Supporting Information

A multiple linear regression approach to the estimation of carboxylic acid ester and lactone alkaline hydrolysis rate constants

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Table S1. Experimental and calculated log(k_b) values for 223 carboxylic acid esters.

ID no.	Name	Expt. log(k_b)	HYDROWIN	SPARC	CAE QSAR	CAE DTC-QSAR	QSAR 1/2	[a]Status	Ref no.
1	Methyl formate	1.56	1.20	0.69	1.52	1.47	2	In-AD	1
2	Ethyl formate	1.41	1.17	0.67	1.10	1.09	2	In	1
3	Propyl formate	1.36	1.10	0.67	1.00	1.00	2	In	1
4	Butyl formate	1.34	1.10	0.67	0.97	0.97	2	In	1
5	Isopropyl formate	1.04	1.05	0.64	0.62	0.63	2	In	1
6	Methyl acetate	-0.75	-0.89	-0.92	-0.38	-0.46	2	In	1
7	Ethyl Acetate	-0.95	-0.92	-1.07	-0.81	-0.85	2	In	1
8	Propyl acetate	-1.01	-0.99	-1.11	-0.91	-0.94	2	In	1
9	Butyl acetate	-1.05	-0.99	-1.13	-0.94	-0.97	2	In	1
10	Isopropyl acetate	-1.58	-1.04	-1.32	-1.28	-1.29	2	In	1
11	s-Butyl acetate	-1.76	-1.20	-1.73	-1.76	-1.74	2	In	1
12	Cyclopropyl acetate	-0.63	-1.23	-0.99	-0.66	-0.70	2	In	2
13	Cyclopentyl acetate	-1.46	-1.02	-1.38	-1.40	-1.39	2	In	2
14	Cyclohexenyl acetate[b]	-0.60	-0.80	-0.11	-0.11	-0.06	2	In	2
15	t-Butyl acetate	-2.82	-1.34	-1.81	-1.81	-1.78	2	In	1
16	3-methylpentan-3-yl acetate	-3.38	-1.34	-2.65	-2.76	-2.68	2	In	1
17	Vinyl acetate	0.68	-0.25	1.10	0.35	0.34	2	In	3
18	Isopropenyl acetate	-0.38	-0.57	0.91	-0.53	-0.50	2	In	2
19	Cyclopentenyl acetate	0.06	-0.80	-0.01	0.01	0.05	2	In	2
20	Allyl Acetate	-0.68	-0.46	0.50	-0.71	-0.75	2	In	1
21	but-3-en-2-yl acetate	-1.14	-1.04	-0.13	-1.52	-1.51	2	In	1
22	3-Methyl-1-penten-3-yl acetate	-2.40	-1.34	-1.05	-2.59	-2.50	2	In	1
23	3-Butyn-2-yl acetate	-0.44	-0.34	0.21	-0.36	-0.37	2	In	1
24	3-Methyl-1-pentyn-3-yl acetate	-1.66	-1.34	-0.77	-1.44	-1.39	2	In	1
25	2-Propyn-1-yl acetate	-0.14	0.67	0.75	0.11	0.07	2	In	1
26	Benzyl acetate	-0.71	-0.39	-0.29	-1.33	-1.38	2	In	1
27	Phenyl acetate	0.00	0.12	0.13	0.16	0.12	2	In	3
28	o-Fluorophenyl acetate	0.44	0.12	0.98	0.67	0.64	2	In	3

29	o-Chlorophenyl acetate	0.30	0.12	1.14	0.55	0.55	2	In	3
30	o-Bromophenyl acetate	0.35	0.12	1.08	0.34	0.36	2	In	3
31	o-Iodophenyl acetate	0.30	0.12	1.05	0.17	0.22	2	In	3
32	o-Methylphenyl acetate	-0.35	0.12	0.34	-0.27	-0.27	2	In	3
33	o-Ethylphenyl acetate	-0.40	0.12	-0.39	-0.60	-0.58	2	In	3
34	o-Isopropylphenyl acetate	-0.44	0.12	-0.55	-0.60	-0.57	2	In	3
35	o-tert-Butylphenyl acetate	-0.72	0.12	-0.70	-1.28	-1.21	2	In	3
36	o-Methoxyphenyl acetate	-0.14	0.12	0.34	-0.26	-0.26	2	In	3
37	o-Nitrophenyl acetate	0.90	0.12	1.77	0.85	0.85	2	In	3
38	o-Cyanophenyl acetate	1.08	0.12	1.80	0.56	0.55	2	In	3
39	m-Fluorophenyl acetate	0.45	0.54	0.57	0.75	0.71	2	In	3
40	m-Bromophenyl acetate	0.45	0.58	0.65	0.80	0.77	2	In	3
41	m-Methylphenyl acetate	-0.06	0.04	0.06	0.18	0.16	2	In	3
42	m-Ethylphenyl acetate	-0.05	0.03	0.06	0.17	0.15	2	In	3
43	m-Methoxyphenyl acetate	0.12	0.27	0.31	0.41	0.39	2	In	3
44	m-Nitrophenyl acetate	0.86	1.04	1.05	1.07	1.02	2	In	3
45	m-Cyanophenyl acetate	0.77	0.89	0.95	0.87	0.83	2	In	3
46	p-Fluorophenyl acetate	0.18	0.19	0.38	0.48	0.44	2	In	3
47	p-Chlorophenyl acetate	0.34	0.42	0.43	0.61	0.58	2	In	3
48	p-Bromophenyl acetate	0.30	0.42	0.44	0.59	0.56	2	In	3
49	p-Methylphenyl acetate	-0.06	-0.06	-0.02	0.02	0.00	2	In	3
50	p-Ethylphenyl acetate	-0.14	-0.07	-0.02	0.02	0.00	2	In	3
51	p-tert-Butylphenyl acetate	-0.16	-0.07	-0.02	0.04	0.03	2	In	3
52	p-Methoxyphenyl acetate	-0.07	0.13	0.02	0.17	0.15	2	In	3
53	p-Nitrophenyl acetate	1.05	1.09	0.90	1.38	1.33	2	In-AD	3
54	p-Cyanophenyl acetate	0.85	0.99	0.80	1.03	0.98	2	In	3
55	p-Methoxymethylphenyl acetate	0.56	0.15	0.07	0.35	0.32	2	In	3
56	Methyl Chloroacetate	2.15	0.97	1.56	1.47	1.42	2	In-AD	1
57	Ethyl Chloroacetate	1.56	0.95	1.40	1.04	1.02	2	In-AD	1
58	p-Nitrophenyl Chloroacetate	3.77	2.96	3.36	3.23	3.20	2	In	1
59	Methyl Dichloroacetate	3.45	2.76	3.24	2.66	2.62	2	In	1
60	Ethyl Dichloroacetate	2.95	2.74	3.09	2.25	2.24	2	In	1

61	Ethyl Trichloroacetate	3.41	3.20	3.47	3.21	3.27	2	Out	3
62	Phenyl Dichloroacetate	4.11	3.77	4.28	3.21	3.22	2	In	1
63	Ethyl Difluoroacetate	3.65	3.22	2.86	3.10	3.16	2	In	1
64	Ethyl Fluoroacetate	1.08	1.27	1.23	1.32	1.32	2	In-AD	3
65	Ethyl (methylthio)acetate	-0.04	0.20	0.15	-0.27	-0.26	2	In-AD	1
66	Ethyl methyl sulfoxide acetate	0.62	0.78	1.70	0.59	0.61	2	In	1
67	Ethyl methyl sulfone acetate	1.11	0.53	2.65	1.58	1.78	2	In-AD	1
68	2,4-D butoxyethyl ester	1.33	0.96	0.23	1.27	1.32	2	In	4
69	2,4-D methyl ester	1.09	0.65	-0.05	1.07	1.08	2	In	4
70	Ethyl Propionate	-1.06	-0.99	-1.35	-1.23	-1.26	2	In	1
71	Isopropyl Propionate	-1.68	-1.12	-1.61	-1.70	-1.70	2	In	3
72	Ethyl Butyrate	-1.32	-1.20	-1.49	-1.40	-1.43	2	In-AD	1
73	Ethyl iso-Butyrate	-1.52	-1.36	-1.62	-1.55	-1.58	2	In-AD	1
74	Isopropyl iso-Butyrate	-2.36	-1.48	-1.88	-2.02	-2.02	2	In	3
75	Ethyl neopentanoate	-2.77	-2.23	-2.04	-1.63	-1.65	2	In	3
76	Methyl acrylate	-0.85	-1.59	-0.59	-0.93	-0.93	2	In	5
77	Ethyl acrylate	-1.11	-1.61	-0.74	-1.35	-1.32	2	In	1
78	Butyl acrylate	-1.28	-1.68	-0.81	-1.48	-1.43	2	In	5
79	Phenyl acrylate	-0.12	-0.58	0.46	-0.42	-0.37	2	In	5
80	p-Chlorophenyl acrylate	0.30	-0.28	0.76	0.04	0.09	2	In-AD	5
81	p-Acetylphenyl Acrylate	0.55	0.01	0.61	0.52	0.55	2	In	5
82	m-Nitrophenyl acrylate	0.75	0.35	1.38	0.34	0.38	2	In	5
83	p-Nitrophenyl acrylate	0.95	0.40	1.22	0.75	0.78	2	In	5
84	trans-Methyl crotonate	-1.47	-2.03	-1.79	-1.22	-1.23	2	In	5
85	trans-Ethyl crotonate	-1.89	-2.05	-1.94	-1.65	-1.63	2	In-AD	1
86	cis-Ethyl crotonate	-1.84	-2.05	-1.94	-1.98	-1.98	2	In	1
87	Methyl methacrylate	-1.23	-2.47	-0.83	-1.55	-1.64	2	In	5
88	Methyl 3,3-Dimethylacrylate	-2.27	-2.18	-3.00	-1.68	-1.71	2	In	5
89	trans-Diethyl fumarate	0.65	-0.11	-0.41	-0.04	0.00	2	In	1
90	cis-Diethyl fumarate	-0.39	-0.11	-0.41	-0.39	-0.35	2	In	1
91	Propyl crotonate	-1.91	-2.13	-1.99	-1.75	-1.72	2	In	5
92	Isopropyl crotonate	-2.41	-2.18	-2.20	-2.11	-2.05	2	In-AD	5

93	Butyl crotonate	-1.95	-2.13	-2.00	-1.77	-1.72	2	In-AD	5
94	Isobutyl crotonate	-1.99	-2.32	-2.00	-2.23	-2.17	2	In	5
95	sec-butyl crotonate	-2.64	-2.34	-2.60	-2.59	-2.50	2	In	5
96	Isoamyl crotonate	-2.00	-2.13	-1.86	-1.89	-1.84	2	In-AD	5
97	Ethyl Propiolate	0.67	-0.11	-0.68	1.02	1.03	2	In	1
98	Ethyl 2-Butynoate	-0.25	-0.32	-2.01	0.31	0.30	2	In-AD	1
99	Diethyl 2-Butynedioate	1.84	-0.02	-0.44	2.20	2.23	2	In	1
100	Methyl Benzoate	-1.10	-1.40	-1.63	-1.23	-1.27	2	In-AD	3
101	Ethyl benzoate	-1.52	-1.42	-1.78	-1.64	-1.65	2	In	1
102	Isopropyl benzoate	-2.21	-1.55	-2.02	-2.10	-2.07	2	In	1
103	Methyl 1-Naphthoate	-1.51	-1.40	-1.81	-1.42	-1.43	2	In	5
104	Ethyl 1-Naphthoate	-1.77	-1.42	-1.96	-1.85	-1.83	2	In	5
105	Isopropyl 1-Naphthoate	-2.59	-1.55	-2.22	-2.31	-2.25	2	In	5
106	p-Nitrophenyl 1-Naphthoate	0.06	0.59	-0.02	0.24	0.27	2	In	5
107	p-Methoxyphenyl 1-Naphthoate	-0.99	-0.38	-0.90	-0.91	-0.86	2	In	5
108	Methyl 5-Nitro-1-Naphthoate	-0.85	-1.40	-1.29	-0.30	-0.25	2	In	5
109	Methyl 2-Naphthoate	-1.11	-1.40	-1.70	-1.47	-1.35	2	In	5
110	2-methoxyethyl acetate	-0.69	-0.58	-0.63	-0.21	-0.25	2	In	3
111	2-chloroethyl acetate	-0.41	-0.39	-0.27	0.09	0.04	2	In	3
112	Trifluoroethyl acetate	0.28	1.02	-0.41	0.93	0.88	2	In	3
113	Chloromethyl acetate	1.79	1.21	1.60	0.86	0.79	2	In	3
114	Dichloromethyl acetate	3.18	3.39	3.27	2.48	2.40	2	In-AD	3
115	Trichloromethyl acetate	4.11	4.66	3.57	3.95	3.87	2	In	3
116	Bromomethyl acetate	1.96	1.33	1.59	1.21	1.13	2	In	3
117	2-(dimethylamino)ethyl acetate	-1.00	-0.80	-0.76	-0.42	-0.45	2	In	3
118	Ethyl 2-methoxyacetate	0.14	0.33	0.00	0.48	0.50	2	In-AD	3
119	Ethyl 2-hydroxyacetate	0.00	0.39	-0.27	-0.29	-0.31	2	In-AD	3
120	Ethyl Bromoacetate	1.70	1.02	1.35	1.58	1.57	2	In-AD	3
121	Ethyl Dibromoacetate	2.31	2.62	2.74	2.96	3.01	2	In	3
122	Ethyl 2-bromopropanoate	1.00	0.44	1.02	1.10	1.12	2	In	3
123	Ethyl Iodoacetate	1.21	0.97	1.21	1.55	1.58	2	In-AD	3
124	Ethyl 2-aminoacetate	-0.19	0.19	-0.61	-0.09	-0.07	2	In	3

125	Ethyl 4-aminobenzoate	-2.57	-2.62	-3.16	-2.93	-2.84	2	In	3
126	Ethyl 4-nitrobenzoate	-0.13	0.21	-0.79	0.12	0.17	2	In	3
127	Ethyl 4-fluorobenzoate	-1.41	-1.30	-1.73	-1.71	-1.74	2	In	3
128	4-(ethoxycarbonyl)benzen-1-olate	-3.58	-2.22	-3.21	-3.05	-2.99	2	In-AD	3
129	Ethyl 3-aminobenzoate	-1.64	-1.42	-2.11	-2.94	-2.85	2	In	3
130	Procaine	-2.42	-2.50	-3.40	-2.62	-2.50	2	In	6
131	4-methylphenyl benzoate	-0.49	-0.56	-0.72	-0.85	-0.83	2	In	3
132	4-cyanophenyl benzoate	0.33	0.49	0.10	0.17	0.16	2	In	3
133	4-nitrophenyl benzoate	0.45	0.59	0.20	0.52	0.50	2	In	3
134	2,4-dinitrophenyl benzoate	1.18	0.59	1.82	0.90	0.91	2	In	3
135	p-Methoxyphenyl acetate	0.04	0.13	0.02	0.17	0.15	2	In	3
136	p-Methoxyphenyl propionate	-0.14	0.05	-0.27	-0.24	-0.26	2	In	3
137	p-Methoxyphenyl butyrate	-0.14	-0.16	-0.41	-0.41	-0.42	2	In	3
138	p-Methoxyphenyl isobutyrate	-0.30	-0.31	-0.55	-0.56	-0.58	2	In	3
139	p-Methoxyphenyl pentanoate	-0.15	-0.16	-0.46	-0.51	-0.52	2	In-AD	3
140	p-Methoxyphenyl 2-methylbutanoate	-0.57	-0.79	-0.98	-0.90	-0.92	2	In	3
141	p-Methoxyphenyl neopentanoate	-0.92	-1.19	-0.98	-0.65	-0.65	2	In	3
142	p-Nitrophenyl acetate	0.98	1.09	0.90	1.38	1.33	2	In	3
143	p-Nitrophenyl propionate	0.90	1.02	0.61	0.96	0.92	2	In	3
144	p-Nitrophenyl butyrate	0.75	0.81	0.47	0.79	0.75	2	In-AD	3
145	p-Nitrophenyl isobutyrate	0.69	0.65	0.33	0.64	0.60	2	In-AD	3
146	p-Nitrophenyl pentanoate	0.71	0.81	0.42	0.69	0.66	2	In-AD	3
147	p-Nitrophenyl 2-methylbutanoate	0.48	0.17	-0.10	0.31	0.26	2	In-AD	3
148	p-Nitrophenyl neopentanoate	0.11	-0.22	-0.10	0.56	0.53	2	In-AD	3
149	2,4-Dinitrophenyl acetate	1.97	1.09	2.53	1.86	1.84	2	In	3
150	Acetoxime acetate	-0.01	-0.18	2.45	-0.13	-0.05	2	In	7
151	p-Methoxyphenyl formate	1.57	2.22	2.22	2.07	2.08	2	In	8
152	p-Methylphenyl formate	1.77	2.03	2.18	1.92	1.92	2	In	8
153	phenyl formate	1.82	2.20	2.33	2.05	2.05	2	In	8
154	m-Nitrophenyl formate	2.70	3.13	3.25	2.96	2.95	2	In	8
155	p-Nitrophenyl formate	3.07	3.18	3.10	3.28	3.25	2	In	8
156	Phenylalanine methyl ester	-0.15	-1.33	-1.19	-0.26	-0.24	2	In	9

157	Imidazole lactic acid methyl ester	1.41	-0.24	-0.69	1.38	1.40	2	In	9
158	Histidine methyl ester	-0.13	-1.33	-1.08	0.21	0.24	2	In	9
159	Acetic anhydride	2.99	3.41	1.32	3.31	3.24	2	In	7
160	Phenyl acetate	-0.30	0.12	0.13	0.28	0.24	2	In	3
161	Phenyl propionate	0.08	0.04	-0.16	-0.14	-0.17	2	In	3
162	Phenyl butyrate	-0.11	-0.17	-0.30	-0.33	-0.36	2	In	3
163	Phenyl Isobutyrate	-0.19	-0.33	-0.44	-0.46	-0.49	2	In	3
164	Phenyl pentanoate	-0.15	-0.17	-0.35	-0.45	-0.47	2	In	3
165	Phenyl 2-methylbutyrate	-0.57	-0.80	-0.86	-0.72	-0.75	2	In	3
166	Phenyl neopentanoate	-0.89	-1.20	-0.87	-0.49	-0.50	2	In	3
167	Phenyl 3,3-dimethylbutanoate	-0.30	-1.38	-0.93	-0.88	-0.91	2	In-AD	3
168	4-ethoxy-4-oxobutanoate	-1.75	-1.05	-1.42	-2.22	-2.24	2	In-AD	10
169	(2E)-4-ethoxy-4-oxobut-2-enoate	-0.80	-0.50	-0.49	-1.39	-1.38	2	In-AD	10
170	(2Z)-4-ethoxy-4-oxobut-2-enoate	-2.31	-0.50	-0.49	-3.69	-3.68	2	In	10
171	4-ethoxy-4-oxobut-2-ynoate	0.38	-0.32	-0.49	0.56	0.58	2	In	10
172	Isobutyl acetate	-1.21	-1.18	-1.16	-1.34	-1.35	2	In	5
173	Methyl tiglate	-1.42	-2.68	-2.04	-1.67	-1.76	2	In-AD	5
174	Methyl dimethylacrylate	-2.12	-2.18	-3.00	-1.77	-1.80	2	In-AD	5
175	n-Hexyl formate	1.14	1.10	0.67	1.01	1.01	2	In	11
176	2-Ethylbutylformate	1.17	0.91	0.67	0.15	0.20	2	In	11
177	Phenyl Phenylacetate	0.04	0.34	0.30	0.23	0.16	2	In	12
178	Phenyl Diphenylacetate	0.09	-0.38	-1.36	0.02	-0.01	2	Out	12
179	p-nitrophenylacetate	1.15	-0.67	-0.38	0.95	1.01	2	In	13
180	methyl 2-phenylacetate	-0.82	-0.67	-0.73	-0.45	-0.55	2	In	14
181	ethyl 2-phenylacetate	-1.00	-0.69	-0.88	-0.88	-0.95	2	In	14
182	propan-2-yl 2-phenylacetate	-1.92	-0.82	-1.14	-1.38	-1.42	2	In-AD	14
183	trifluoromethyl 2-phenylacetate	0.61	1.25	-0.23	0.88	0.80	2	In	14
184	1,1,1,3,3,3-hexafluoropropan-2-yl 2-phenylacetate	1.93	-0.82	-2.19	1.81	1.76	2	In	14
185	phenyl 2-phenylpropanoate	0.04	0.34	0.30	0.23	0.16	2	In	14
186	phenyl 3-phenylpropanoate	0.16	-0.06	-0.22	1.53	1.58	2	In	14
187	1-phenylethyl 3-phenylpropanoate	-1.70	-0.69	-0.95	-1.33	-1.39	2	In	14
188	pentan-2-yl 3-phenylpropanoate	-1.62	-0.98	-1.54	-2.02	-2.02	2	In	14

189	2-phenylpropyl 3-phenylpropanoate	-1.57	-0.96	-1.58	-2.05	-2.07	2	In	14
190	ISOAMYLACETATE	-1.02	-0.99	-0.99	-1.12	-1.13	2	In-AD	15
191	methyl 4-hydroxybenzoate(MeP)	-3.10	-2.20	-2.27	-2.64	-2.59	2	In	16
192	propyl 4-hydroxybenzoate(PrP)	-3.53	-2.29	-2.45	-3.21	-3.11	2	In-AD	16
193	butyl 4-hydroxybenzoate(BuP)	-3.61	-2.29	-2.46	-3.26	-3.15	2	In-AD	16
194	propan-2-yl 4-hydroxybenzoate(iPrP)	-4.09	-2.34	-2.65	-3.56	-3.44	2	In-AD	16
195	2-methylpropyl 4-hydroxybenzoate(iBuP)	-3.71	-2.48	-2.48	-3.57	-3.44	2	In	16
196	benzyl 4-hydroxybenzoate(BzP)	-3.12	-1.70	-1.61	-3.48	-3.40	2	In	16
197	benzyl benzoate	-2.10	-0.90	-0.98	-2.22	-2.23	2	In	17
198	ethyl trimethyl acetate (ethyl pivalate)	-2.77	-2.23	-2.04	-1.62	-1.64	2	In	17
199	1-butyl 2,4-dichlorophenoxyacetate	0.60	0.55	-0.27	0.45	0.52	2	In-AD	4
200	1-octyl 2,4-dichlorophenoxyacetate	0.60	0.20	-0.28	0.73	0.80	2	In	4
201	glycol monoacetate	-0.63	-0.92	-0.75	-0.15	-0.20	2	In-AD	18
202	Tetracaine	-2.45	-2.37	-2.80	-2.51	-2.39	2	In	19
203	chloroprocaine	-1.77	-2.50	-2.75	-1.66	-1.53	2	In	20
204	2,2,4-Trimethyl-1,3-pentanediol monoisobutyrate	-2.01	-1.84	-3.04	-2.36	-2.28	2	In	21
205	butylparaben	-3.91	-2.29	-2.46	-3.26	-3.15	2	In	21
206	methyl 2-phenylacetate	-0.82	-0.67	-0.73	-0.37	-0.47	2	In	14
207	methyl 3-phenylpropanoate	-0.82	-1.07	-1.26	-1.16	-1.20	2	In	14
208	methyl 3-(2-hydroxyphenyl)propanoate	-0.64	-1.07	-1.51	-0.79	-0.81	2	In	14
209	methyl 2-chloropropanoate	0.41	0.70	1.35	0.84	0.81	2	In-AD	14
210	methyl 2-(2-phenylacetamido) propanoate	-0.03	-1.33	-0.55	-0.54	-0.53	2	In	14
211	methyl 3-phenyl-2-(2-phenylacetamido) propanoate	-0.26	-1.33	-1.07	-0.99	-0.89	2	In	14
212	methyl 2-phenylpropanoate	-1.42	-1.48	-1.38	-0.61	-0.71	2	In	14
213	methyl 3-phenylbutanoate	-0.60	-1.75	-2.07	-1.73	-1.77	2	In-AD	14
214	methyl 4-hydroxy-4-phenylbutanoate	-1.10	-1.18	-1.80	-0.85	-0.84	2	In-AD	14
215	p-Nitrophenyl B-phenylpropionate	1.16	0.91	0.54	0.51	0.50	2	In	22
216	p-Nitrophenylphenylacetate	1.79	1.32	1.07	1.30	1.22	2	In	22
217	p-Nitrophenyl m-nitrophenylacetate	2.04	1.32	1.29	2.62	2.73	2	In	22
218	Ethyl palmitate	-3.02	-1.55	-1.56	-2.89	-2.92	1	In	23
219	n-Butyl palmitate	-3.07	-1.62	-1.62	-3.08	-3.13	1	In	23
220	Methyl stearate	-3.32	-1.52	-1.41	-2.68	-2.71	1	In	23

221	Octadecyl acetate	-0.56	-1.34	-1.14	-1.27	-1.29	1	In	23
222	Ethyl stearate	-4.00	-1.55	-1.56	-3.12	-3.17	1	In	23
223	Cetyl propionate	-2.85	-1.41	-1.42	-1.64	-1.64	1	In	23

[a]Applicability domain status determined from DTC-QSAR: In and Out applies to training set, and In-AD and Out-AD applies to test set.
[b]Corrected name.

Table S2. Experimental and calculated log(k_b) values for 108 lactones.

ID no.	Name	Ring size	Expt. log(k_b)[a]	Lactone QSAR	Lactone DTC-QSAR	QSAR 1/2	Status[b]	Ref. no.
1	Coumarin	6	**-0.23**	-0.38	-0.29	1	In-AD	14, 24
2	Ethyl coumarin-3-carbaoxylate	6	0.39	1.07	1.10	1	In	25
3	β-Butyrolactone	4	0.44	0.19	0.21	1	In	26
4	6-Nitro-3,4-dihydrocoumarin	6	3.44	3.23	3.39	1	In	22
5	3,4-dihydrocoumarin	6	**2.66**	1.53	1.58	1	In	14, 22
6	diketene	4	1.18	1.57	1.60	1	In	27
7	3-Chloro-coumarin	6	1.26	0.93	0.97	1	In	28
8	3-Bromo-coumarin	6	1.20	1.31	1.43	1	In	28
9	3-Phenyl-coumarin	6	-0.10	-0.10	-0.05	1	In	28
10	3-Methyl-Coumarin	6	-0.28	-0.88	-0.82	1	In	28
11	4-Methyl-Coumarin	6	-1.00	-1.09	-1.03	1	In	28
12	salinosporamide A	4	1.89	1.98	1.99	1	In	29
13	6H-benzo[c]chromen-6-one	6	1.08	0.16	0.23	1	In	30
14	4,4-dimethyl-3,4-dihydro-2H-1-benzopyran-2-one	6	0.62	1.06	1.08	1	In	30
15	4,4,5,7-tetramethyl-3,4-dihydro-2H-1-benzopyran-2-one	6	-0.40	0.45	0.44	1	In	30
16	δ-Valerolactone	6	**1.24**	0.86	0.90	1	In	14, 31
17	2-Oxabicyclo [2.2.2]-octan-3-one	6	-1.57	-0.59	-0.62	1	In	31
18	Tetra-O-methylglucono-δ-lactone	6	3.53	3.45	3.49	1	In	32
19	Tri-O-methyl - 2- deoxyglucono-δ-lactone	6	2.26	2.45	2.55	1	In	32
20	D-Glucono-δ-lactone	6	3.26	3.66	3.73	1	In-AD	33
21	P-CPT (prodrug of Camptothecin)	6	1.96	1.64	1.62	1	In	34
22	β-propiolactone	4	**0.70**	0.79	0.84	1	In	14, 35
23	Isochroman-3-one	6	0.74	0.32	0.33	1	In	14
24	6-Methyl-3,4-dihydropyran-2-one	6	1.90	1.70	1.73	1	In	14
25	Warfarin	6	**-3.70**	-3.39	-3.45	1	In	36
26	camptothecin	6	2.63	2.52	2.53	1	In	37
27	10-OH camptothecin	6	2.88	2.47	2.48	1	In	37
28	9-$CH_2NH(CH_3)^{2+}$, 10-OH camptothecin	6	2.63	2.40	2.41	1	In-AD	37

29	9-NH_2 camptothecin	6	2.67	2.50	2.51	1	In-AD	37
30	10,11-O$(CH_2)_2$O- camptothecin	6	2.63	2.69	2.71	1	In	37
31	6-nitro-2H-chromen-2-one	6	0.70	1.07	1.26	1	In-AD	38
32	6-nitro-2H-chromen-2-one-3- carboxylic acid	6	0.81	0.23	0.27	1	In	38
33	7-dimethylamino-4-methyl-2H-chromen-2-one	6	-2.11	-2.50	-2.50	1	In	39
34	7-diethylamino-4-methyl-2H-chromen-2-one	6	-2.40	-2.20	-2.18	1	In-AD	39
35	7-hydroxy-2H-chromen-2-one	6	-2.01	-1.83	-1.76	1	In	40
36	7-hydroxy-2H-chromen-2-one-4-acetic acid	6	-1.89	-1.97	-1.90	1	In	40
37	coumalic acid	6	-1.15	-0.58	-0.49	1	In	41
38	4,4-dimethyl-3H-1-benzopyran-2-one	6	0.90	1.05	1.07	1	In-AD	42
39	Bergenin	6	0.89	0.49	0.61	1	In	43
40	Dalvastatin	6	0.81	1.41	1.49	1	In	44
41	Simvastatin	6	0.53	0.64	0.68	1	In-AD	45
42	4-hexadecylidene-3-pentadecyloxetan-2-one	4	0.20	-0.17	-0.23	1	In	46
	4-Pentadecylidene-3-tetradecyl-2-oxetanone[c]	4	0.20	-0.17	-0.23	1		46
43	β-Isovalerolactone	4	-0.66	-0.54	-0.56	1	In	47
44	coumarin-3- thiocarboxamide	6	-0.77	-1.22	-1.22	1	In	48
45	Decan-5-olide	6	-1.07	-1.25	-1.30	1	In	49
46	9-Nitrocamptothecin	6	2.46	2.75	2.77	1	In-AD	50
47	3-BROMOCOUMARIN	6	0.93	1.33	1.44	1	In	51
48	COUMARIN-3-CARBOXYLIC ACID	6	-1.91	-1.17	-1.23	1	In	51
49	Psoralen	6	-0.41	-0.04	0.08	1	In-AD	52
50	8-Hydroxypsoralen	6	-2.03	-2.29	-2.22	1	In	52
51	2-furanone	5	-1.43	-0.77	-0.59	2	In-AD	27
52	3-(m-nitrophenyl)-3-methoxyphthalide	5	-0.06	-0.25	-0.21	2	In	53
53	2-Coumaranone	5	**1.83**	2.29	2.30	2	In-AD	12, 14, 22
54	Phthalide	5	**-0.29**	-0.58	-0.42	2	In	14, 54, 55
55	γ-Butyrolactone	5	**-0.02**	0.18	0.30	2	In	31, 55
56	γ-Valerolactone	5	**-0.41**	-0.11	-0.04	2	In	31, 55
57	5- Aminophthalide	5	-0.75	-1.04	-0.89	2	In	55
58	3-phenylcoumaran-2-one	5	2.70	1.92	1.91	2	In	12
59	2,3-dihydro-1-benzofuran-2-one	5	2.21	1.94	1.93	2	In	12

60	2-oxo-3-phenyl-2,3-dihydro-1-benzofuran-5-olate	5	1.75	1.67	1.66	2	In-AD	12
61	5-hydroxy-3-phenyl-2,3-dihydro-1-benzofuran-2-one	5	2.26	2.00	1.99	2	In	12
62	5-methoxy-3-methyl-3-phenyl-2,3-dihydro-1-benzofuran-2-one	5	0.91	1.72	1.70	2	In	12
63	5-Nitro-2-coumaranone	5	**3.07**	2.90	2.92	2	In	12, 56
64	N-Butyryl-L-homoserine lactone	5	1.13	0.92	0.98	2	In	57
65	N-hexanoyl-L-homoserine lactone	5	1.13	0.82	0.88	2	In	57
66	N-octanoyl-L-homoserine lactone	5	1.31	0.90	0.96	2	In	57
67	3-oxo-N-hexanoyl-L-homoserine lactone	5	0.97	1.63	1.66	2	In	57
68	3-oxo-N-octanoyl-L-homoserine lactone	5	1.24	1.02	1.09	2	In	57
69	8-Hydroxy-1-naphthoic acid lactone	5	1.91	1.25	1.33	2	In	30
70	e-Caprolactone	7	-0.11	-0.28	-0.18	2	In	31
71	6-Oxabicyclo[3.2.1]-octan-7-one	7	-0.44	-0.42	-0.36	2	In	31
72	γ- Ethoxy- γ-butyrolactone	5	0.69	0.79	0.85	2	In	58
73	Phenyl N-acyl homoserine lactone	5	1.19	1.06	1.13	2	In	59
74	2-methoxyphenyl N-acyl homoserine lactone	5	1.37	1.13	1.20	2	In	59
75	3-methoxyphenyl N-acyl homoserine lactone	5	1.22	1.15	1.22	2	In	59
76	4-methoxyphenyl N-acyl homoserine lactone	5	1.17	1.26	1.33	2	In	59
77	2-nitrophenyl N-acyl homoserine lactone	5	1.36	1.40	1.47	2	In	59
78	3-nitrophenyl N-acyl homoserine lactone	5	1.32	1.43	1.51	2	In-AD	59
79	4-nitrophenyl N-acyl homoserine lactone	5	1.40	1.44	1.51	2	In-AD	59
80	2,3-dihydro-1-benzofuran-2-one	5	2.64	2.29	2.30	2	In-AD	42
81	4,6-dimethyl-2,3-dihydro-1-benzofuran-2-one	5	2.28	2.00	2.00	2	In	42
82	3,3-dimethyl-2,3-dihydro-1-benzofuran-2-one	5	1.30	1.80	1.80	2	In	42
83	3,3,4,6-tetramethyl-2,3-dihydro-1-benzofuran-2-one	5	0.90	1.53	1.52	2	In	42
84	Canrenone	5	-0.96	-0.90	-0.93	2	In	60
85	Gibberellic acid	7	-0.38	-1.08	-1.11	2	In	61
86	Spirodiclofen	5	-0.37	-0.75	-0.74	2	In	62
87	Spiromesifen	5	-0.73	-0.84	-0.83	2	In-AD	63
88	Pilocarpine	5	-1.02	-0.37	-0.27	2	In-AD	64
89	isopilocarpine	5	-0.98	-0.37	-0.27	2	In	64
90	phenolphthalein	5	-1.74	-1.34	-1.32	2	In	65
91	N,N-Dimethylaminophenolphthalein	5	-1.59	-1.36	-1.35	2	In	66

92	securinine	5	-1.62	-1.60	-1.55	2	In	67
93	4'-Demethylepipicropodophylline (DEPP)	5	1.46	1.49	1.43	2	Out	68
94	4'-Demethylpicropodophylline (DPP)	5	1.39	1.49	1.43	2	Out	68
95	Picropodophylline	5	1.61	1.49	1.43	2	Out-AD	68
96	Epothilone-D	16	0.99	1.34	1.18	2	In	69
97	D-Glucuronolactone	5	2.32	2.21	2.16	2	In	70
98	Brassinolide	7	-1.31	-1.21	-1.15	2	In-AD	71
99	5-octyl-2,5-dihydrofuran-2-one	5	-1.25	-1.35	-1.23	2	In	72
100	3,4-dichloro-5-hydroxyfuran-2(5H)-one	5	1.49	1.85	1.88	2	In-AD	73
101	3,4-dibromo-5-hydroxyfuran-2(5H)-one	5	1.03	1.23	1.30	2	Out	73
102	N-acylhomoserine homoserine C6	5	1.20	0.60	0.65	2	In	74
103	N-acylhomoserine homoserine C7	5	1.22	0.58	0.62	2	In	74
104	N-acylhomoserine homoserine C8	5	1.09	0.67	0.72	2	In	74
105	N-acylhomoserine homoserine C10	5	0.92	0.66	0.71	2	In	74
106	N-acylhomoserine homoserine C12	5	0.55	0.66	0.71	2	In	74
107	N-acylhomoserine homoserine C14	5	0.03	0.66	0.71	2	In	74
108	2-Coumaranone	5	1.93	2.29	2.30	2	In	75

[a]Bold font indicates experimental values determined from mean of multiple references. [b]Applicability domain status determined from DTC-QSAR: In and Out applies to training set, and In-AD and Out-AD applies to test set. [c]Not included in model development (see datapoint after no. 42).

Table S3. Correlation coefficients for pairs of descriptors for the carboxylic acid ester data set (n=223). See Table 1 for abbreviation key.

	bpK_a OC=O	pK_a COOH	pK_a OH	SH *COOH	SH *OH	SEI *OH	SEI: C=O*	ρ *C=O	AAC	*E* COOH	Sum π χ	molec pol	opt-*E* COOH	μ COOH
pK_a COOH	0.519													
pK_a OH	0.282	-0.207												
SH *COOH	-0.139	-0.263	0.198											
SH *OH	-0.178	0.273	-0.770	-0.327										
SEI *OH	-0.123	0.257	-0.670	-0.325	0.955									
SEI C=O*	-0.274	-0.237	-0.058	0.893	0.000	0.002								
ρ *C=O	-0.252	-0.080	0.015	-0.387	0.054	0.066	-0.304							
AAC	-0.110	0.037	-0.519	0.279	0.386	0.307	0.454	-0.391						
E COOH	-0.150	-0.407	0.182	0.594	-0.354	-0.357	0.537	-0.507	0.487					
Sum π χ	-0.152	-0.052	-0.639	0.294	0.423	0.338	0.443	-0.402	0.903	0.447				
molec α	-0.082	0.063	-0.183	0.380	0.201	0.169	0.525	-0.260	0.628	0.365	0.563			
opt-*E* COOH	-0.318	-0.432	0.118	0.478	-0.270	-0.278	0.508	-0.329	0.475	0.940	0.389	0.338		
$^{k}\mu$ COOH	0.360	-0.066	0.192	0.459	-0.222	-0.204	0.365	-0.291	0.342	0.431	0.310	0.316	0.301	
molec α OH	-0.081	0.228	-0.529	-0.276	0.757	0.711	-0.007	0.052	0.359	-0.275	0.352	0.467	-0.206	-0.103

Table S4. Correlation coefficients for pairs of descriptors for the Lactone QSAR1 data set (n=50). See Table 2 for abbreviation key.

	LRS	pK_a OC=O	apK_a1	pK_a COOH	pK_a OH	ρ C=O*	π q *OC=O
pK_a OC=O	-0.050						
apK_a1	-0.118	0.268					
pK_a COOH	-0.381	0.161	0.117				
pK_a OH	-0.134	-0.298	-0.088	0.422			
ρ C=O*	-0.302	-0.501	-0.015	0.593	0.658		
π q *OC=O	0.159	0.063	0.120	-0.402	-0.893	-0.500	
SEI *OC=O	0.696	-0.080	-0.037	-0.543	-0.370	-0.426	0.365

Table S5. Correlation coefficients for pairs of descriptors for the Lactone QSAR2 data set (n=58). See Table 2 for abbreviation key.

	pK_a OC=O	pK_a COOH	q *OC=O	SEI *C=O	SEI *OC=O
pK_a COOH	0.224				
q *OC=O	-0.368	-0.144			
SEI *C=O	-0.179	-0.419	0.205		
SEI *OC=O	0.078	-0.140	0.336	0.674	
RSCS	0.132	-0.151	-0.184	0.219	-0.029

Table S6. Values of the regression coefficient, significance level (p-value), correlation (R), and standard error of lactone hydrolysis rate constants against various physicochemical and molecular descriptors for two models: Lactone-fulldata QSAR and Lactone-fulldata DTC-QSAR.

		Lactone-fulldata QSAR			Lactone-fulldata DTC-QSAR	
Variable	*Correl.(R)*	*Coefficient*	*[a](+/-)*	*P-value*	*Coefficient*	*[a](+/-)*
Intercept	-	-34.244	4.732	1.13E-10	-34.111	5.267
[b]pK_a OC=O	-0.690	-4.733	0.564	4.31E-13	-4.912	0.665
[c]apK_a1	-0.074	0.019	0.008	2.62E-02	0.028	0.010
[d]pK_a COOH	-0.157	-0.543	0.157	8.10E-04	-0.518	0.170
[e]pK_a OH	-0.009	-0.470	0.086	3.51E-07	-0.471	0.103
[f]SH *OC=O	-0.203	-5.022	1.508	1.23E-03	-4.197	1.882
[g]SH *C=O	-0.107	-10.578	2.488	4.92E-05	-9.128	2.892
[h]SEI C=O*	0.076	14.826	4.662	1.98E-03	11.276	5.652
[i]*q* *OC=O	0.001	-37.744	9.981	2.71E-04	-40.704	12.128
[j]HRA	-0.420	-1.362	0.331	8.28E-05	-1.435	0.385
[k]HARC	-0.084	-0.565	0.188	3.34E-03	-0.375	0.228
LRSS	0.122	0.308	0.088	7.64E-04	0.252	0.115

[a]Standard Error (+/-); [b]basic micro pK_a on oxygen of carbonyl (parent compound); [c] [c]Lowest acidic micro pK_a on parent compound; [d]Acidic micro pK_a on carboxylic group of product; [e]Acidic macro-pK_a on alcohol group of product; [f]Steric hinderance on sp^3 alpha oxygen connected to carbonyl (parent compound); [g]Steric hinderance on sp^2 carbon of carbonyl (parent compound); [h]Steric effect index on sp^2 oxygen of carbonyl (parent compound); [i]Charge on sp^3 alpha oxygen connected to carbonyl (parent compound); [j]Hetero ring analysis (user-determined/not available in ChemAxon); [k]Heteroaromatic ring count; [l]Largest ring system size.

Table S7. Overall performance statistics for CAE and Lactone QSAR1 and QSAR2, and comparisons with other existing models when applicable.

Model	n	R^2	R_a^2	s	MAE	RMSE	mne	mpe
CAE QSAR1	223	0.93	0.92	0.45	0.339	0.433	-1.39	1.25
CAE DTC-QSAR1	223	0.93	0.92	0.46	0.341	0.438	-1.30	1.22
HYDROWIN	223	0.82	-	-	0.489	0.690	-2.75	2.45
SPARC	223	0.77	-	-	0.546	0.770	-4.12	2.46
CAE QSAR2	217	0.93	0.93	0.42	0.318	0.410	-1.38	1.37
CAE DTC-QSAR2	217	0.93	0.93	0.42	0.318	0.413	-1.37	1.42
HYDROWIN	217	0.83	-	-	0.459	0.643	-2.75	2.04
SPARC	217	0.79	-	-	0.519	0.733	-4.12	2.46
Lactone QSAR1	50	0.94	0.92	0.47	0.347	0.429	-1.13	0.97
Lactone DTC-QSAR1	50	0.94	0.92	0.48	0.352	0.434	-1.08	0.95
Lactone QSAR2	58	0.90	0.89	0.40	0.304	0.338	-0.78	0.81
Lactone DTC-QSAR2	58	0.90	0.89	0.41	0.303	0.383	-0.79	0.84

[a]Statistical parameters: n = Observations; R^2 = squared correlation coefficient, adjusted R_a^2 s = Standard error or standard deviation of estimate (SEE), MAE = Mean Absolute Error, RMSE = Root Mean Square Error, mne = maximum negative error (largest underestimation), mpe = maximum positive error (largest overestimation)

Table S8. Training and test sets' validation statistics for Lactone-fulldata DTC-QSARs. See Table 6 for abbreviations.[a]

Validation Statistics	Lactone-fulldata DTC-QSAR	*Validation Statistics*	Lactone-fulldata DTC-QSAR
Internal	*Training Set*	*External*	*Test Set*
Observations (n)	87	Observations (n)	21
no. of outliers	0	no. of outliers	0
[b]R^2	0.80	[b]R^2	0.80
[b]R_a^2	0.77	[b]Q^2(F1)	0.78
[b]Q^2(LOO)	0.73	[b]Q^2(F2)	0.77
[b]SEE	0.71	[b]CCC	0.86
MAE	0.595[b] (0.507)[c]	[b]MAE	0.591
[c]RMSD	0.656	[c]RMSD	0.663

[a]Statistical parameters: R^2 = squared correlation coefficient, R_a^2 = adjusted squared correlation coefficient, SEE = Standard error or standard deviation of estimate (s), MAE = Mean Absolute Error, RMSE = Root Mean Square Error, mne = maximum negative error (largest underestimation), mpe = maximum positive error (largest overestimation); [b]Taken from DTC-QSAR; [c]Calculated.

Table S9. Experimental and calculated log(k_b) values for various alkyl chain carboxylic acid esters.[a]

Chemical Name	Chain length	R1/R2[b]	Expt. log(k_b)	CAE QSAR1		CAE QSAR2		SPARC		HYDROWIN	
Methyl formate	C1	R2	1.56	1.47	(-0.09)	1.52	(-0.05)	0.69	(-0.88)	1.20	(-0.37)
Ethyl formate	C2	R2	1.41	1.07	(-0.34)	1.10	(-0.31)	0.67	(-0.74)	1.17	(-0.24)
Propyl formate	C3	R2	1.36	0.97	(-0.39)	1.00	(-0.36)	0.67	(-0.69)	1.10	(-0.26)
Butyl formate	C4	R2	1.34	0.91	(-0.43)	0.97	(-0.37)	0.67	(-0.67)	1.10	(-0.24)
n-Hexyl formate	C6	R2	1.14	0.89	(-0.26)	1.01	(-0.14)	0.67	(-0.48)	1.10	(-0.05)
Methyl acetate	C1	R2	-0.75	-0.35	(0.39)	-0.38	(0.36)	-0.92	(-0.17)	-0.89	(-0.15)
Ethyl acetate	C2	R2	-0.95	-0.78	(0.18)	-0.81	(0.14)	-1.07	(-0.12)	-0.92	(0.04)
Propyl acetate	C3	R2	-1.01	-0.88	(0.14)	-0.91	(0.10)	-1.11	(-0.10)	-0.99	(0.02)
Butyl acetate	C4	R2	-1.05	-0.93	(0.12)	-0.94	(0.11)	-1.13	(-0.08)	-0.99	(0.07)
1-octyl 2,4-dichlorophenoxyacetate	C8	R2	0.60	0.55	(-0.05)	0.73	(0.13)	-0.28	(-0.88)	0.20	(-0.40)
Methyl decanoate[c]	C9	R1	-2.64	-1.73	(0.91)	-0.93	(1.71)	-1.41	(1.23)	-1.52	(1.12)
Ethyl palmitate	C16	R1	-3.02	-2.89	(0.13)	-2.45	(0.57)	-1.56	(1.46)	-1.55	(1.48)
n-Butyl palmitate	C16	R1	-3.07	-3.08	(-0.01)	-2.62	(0.45)	-1.62	(1.45)	-1.62	(1.46)
Methyl stearate	C17	R1	-3.32	-2.68	(0.64)	-2.00	(1.32)	-1.41	(1.91)	-1.52	(1.80)
Ethyl stearate	C17	R1	-4.00	-3.12	(0.88)	-2.45	(1.55)	-1.56	(2.44)	-1.55	(2.45)
Cetyl propionate	C15	R2	-2.85	-1.64	(1.22)	-2.29	(0.56)	-1.42	(1.43)	-1.41	(1.44)
Octadecyl acetate	C18	R2	-0.56	-1.27	(-0.71)	-1.85	(-1.29)	-1.14	-0.58)	-1.34	(-0.78)

[a] The values in parenthesis are prediction errors (negative and positive errors are underestimation and overestimation values respectively). Note that chain lengths of C8 to C18 were used for assessing statistical performance of long-chain alkyl esters (in Table 4) for carboxylic acid ester models: CAE QSAR1 and CAE QSAR2. Reference to all the chemicals in this table can be found in Table S1 except for methyl decanoate.[b]R1 and R2 refers to R-group attached to carbonyl and oxygen, respectively (in Scheme 1). [d]Was not included in original carboxylic acid ester dataset of Table S1; See reference no.[76]

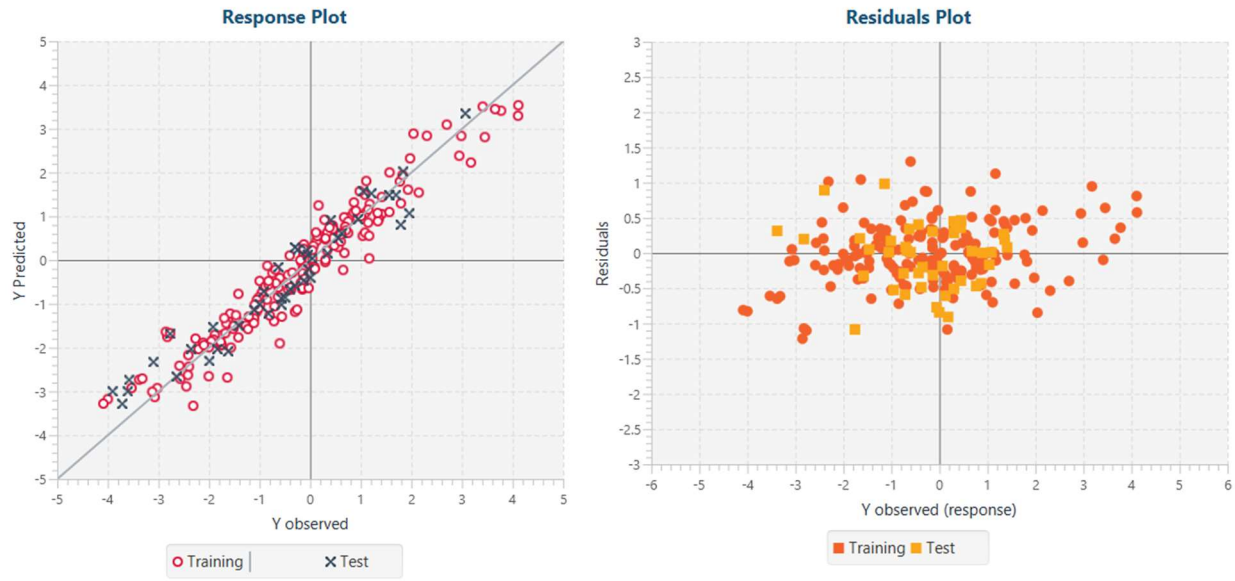

Figure S1. Regression (response) and residuals plot of CAE DTC-QSAR1.

Figure S2. Regression (response) and residuals plot of CAE DTC-QSAR2

Figure S3. Regression (response) and residuals plot of Lactone DTC-QSAR1.

Figure S4. Regression (response) and residuals plot of Lactone DTC-QSAR2.

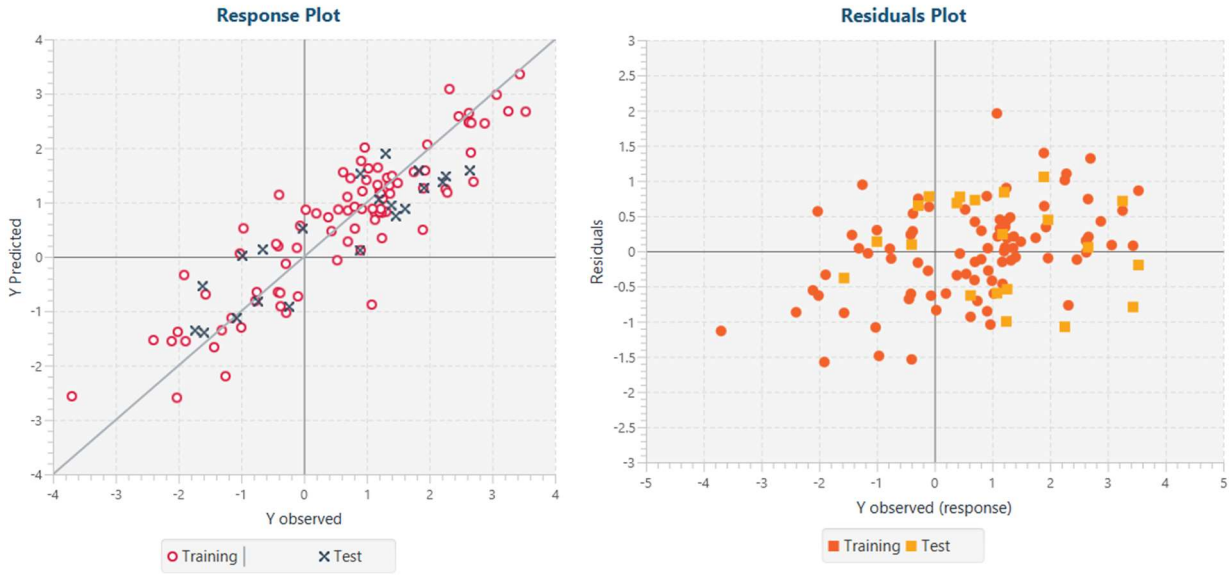

Figure S5. Regression (response) and residuals plot of Lactone-fulldata DTC-QSAR.

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