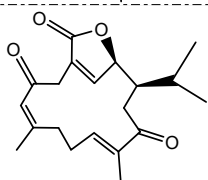
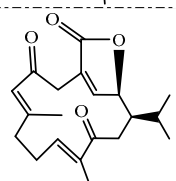
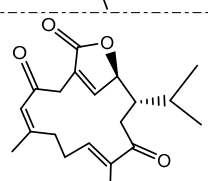
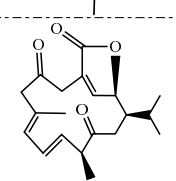
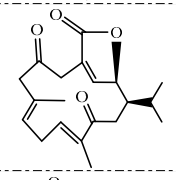
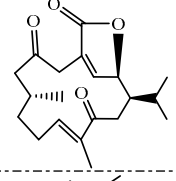
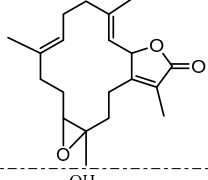
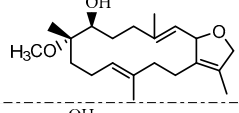
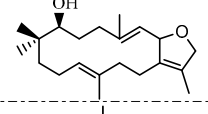
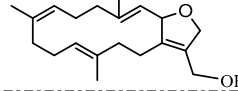
44	Sarcophytonolide G	<i>S. latum</i>		-7.8
45	Sarcophytonolide H	<i>S. latum</i>		-8.0
46	Sarcophytonolide I	<i>S. latum</i>		-7.7
47	Sarcophytonolide J	<i>S. infundibuliforme</i>		-7.5
48	Sarcophytonolide K	<i>S. trocheliophorum</i>		-8.1
49	Sarcophytonolide L	<i>S. latum</i>		-7.6
50	Sarcophytonolide N	<i>S. trocheliophorum</i>		-7.3
51	Sarcophytonolide O	<i>S. trocheliophorum</i>		-8.2
52	Sarcophytonolide P	<i>S. trocheliophorum</i>		-8.2
53	Sarcophytonolide Q	<i>S. trocheliophorum</i>		-8.2
54	Sarcophytonolide R	<i>S. trocheliophorum</i>		-7.3

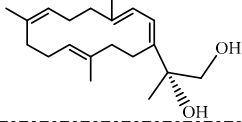
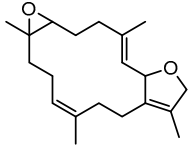
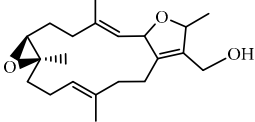
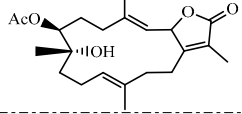
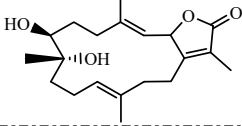
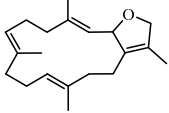
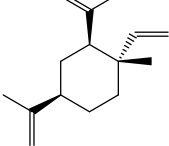
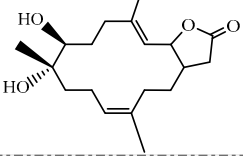
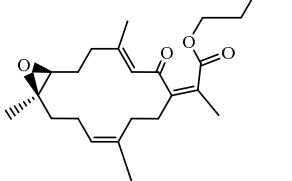
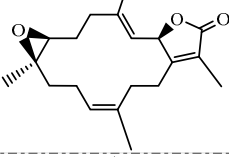
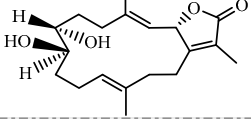
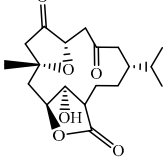
55	ketoemblide	<i>S.</i> <i>trocheliophorum</i>		-8.2
56	(E,E,E)-1-isopropenyl-4,8,12-trimethylcyclotetradeca-3,7,11-tiene	<i>S.</i> <i>trocheliophorum</i>		-7.7
57	Sarcophytonolide S	<i>S.</i> <i>trocheliophorum</i>		-7.9
58	Sarcophytonolide T	<i>S.</i> <i>trocheliophorum</i>		-8.1
59	Sarcophytonolide U	<i>S.</i> <i>trocheliophorum</i>		-8.1
60	Sartrolide H	<i>S.</i> <i>trocheliophorum</i>		-7.4
61	Sartrolide I	<i>S.</i> <i>trocheliophorum</i>		-7.3
62	Sartrolide J	<i>S.</i> <i>trocheliophorum</i>		-7.5
63	Sartrolide A	<i>S.</i> <i>trocheliophorum</i>		-7.0
64	Sartrolide B	<i>S.</i> <i>trocheliophorum</i>		-7.3
65	Sartrolide C	<i>S.</i> <i>trocheliophorum</i>		-6.7
66	Sartrolide D	<i>S.</i> <i>trocheliophorum</i>		-7.9
67	Sartrolide E	<i>S.</i> <i>trocheliophorum</i>		-7.5

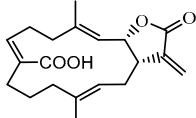
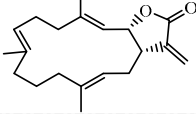
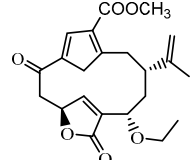
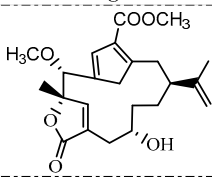
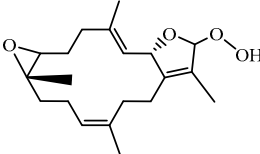
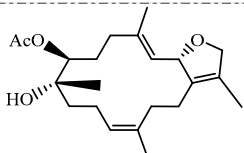
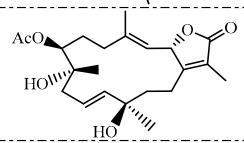
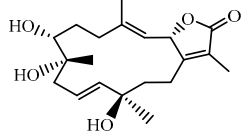
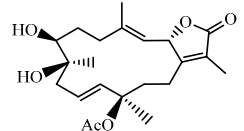
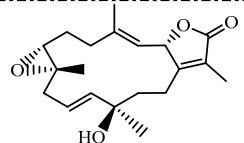
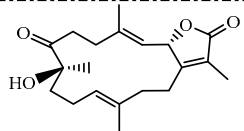
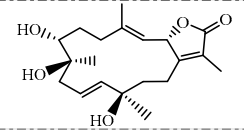
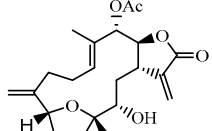
68	Sartrolide F	<i>S. trocheliophorum</i>		-7.6
69	Sartrolide G	<i>S. trocheliophorum</i>		-8.2
70	Bissartrolide dimer	<i>S. trocheliophorum</i>		-8.1
71	Yalongene A	<i>S. trocheliophorum</i>		-8.0
72	Yalongene A	<i>S. trocheliophorum</i>		-6.5
73	Trochelioid A	<i>S. trocheliophorum</i>		-7.8
74	Trochelioid B	<i>S. trocheliophorum</i>		-8.1
75	16-oxosarcophytonin E	<i>S. trocheliophorum</i>		-7.5
76	Sarcassin A	<i>S. crassocaule</i>		-8.2
77	Sarcassin B	<i>S. crassocaule</i>		-6.4
78	Sarcassin C	<i>S. crassocaule</i>		-7.8
79	Sarcassin D	<i>S. crassocaule</i>		-8.2

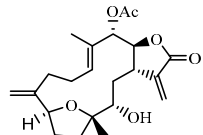
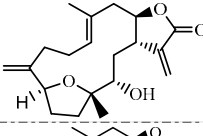
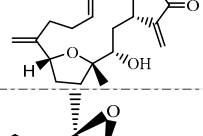
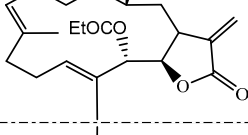
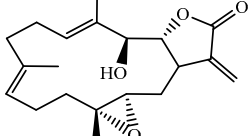
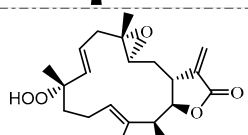
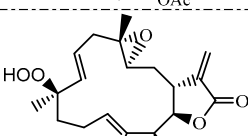
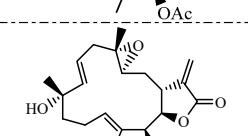
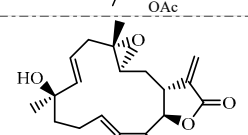
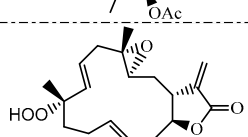
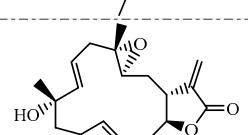
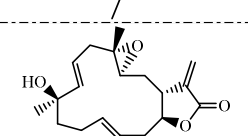
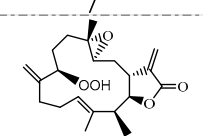
80	Sarcassin E	<i>S. crassocaule</i>		-8.1
81	Emblide	<i>S. crassocaule</i> <i>S. tortuosum</i>		-8.2
82	Crassocolide A	<i>S. crassocaule</i>		-8.1
83	Crassocolide B	<i>S. crassocaule</i>		-7.4
84	Crassocolide C	<i>S. crassocaule</i>		-6.5
85	Crassocolide D	<i>S. crassocaule</i>		-7.7
86	Crassocolide E	<i>S. crassocaule</i>		-8.2
87	Crassocolide F	<i>S. crassocaule</i>		-8.1
88	Lobophytolide	<i>S. crassocaule</i>		-7.5
89	Crassocolide G	<i>S. crassocaule</i>		-6.3

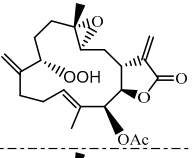
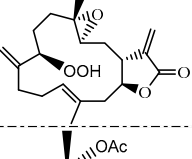
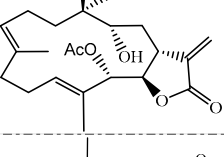
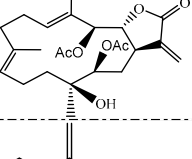
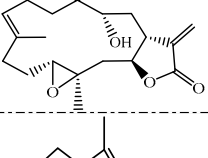
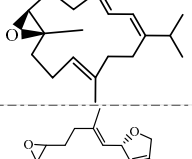
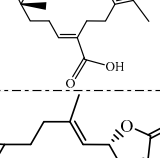
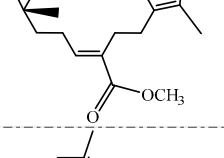
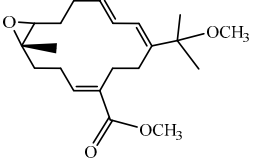
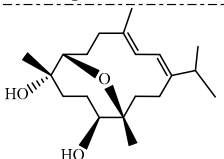
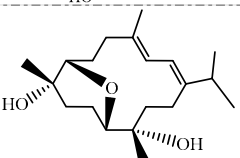
90	Crassocolide H	<i>S. crassocaule</i>		-7.0
91	Crassocolide I	<i>S. crassocaule</i>		-7.0
92	Crassocolide J	<i>S. crassocaule</i>		-7.7
93	Crassocolide K	<i>S. crassocaule</i>		-8.1
94	Crassocolide L	<i>S. crassocaule</i>		-8.0
95	Crassocolide M	<i>S. crassocaule</i>		-7.7
96	Crassocolide N	<i>S. crassocaule</i>		-7.6
97	Crassocolide O	<i>S. crassocaule</i>		-8.1
98	Crassocolide P	<i>S. crassocaule</i>		-8.1
99	Flexusine A	<i>S. flexuosum</i>		-7.4
100	Flexusine B	<i>S. flexuosum</i>		-8.1

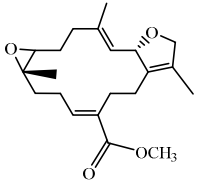
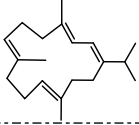
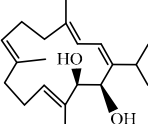
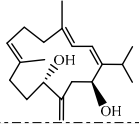
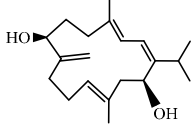
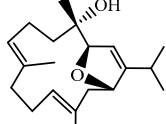
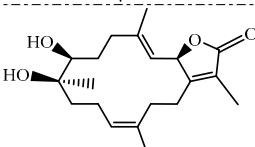
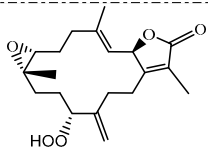
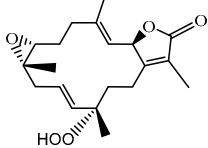
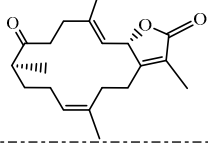
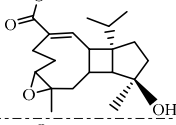
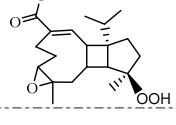
101	Epimukulol	<i>S. flexuosum</i>		-7.4
102	Sarcostolide A	<i>S. stolidotum</i>		-8.2
103	Sarcostolide B	<i>S. stolidotum</i>		-8.2
104	Sarcostolide C	<i>S. stolidotum</i>		-8.0
105	Sarcostolide D	<i>S. stolidotum</i>		-8.4
106	Sarcostolide E	<i>S. stolidotum</i>		-7.6
107	Sarcostolide F	<i>S. stolidotum</i>		-7.8
108	Sarcostolide G	<i>S. stolidotum</i>		-7.4
109	Isosarcophin	<i>S. stolidotum</i>		-6.9
110	(-)-7 $\beta$ -hydroxy-8 $\alpha$ -methoxy-deepoxy-sarcophytoxide	<i>S. mililatensis</i>		-6.9
111	(+)-7 $\beta$ ,8 $\beta$ -Dihydroxy-deepoxy-sarcophytoxide	<i>S. mililatensis</i>		-6.6
112	(-)-17-hydroxysarcophytonin A	<i>S. mililatensis</i>		-7.3

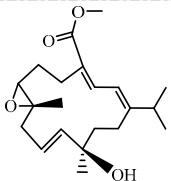

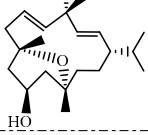
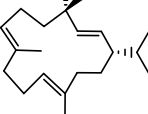
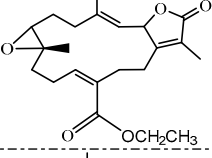
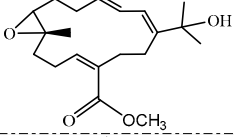
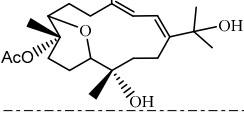
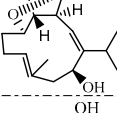
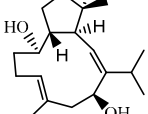
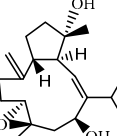
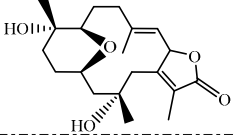
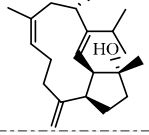
113	Sarcophytol V	<i>S. mililatensis</i>		-6.8
114	Sarcophytoxide	<i>S. mililatensis</i> <i>S. glaucum</i> <i>Sarcophyton</i> sp. <i>S.</i> <i>trocheliophorum</i>		-6.9
115	17-hydroxysarcophytoxide	<i>S. glaucum</i>		-6.7
116	7β-acetoxy-8α-hydroxydeepoxysarcophine	<i>S. glaucum</i>		-7.6
117	7α,8βDihydroxydeepoxysarcophine	<i>S. elegans</i> <i>S. auritum</i> <i>S. glaucum</i>		-7.2
118	Sarcophytonin A	<i>S. mililatensis</i>		-6.8
119	(-)-β-Elemene	<i>Sarcophyton</i> sp.		-4.3
120	(7R,8S)-dihydroxydeepoxy-ent-sarcophine	<i>S. glaucum</i>		-7.5
121	Secosarcophinolide	<i>S. glaucum</i>		-8.4
122	Ent-sarcophine	<i>S. glaucum</i>		-8.6
123	(7S,8R)-dihydroxydeepoxysarcophine	<i>S. glaucum</i>		-7.2
124	5-epi-sinuleptolide	<i>Sarcophyton</i> sp.		-7.3

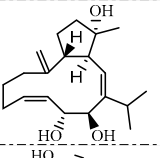
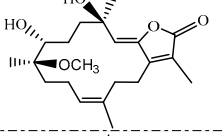
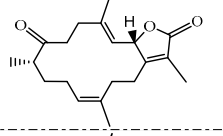
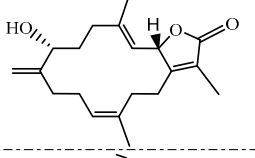
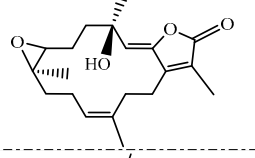
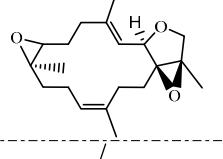
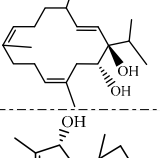
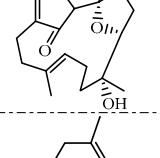
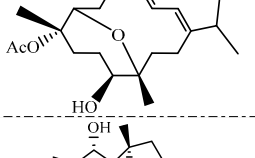
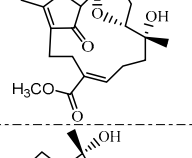
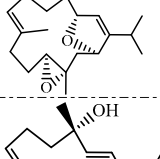
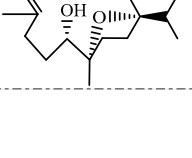
125	Lobohedleolide	<i>Sarcophyton</i> <i>sp.</i>		-8.2
126	(7Z)-lobohedleolide	<i>Sarcophyton</i> <i>sp.</i>		-8.2
127	Sarcofuranocembrenolide A	<i>Sarcophyton</i> <i>sp.</i>		-8.5
128	Sarcofuranocembrenolide B	<i>Sarcophyton</i> <i>sp.</i>		-7.7
129	Sarcophytonins F	<i>Sarcophyton</i> <i>sp.</i>		-8.3
130	Sarcophytonin G	<i>Sarcophyton</i> <i>sp.</i>		-6.9
131	7-Acetyl-8-epi- sinumaximol G	<i>S. ehrenbergi</i>		-8.3
132	8-epi-sinumaximol G	<i>Sarcophyton</i> <i>sp.</i>		-7.9
133	12-acetyl-7, 12-episinumaximol G	<i>Sarcophyton</i> <i>sp.</i>		-8.0
134	12-hydroxysarcoph-10-ene	<i>S. ehrenbergi</i>		-7.7
135	8-hydroxy-epi-sarcophinone	<i>S. ehrenbergi</i>		-7.3
136	Sinumaximol G	<i>S. ehrenbergi</i>		-7.4
137	Sarcocrassocolide A	<i>S. crassocaule</i>		-8.3

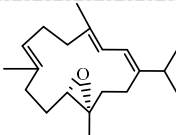
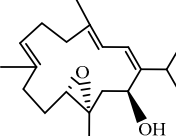
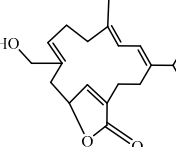
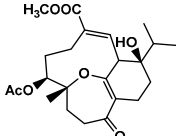
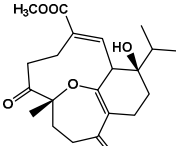
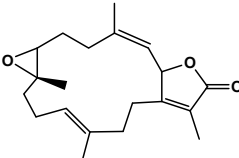
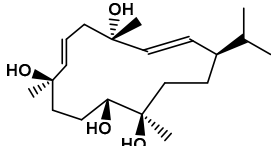
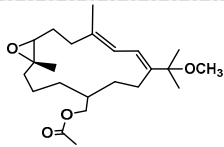
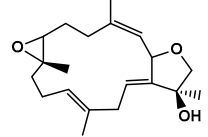
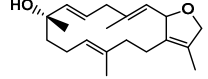
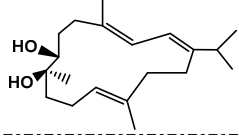
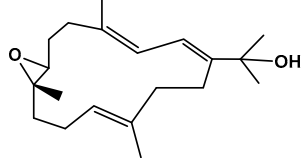
138	Sarcocrassocolide B	<i>S. crassocaule</i>		-8.6
139	Sarcocrassocolide C	<i>S. crassocaule</i>		-8.2
140	Sarcocrassocolide D	<i>S. crassocaule</i>		-8.1
141	Sarcocrassocolide E	<i>S. crassocaule</i>		-8.3
142	Sinularolide	<i>S. crassocaule</i>		-7.9
143	Sarcocrassocolide F	<i>S. crassocaule</i>		-9.0
144	Sarcocrassocolide G	<i>S. crassocaule</i>		-8.5
145	Sarcocrassocolide H	<i>S. crassocaule</i>		-8.3
146	Sarcocrassocolide I	<i>S. crassocaule</i>		-8.3
147	Sarcocrassocolide J	<i>S. crassocaule</i>		-9.1
148	Sarcocrassocolide K	<i>S. crassocaule</i>		-8.3
149	Sarcocrassocolide L	<i>S. crassocaule</i>		-8.1
150	Sarcocrassocolide M	<i>S. crassocaule</i>		-7.5

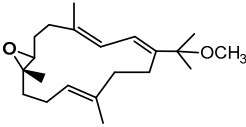
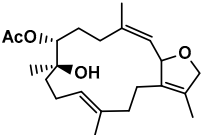
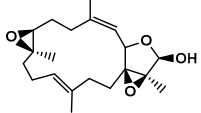
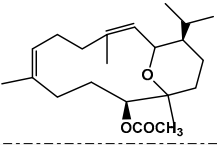
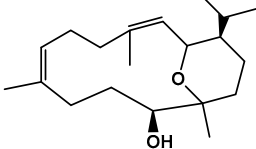
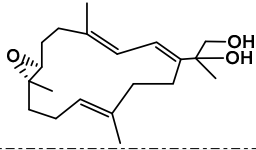
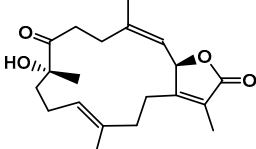
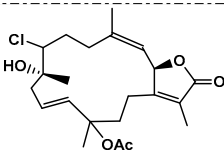
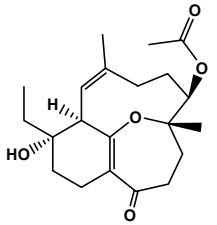
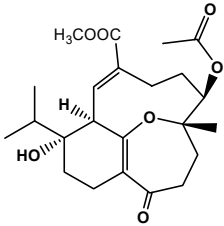
151	Sarcocrassocolide N	<i>S. crassocaule</i>		-9.4
152	Sarcocrassocolide O	<i>S. crassocaule</i>		-7.5
153	Sarcocrassocolide P	<i>S. crassocaule</i>		-7.1
154	Sarcocrassocolide Q	<i>S. crassocaule</i>		-7.8
155	Sarcocrassocolide R	<i>S. crassocaule</i>		-7.3
156	(+)-7,8-epoxy-7,8-dihydrocembrene C	<i>S. ehrenbergi</i>		-8.0
157	(+)-12-carboxy-11Z-sarcophytoxide	<i>S. ehrenbergi</i>		-8.0
158	(+)-12-methoxycarbonyl-11Z-sarcophine	<i>S. ehrenbergi</i>		-8.9
159	Ehrenberoxide A	<i>S. ehrenbergi</i>		-8.1
160	Ehrenberoxide B	<i>S. ehrenbergi</i>		-7.0
161	Ehrenberoxide C	<i>S. ehrenbergi</i>		-7.2

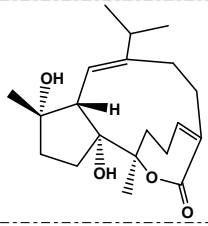
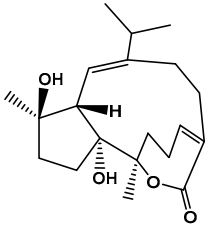
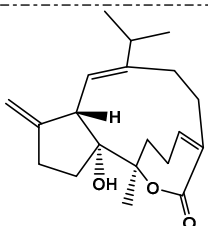
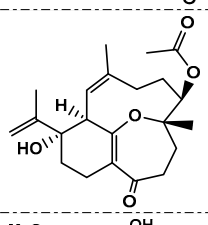
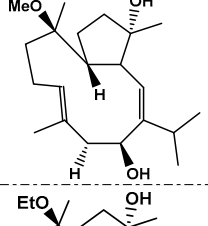
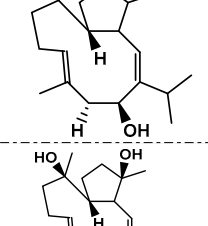
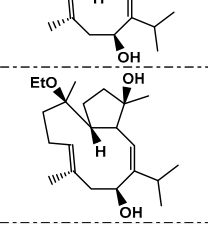
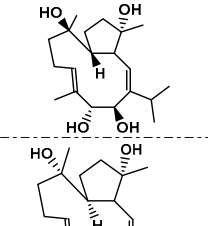
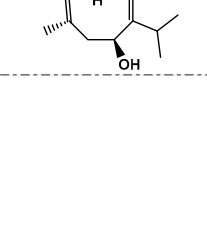

162	Lobophynin C	<i>S. ehrenbergi</i>		-8.5
163	Cembrene C	<i>S. trocheliophorum</i>		-7.5
164	Sarcophytol B	<i>Sarcophyton sp.</i>		-7.9
165	Sarcophytol E	<i>S. infundibuliforme</i>		-7.7
166	Sarcophytol H	<i>S. infundibuliforme</i>		-7.5
167	(-)-marasol	<i>S. infundibuliforme</i> <i>S. glaucum</i>		-7.2
168	2R,7R,8R-dihydroxydeepoxysarcophine	<i>S. glaucum</i>		-7.8
169	11(S)-hydroperoxysarcoph-12(20)-ene	<i>S. glaucum</i>		-8.3
170	12(S)-hydroperoxysarcoph-10-ene	<i>S. glaucum</i>		-8.2
171	8-epi-sarcophinone	<i>S. glaucum</i>		-6.7
172	Methyl sarcotroate A	<i>S. trocheliophorum</i>		-8.1
173	Methyl sarcotroate B	<i>S. trocheliophorum</i>		-8.5

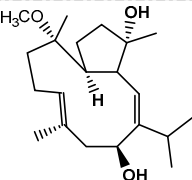
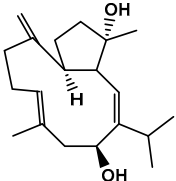
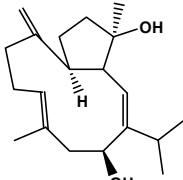
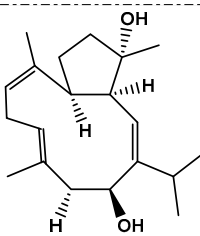
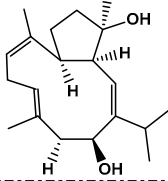
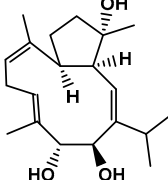
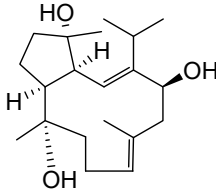
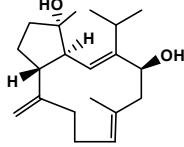
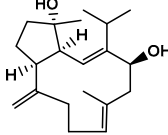
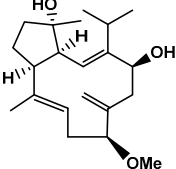
174	Sarcophytonolide M	<i>S. trocheliophorum</i>		-9.0
175	(1S,2E,4R,6E,8S,11R,12S)-8,11-epoxy-4,12-epoxy-2,6-cembradiene	<i>S. glaucum</i>		-7.6
176	(1S,2E,4R,6E,8R,11S,12R)-8,12-epoxy-2,6-cembradiene-4,11-diol	<i>S. glaucum</i>		-7.7
177	(1S,4R,13S)-cembra-2E,7E,11E-trien-4,13-diol	<i>S. glaucum</i>		-7.8
178	(+)-12-ethoxycarbonyl-11Z-sarcophine	<i>S. ehrenbergi</i>		-7.9
179	Ehrenbergol A	<i>S. ehrenbergi</i>		-8.0
180	Ehrenbergol B	<i>S. ehrenbergi</i>		-8.8
181	Sarcophylolide B	<i>S. elegans</i>		-7.2
182	Sarcophylolide C	<i>S. elegans</i>		-7.8
183	Sarcophylolide D	<i>S. elegans</i>		-6.9
184	Sarcophylolide E	<i>S. elegans</i>		-7.9
185	Sarcophytol L	<i>S. elegans</i>		-7.2

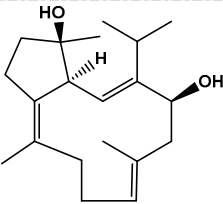
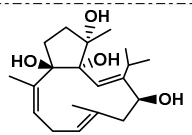
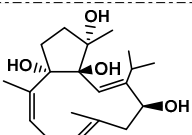
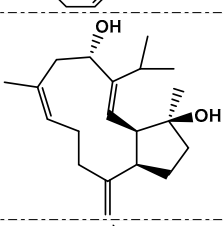
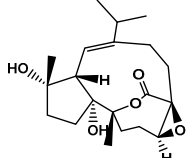
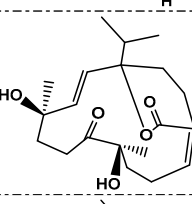
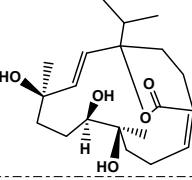
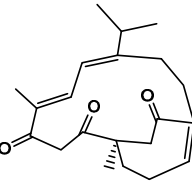
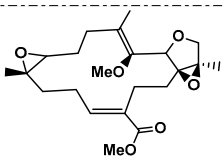
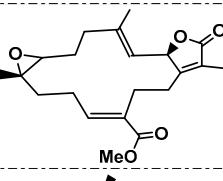
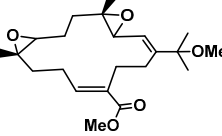
186	13 $\alpha$ -hydroxysarcophytol L	<i>S. elegans</i>		-7.3
187	Sarcophylide A	<i>S. elegans</i>		-9.3
188	Sarcophinone	<i>S. elegans</i>		-6.7
189	7 $\alpha$ -hydroxy- $\Delta^8(19)$ -deepoxysarcophine	<i>S. elegans</i>		-7.1
190	4 $\beta$ -hydroxy- $\Delta^2(3)$ -sarcophine	<i>S. elegans</i>		-7.6
191	1,15 $\beta$ -epoxy-2-epi-16-deoxysarcophine	<i>S. elegans</i>		-7.6
192	Sarcophytol Q	<i>S. elegans</i>		-7.8
193	Lobocrasol	<i>S. elegans</i>		-6.6
194	Acetyl ehrenberoxide B	<i>S. ehrenbergi</i>		-8.4
195	Ehrenbergol C	<i>S. ehrenbergi</i>		-7.4
196	Sarcophytol W	<i>S. infundibuliforme</i>		-7.5
197	(2E,7E)-4,11-dihydroxy-1,12-oxidocembra-2,7-dien	<i>S. glaucum</i>		-7.5

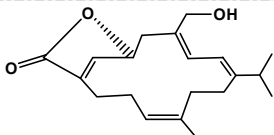
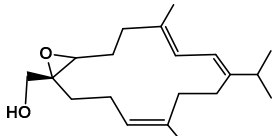
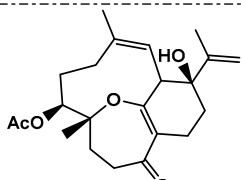
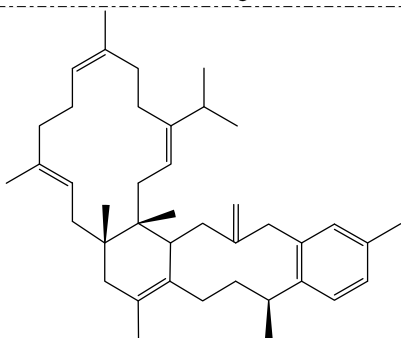
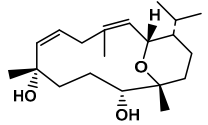
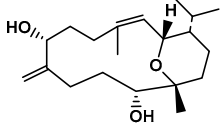
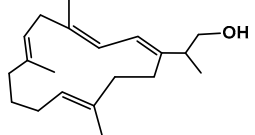
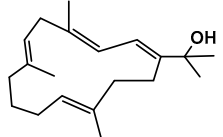
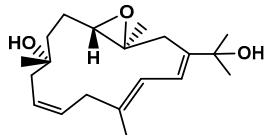
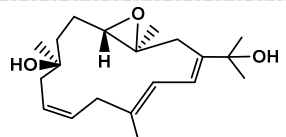
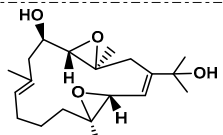
198	(+)-11,12-epoxy-11,12-dihydrocembrene-C	<i>Sarcophyton sp.</i>		-7.3
199	(+)-11,12-epoxysarcophytol A	<i>Sarcophyton sp.</i>		-7.2
200	Sarcolactone A	<i>Sarcophyton sp.</i>		-7.9
201	Tortuosene A	<i>S. tortuosum</i>		-8.5
202	Tortuosene B	<i>S. tortuosum</i>		-8.0
203	2-epi-sarcophine	<i>S. auritum</i>		-7.6
204	(1R,2E,4S,6E,8R,11R,12R)-2,6-cembradiene-4,8,11,12-tetrol	<i>S. auritum</i>		-8.3
205	Sarcophyton A	<i>Sarcophyton sp.</i>		-8.2
206	Sarcophyton B	<i>Sarcophyton sp.</i>		-7.8
207	Sarcophyton C	<i>Sarcophyton sp.</i>		-7.2
208	Sarcophyton D	<i>Sarcophyton sp.</i>		-7.2
209	2-[(E,E,E)-7',80-epoxy-4',8',12'-trimethylcyclotetradeca-1',3',11-trienyl]propan-2-ol	<i>Sarcophyton sp.</i>		-8.2

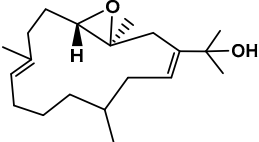
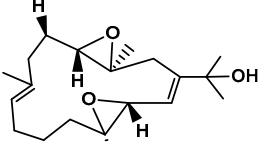
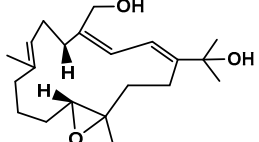
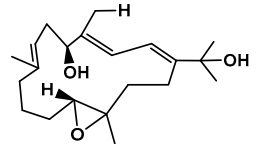
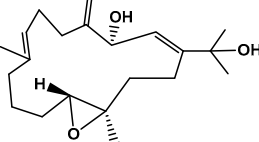
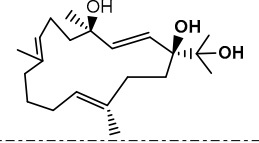
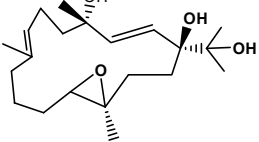
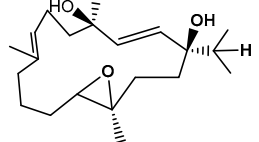
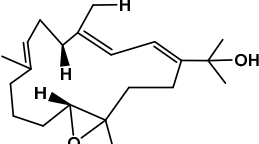
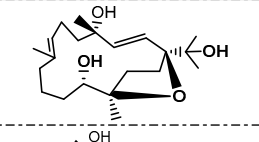
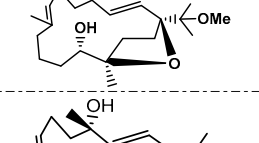
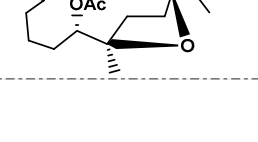
210	(1E,3E,7R*,8R*,11E)-1-(2-methoxy-propan-2-yl)-4,8,12-trimethyloxabicyclo[12.1.0]-pentadeca-1,3,11-triene	<i>Sarcophyton sp.</i>		-7.5
211	Crassumol C	<i>Sarcophyton sp.</i>		-7.4
212	Laevigatol A	<i>Sarcophyton sp.</i>		-7.0
213	Sarcotrocheliol acetate	<i>S. glaucum</i> <i>S. trocheliophorum</i>		-7.3
214	Sarcotrocheliol	<i>S. trocheliophorum</i>		-7.6
215	Sarcophinediol	<i>S. glaucum</i>		-8.6
216	7-keto-8α-hydroxy-deepoxysarcophine	<i>S. ehrenbergi</i>		-7.8
217	7β-chloro-8α-hydroxy-12-acetoxy-deepoxysarcophine	<i>S. ehrenbergi</i>		-7.4
218	Dihydrosarsolenone	<i>S. trocheliophorum</i>		-8.1
219	Methyl dihydrosarsolenoneate	<i>S. solidum</i>		-8.1

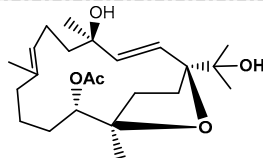
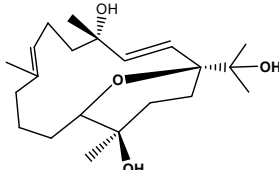
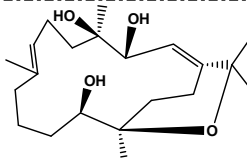
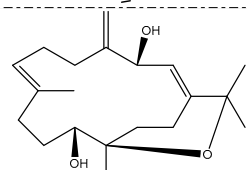
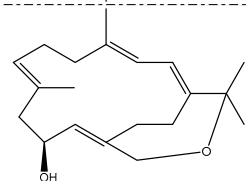
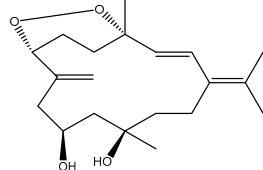
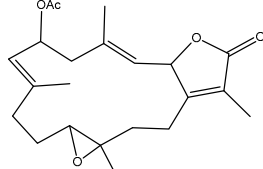
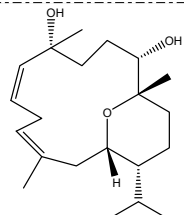
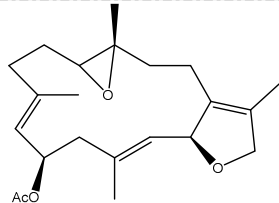
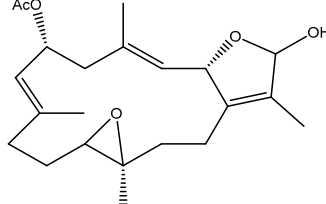
220	Sarsolilide B	<i>S. trocheliophorum</i>		-7.4
221	Sarsolilide C	<i>S. trocheliophorum</i>		-7.1
222	Sarsolilide A	<i>S. solidum</i>		-7.4
223	Sarsolenone	<i>S. solidum</i>		-8.9
224	Trocheliophol A	<i>S. trocheliophorum</i>		-7.3
225	Trocheliophol B	<i>S. trocheliophorum</i>		-7.4
226	Trocheliophols C	<i>S. trocheliophorum</i>		-6.8
227	Trocheliophol D	<i>S. trocheliophorum</i>		-6.8
228	Trocheliophol E	<i>S. trocheliophorum</i>		-6.9
229	Trocheliophol F	<i>S. trocheliophorum</i>		-7.4

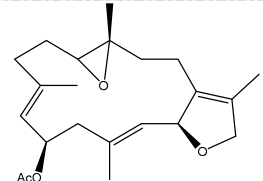
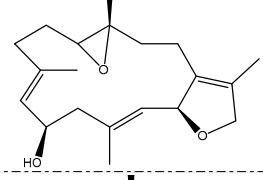
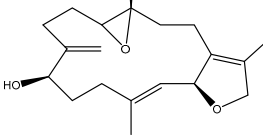
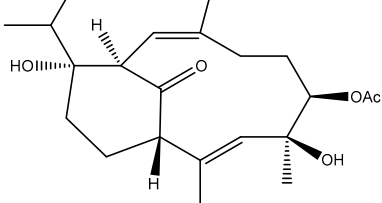
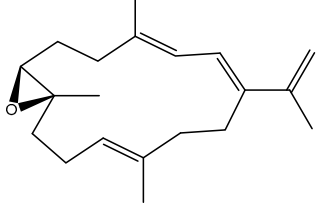
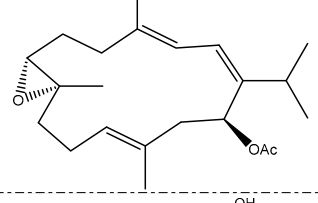
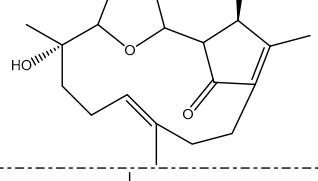
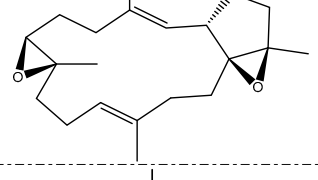
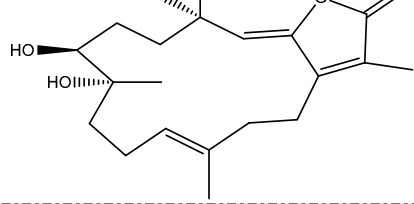
230	Trocheliophol G	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.3
231	Trocheliophol H	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.3
232	Trocheliophol I	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.9
233	Trocheliophol J	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.1
234	Trocheliophol K	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.7
235	Trocheliophol L	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.6
236	Trocheliophol M	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.6
237	Trocheliophol N	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.9
238	Trocheliophol O	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.9
239	Trocheliophol P	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.6

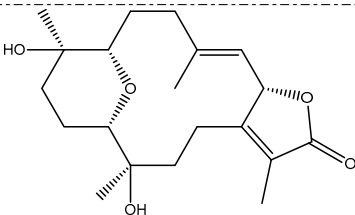
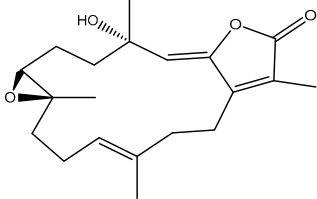
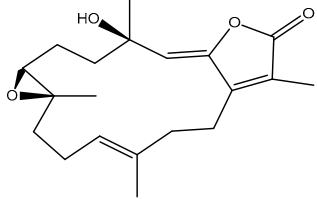
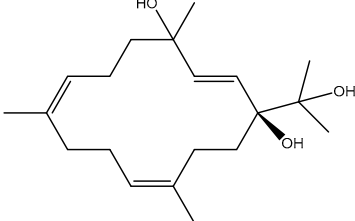
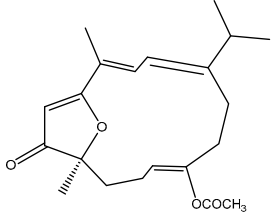
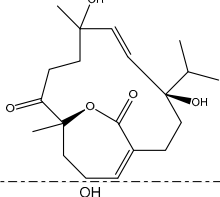
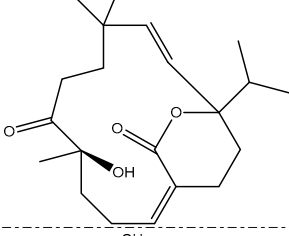
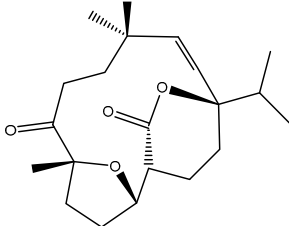
240	Trocheliophol Q	<i>S. trocheliophorum</i>		-6.9
241	Trocheliophol R	<i>S. trocheliophorum</i>		-6.9
242	Trocheliophol S	<i>S. trocheliophorum</i>		-6.1
243	4-epi-sarcophytol L	<i>S. elegans</i>		-8.0
244	Sarcophelegan A	<i>S. elegans</i>		-7.4
245	Sarcophelegan B	<i>S. elegans</i>		-7.5
246	Sarcophelegan C	<i>S. elegans</i>		-7.8
247	Sarcophelegan D	<i>S. elegans</i>		-7.9
248	(+)-1,15-epoxy-2-methoxy-12methoxycarbonyl-11E-sarcophytoxide	<i>S. ehrenbergi</i>		-8.4
249	(+)-2-epi-12-methoxycarbonyl-11E-sarcophine	<i>S. ehrenbergi</i>		-7.4
250	3,4-epoxyehrenberoxide A	<i>S. ehrenbergi</i>		-6.9

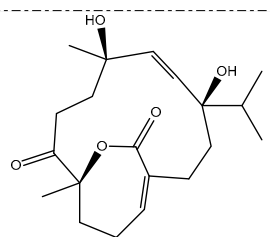
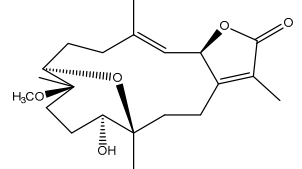
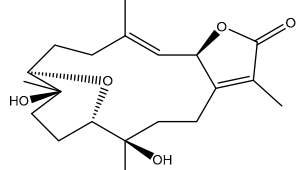
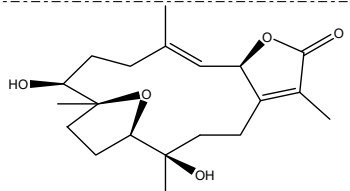
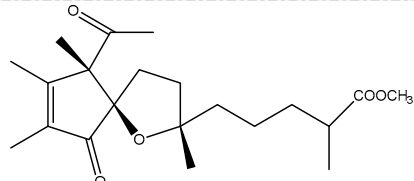
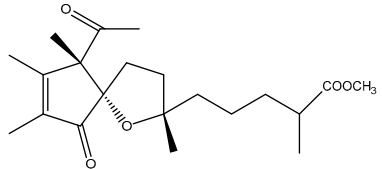
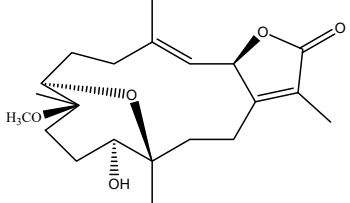
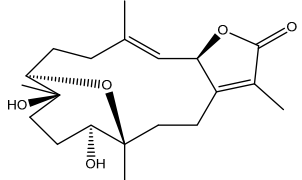
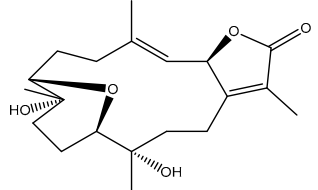
251	Ehrenbergol D	<i>S. ehrenbergi</i>		-6.7
252	Ehrenbergol E	<i>S. ehrenbergi</i>		-7.7
253	7-deacetyl-sarsolenone	<i>S. solidum</i>		-8.0
254	Trocheliame	<i>S. trocheliophorum</i>		-6.9
255	Sarcotrocheldiol A	<i>S. trocheliophorum</i>		-8.2
256	Sarcotrocheldiol B	<i>S. trocheliophorum</i>		-6.8
257	16-hydroxycembra-1,3,7,11-tetraene	<i>Sarcophyton sp.</i>		-7.8
258	15-hydroxycembra-1,3,7,11-tetraene	<i>Sarcophyton sp.</i>		-8.0
259	Sarcophytol D	<i>S. trocheliophorum</i>		-7.4
260	Sarcophytol E	<i>S. trocheliophorum</i>		-7.9
261	Sarcophytol F	<i>S. trocheliophorum</i>		-7.2

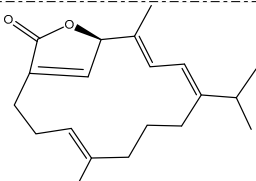
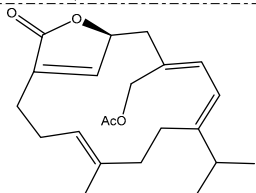
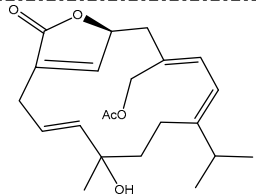
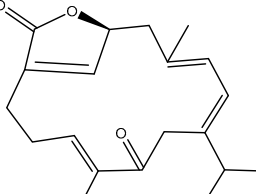
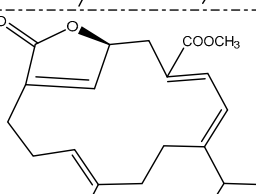
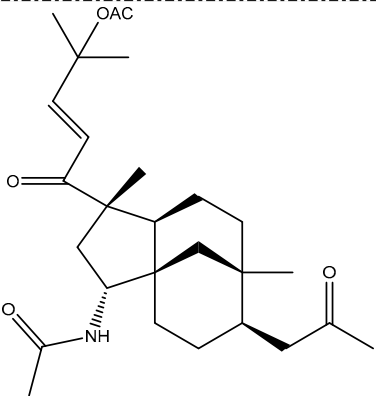
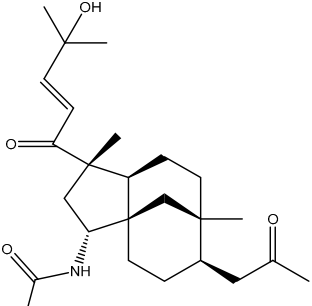
262	11,12-epoxy-1(E),3(E), 7(E)- cembratrien-15-ol	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.9
263	Sinugibberol	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.7
264	Sarcophytol G	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-8.3
265	Sarcophytol H	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.8
266	Sarcophytol I	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.8
267	Sarcophytol J	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.1
268	Sarcophytol K	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.6
269	Sarcophytol L	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-6.4
270	Crassumol A	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-8.0
271	Sarcophytol M	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.0
272	Sarcophytol N	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.0
273	Sarcostolide O	<i>S.</i> <i>trocheliophoru</i> <i>m</i>		-7.6

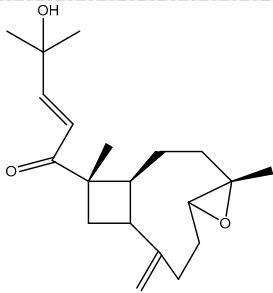
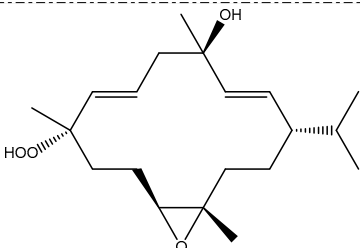
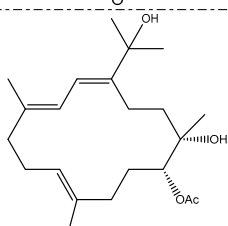
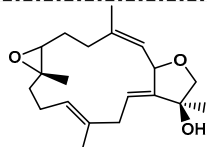
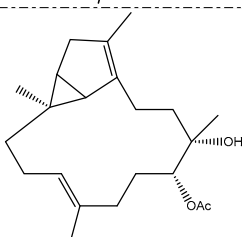
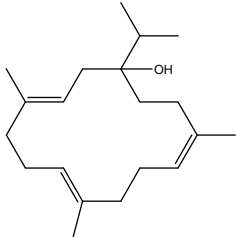
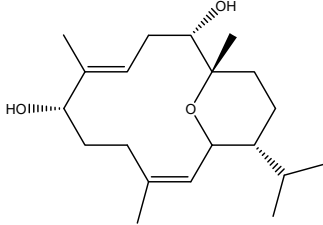
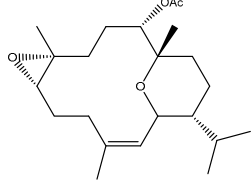
274	Sarcophytrol P	<i>S. trocheliophoru m</i>		-6.9
275	Sarcophytrol Q	<i>S. trocheliophoru m</i>		-7.5
276	Sarcophytrols R	<i>S. trocheliophoru m</i>		-7.4
277	Sarcophytrol S	<i>S. trocheliophoru m</i>		-6.5
278	Sarcophytrol T	<i>S. trocheliophoru m</i>		-7.0
279	Sarcophytrol U	<i>S. trocheliophoru m</i>		-8.0
280	Trocheliolide B	<i>S. trocheliophoru m</i>		-7.0
281	9-Hydroxy-10,11-dehydro-sarcotrocheliol	<i>S. trocheliophoru m</i>		-7.7
282	Sarcophytonoxide A	<i>S. ehrenbergi</i>		-7.3
283	Sarcophytonoxide B	<i>S. ehrenbergi</i>		-7.9

284	Sarcophytonoxide C	<i>S. ehrenbergi</i>		-6.9
285	Sarcophytonoxide D	<i>S. ehrenbergi</i>		-6.5
286	Sarcophytonoxide E	<i>S. ehrenbergi</i>		-8.0
287	Secodihydrosarsolenone	<i>S. trocheliophorum</i>		-8.1
288	(+)-(1E,3E,11E)-7,8-epoxycembra-1,3,11,15-tetraene	<i>S. stellatum</i>		-7.8
289	(+)-(7R,8R,14S,1Z,3E,11E)-14-acetoxy-7,8-epoxycembra-1,3,11-Triene	<i>S. stellatum</i>		-7.6
290	3,4,8,16-tetra-epi-lobocrasol	<i>S. glaucum</i>		-7.1
291	1,15β-epoxy-deoxysarcophine	<i>S. glaucum</i>		-7.3
292	3,4-dihydro-4α,7β,8α-trihydroxy-Δ <sup>2</sup> -sarcophine	<i>S. glaucum</i>		-8.6

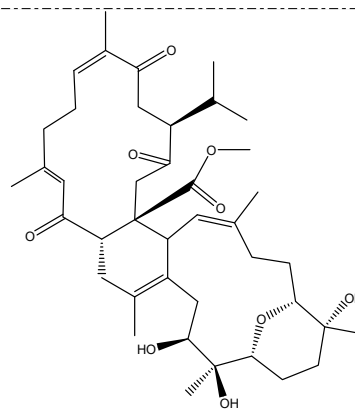
293	<i>ent</i> -sarcophylide E	<i>S. glaucum</i>		-7.8
294	3,4-dihydro-4 $\alpha$ -hydroxy- $\Delta^2$ -sarcophine	<i>S. glaucum</i>		-7.3
295	3,4-dihydro-4 $\beta$ -hydroxy- $\Delta^2$ -sarcophine	<i>S. glaucum</i>		-7.7
296	Klyflaccicembranol F	<i>S. glaucum</i>		-7.6
297	Sarelengan C	<i>S. elegans</i>		-8.2
298	Sarelengan D	<i>S. elegans</i>		-6.7
299	Sarelengan E	<i>S. elegans</i>		-8.4
300	Sarelengan F	<i>S. elegans</i>		-7.8

301	Sarelengan G	<i>S. elegans</i>		-7.4
302	Sarcoehrenbergilid A	<i>S. ehrenbergi</i>		-6.9
303	Sarcoehrenbergilid B	<i>S. ehrenbergi</i>		-8.8
304	Sarcoehrenbergilid C	<i>S. ehrenbergi</i>		-8.2
305	Sinulolides A	<i>S. ehrenbergi</i>		-7.4
306	Sinulolide B	<i>S. ehrenbergi</i>		-7.3
307	Sarcoehrenbergilid D	<i>S. ehrenbergi</i>		-7.2
308	Sarcoehrenbergilid E	<i>S. ehrenbergi</i>		-7.0
309	Sarcoehrenbergilid F	<i>S. ehrenbergi</i>		-7.8

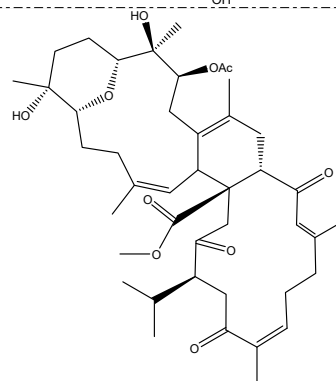
310	Sarcoehrenolide A	<i>S. ehrenberg</i>		-7.7
311	Sarcoehrenolide B	<i>S. ehrenbergi</i>		-7.0
312	Sarcoehrenolide C	<i>S. ehrenbergi</i>		-6.8
313	Sarcoehrenolide D	<i>S. ehrenbergi</i>		-7.6
314	Sarcoehrenolide E	<i>S. ehrenbergi</i>		-7.5
315	Sarinfacetamide A	<i>S. infundibuliforme</i>		-7.4
316	Sarinfacetamides B	<i>S. infundibuliforme</i>		-8.4

317	Nanolobatin B	<i>S. infundibuliforme</i>		-8.1
318	(1S,2E,4R,6E,8S,11S,12S)-11,12-epoxy-8-hydroperoxy-4-hydroxy-2,6-cembradiene	<i>Sarcophyton sp.</i>		-8.6
319	Sarcomililatol A	<i>S. mililatensis</i>		-7.2
320	Sarcomililatol B	<i>S. mililatensis</i>		-7.8
321	Sarcomililate A	<i>S. mililatensis</i>		-5.9
322	Sarcophytol M	<i>S. mililatensis</i>		-7.7
323	9-hydroxy-7,8dehydro-sarcotrocheliol	<i>S. trocheliophorum</i>		-6.6
324	8,9-expoy-sarcotrocheliol acetate	<i>S. trocheliophorum</i>		-6.9

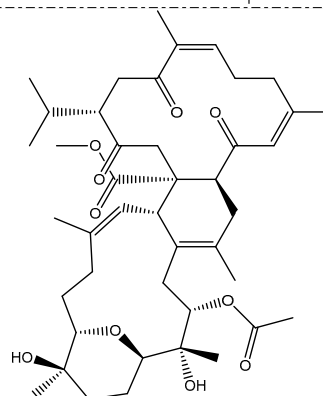
325 Bisglaucumlide A *S. glaucum* -9.6



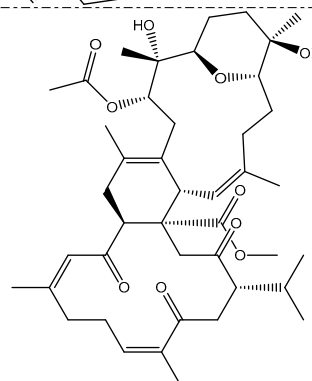
326 Bisglaucumlide B *S. glaucum* -8.1



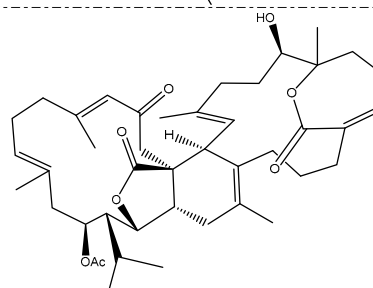
327 Bisglaucumlide C *S. glaucum* -5.1



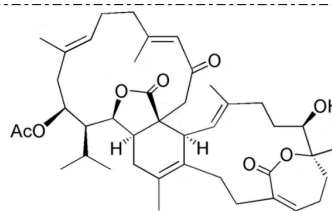
328 Bisglaucumlide D *S. glaucum* -5.7



329 Glaucumolide A *S. glaucum* -8.0

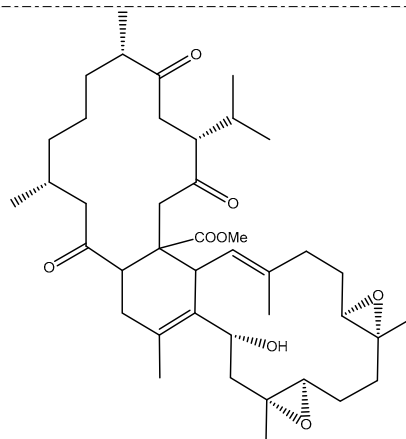


330      Glaucumolide B      *S. glaucum*



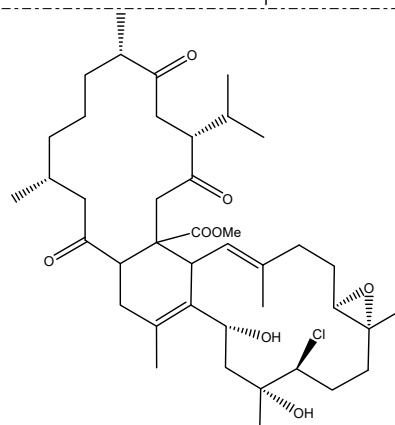
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331      Ximaolide A      *S. tortuosum*



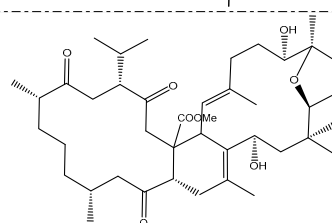
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332      Ximaolide B      *S. tortuosum*



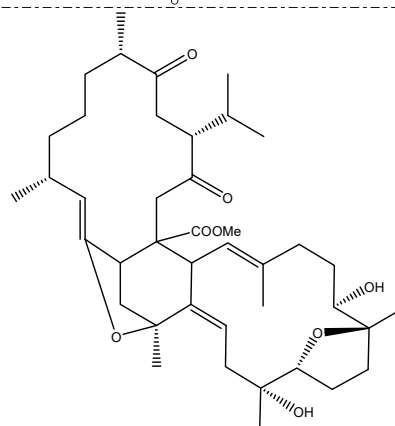
−8.2

333      Ximaolide C      *S. tortuosum*



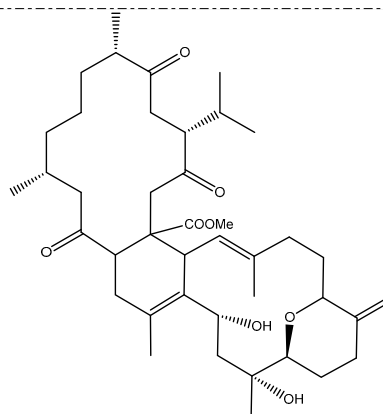
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334      Ximaolide D      *S. tortuosum*

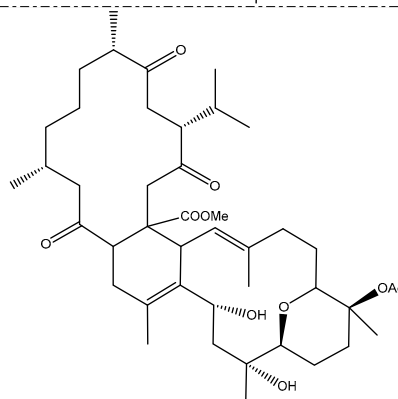


−8.0

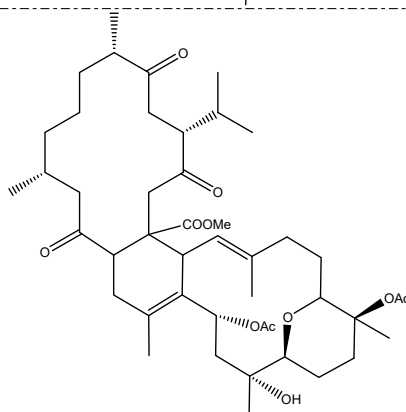
335 Ximaolide E *S. tortuosum* -9.0



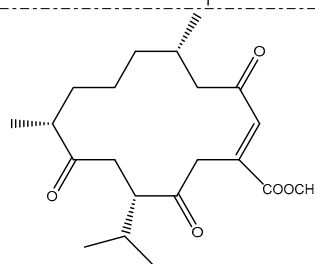
336 Ximaolide F *S. tortuosum* -9.5



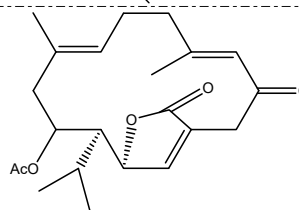
337 Ximaolide G *S. tortuosum* -7.3



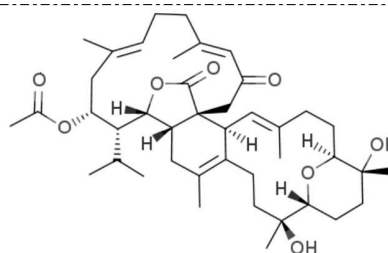
338 Methyl tortuosoate A *S. tortuosum* -8.4



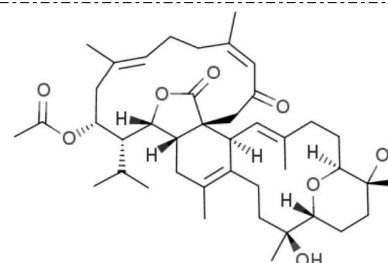
339 Isosarcophytonolide D *S. tortuosum* -7.6



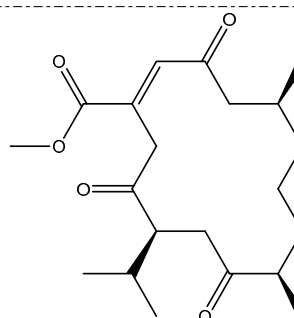
340 Bislatumlide A *S. latum* -9.6



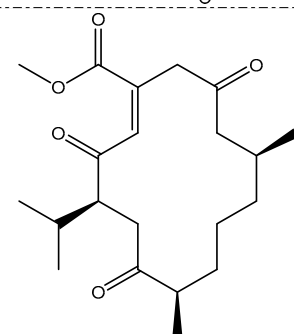
341 Bislatumlide B *S. latum* -8.2



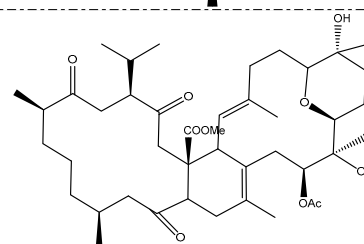
342 Methyl tetrahydrosarcoate *S. elegans* -8.1



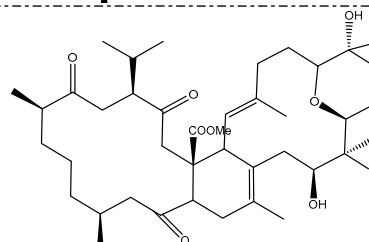
343 Methyl tetrahydroisosarcoate *S. elegans* -7.4



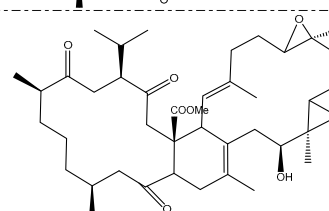
344 Nyalolide *S. elegans* -7.5



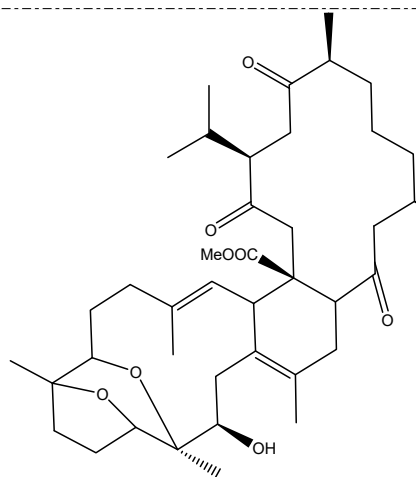
345 Desacetylnyalolide *S. elegans* -8.3



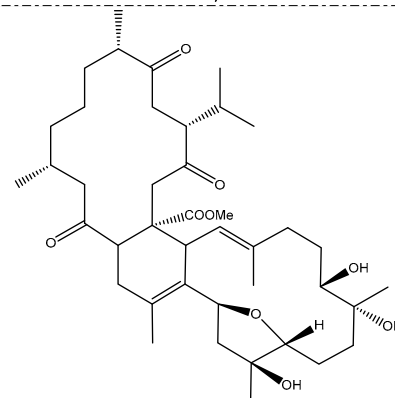
346 Diepoxynyalolide *S. elegans* -7.7



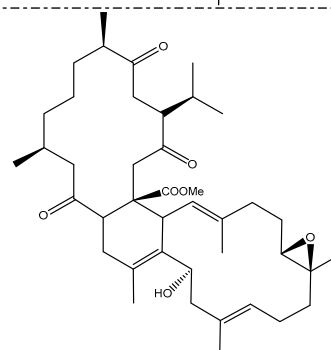
347      Dioxanyalolide      *S. elegans*      -9.5



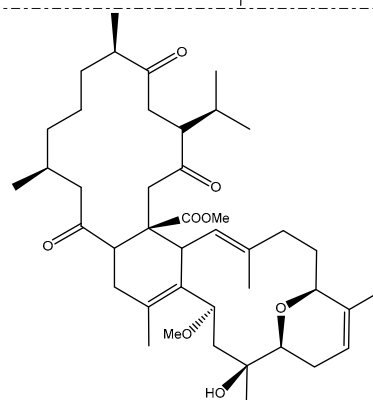
348      Sarcophytolide G      *S. elegans*      -7.4



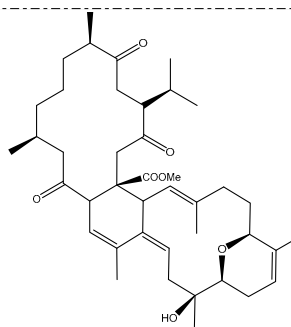
349      Sarcophytolide H      *S. glaucum*      -8.5



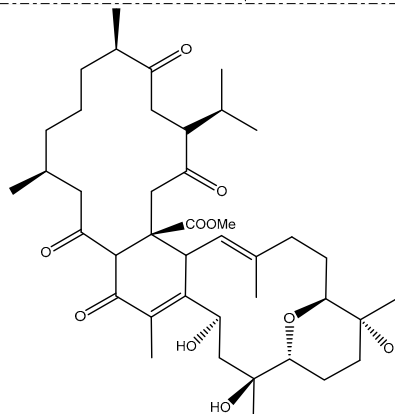
350      Sarcophytolide I      *S. elegans*      -7.5



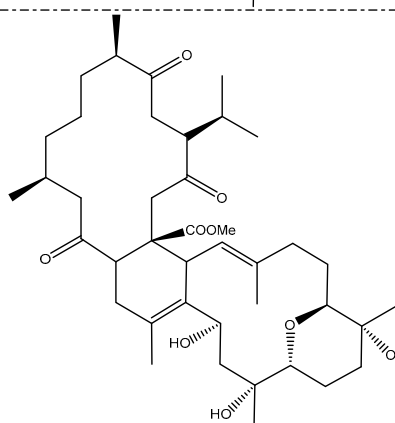
351 Sarcophytolide J *S. elegans* -8.0



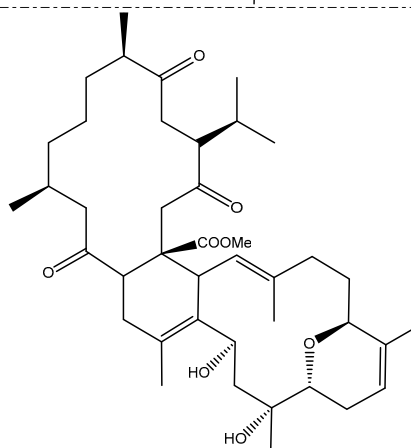
352 Sarcophytolide K *S. elegans* -7.1



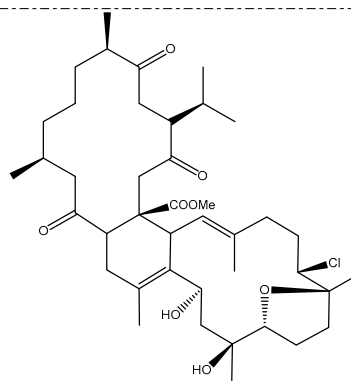
353 Sarcophytolide L *S. elegans* -6.9



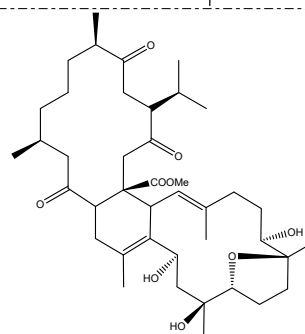
354 Lobophytone H *S. elegans* -8.1



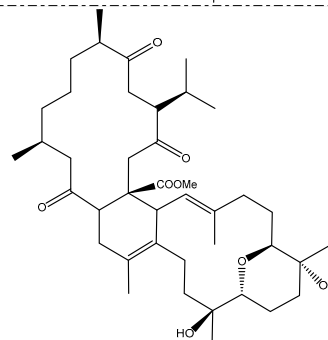
355 Lobophytone I *S. elegans* -8.5



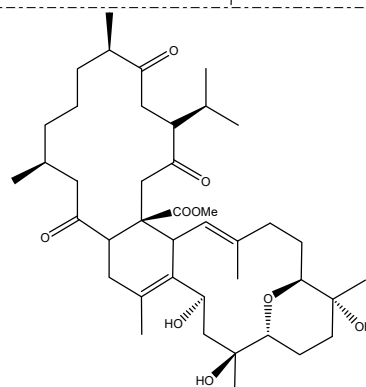
356 Lobophytone K *S. elegans* -8.3



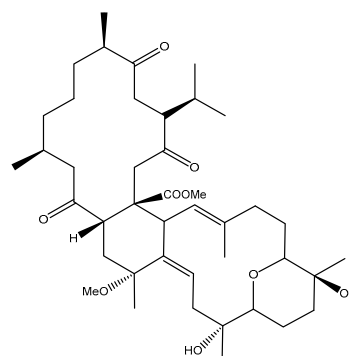
357 Lobophytone W *S. elegans* -8.7



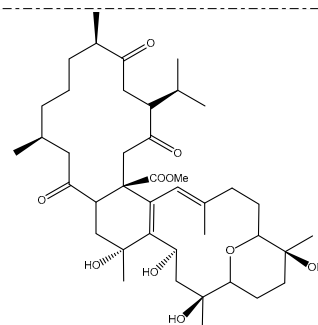
358 Lobophytone U *S. pauciplicatum* -8.6



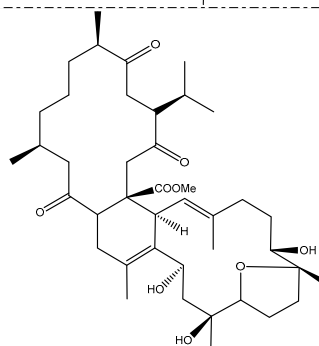
359 Sarcophytolide M *S. pauciplicatum* -7.2



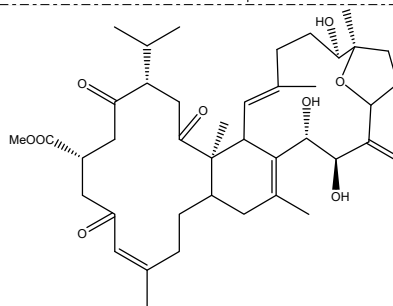
360 Sarcophytolide N *S. pauciplicatum* -7.0



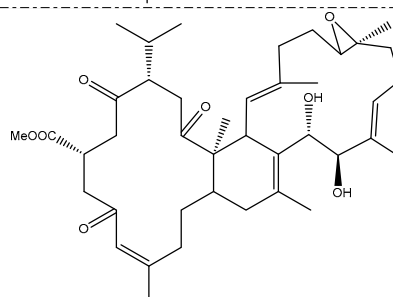
361 Lobophytone O *S. pauciplicatum* -8.6



362 Sarelengan A *S. elegans* -8.1



363 Sarelengan B *S. elegans* -9.8



<sup>a</sup>Data sorted according to the order of the compounds in Ref. (Elkhawas et al., 2020).

**Table S2.** Computed Autodock and MM/GBSA binding energies (in kcal/mol) for darunavir and the top 58 potent *Sarcophyton* cembranoid diterpenes metabolites against SARS-CoV-2 main protease (M<sup>pro</sup>) over 250 ps implicit solvent MD simulations<sup>a</sup>.

Compound Name	Docking Score (kcal/mol)	MM/GBSA Binding Energy (kcal/mol)
Darunavir	-8.2	-31.1
Bislatulide A, B (340)	-9.6	-45.1
Desacetylinalolide (345)	-8.3	-43.3
Dioxanyalolide (347)	-9.5	-40.8
Sarelengan B (363)	-9.8	-40.7
Lobophytone W (357)	-8.7	-39.2
Bisglaucumide A (325)	-9.6	-31.0
Sarinacetamides B (316)	-8.4	-31.0
Methyl sarcotroate B (173)	-8.5	-30.9
Sarcophytonolide B (39)	-8.7	-30.8
Sarcophytolide H (349)	-8.5	-30.8
Sarcocrassocolide E (141)	-8.3	-30.7
Sarcocrassocolide N (151)	-9.4	-30.7
Ximaolide A (331)	-9.3	-30.6
7-Acetyl-8-epi- sinumaximol G (131)	-8.3	-30.6
Ximaolide E (335)	-9.0	-30.5
Methyl tetrahydrosarcoate and methyl tetrahydroisosarcoate (342)	-8.3	-30.5
Sarcophinediol (215)	-8.6	-30.5
Lobophytone K (356)	-8.3	-30.5
Sarcocrassocolide H (145)	-8.3	-30.2
Sarcocrassocolide J (147)	-9.1	-30.1
Sarcocrassocolide I (146)	-8.3	-30.1
Lobophytone O (361)	-8.6	-30.0
Sarcofuranocembrenolide A (127)	-8.5	-29.9
Ent-sarcophine (122)	-8.6	-29.8
Lobophytone U (358)	-8.6	-29.6
Lobophytone I (355)	-8.5	-29.4
Tortuosene A (201)	-8.5	-29.4
Sarcophytolide A (187)	-9.3	-29.3
(1R,2E,4S,6E,8R,11R,12R)-2,6-cembradiene- 4,8,11,12-tetrol (204)	-8.3	-29.2
Sarcophytol G (264)	-8.3	-29.0
(+)-12-methoxycarbonyl-11Z-sarcophine (158)	-8.9	-28.8
(+)-1,15-epoxy-2-methoxy-12methoxycarbonyl-11E- sarcophytoxide (248)	-8.4	-28.5
Ximaolide F (336)	-9.5	-28.5
Sarcocrassocolide F (143)	-9.0	-28.5
Sarcophytonolide M (174)	-9.0	-28.3
3,4-dihydro-4 $\alpha$ ,7 $\beta$ ,8 $\alpha$ -trihydroxy- $\Delta^2$ -sarcophine (292)	-8.6	-28.1
Glaucomolide A (329)	-9.4	-27.9
Sarelengan E (299)	-8.4	-27.4
Sarcocrassolide A (8)	-9.0	-27.2
Methyl tortuosoate A (338)	-8.4	-27.2
(4Z,12Z,14E)-sarcophytolide (31)	-8.8	-26.2

Sarcoehrenbergilid B ( <b>303</b> )	−8.8	−26.2
Ehrenbergol B ( <b>180</b> )	−8.8	−26.0
Sarcocrassocolide G ( <b>144</b> )	−8.5	−25.9
Sarsolenone ( <b>223</b> )	−8.9	−25.4
Crassolide ( <b>7</b> )	−8.5	−25.3
Sarcophytonins F ( <b>129</b> )	−8.3	−25.2
Lobophynin C ( <b>162</b> )	−8.5	−25.2
(1S,2E,4R,6E,8S,11S,12S)-11,12-Epoxy-2,6-cembrane-4,8-diol ( <b>17</b> )	−8.3	−24.9
Secosarcophinolide ( <b>121</b> )	−8.4	−24.8
Sacostolide D ( <b>105</b> )	−8.4	−24.3
Acetyl ehrenberoxide B ( <b>194</b> )	−8.4	−24.2
Sarcophytonolide C ( <b>40</b> )	−8.4	−23.6
Sarcocrassocolide B ( <b>138</b> )	−8.6	−23.6
Denticulatolide ( <b>10</b> )	−9.9	−23.3
(1S,2E,4R,6E,8S,11S,12S)-11,12-epoxy-8-hydroperoxy-4-hydroxy-2,6-cembradiene ( <b>318</b> )	−8.6	−22.8
11(S)-hydroperoxylsarcoph-12(20)-ene ( <b>169</b> )	−8.3	−22.3
Sarcocrassocolide A ( <b>137</b> )	−8.3	−21.1
Sarcocrassocolide K ( <b>148</b> )	−8.3	−20.0

<sup>a</sup>Data sorted according to the calculated MM/GBSA binding energies.

**Table S3.** Network topological analysis for the predicted targets for bislatumlide A (**340**).

<b>Target</b>	<b>Betweenness Centrality</b>	<b>Closeness Centrality</b>	<b>Degree</b>
SRC	0.140277931	0.674603175	46
MAPK1	0.097973132	0.625000000	37
AR	0.076882543	0.586206897	32
MAPK8	0.043685125	0.582191781	29
MDM2	0.05093431	0.548387097	27
ERBB2	0.060499285	0.551948052	26
PTGS2	0.062644806	0.562913907	24
IGF1R	0.019882126	0.534591195	22
HSP90AB1	0.031359945	0.521472393	22
MMP2	0.045495406	0.53125000	21
GSK3B	0.020712726	0.537974684	21
PRKCA	0.031388573	0.527950311	21
PLCG1	0.015506616	0.515151515	21
CDKN1B	0.014823023	0.518292683	20
LCK	0.026151452	0.518292683	19
RPS6KB1	0.01034058	0.515151515	19
CASR	0.043481068	0.459459459	18
MAPK14	0.013888034	0.512048193	18
NR3C1	0.034134996	0.534591195	18
CDK4	0.015939274	0.505952381	18

**Table S4.** Interactors list showing the top 10 genes stimulated by bislatumlide A (**340**), their UniProt Ids and list of genes Ids which Interacts with SARS-CoV-2.

<b>Input</b>	<b>UniProt Id</b>	<b>Interacts with</b>
<b>APP</b>	P05067-4, P05067, P05067-PRO_0000000093, P05067-PRO_0000000092,	P21359, P29353, P02649, P04629, P78352, P00533, P49841, 28815, P08138, Q96FE5, P01100
<b>JAK2</b>	O60674, Q62120	P46527, O60674, P18031
<b>AR</b>	P10275	P24385, Q92793, Q92993, O14686, P35222, O75593, P55317, Q15596, Q02790, Q9NSA3, Q9UBL3
<b>JUN</b>	P05412	P05412, O95644, P07900, Q9UPN9, P15336, P18846, Q00987, P16220, P17275, P52292, P45983, Q15796, Q99966, P01100
<b>LYN</b>	P07948-1, P07948	P46527, Q07666, Q9NWQ8, P12931, P00533, Q05397
<b>MAPK1</b>	P28482	P35813, P10415, Q9BUB5, P28482, P27361, Q15121, P35236, P32121, P46531, Q02750, Q12913, P29353-2
<b>MAPK3</b>	P27361	Q14160, P19419, P28482, P27361, Q15121, Q02750, Q12913
<b>MAPK3</b>	P27361	Q14160, P19419, P28482, P27361, Q15121, Q02750, Q12913
<b>MAPK8</b>	P45983	P05412, Q07817, P00533, P27986, P46108, P60953
<b>MDM2</b>	Q00987, EBI-2694074	P05412, P49674, Q13547, Q15648, P31749, P32121, P29590, P48729, Q00987, P04271, P08047, Q9Y297, P78352, Q93009, P49757
<b>SRC</b>	P05480, P00523, P12931, Q9WUD9	P35968, P07900, Q68CZ2, P22681, P18031, Q07666, P32121, P35222, P56945, Q05397, P00519, P08581, Q9Y4D1, P41240, P06241, P07550, P00533, 15532, P27986, Q14289, Q13177, P40763