Supporting information

Development of a fragment-based *in silico* profiler for Michael addition thiol reactivity

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Table S1: all 72 chemicals (13 aldehydes, 17 ketones, 24 esters, nine nitro chemicals, three nitrile containing chemicals and six cyclic ketones). Containing chemical names, SMILES, experimental values (RC_{50} average, RC_{50} –Log RC_{50}), calculated values (fragment Eact and fragment SAS A), the fragment used and predicted –Log RC_{50} values for models 1-4 (M1, M2, M3 and M4)

ID	Chemical	SMILES	RC50 Average	RC50 SD	-Log RC50 Average (mM)	Fragment Eact	Fragment SAS A	Fragment used	M 1	M 2	M 3	M 4
1	*Trans*-2-pentenal	O=C/C=C/CC	0.33	0.02	0.48	0.40	15.80	*Trans*-2-pentenal	0.02	0.81	0.57	0.55
2	*Trans*-2-octenal	O=C/C=C/CCCCC	0.28	0.02	0.55	0.40	15.80	*Trans*-2-pentenal	0.02	0.81	0.57	0.55
3	*Trans*-2-nonenal	O=C/C=C/CCCCCC	0.41	0.05	0.39	0.40	15.80	*Trans*-2-pentenal	0.02	0.81	0.57	0.55
4	*Trans*-2-hexenal	O=C/C=C/CCC	0.43	0.11	0.37	0.40	15.80	*Trans*-2-pentenal	0.02	0.81	0.57	0.55
5	Acrolein	O=CC=C	0.07	0.03	1.15	-5.40	19.20	Acrolein	0.89	1.74	1.38	1.34
6	*Trans*-2-methyl-2-butenal	O=C/C(C)=C/C	11.71	1.88	-1.07	3.40	5.60	*Trans*-2-methyl-2-butenal	-0.43	-0.68	-0.87	-0.96
7	2-Methyl-2-pentenal	O=CC(=CCC)C	20.74	1.21	-1.32	4.90	5.60	2-Methyl-2-pentenal	-0.66	-0.82	-0.97	-1.05
8	4-Methyl-2-pentenal	O=CC=CC(C)C	1.15	0.15	-0.06	3.70	14.02	4-Methyl-2-pentenal	-0.48	0.30	0.12	0.12
9	*Trans*-2-butenal	O=C/C=C/C	0.21	0.02	0.68	-1.50	15.80	*Trans*-2-butenal	0.31	0.98	0.70	0.66
10	(E)-2-decen-1-al	O=C/C=C\CCCCCCC	0.21	0.05	0.68	0.40	15.80	*Trans*-2-pentenal	0.02	0.81	0.57	0.55
11	*Trans*-2-decenal	O=C/C=C/CCCCCCC	0.17	0.02	0.77	0.40	15.80	*Trans*-2-pentenal	0.02	0.81	0.57	0.55
12	*Trans*-cinnamaldehyde	O=C\C=C\C1=CC=CC=C1	0.96	0.24	0.02	3.40	13.32	*Trans*-cinalamdehyde	-0.43	0.24	0.06	0.05
13	α-Methyl-*trans*-cinnamaldehyde *	C\C(C=O)=C/C1=CC=CC=C1	21.60	7.04	-1.33	5.30	4.10	α-Methyl-*trans*-cinnamaldehyde	-0.72	-1.04	-1.18	-1.27
14	Methyl vinyl ketone	O=C(C=C)C	0.06	0.03	1.22	-0.80	18.10	Methyl vinyl ketone	0.20	1.19	0.93	0.92
15	1-Hexen-3-one	O=C(C=C)CCC	0.06	0.00	1.22	-0.80	18.10	Methyl vinyl ketone	0.20	1.19	0.93	0.92
16	1-Penten-3-one	O=C(C=C)CC	0.05	0.00	1.30	-0.80	18.10	Methyl vinyl ketone	0.20	1.19	0.93	0.92
17	3-Penten-2-one	O=C(C=CC)C	0.15	0.09	0.82	4.50	14.60	3-Penten-2-one	-0.60	0.30	0.14	0.15
18	3-Hepten-2-one	O=C(C=CCCC)C	0.67	0.11	0.17	6.90	14.60	3-Hexen-2-one	-0.96	0.08	-0.03	0.00
19	3-Octen-2-one	O=C(C=CCCCC)C	0.57	0.01	0.24	6.90	14.60	3-Hexen-2-one	-0.96	0.08	-0.03	0.00
20	3-Nonen-2-one	O=C(C=CCCCCC)C	0.54	0.11	0.27	6.90	14.60	3-Hexen-2-one	-0.96	0.08	-0.03	0.00
21	3-Decen-2-one	O=C(C=CCCCCCC)C	0.58	0.16	0.24	6.90	14.60	3-Hexen-2-one	-0.96	0.08	-0.03	0.00
22	4-Hexen-3-one	O=C(C=CC)CC	0.34	0.05	0.47	5.30	14.60	4-Hexen-3-one	-0.72	0.23	0.08	0.10
23	1-Octen-3-one	O=C(C=C)CCCCC	0.02	0.01	1.70	-0.80	18.10	Methyl vinyl	0.20	1.19	0.93	0.92

								ketone				
24	3-Methyl-3-penten-2-one	O=C(C(=CC)C)C	9.77	1.23	-0.99	9.40	6.10	3-Methyl-3-penten-2-one	-1.33	-1.16	-1.23	-1.25
25	5-Methyl-2-hepten-4-one	CC(C)C(=O)C=CC	0.37	0.02	0.43	7.20	14.60	5-Methyl-2-hexen-4-one	-1.00	0.05	-0.05	-0.01
26	*Trans*-3-nonen-2-one	CC(=O)/C=C/CCCCC	0.60	0.03	0.22	6.90	14.60	3-Hexen-2-one	-0.96	0.08	-0.03	0.00
27	4-phenyl-3-buten-2-one	CC(=O)\C=C\C1=CC=CC=C1	3.53	0.30	-0.55	7.20	10.49	4-Phenyl-3-buten-2-one	-1.00	-0.44	-0.55	-0.55
28	*Trans*-chalcone *	O=C(\C=C\C1=CC=CC=C1)C1=CC=CC=C1	0.40	0.07	0.40	5.50	10.49	*Trans*-chalcone	-0.75	-0.29	-0.43	-
29	2-Hydroxychalcone	OC1=CC=CC=C1\C=C\C(=O)C1=CC=CC=C1	0.28	0.08	0.55	5.50	10.49	*Trans*-chalcone	-0.75	-0.29	-0.43	-
30	4-Hydroxychalcone	OC1=CC=C(\C=C\C(=O)C2=CC=CC=C2)C=C1	0.41	0.29	0.39	5.50	10.49	*Trans*-chalcone	-0.75	-0.29	-0.43	-
31	Isobutyl acrylate	CC(C)COC(=O)C=C	0.48	0.06	0.32	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
32	n-Hexylacrylate	CCCCCCOC(=O)C=C	0.82	0.08	0.09	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
33	Butyl acrylate	CCCCOC(=O)C=C	0.77	0.02	0.11	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
34	Methyl crotonate	COC(=O)\C=C\C	21.25	4.95	-1.33	10.20	14.60	Methyl crotonate	-1.45	-0.22	-	-
35	Ethyl acrylate	CCOC(=O)C=C	0.52	0.05	0.28	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
36	Methyl acrylate	COC(=O)C=C	0.49	0.10	0.31	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
37	Methyl methacrylate	COC(=O)C(C)=C	69.19	7.12	-1.84	9.70	5.08	Methyl methacrylate	-1.38	-1.31	-1.37	-1.40
38	Tert-butyl acrylate	CC(C)(C)OC(=O)C=C	1.28	0.30	-0.11	7.00	17.50	Tert-butyl acrylate	-0.97	0.42	0.31	0.38
39	Propyl acrylate	CCCOC(=O)C=C	0.85	0.07	0.07	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
40	2-Hydroxy ethyl acrylate	OCCOC(=O)C=C	0.27	0.03	0.57	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
41	2-Hydroxyethyl methacrylate	CC(=C)C(=O)OCCO	33.40	1.33	-1.52	9.70	5.08	Methyl methacrylate	-1.38	-1.31	-1.37	-1.40
42	2-Hydroxypropyl methacrylate	CC(O)COC(=O)C(C)=C	21.15	9.20	-1.33	9.70	5.08	Methyl methacrylate	-1.38	-1.31	-1.37	-1.40
43	Phenyl acrylate	CC(=C)C(=O)OC1=CC=CC=C1	0.02	0.01	1.70	-0.10	17.50	Phenyl acrylate	0.10	1.06	0.81	-
44	Isoamyl acrylate	CC(C)CCOC(=O)C=C	0.68	0.22	0.17	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
45	N-pentylacrylate	CCCCCOC(=O)C=C	0.81	0.02	0.09	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
46	Ethyl crotonate	CCOC(=O)\C=C\C	17.95	0.78	-1.25	10.20	14.60	Methyl crotonate	-1.45	-0.22	-	-
47	Methyl *trans*-2-pentenoate	CC\C=C\C(=O)OC	5.05	0.42	-0.70	10.70	14.60	Methyl trans-2-pentenoate	-1.53	-0.26	-	-
48	Ethyl *trans*-2-hexenoate	CCC\C=C\C(=O)OCC	0.76	0.10	0.12	10.70	14.60	Methyl trans-2-pentenoate	-1.53	-0.26	-0.30	-0.22

49	Methyl-2-hexenoate	CCC\C=C\C(=O)OC	2.46	1.37	-0.39	10.70	14.60	Methyl trans-2-pentenoate	-1.53	-0.26	-0.30	-0.22
50	Methyl-4-methyl-2-pentenoate	COC(=O)\C=C\C(C)C	1.28	0.25	-0.11	14.40	14.60	Methyl-4-methyl-2-pentenoate	-2.08	-0.59	-0.56	-0.45
51	Ethyl tiglate	CCOC(=O)C(\C)=C\C	14.34	3.32	-1.16	14.40	5.41	Methyl tiglate	-2.08	-1.70	-1.66	-1.64
52	Ethyl methacrylate *	CCOC(=O)C(C)=C	33.75	-	-1.53	9.70	5.08	Methyl methacrylate	-1.38	-1.31	-1.37	-1.40
53	Butyl methacrylate *	CCCCOC(=O)C(C)=C	43.27	-	-1.64	9.70	5.08	Methyl methacrylate	-1.38	-1.31	-1.37	-1.40
54	2-Ethylhexyl acrylate *	CCCCC(CC)COC(=O)C=C	0.44	0.03	0.36	4.90	17.50	Methyl acrylate	-0.66	0.61	0.46	0.50
55	1-Nitro-1-cyclohexene	C1CCCC=C1N(=O)(=O)	0.03	0.01	1.52	-9.84	14.23	2-Nitrobut-2-ene	-	-	-	0.96
56	4-Methyl-β-nitrostyrene	N(=O)(=O)C=Cc1ccc(C)cc1	0.10	0.03	1.00	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
57	*Trans*-β-Nitrostyrene	c1ccccc1/C=C/N(=O)=O	0.09	0.02	1.05	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
58	*Trans*-4-Methyl-β-nitrostyrene	O=N(=O)/C=C/c1ccc(C)cc1	0.08	0.01	1.10	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
59	*Trans*-4-Chloro-β-nitrostyrene	c1cc(Cl)ccc1/C=C/N(=O)(=O)	0.07	0.03	1.15	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
60	*Trans*-4-Bromo-β-nitrostyrene	O=N(=O)/C=C/c1ccc(Br)cc1	0.07	0.00	1.15	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
61	*Trans*-4-Fluoro-β-nitrostyrene	O=N(=O)C=Cc1ccc(F)cc1	0.05	0.01	1.30	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
62	*Trans*-Methoxy-β-nitrostyrene	O=N(=O)/C=C/c1ccc(OC)cc1	0.04	0.02	1.40	-8.08	14.23	2-Nitroethylbezene	-	-	-	0.85
63	*Trans*-b-methyl-β-nitrostyrene	c1ccccc1/C=C/(C)N(=O)(=O)	0.06	0.01	1.22	-7.43	14.23	2-Nitroprop-1en-1-yl-benzene	-	-	-	0.82
64	2-Methyleneglutaronitrile	N#CC(=C)CCC#N	22.92	3.45	-1.36	10.03	6.16	2-Methylprop-2-ene-nitrile	-	-	-	-1.28
65	Cyclohexene-1-carbonitrile (1-cyanocyclohexene)	C1(C#N)=CCCCC1	28.16	40.45	-1.45	14.97	6.19	2-Methylbut-2-ene-nitrile	-	-	-	-1.57
66	1-Cyclopentene-1-carbonitrile	N#CC1=CCCC1	20.51	0.95	-1.31	14.97	6.19	2-Methylbut-2-ene-nitrile	-	-	-	-1.57
67	2-Cyclohexen-1-one	O=C1CCCC=C1	0.32	0.13	0.49	6.90	14.60	3-Hexen-2-one	-	-	-	0.00
68	2-cyclopenten-1-one	O=C1CCC=C1	0.67	0.17	0.17	6.90	14.60	3-Hexen-2-one	-	-	-	0.00
69	2-Methyl-2-cyclopenten-1-one	CC1=CCCC1=O	9.92	1.24	-1.00	11.00	6.10	3-Methyl-3-hexen-2-one	-	-	-	-1.35
70	4,4-Dimethyl-2-cyclohexen-1-one	CC1(C)CCC(=O)C=C1	1.01	0.11	0.00	8.64	14.60	5-Methyl-3-hexen-2-one	-	-	-	-0.10
71	1-Acetyl-1-cyclohexene	CC(=O)C1=CCCCC1	2.06	0.54	-0.31	11.00	6.10	3-Methyl-3-hexen-	-	-	-	-1.35

									2-one				
72	1-Acetyl-1-cyclopentene	CC(=O)C1=CCCC1	3.90	4.19	-0.59	11.00	6.10	3-Methyl-3-hexen-2-one	-	-	-	-1.35