

Concentration Addition Prediction for the Multiple-component Mixture Containing No Effect Chemicals

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Table S1 Physicochemical properties of five chemicals*

No	Chemical	Abbr.	CAS RN	Formula	MW (g/mol)	Stock (mol/L)
1	Apramycin sulfate	APR	65710-07-8	$C_{21}H_{41}N_5O_{11} \cdot H_2SO_4$	637.66	1.978×10^{-5}
2	Imidacloprid	IMI	138261-41-3	$C_9H_{10}ClN_5O_2$	255.66	1.580×10^{-3}
3	Metalaxyl	MEL	57837-19-1	$C_{15}H_{21}NO_4$	279.33	6.787×10^{-3}
4	Neomycin sulfate	NEO	1405-10-3	$C_{23}H_{46}N_6O_{13} \cdot 3H_2SO_4$	908.87	1.222×10^{-5}
5	1-Butylpyridiniumbromide	[bpy]Br	874-80-6	$C_9H_{14}BrN$	216.12	2.262×10^{-2}

*MW: Molecular weight

Table S2 The fitted concentration-response curve (α and β) and some statistics (R^2 and RMSE) of five chemicals

No	Abbr.	Exposure time	Fit function	α	β	R^2	RMSE
1	APR	15 min	-				
		12 h	Weibull	13.97	2.57	0.9895	0.03296
2	IMI	15 min	Logit	7.74	2.22	0.9964	0.01371
3	MEL	15 min	Weibull	6.30	2.30	0.9937	0.02339
4	NEO	15 min	-				
		12 h	Weibull	16.33	2.66	0.9972	0.03327
5	[bpy]Br	15 min	Logit	10.78	4.05	0.9950	0.02860

Table S3 The experimental concentration (Cmix), individual inhibitions (x1, x2, and x3), fitted inhibition (Fit_x), upper (Upper) and lower inhibition (Lower) of the 95% observation-based confidence intervals, and inhibition predicted by concentration addition (CA) in Figure 2

(a) R1

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
1.08283E-4	0.004600	0.068620	-0.059420	1.57785E-2	-0.061147	-0.016679	-0.047822
1.59005E-4	0.008700	0.072845	-0.055445	2.54114E-2	-0.067396	0.012597	-0.033781
2.33488E-4	0.016400	0.080862	-0.048062	4.13208E-2	0.043969	0.033123	-0.025039
3.42860E-4	0.030400	0.095600	-0.034800	6.76268E-2	0.071706	0.037663	0.027214
5.03466E-4	0.056000	0.122714	-0.010714	1.10668E-1	0.133659	0.102909	0.093438
7.39304E-4	0.100700	0.169904	0.031496	1.78947E-1	0.113382	0.124551	0.138684
1.08562E-3	0.174500	0.246421	0.102579	2.80626E-1	0.157382	0.160927	0.160001
1.59415E-3	0.285300	0.358247	0.212353	4.16573E-1	0.244770	0.282124	0.270516
2.34089E-3	0.429800	0.503272	0.356328	5.72048E-1	0.426586	0.426001	0.417610
3.43744E-3	0.587400	0.665175	0.509625	7.19004E-1	0.591964	0.572254	0.589185
5.04763E-3	0.728800	0.801547	0.656053	8.33501E-1	0.753844	0.731819	0.736414
7.41209E-3	0.835400	0.899883	0.770917	9.09195E-1	0.848024	0.838745	0.841556

(b) R2

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
7.83461E-5	0.013200	0.069755	-0.043355	2.21108E-2	0.002503	-0.028140	-0.004004
1.15046E-4	0.020500	0.077375	-0.036375	3.34870E-2	0.000294	-0.031642	-0.015527
1.68936E-4	0.031700	0.089114	-0.025714	5.08623E-2	-0.047031	0.017341	0.032342
2.48071E-4	0.049000	0.107244	-0.009244	7.73387E-2	0.018446	0.030462	0.055334
3.64275E-4	0.075400	0.134760	0.016040	1.17322E-1	0.113659	0.083607	0.127349
5.34911E-4	0.115000	0.175567	0.054433	1.76486E-1	0.154327	0.107788	0.169811
7.85479E-4	0.173300	0.234735	0.111865	2.60726E-1	0.112190	0.127873	0.197368
1.15342E-3	0.256700	0.318252	0.195148	3.73078E-1	0.253886	0.250200	0.243072
1.69372E-3	0.370200	0.431409	0.308991	5.08637E-1	0.366126	0.378781	0.376947
2.48710E-3	0.513600	0.575399	0.451801	6.51239E-1	0.517121	0.518917	0.527859
3.65213E-3	0.674800	0.739214	0.610386	7.78516E-1	0.677405	0.682727	0.700249
5.36289E-3	0.826400	0.894254	0.758546	8.74253E-1	0.804136	0.803141	0.810345

(c) R3

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
5.51208E-5	0.012700	0.066392	-0.040992	2.26750E-2	-0.037122	-0.062118	-0.004028
8.09409E-5	0.019400	0.073392	-0.034592	3.37125E-2	0.008941	-0.011508	-0.021937
1.18856E-4	0.029500	0.083984	-0.024984	5.01663E-2	0.033280	-0.012712	0.022821
1.74532E-4	0.044700	0.099925	-0.010525	7.45807E-2	0.016902	0.056751	0.087079
2.56287E-4	0.067400	0.123608	0.011192	1.10428E-1	0.084627	0.078186	0.080305
3.76339E-4	0.101200	0.158484	0.043916	1.62025E-1	0.116809	0.117676	0.161832
5.52628E-4	0.150400	0.208508	0.092292	2.33815E-1	0.150934	0.150713	0.164383
8.11494E-4	0.220400	0.278708	0.162092	3.28499E-1	0.186943	0.211633	0.179569
1.19162E-3	0.316400	0.374417	0.258383	4.44028E-1	0.327536	0.328260	0.288870
1.74981E-3	0.440700	0.499122	0.382278	5.71124E-1	0.446696	0.457402	0.441981
2.56947E-3	0.588400	0.649395	0.527405	6.94625E-1	0.605346	0.604599	0.604428
3.77309E-3	0.742400	0.807732	0.677068	7.99687E-1	0.726695	0.733049	0.727855

(d) R4

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
9.54511E-5	0.006500	0.055053	-0.042053	1.44381E-2	0.007902	-0.035848	-0.043644
1.40163E-4	0.011800	0.060486	-0.036886	2.29997E-2	0.022776	-0.008516	-0.055285
2.05820E-4	0.021100	0.070093	-0.027893	3.69703E-2	0.020683	-0.024024	-0.003704
3.02231E-4	0.037500	0.087141	-0.012141	5.98427E-2	-0.009265	0.027465	0.053687
4.43805E-4	0.065800	0.116639	0.014961	9.70869E-2	0.095137	0.051303	0.138030
6.51696E-4	0.113000	0.165609	0.060391	1.56447E-1	0.128764	0.103848	0.208982
9.56970E-4	0.187300	0.241620	0.132980	2.46612E-1	0.163696	0.163716	0.230597
1.40524E-3	0.294100	0.348944	0.239256	3.72050E-1	0.253095	0.297526	0.288029
2.06350E-3	0.429700	0.484919	0.374481	5.24210E-1	0.410930	0.438471	0.434673
3.03010E-3	0.576700	0.634832	0.518568	6.78203E-1	0.550199	0.574974	0.576998
4.44949E-3	0.711300	0.767122	0.655478	8.05845E-1	0.712576	0.704196	0.727284
6.53375E-3	0.816700	0.866056	0.767344	8.93925E-1	0.823955	0.817000	0.839312

(e) R5

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
7.76165E-5	0.011000	0.050219	-0.028219	1.11645E-2	0.013523	-0.023134	0.002353
1.13974E-4	0.017100	0.056512	-0.022312	1.77472E-2	0.001750	-0.013818	0.022235
1.67363E-4	0.026600	0.066344	-0.013144	2.85173E-2	0.001142	-0.032947	0.040742
2.45761E-4	0.041200	0.081470	0.000930	4.62505E-2	0.031333	0.009526	0.049336
3.60882E-4	0.063600	0.104610	0.022590	7.54180E-2	0.052284	0.065999	0.074411
5.29930E-4	0.097600	0.139469	0.055731	1.22699E-1	0.119236	0.102919	0.129189
7.78165E-4	0.148100	0.190679	0.105521	1.96530E-1	0.154323	0.132446	0.173525
1.14268E-3	0.221400	0.264203	0.178597	3.03829E-1	0.206149	0.190303	0.209818
1.67794E-3	0.323400	0.365982	0.280818	4.42629E-1	0.302945	0.325691	0.316323
2.46394E-3	0.456600	0.499432	0.413768	5.95531E-1	0.481374	0.474952	0.474647
3.61812E-3	0.614200	0.658900	0.569500	7.35296E-1	0.637288	0.631298	0.617916
5.31295E-3	0.773900	0.821632	0.726168	8.41900E-1	0.762296	0.748314	0.741964

(f) R6

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
5.65584E-5	0.016100	0.088236	-0.056036	1.77990E-2	-0.050572	-0.044723	-0.018610
8.30520E-5	0.024000	0.096616	-0.048616	2.67422E-2	-0.034596	-0.028170	-0.011157
1.21956E-4	0.035800	0.109160	-0.037560	4.02950E-2	0.035127	0.007946	-0.011570
1.79084E-4	0.053300	0.127710	-0.021110	6.08169E-2	0.075182	0.069379	0.031530
2.62972E-4	0.078800	0.154503	0.003097	9.17161E-2	0.101672	0.114384	0.105169
3.86155E-4	0.115900	0.192885	0.038915	1.37597E-1	0.170079	0.167611	0.143334
5.67041E-4	0.168700	0.246511	0.090889	2.03892E-1	0.192321	0.187602	0.174732
8.32660E-4	0.242000	0.319839	0.164161	2.95245E-1	0.269910	0.205497	0.235615
1.22270E-3	0.340100	0.417572	0.262628	4.12041E-1	0.323304	0.292052	0.308403
1.79545E-3	0.464000	0.542255	0.385745	5.46204E-1	0.466585	0.471130	0.452946
2.63649E-3	0.607500	0.689174	0.525826	6.80638E-1	0.615956	0.620753	0.629914
3.87150E-3	0.754100	0.841036	0.667164	7.96203E-1	0.755374	0.743874	0.750162

(g) R7

Cmix	Fit_X	Upper	Lower	CA	x1	x2	x3
5.83233E-5	0.013700	0.086283	-0.058883	2.03647E-2	-0.098203	-0.036401	-0.042289
8.56436E-5	0.020800	0.093811	-0.052211	3.04516E-2	-0.046623	-0.017878	-0.015575
1.25762E-4	0.031600	0.105305	-0.042105	4.56158E-2	0.020656	0.011168	0.006171
1.84672E-4	0.047900	0.122638	-0.026838	6.83529E-2	0.037730	0.062972	0.042956
2.71177E-4	0.072300	0.148389	-0.003789	1.02180E-1	0.088964	0.082696	0.109909
3.98205E-4	0.108300	0.185826	0.030774	1.51686E-1	0.128761	0.128100	0.146470
5.84735E-4	0.160700	0.239266	0.082134	2.21996E-1	0.170181	0.181009	0.191317
8.58642E-4	0.234800	0.313540	0.156060	3.16986E-1	0.215386	0.212448	0.202857
1.26086E-3	0.335600	0.413936	0.257264	4.35854E-1	0.342243	0.335676	0.302052
1.85148E-3	0.464600	0.543596	0.385604	5.69481E-1	0.467639	0.474676	0.481018
2.71876E-3	0.614900	0.697347	0.532453	7.00776E-1	0.626422	0.618706	0.626169
3.99231E-3	0.767300	0.855111	0.679489	8.11793E-1	0.760602	0.749922	0.754682

Table S4 The fitted inhibition (Fit_x), combination indice (CI), and the upper (Upper) and lower CIs (Lower) of the 95% observation-based confidence intervals in Figure 3

(a) R1

No	Fit_X	CI	Upper	Lower
1	0.050000	1.718754	3.118424	0.467834
2	0.100000	1.581925	2.308040	0.822015
3	0.150000	1.514781	2.041034	1.012414
4	0.200000	1.483948	1.896396	1.080009
5	0.250000	1.461365	1.816769	1.124387
6	0.300000	1.447748	1.775947	1.148833
7	0.350000	1.444781	1.729140	1.162484
8	0.400000	1.431941	1.718713	1.184592
9	0.450000	1.430288	1.735490	1.182214
10	0.500000	1.441386	1.716111	1.181268
11	0.550000	1.432619	1.715288	1.198218
12	0.600000	1.427509	1.766487	1.181441
13	0.650000	1.457116	1.748786	1.143931
14	0.700000	1.448897	1.792122	1.181497
15	0.750000	1.463833	1.852122	1.145738
16	0.800000	1.490739	1.802037	1.127108

(b) R2

No	Fit_X	CI	Upper	Lower
1	0.050000	1.518110	3.102547	0.045086
2	0.100000	1.496662	2.335913	0.692654
3	0.150000	1.495193	2.080594	0.932954
4	0.200000	1.496701	1.946701	1.056118
5	0.250000	1.493102	1.877563	1.132896
6	0.300000	1.496477	1.817347	1.177029
7	0.350000	1.488268	1.786616	1.215729
8	0.400000	1.486439	1.758939	1.230678
9	0.450000	1.480034	1.717010	1.245012
10	0.500000	1.457577	1.713358	1.251975
11	0.550000	1.453461	1.695693	1.233209
12	0.600000	1.438560	1.653219	1.230753
13	0.650000	1.401162	1.645384	1.217491
14	0.700000	1.378034	1.640713	1.171128
15	0.750000	1.353313	1.582878	1.133931
16	0.800000	1.286468	1.483713	1.097980

(c) R3

No	Fit_X	CI	Upper	Lower
1	0.050000	1.634267	3.366954	0.021482
2	0.100000	1.600807	2.498483	0.752169
3	0.150000	1.583976	2.203118	0.995903
4	0.200000	1.573032	2.052366	1.114141
5	0.250000	1.562352	1.948988	1.184753
6	0.300000	1.544170	1.888114	1.228096
7	0.350000	1.532668	1.831634	1.246560
8	0.400000	1.512352	1.777617	1.260550
9	0.450000	1.483973	1.756537	1.259075
10	0.500000	1.470317	1.707816	1.240959
11	0.550000	1.434592	1.662248	1.234260
12	0.600000	1.393562	1.651920	1.202209
13	0.650000	1.370402	1.597002	1.156213
14	0.700000	1.315802	1.513004	1.129407
15	0.750000	1.231620	1.401023	1.071497
16	0.800000	1.117862	1.260388	0.983143

(d) R4

No	Fit_X	CI	Upper	Lower
1	0.050000	1.392272	2.307614	0.545680
2	0.100000	1.308234	1.801573	0.801116
3	0.150000	1.276415	1.633763	0.930320
4	0.200000	1.264202	1.551235	0.988154
5	0.250000	1.259788	1.502024	1.024207
6	0.300000	1.255809	1.489694	1.051366
7	0.350000	1.267856	1.470313	1.066518
8	0.400000	1.267905	1.472149	1.091580
9	0.450000	1.277413	1.494370	1.099543
10	0.500000	1.298278	1.493487	1.110651
11	0.550000	1.299384	1.520877	1.130321
12	0.600000	1.319526	1.560623	1.124097
13	0.650000	1.350958	1.560411	1.134187
14	0.700000	1.347527	1.640796	1.160501
15	0.750000	1.405851	1.674314	1.137172
16	0.800000	1.423102	1.638437	1.179624

(e) R5

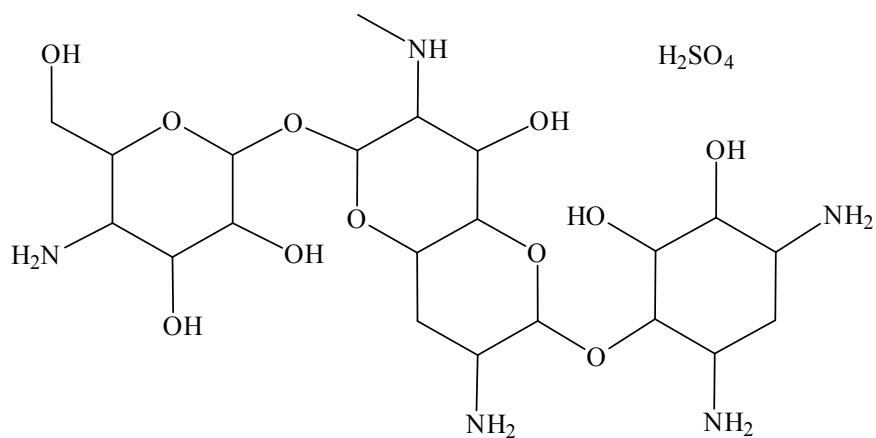
No	Fit_X	CI	Upper	Lower
1	0.050000	1.113491	1.913309	0.355485
2	0.100000	1.202350	1.666037	0.748151
3	0.150000	1.264629	1.605703	0.932897
4	0.200000	1.312199	1.589843	1.043893
5	0.250000	1.350637	1.584469	1.121573
6	0.300000	1.377203	1.588436	1.178644
7	0.350000	1.401247	1.593721	1.219090
8	0.400000	1.418438	1.586647	1.250850
9	0.450000	1.418265	1.598869	1.270769
10	0.500000	1.434414	1.600065	1.276583
11	0.550000	1.432887	1.581118	1.288134
12	0.600000	1.410060	1.585984	1.280731
13	0.650000	1.408256	1.581175	1.256132
14	0.700000	1.389595	1.543380	1.241539
15	0.750000	1.335578	1.470595	
16	0.800000	1.244376	1.360520	

(f) R6

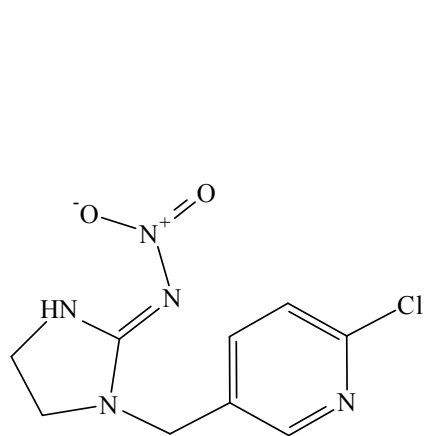
No	Fit_X	CI	Upper	Lower
1	0.050000	1.128247	2.846845	-0.443975
2	0.100000	1.168680	2.097821	0.321793
3	0.150000	1.198797	1.858655	0.585327
4	0.200000	1.223367	1.738115	0.729712
5	0.250000	1.238548	1.680120	0.828181
6	0.300000	1.254957	1.630291	0.889337
7	0.350000	1.260155	1.618497	0.943482
8	0.400000	1.272042	1.579245	0.968686
9	0.450000	1.265437	1.586666	1.002906
10	0.500000	1.271870	1.572967	1.000477
11	0.550000	1.267236	1.532941	1.013892
12	0.600000	1.242056	1.567037	1.018555
13	0.650000	1.243474	1.545359	0.974863
14	0.700000	1.221426	1.486996	0.974254
15	0.750000	1.168373	1.399298	0.953450
16	0.800000	1.084072	1.281134	0.900670

(g) R7

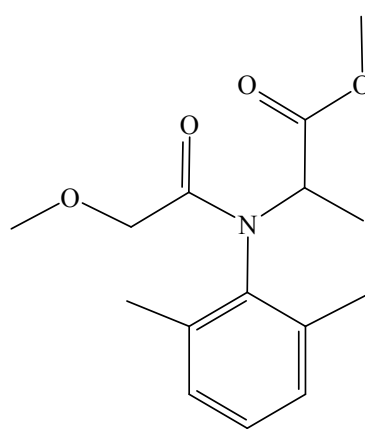
No	Fit_X	CI	Upper	Lower
1	0.050000	1.400149	3.423871	-0.442695
2	0.100000	1.388924	2.446502	0.407195
3	0.150000	1.387990	2.122052	0.696849
4	0.200000	1.389779	1.956935	0.843944
5	0.250000	1.387998	1.860130	0.938457
6	0.300000	1.386009	1.789855	0.996497
7	0.350000	1.378708	1.753668	1.039323
8	0.400000	1.376182	1.696423	1.059203
9	0.450000	1.357181	1.688504	1.083790
10	0.500000	1.352256	1.662308	1.072554
11	0.550000	1.337899	1.610765	1.077273
12	0.600000	1.303943	1.622469	1.074568
13	0.650000	1.291114	1.601800	1.027325
14	0.700000	1.264613	1.537472	1.010310
15	0.750000	1.207192	1.444160	0.986339
16	0.800000	1.118740	1.320831	0.930391



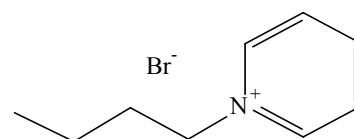
Apramycin sulfate (APR)



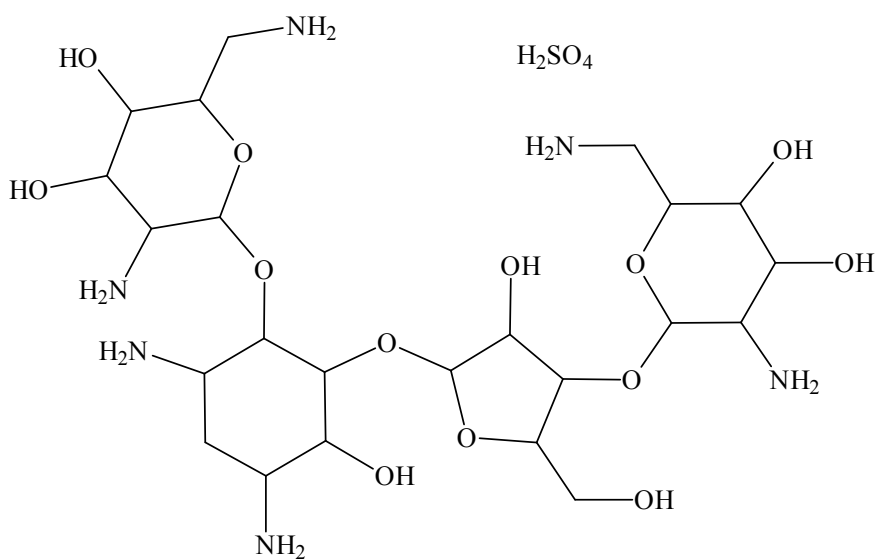
Imidacloprid (IMI)



Metalaxyl (MEL)



1-Butylpyridiniumbromide
([bpy]Br)



Neomycin sulfate (NEO)

Figure S1 Molecular structures of five chemicals

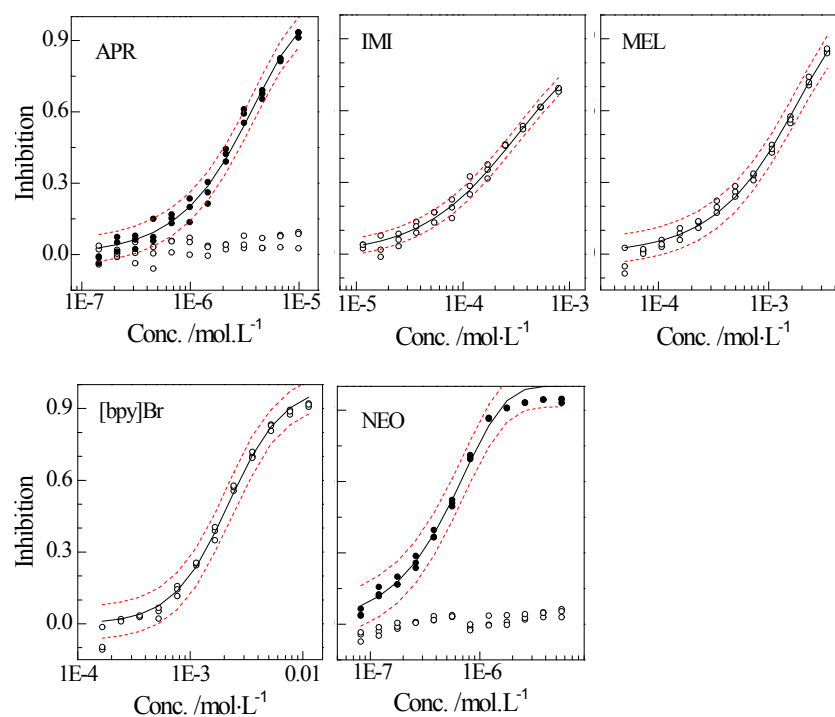


Figure S2 Concentration-response curves of five chemicals (⊙: experimental scatters at the exposure of 15 min; ⊗: experimental scatters at the exposure of 12 h; black solid line: fitted curves; red dash line: 95% observation-based confidence intervals)