

SUPPLEMENTARY MATERIALS for

Structures, activities and drug-likeness of anti-infective xanthone derivatives isolated from marine environment: a review

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Table S1. Molecular descriptors of marine anti-infective xanthenes.

ID	Molecular Formula	MW (g mol ⁻¹)	Stereogenic centers	N ^o HBA	N ^o HBD	Rotatable bonds	N ^o rings	Fraction Csp ³	FAr
Xanthone derivatives									
1	C ₁₉ H ₁₆ O ₇	356.33	2	7	1	2	3	0.32	0.54
2	C ₁₈ H ₁₄ O ₇	342.30	0	7	2	1	5	0.28	0.56
3	C ₂₀ H ₁₆ O ₈	384.34	0	8	1	3	5	0.30	0.50
4	C ₁₄ H ₁₀ O ₅	274.27	0	5	2	1	3	0.27	0.30
5	C ₂₀ H ₂₀ O ₄	324.37	0	4	2	3	3	0.25	0.58
6	C ₁₆ H ₁₂ O ₆	300.26	0	6	2	2	3	0.12	0.64
7	C ₁₇ H ₁₄ O ₆	314.29	0	6	1	3	3	0.18	0.61
8	C ₁₄ H ₁₀ O ₅	258.23	0	5	3	0	3	0.07	0.74
9	C ₁₄ H ₁₀ O ₅	258.23	0	5	3	0	3	0.07	0.74
10	C ₃₀ H ₂₇ NO ₁₂	593.53	2	12	7	8	5	0.27	0.47
11	C ₂₇ H ₂₀ O ₁₁	520.44	0	11	5	2	6	0.22	0.53
12	C ₃₀ H ₂₅ NO ₁₁	575.52	4	11	5	2	7	0.30	0.48
13	C ₃₀ H ₂₅ NO ₁₁	575.52	4	11	5	2	7	0.30	0.48
14	C ₂₇ H ₂₀ O ₁₀	504.44	0	10	4	2	6	0.22	0.54
15	C ₂₆ H ₂₈ O ₈	468.50	3	8	3	6	4	0.38	0.41
16	C ₂₅ H ₂₇ ClO ₆	458.93	3	6	3	4	4	0.40	0.44
17	C ₂₆ H ₃₀ O ₈	470.51	3	8	2	6	4	0.46	0.41
18	C ₁₇ H ₁₄ O ₆	314.29	0	6	2	3	3	0.18	0.61
19	C ₂₇ H ₃₀ O ₉	498.52	4	9	4	6	4	0.41	0.39
37	C ₁₅ H ₁₂ O ₄	256.25	0	4	2	1	3	0.13	0.74
38	C ₁₄ H ₁₀ O ₆	274.23	0	6	4	0	3	0.07	0.70
39	C ₁₆ H ₁₂ O ₅	284.26	0	5	1	2	3	0.12	0.67

40	C ₁₈ H ₁₄ O ₇	342.30	0	7	0	5	3	0.17	0.56
41	C ₁₇ H ₁₃ ClO ₆	348.73	0	6	2	3	3	0.18	0.58
42	C ₂₁ H ₂₂ O ₅	354.40	0	5	1	5	3	0.29	0.54
43	C ₂₂ H ₂₄ O ₆	384.42	0	6	1	6	3	0.32	0.50
44	C ₂₁ H ₂₂ O ₆	370.40	0	5	2	5	3	0.29	0.52
45	C ₂₁ H ₂₂ O ₅	354.40	0	5	1	5	3	0.29	0.54
46	C ₂₀ H ₂₀ O ₅	340.37	0	5	2	4	3	0.25	0.56
47	C ₂₆ H ₂₈ O ₈	468.50	3	9	3	6	4	0.42	0.41
49	C ₂₀ H ₁₈ O ₇	370.35	5	7	2	1	4	0.35	0.52
50	C ₂₀ H ₁₈ O ₆	354.35	5	6	1	1	4	0.35	0.54
51	C ₂₀ H ₁₉ ClO ₆	390.81	3	6	2	2	4	0.35	0.52
52	C ₁₆ H ₁₂ O ₆	300.26	0	6	2	2	3	0.12	0.64
Hydroxanthones									
20	C ₁₆ H ₁₄ O ₇	318.28	1	7	3	3	3	0.25	0.43
21	C ₁₆ H ₁₄ O ₇	318.28	2	7	3	3	3	0.25	0.43
22	C ₁₆ H ₁₆ O ₈	336.29	3	8	4	3	3	0.38	0.42
23	C ₃₂ H ₃₀ O ₁₄	638.57	6	14	6	5	6	0.38	0.26
24	C ₃₂ H ₃₂ O ₁₄	640.59	6	14	6	5	6	0.44	0.13
25	C ₄₀ H ₄₂ O ₁₄	746.75	6	14	4	11	6	0.45	0.22
26	C ₃₂ H ₃₀ O ₁₄	638.57	6	14	6	5	6	0.38	0.13
27	C ₃₂ H ₃₀ O ₁₄	638.57	6	14	6	5	6	0.38	0.26
28	C ₃₄ H ₃₀ O ₁₂	628.19	0	12	5	4	7	0.35	0.25
29	C ₃₄ H ₃₀ O ₁₂	628.19	4	12	5	4	7	0.35	0.26
30	C ₃₅ H ₃₂ O ₁₁	628.62	5	11	5	4	7	0.37	0.26
31	C ₃₅ H ₃₂ O ₁₁	628.62	5	11	5	4	7	0.37	0.26
48	C ₁₅ H ₁₂ O ₇	304.25	3	7	3	2	3	0.20	0.45
53	C ₃₀ H ₂₆ O ₁₂	578.52	1	12	3	4	7	0.40	0.38
Glycosylated and other derivatives									
32	C ₃₆ H ₃₄ O ₁₃	674.65	0	13	1	6	6	0.39	0.41
33	C ₄₀ H ₃₈ O ₁₈	806.72	0	18	8	13	5	0.33	0.45
34	C ₃₆ H ₃₁ NO ₁₁	653.63	0	11	2	6	7	0.33	0.42
35	C ₄₄ H ₄₃ NO ₁₅	825.81	4	15	2	10	8	0.43	0.33
36	C ₃₆ H ₃₁ NO ₁₂	669.63	0	12	1	7	7	0.33	0.41

Table S2. Biophysiochemical properties of marine anti-infective xanthoness.

ID	Molar refractivity	PSA (Å ²)	Log P (iLOGP)	Log P (XLOGP3)	Log P (WLOGP)	Log P (MLOGP)	Log P (SILICOS-IT)	Log P (ACDlabs)	Log D _{7.4} (ACDLabs)	Log S (Ali)	Log S (ESOL)	Log S (SILICOS-IT)
Xanthone derivatives												
1	92.93	87.36	3.14	3.05	2.89	0.85	3.18	3.84	3.84	-4.55	-4.24	-5.05
2	87.6	98.36	2.44	2.55	2.20	0.75	2.24	2.44	2.44	-4.26	-3.92	-4.12
3	97.33	104.43	2.70	3.13	2.77	0.76	2.69	3.07	3.07	-4.99	-4.37	-4.74
4	71.03	75.99	1.88	1.69	2.25	0.25	1.59	2.53	2.39	-2.90	-2.76	-2.37
5	96.83	70.67	3.51	4.56	3.81	2.23	5.03	4.42	4.42	-5.77	-4.96	-6.17
6	80.43	96.97	2.28	3.02	2.67	1.00	2.90	3.48	-0.23	-4.72	-3.94	-4.59
7	84.75	85.97	2.41	3.35	2.76	1.24	3.43	3.69	3.69	-4.83	-4.15	-5.29
8	71.03	90.90	1.91	2.81	2.37	0.57	2.47	2.74	2.72	-4.38	-3.76	-3.95
9	71.03	90.90	2.04	2.81	2.37	0.57	2.47	2.76	2.74	-4.38	-3.76	-3.95
10	153	224.06	1.76	2.57	2.24	-0.80	3.59	2.05	-2.37	-6.92	-4.96	-6.27
11	133.16	183.96	2.59	4.73	3.31	0.59	3.72	4.89	1.84	-8.32	-6.30	-6.19
12	152.13	187.20	2.38	4.16	2.18	0.28	3.55	1.29	2.47	-7.80	-6.25	-6.73
13	152.13	187.20	3.37	4.16	2.18	0.28	3.55	2.47	1.29	-7.80	-6.25	-6.73
14	131.14	163.73	3.04	5.09	3.60	1.49	4.19	5.32	2.29	-8.27	-6.44	-6.78
15	126.95	126.43	3.49	4.10	3.11	1.29	4.65	4.05	4.05	-6.46	-5.24	-5.71
16	126.43	100.13	3.97	4.79	4.17	2.14	5.50	5.02	5.02	-6.62	-5.76	-6.65
17	128.12	115.43	3.76	3.31	3.25	0.55	4.80	4.02	4.02	-5.41	-4.75	-6.36
18	84.39	96.97	2.82	2.49	2.09	0.97	3.28	3.13	3.13	-4.17	-3.61	-4.99
19	133.69	146.66	3.46	2.98	2.67	0.71	4.14	3.20	3.2	-5.72	-4.70	-5.14
37	73.11	70.67	2.34	2.64	2.30	1.12	3.32	3.11	3.11	-3.77	-3.57	-4.93
38	73.05	111.13	1.88	2.46	2.08	0.02	1.98	2.91	2.78	-4.44	-3.61	-3.37

39	78.26	76.74	2.83	3.38	2.75	1.54	3.38	3.59	3.59	-4.67	-4.09	-5.17
40	89.04	92.04	2.89	2.64	2.53	1.42	3.39	3.37	3.37	-4.22	-3.71	-5.53
41	89.4	96.97	2.88	3.12	2.74	1.21	3.93	4.10	4.1	-4.83	-4.20	-5.58
42	102.82	68.90	3.36	3.88	3.95	1.89	5.12	4.24	4.24	-5.02	-4.55	-6.60
43	102.82	78.13	3.43	3.85	3.96	1.57	5.21	3.67	3.67	-5.19	-4.62	-6.70
44	109.31	89.13	3.25	3.53	3.65	1.35	4.65	3.67	3.67	-5.09	-4.41	-6.01
45	103.12	68.90	3.60	3.83	4.30	1.89	5.12	5.24	5.25	-4.97	-4.52	-6.60
46	98.35	79.90	3.32	4.11	3.65	1.67	4.58	3.86	3.86	-5.49	-4.69	-5.91
47	128.4	143.50	2.92	2.81	2.51	0.51	4.21	3.14	3.14	-5.48	-4.51	-5.59
49	97.25	98.36	3.14	2.78	2.66	0.81	2.96	3.01	3.01	-4.50	-4.21	-4.99
50	96.09	78.13	3.43	3.75	3.69	1.61	3.86	3.85	3.85	-5.08	-4.73	-5.80
51	103.51	89.13	3.37	4.37	4.33	1.69	4.26	4.95	4.22	-5.96	-5.27	-5.87
52	80.28	96.97	2.43	3.02	2.45	0.73	2.90	3.56	3.55	-4.72	-3.94	-4.59
Hydroxanthone derivatives												
20	80.45	117.20	2.38	0.96	0.37	-0.49	1.40	1.20	1.2	-3.01	-2.54	-2.53
21	103.47	117.20	2.34	0.96	0.37	-0.49	1.40	1.20	1.2	-3.01	-2.54	-2.53
22	81.17	137.43	1.26	0.26	-0.60	-1.21	1.31	0.32	0.29	-2.71	-2.20	-2.63
23	155.3	226.58	3.79	3.80	2.16	-1.36	1.85	1.62	-1.05	-8.25	-6.06	-4.17
24	155.17	226.58	3.67	2.30	1.50	-1.82	0.29	0.79	0.78	-6.70	-5.03	-1.91
25	191.84	220.26	4.75	3.54	5.41	-0.07	5.11	4.63	3.52	-7.85	-6.14	-7.00
26	155.1	226.58	3.62	2.36	2.33	-1.90	0.67	0.64	0.63	-6.76	-5.05	-2.34
27	155.3	226.58	4.58	3.80	2.16	-1.36	1.85	1.63	-1.01	-8.25	-6.06	-4.17
28	158.55	197.12	4.28	3.57	3.52	0.16	3.06	3.03	1.55	-7.40	-5.93	-5.44
29	161.54	197.12	4.26	3.57	3.52	0.16	3.06	3.03	1.55	-7.40	-5.93	-5.44
30	161.54	187.89	3.15	3.76	3.93	0.83	3.71	3.80	3.04	-7.40	-6.04	-5.98
31	161.54	187.89	3.73	3.76	3.93	0.83	3.71	3.80	3.04	-7.40	-6.04	-5.98
48	75.36	117.20	2.70	1.08	0.03	-0.74	1.00	0.76	0.74	-3.13	-2.61	-2.35

53	142.3	179.03	3.90	2.91	1.77	0.13	3.08	3.64	3.63	-6.33	-5.28	-5.74
Glycosylated and other derivatives												
32	173.33	166.26	4.09	5.44	4.34	-0.23	5.31	5.08	5.08	-8.69	-7.36	-8.77
33	196.41	281.57	2.61	1.56	0.49	-2.39	0.69	1.65	1.55	-7.08	-5.30	-5.14
34	175.42	177.72	3.50	5.84	4.01	0.93	6.05	3.70	3.63	-9.34	-7.48	-9.35
35	214.95	222.48	4.31	6.09	4.11	0.48	6.01	3.55	3.54	-10.54	-8.38	-9.50
36	176.76	175.95	3.98	5.21	3.68	0.18	6.05	2.52	2.52	-8.65	-7.11	-9.72

Table S3. Violations of drug-likeness rules by the marine anti-infective xanthones. For each compound, the type of violations of each rule was described.

ID	Lipinski	Ghose	Veber	Egan	Muegge
Xanthone derivatives					
1	0	0	0	0	0
2	0	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0
6	0	0	0	0	0
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	MW>500, HBA>10, HBA>5	MW>480, MR>130	PSA>140	PSA>131.6	PSA>150, HBA>10, HBD>5
11	MW>500, HBA>10	MW>480, MR>130	PSA>140	PSA>131.6	PSA>150, HBA>10
12	MW>500, HBA>10	MW>480, MR>130	PSA>140	PSA>131.6	PSA>150, HBA>10
13	MW>500, HBA>10	MW>480, MR>130	PSA>140	PSA>131.6	PSA>150, HBA>10
14	0	MW>480, MR>130	PSA>140	PSA>131.6	PSA>150, HBA>10
15	0	0	0	0	0
16	0	0	0	0	0
17	0	0	0	0	0
18	0	0	0	0	0
19	0	MW>480, MR>130	PSA>140	PSA>131.6	0
37	0	0	0	0	0
38	0	0	0	0	0
39	0	0	0	0	0
40	0	0	0	0	0
41	0	0	0	0	0
42	0	0	0	0	0
43	0	0	0	0	0
44	0	0	0	0	0
45	0	0	0	0	0
46	0	0	0	0	0
47	0	MR>130	PSA>140	PSA>131.6	0
49	0	0	0	0	0
50	0	0	0	0	0
51	0	0	0	0	0

52	0	0	0	0	0
Hydroxanthones derivatives					
20	0	0	0	0	0
21	0	0	0	0	0
22	0	TNA>70	0	PSA>131.6	0
23	MW>500, HBA>10, HBA>5	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, HBD>5
24	MW>500, HBA>10, HBA>5	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, HBD>5
25	MW>500, HBA>10	MW>480, MR>130, TNA>70	PSA>140, RB>10	PSA>131.6	MW>600, PSA>150, HBA>10
26	MW>500, HBA>10, HBA>5	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, HBD>5
27	MW>500, HBA>10, HBA>5	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, HBD>5
28	MW>500, HBA>10	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10
29	MW>500, HBA>11	MW>480, MR>130, TNA>71	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10
30	MW>500, HBA>12	MW>480, MR>130, TNA>72	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10
31	MW>500, HBA>13	MW>480, MR>130, TNA>73	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10
48	0	0	0	0	0
53	MW>500, HBA>10	MW>480, MR>130	PSA>140	PSA>131.6	PSA>150, HBA>10
Glycosylated and other derivatives					
32	MW>500, HBA>10	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, LOG P>5

33	MW>500, HBA>10, HBA>5	MW>480, MR>130, TNA>70	PSA>140, RB>10	PSA>131.6	MW>600, PSA>150, HBA>10, HBD>5
34	MW>500, HBA>10	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, LOG P>5
35	MW>500, HBA>10	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, HBD>5, LOG P>5
36	MW>500, HBA>10	MW>480, MR>130, TNA>70	PSA>140	PSA>131.6	MW>600, PSA>150, HBA>10, LOG P>5

MW – molecular weight, MR - molar refractivity, TNA - total number of atoms, PSA – polar surface area, HBA – hydrogen bond acceptor, HBD – hydrogen bond donor, RB - rotatable bonds, LOG P – considered log P value calculated by XLOGP3.

Table S4. Absorption and Metabolism parameters of marine antimicrobial xanthenes.

ID	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor
Xanthone derivatives								
1	High	No	No	Yes	Yes	Yes	Yes	Yes
2	High	No	No	Yes	No	No	Yes	No
3	High	No	No	No	No	Yes	Yes	No
4	High	Yes	No	No	No	No	No	No
5	High	Yes	No	Yes	Yes	Yes	No	Yes
6	High	No	No	Yes	No	Yes	No	No
7	High	No	No	Yes	No	Yes	No	No
8	High	No	No	Yes	No	No	Yes	Yes
9	High	No	No	Yes	No	No	Yes	Yes
10	Low	No	No	No	No	Yes	No	No
11	Low	No	No	No	No	Yes	No	No
12	Low	No	No	No	No	Yes	No	No
13	Low	No	No	No	No	Yes	No	No
14	Low	No	No	No	No	Yes	No	No
15	High	No	Yes	No	No	Yes	No	Yes
16	High	No	Yes	No	No	Yes	No	Yes
17	High	No	Yes	No	No	No	No	Yes
18	High	No	No	Yes	No	Yes	No	Yes
19	Low	No	Yes	No	No	No	No	Yes
37	High	Yes	No	Yes	No	No	Yes	Yes
38	High	No	No	Yes	No	No	Yes	Yes

39	High	Yes	No	Yes	No	Yes	No	No
40	High	No	No	Yes	Yes	Yes	No	Yes
41	High	No	No	Yes	No	Yes	No	Yes
42	High	Yes	No	Yes	Yes	Yes	No	Yes
43	High	No	No	No	Yes	Yes	No	Yes
44	High	No	No	Yes	No	Yes	No	No
45	High	Yes	No	Yes	Yes	Yes	No	Yes
46	High	No	No	Yes	Yes	Yes	No	Yes
47	Low	No	Yes	No	No	No	No	Yes
49	High	No	No	No	No	Yes	Yes	Yes
50	High	No	Yes	Yes	Yes	Yes	Yes	Yes
51	High	No	No	No	Yes	Yes	No	Yes
52	High	No	No	Yes	No	Yes	No	No

Hydroxanthones derivatives

20	High	No	No	No	No	No	No	No
21	High	No	No	No	No	No	No	No
22	Low	No	No	No	No	No	No	No
23	Low	No	No	No	No	Yes	No	No
24	Low	No	Yes	No	No	No	No	No
25	Low	No	Yes	No	No	No	No	No
26	Low	No	Yes	No	No	Yes	No	No
27	Low	No	No	No	No	Yes	No	No
28	Low	No	Yes	No	No	Yes	No	No
29	Low	No	Yes	No	No	Yes	No	No
30	Low	No	Yes	No	No	Yes	No	No

31	Low	No	Yes	No	No	Yes	No	No
48	High	No	No	No	No	No	No	No
53	Low	No	No	No	No	Yes	No	No

Glycosylated and other derivatives

32	Low	No	Yes	No	No	Yes	No	No
33	Low	No	Yes	No	No	No	No	No
34	Low	No	Yes	No	No	Yes	No	No
35	Low	No	Yes	No	No	Yes	No	No
36	Low	No	Yes	No	No	Yes	No	No