Mutagenicity of *N*-acyloxy-*N*-alkoxyamides as an indicator of DNA intercalation part 1: evidence for naphthalene as a DNA intercalator.

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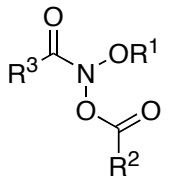
Supplementary Table . Data for linear QSAR Equation 3 and bilinear QSAR Equation 4



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QSAR parameters Log*P*, pK_A, E_S^1, E_S^2, E_S^3, *I* and Log(βP+1) for *N*-acyloxy-*N*-alkoxyamides **1**

Structure[a]	R^1, R^2, R^3	Experimental LogTA100[b]	LogP[c]	pK_A[d]	E_S^1[e]	E_s^2[f]	E_S^3[g]	*I*[h]	Log(βP+1)[i]
1	Et, Me, Ph	2.49	1.54	4.76	0	0	0	0	-2.97223E-06
2	Pr, Me, Ph	2.53	2.02	4.76	0	0	0	0	-8.97594E-06
3	Oct, Me, Ph	2.88	4.11	4.76	0	0	0	0	-0.001102891
4	Pr^i, Me, Ph	2.40	1.86	4.76	0	0	0	0	-6.20985E-06
5[**14**]	Bu, Me, Ph	2.50	2.44	4.76	0	0	0	0	-2.36087E-05
6	Bu, Me, (4-MeO)Ph	2.73	2.32	4.76	-0.55	0	0	0	-1.79092E-05
7	Bu, Me, (4-Ph)Ph	2.92	4.12	4.76	-2.41	0	0	0	-0.001128548
8	Bu, Me, (4-Me)Ph	2.48	2.93	4.76	-1.24	0	0	0	-7.29538E-05
9	Bu, Me, (4-Cl)Ph	2.54	3.00	4.76	-0.97	0	0	0	-8.5712E-05
10	Bu, Me, (4-Br)Ph	2.69	3.27	4.76	-1.16	0	0	0	-0.00015959
11	Bu, Me, (4-NO_2)Ph	2.16	2.48	4.76	-1.76	0	0	0	-2.58864E-05
12	Bu, Me, (3-NO_2)Ph	2.45	2.48	4.76	0	0	0	0	-2.58864E-05
13	Bu, Me, (4-Bu^t)Ph	2.37	4.15	4.76	-2.78	0	0	0	-0.001209148
14	Bn, Me, Ph	2.63	2.93	4.76	0	0	0	0	-7.29538E-05
15	(4-MeO)Bn, Me, Ph	2.70	2.81	4.76	0	-0.55	0	0	-5.53422E-05
16	(4-PhO)Bn, Me, Ph	3.06	3.96	4.76	0	-0.55	0	0	-0.000781077
17	(4-Ph)Bn, Me, Ph	3.09	4.61	4.76	0	-2.41	0	0	-0.003478116
18	(4-Me)Bn, Me, Ph	2.78	3.42	4.76	0	-1.24	0	0	-0.000225409

19	(4-Cl)Bn, Me, Ph	2.76	3.49	4.76	0	-0.97	0	0	-0.000264821
20	(4-Br)Bn, Me, Ph	2.74	3.76	4.76	0	-1.16	0	0	-0.00049299
21	(4-Bu^t)Bn, Me, Ph	2.60	4.64	4.76	0	-2.78	0	0	-0.003725805
22	Bn, Ph, Ph	3.22	4.83	4.20	0	0	0	0	-0.005757084
23	Bn, (4-MeO)Ph, Ph	3.06	4.70	4.31	0	0	-0.55	0	-0.004275088
24	Bn, (4-Ph)Ph, Ph	3.70	6.51	4.21	0	0	-2.41	0	-0.214500656
25	Bn, (4-Me)Ph, Ph	3.29	5.32	4.37	0	0	-1.24	0	-0.017550105
26	Bn, (4-Cl)Ph, Ph	3.12	5.39	3.99	0	0	-0.97	0	-0.020548011
27	Bn, (4-CHO)Ph, Ph	2.87	4.58	3.73	0	0	-1.01	0	-0.003246832
28	Bn, (4-CN)Ph, Ph	2.96	4.86	3.55	0	0	-0.51	0	-0.006165917
29	Bn, (4-NO_2)Ph, Ph	2.69	4.86	3.42	0	0	-1.76	0	-0.006165917
30	Bn, (4-Bu^t)Ph, Ph	3.20	6.54	4.35	0	0	-2.78	0	-0.226441169
31	Bn, (3-NO_2)Bn, Ph	2.94	4.86	3.45	0	0	0	0	-0.006165917
32	Bn, (3-MeO)Bn, Ph	3.23	4.70	4.09	0	0	0	0	-0.004275088
33	-$(CH_2)_6$-, Me, Ph	2.96	3.55	4.76	0	0	0	0	-0.000304041
34	Bu, Ph, Ph	2.70	4.34	4.20	0	0	0	0	-0.001871321
35	Bu, Me, Me	1.94	0.54	4.76	0	0	0	0	-2.97224E-07
36[**15**]	Bu, Ph, Me	2.65	2.44	4.20	0	0	0	0	-2.36087E-05
37	Bn, Me, Me	2.22	1.04	4.76	0	0	0	0	-9.39905E-07
38	Bn, Ph, Me	2.90	2.93	4.20	0	0	0	0	-7.29538E-05
39	(2,6-diMe)Bn, Me, Ph	3.04	3.91	4.76	0	0	0	0	-0.000696203
40	Bu, Me, (3,5-diMe)Ph	2.74	3.42	4.76	0	0	0	0	-0.000225409
41	Bn, Ph, (4-Bu^t)Ph	3.50	6.54	4.20	-2.78	0	0	0	-0.226441169
42	(4-Bu^t)Bn, Ph, Ph	3.05	6.54	4.20	0	-2.78	0	0	-0.226441169
43	(4-Bu^t)Bn, Me, (4-Bu^t)Ph	2.89	6.31	4.76	-2.78	-2.78	0	0	-0.147056222
44	2-Bu, Me, Ph	2.59	2.07	4.76	0	0	0	0	-1.00712E-05
45	Bu^t, Me, Ph	2.47	2.34	4.76	0	0	0	0	-1.87532E-05
46	(2-Me)Bn, Me, Ph	2.71	3.42	4.76	0	0	0	0	-0.000225409
47	(3-Me)Bn, Me, Ph	2.86	3.42	4.76	0	0	0	0	-0.000225409
48	(3,5-diMe)Bn, Me, Ph	2.95	3.91	4.76	0	0	0	0	-0.000696203
49	Bu, (4-Me)Ph, Ph	2.91	4.83	4.37	0	0	-1.24	0	-0.005757084
50	Bu, (4-MeO)Ph, Ph	2.87	4.21	4.47	0	0	-0.55	0	-0.001388002
51[**2**]	Bu, Me, 2-Np	3.59	3.44	4.76	0	0	0	1	-0.00023603
52[**3**]	Bu, 2-Np, Me	3.64	3.44	4.16	0	0	0	1	-0.00023603
53[**4**]	Bu,2-NpCH_2, Me	3.4	3.38	4.24	0	0	0	1	-0.00020558
54[**5**]	Bu, 2-Np$(CH_2)_2$, Me	3.46	3.8	4.57	0	0	0	1	-0.000540523
55[**6**]	1-NpCH_2, Me, Me	3.53	2.03	4.76	0	0	0	1	-9.18501E-06
56[**7**]	2-NpCH_2, Me, Me	3.57	2.03	4.76	0	0	0	1	-9.18501E-06
57[**8**]	2-Np$(CH_2)_2$, Me, Me	3.41	2.31	4.76	0	0	0	1	-1.75015E-05
58[**9**]	2-Np$(CH_2)_3$, Me, Me	3.48	2.73	4.76	0	0	0	1	-4.60322E-05
59	n-Hex, n-Pent, Ph	3.42	5.18	4.86	0	0	0	0	-0.012784286

60	n-Hept, n-Hex, Ph	3.25	6.02	4.78	0	0	0	0	-0.08159238
61	n-Oct, n-Hept, Ph	3.02	6.85	4.78	0	0	0	0	-0.379728413
62	n-Non, n-Oct, Ph	2.95	7.69	4.78	0	0	0	0	-1.0280498
63	n-Dec, n-Non, Ph	2.88	8.52	4.79	0	0	0	0	-1.821894515

[a] Structures in [square brackets] correspond to those in the paper; Data for structures 1-58 used for Equations 3, 1-63 for Equation 4

[b] LogTA100 = $\log_{10}$(revertants at 1μmol/plate);

[c] Log *P* calculated according to Ghose-Crippen;

[d] pK_A of the carboxylic acid corresponding to the acyloxyl group;

[e] E_s^1 Taft steric parameter for *para* –substituent on a benzamide side chain;

[f] E_s^2 Taft steric parameter for *para* –substituent on a benzyloxyl side chain;

[g] E_s^3 Taft steric parameter for *para* –substituent on a benzoyloxyl side chain;

[h] Indicator variable *I*=1 for naphthalene bearing mutagens (entries 51-58) otherwise 0;

[i] Logβ=-6.705

Regression analyses for Supplementary Table 1

Supplementary data for QSAR in Equation 3 (entries 1-58):

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.922063865
R Square	0.850201771
Adjusted R Square	0.83257845
Standard Error	0.161997269
Observations	58

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	6	7.596278708	1.266046451	48.24299398	2.52224E-19
Residual	51	1.338398878	0.026243115		
Total	57	8.934677586			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.117236054	0.412343627	2.709478168	0.009153984	0.289421699	1.94505041	0.289421699	1.94505041
Log*P*	0.261967633	0.026913102	9.733832623	3.20956E-13	0.207937327	0.315997939	0.207937327	0.315997939
pK_A	0.174888546	0.079324165	2.204732261	0.032009431	0.015638643	0.33413845	0.015638643	0.33413845
E_S^1	0.124967737	0.0333362	3.748709701	0.00045455	0.058042524	0.19189295	0.058042524	0.19189295
E_s^2	0.135876125	0.038020244	3.573783632	0.000779782	0.059547302	0.212204948	0.059547302	0.212204948

E_S^3	0.083179961	0.050580411	1.644509384	0.106221948	-0.01836445	0.184724372	-0.01836445	0.184724372
I	0.830536168	0.064360632	12.90441283	1.09189E-17	0.70132681	0.959745526	0.70132681	0.959745526

Log TA100 = 0.26 (±0.03) Log$P$ + 0.17 (±0.08) pK_A + 0.12 (±0.03) E_S^1 + 0.14 (±0.04) E_s^2 + 0.08 (±0.05) E_S^3 + 0.83 (±0.06) I + 1.12 (±0.41)

n = 58, R^2 = 0.85, adj. R^2 = 0.83, s = 0.16, F = 48.2; LOO CV Q^2= 0.85

Supplementary data for QSAR in Equation 4 (entries 1-63):

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.902272575
R Square	0.814095799
Adjusted R Square	0.790435264
Standard Error	0.177690657
Observations	63

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	7	7.604631675	1.086375954	34.40732886	6.82835E-18
Residual	55	1.736568325	0.03157397		
Total	62	9.3412			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.484559313	0.396839985	3.740951944	0.000439186	0.689274217	2.279844409	0.689274217	2.279844409
LogP	0.230836382	0.02381045	9.694751016	1.67405E-13	0.183119175	0.278553589	0.183119175	0.278553589
Log(βP+1)	0.651851424	0.12362435	5.272840064	2.32547E-06	0.404102692	0.899600155	0.404102692	0.899600155
pK_A	0.111078999	0.078360811	1.417532546	0.161967828	-0.045959573	0.268117572	-0.045959573	0.268117572
E_S^1	0.085502071	0.033419717	2.558431952	0.013298028	0.018527463	0.15247668	0.018527463	0.15247668
E_s^2	0.086013203	0.036545126	2.353616263	0.022193027	0.012775134	0.159251272	0.012775134	0.159251272
E_S^3	0.009313227	0.049657727	0.187548395	0.851920877	-0.090203081	0.108829535	-0.090203081	0.108829535
I	0.846728441	0.070324683	12.0402738	4.78996E-17	0.705794627	0.987662255	0.705794627	0.987662255

LogTA100 = 0.23 (±0.02) Log$P$ - 0.65 (±0.12) Log(βP + 1) + 0.11 (±0.08) pK_A + 0.09 (±0.03) E_S^1 + 0.09 (±0.04) E_S^2 + 0.01 (±0.05) E_S^3 + 0.85 (±0.07) I + 1.48 (±0.40)

Logβ = -6.705, n = 63, R^2 = 0.81, adj. R^2 = 0.79, s = 0.18, F = 29.6; LOO CV Q^2= 0.76

Supplementary Experimental

Synthesis of alcohols 2-(2'-naphthyl)ethanol and 3-(2'-naphthyl)-1-propanol.

2-(2'-Naphthyl)ethanol

2-Naphthylacetic acid. 2-Bromomethylnaphthalene (20.0 g, 0.091 mol) and potassium cyanide (17.7 g, 0.271 mol) were stirred overnight with sodium carbonate (12.4 g, 0.117 mol) in 25% aqueous ethanol (120 ml), then refluxed for 2hr. The ethanol was removed under reduced pressure. 50 ml of water was added and the residue extracted with ether (3 x 50 ml) and concentrated under reduced pressure. The impure nitrile was acidified with concentrated hydrochloric acid (30 ml) and refluxed for 5 hours. Ammonia was added until basic and the solution decolourised with charcoal and filtered. After acidification with dilute HCl, 2-naphthylacetic acid (6.40 g, 38%) was filtered off as a white solid and used without further purification, mp 139-140 °C (lit.,[1] 138°C); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710s (C=O); δ_H(300 MHz; $CDCl_3$) 3.84 (2H, s, $\underline{CH_2}CO_2H$), 7.43 (1H, d, Ar-H), 7.49 (2H, m, Ar-H), 7.76 (1H, s, Ar-H), 7.78-7.87 (3H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 41.0 (t), 125.9 (d), 126.3 (d), 127.3 (d), 127.7 (d), 127.7 (d), 128.2 (d), 128.4 (d), 130.7 (s), 133.4 (s), 176.6 (s).

2-(2'-Naphthyl)ethanol. 2-Naphthylacetic acid (5 g, 0.0269 mole) in dry ether (125 ml) was added slowly to a 2 molar excess of lithium aluminium hydride (3.80 g, 0.0537 mole) in dry ether (25 ml) and refluxed overnight. The crude reaction mixture was cooled in ice and dilute HCl added. The ether layer was separated, washed with 10% Na_2CO_3 solution then water and dried with Na_2SO_4. Removal of the ether gave 2-(2'-naphthyl)ethanol (4.12 g, 89%) as a yellow oil which solidified on standing and this was used without further purification, mp 65-66 °C (lit.,[2] 66-67 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3618br (OH), 1600s (C=C), 1044; δ_H(300 MHz; $CDCl_3$) 3.06 (2H, t, $ArCH_2$), 3.98 (2H, br, $\underline{CH_2}OH$), 7.39 (1H, d, Ar-H), 7.48 (2H, m, Ar-H), 7.71 (1H, s, Ar-H), 7.83 (3H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 39.4 (t), 63.5 (t), 125.5 (d), 126.1 (d), 127.4 (d), 127.5 (d), 127.7 (d), 128.2 (d), 128.3 (d), 132.3 (s), 133.6 (s), 136.0 (s).

3-(2'-Naphthyl)-1-propanol

3-(2'-Naphthyl)propenoic acid. A mixture containing 2-naphthaldehyde (10 g, 0.0640 mol), malonic acid (6.66 g, 0.06402 mol) and α-picoline (5.96 g, 0.06402 mol) was heated overnight at 70ºC. The reaction mixture was treated with water (100 ml) and concentrated HCl (25 ml), heated to 100ºC and filtered to remove unreacted 2-naphthaldehyde. The mixture was cooled and filtered. The crude solid was then dissolved in a minimum of boiling NaOH (5%) and Norit added. The mixture was

then filtered at 100ºC and acidified with HCl, cooled and filtered to give 3-(2'-naphthyl)propenoic acid (10.83g 85%), mp 204-205 °C (lit.,[3] 206 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 1686s (C=O), 1626s (C=C), 1288s; δ_H(300 MHz, $CDCl_3$) 6.58 (1H, d, Ar-CH=<u>CH</u>), 7.55 (2H, m, Ar-H), 7.72 (1H, d, Ar-H), 7.87-8.0 (5H, m, Ar-H, Ar-<u>CH</u>=CH); δ_C(75 MHz; $CDCl_3$) 117.2 (d), 123.5 (d), 126.8 (d), 127.5 (d), 127.8 (d), 128.7 (d), 128.8 (d), 130.4 (d), 131.6 (s), 133.3 (s), 134.5 (s), 147.1 (d), 171.0 (s).

3-(2'-Naphthyl)propanoic acid. A mixture of 5% palladium/carbon catalyst (300 mg) and methanol (250 ml) was stirred under hydrogen for 1 hour. 3-(2'-naphthyl)propenoic acid (10 g) was added and the mixture was stirred for 5 hours under hydrogen. Filtration and concentration yielded 3-(2' naphthyl)propanoic acid almost quantitatively, mp 130-131 °C (lit.,[4] 135-136 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710s (C=O); δ_H(300 MHz; $CDCl_3$) 2.81 (2H, t, $ArCH_2\underline{CH_2}$), 3.16 (2H, t, $ArCH_2$), 7.37 (1H, d, Ar-H), 7.47 (2H, m, Ar-H), 7.68 (1H, s, Ar-H), 7.82 (3H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 30.8 (t), 35.4 (t), 125.5 (d), 126.1 (d), 126.5 (d), 126.9 (d), 127.5 (d), 127.6 (d), 128.2 (d), 132.2 (s), 133.6 (s), 137.6 (s), 178.5 (s).

3-(2'-Naphthyl)-1-propanol. 3-(2'-Naphthyl)propanoic acid (10 g, 0.05 mole) in dry ether (250 ml) was added slowly to a 2 molar excess of lithium aluminium hydride (3.80 g, 0.10 mole) in dry ether (50 ml) and refluxed overnight. The crude reaction mixture was cooled in ice and dilute HCl added. The ether layer was separated, washed with 10% Na_2CO_3 solution then water and dried with Na_2SO_4. Removal of the ether gave 3-(2'-naphthyl)-1-propanol (8.56 g, 92%) as a yellow oil which solidified upon standing was used without further purification, mp 31-32 °C (lit.,[5] 33 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3625br (OH), 1600m (C=C), 1507m, 1040s; δ_H(300 MHz; $CDCl_3$) 2.02 (2H, qui, $OCH_2\underline{CH_2}$), 2.91 (2H, t, $ArCH_2$), 3.73 (2H, t, OCH_2), 7.38 (1H, d, Ar-H), 7.47 (2H, m, Ar-H), 7.67 (1H, s, Ar-H), 7.82 (3H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 32.2 (t), 34.1 (t), 62.2 (t), 125.2 (d), 126.0 (d), 126.4 (d), 127.3 (d), 127.4 (d), 127.6 (d), 128.0 (d), 132.1 (s), 133.7 (s), 139.3 (s).

Synthesis alkyl bromides

Method 1. The alkyl bromides were prepared from the appropriate alcohols by refluxing with HBr-H_2SO_4 in ether. The mixtures were washed with conc. HCl, H_2O, 10% aq. Na_2CO_3, H_2O and extracted with DCM. Concentration *in vacuo* provided the alkyl bromides in good yield (>90%) and high purity (^1H, ^{13}C NMR).

Method 2. Alkyl Bromides were prepared from the appropriate arylmethyl compound by refluxing with a slight excess of *N*-bromosuccinimde in carbon tetrachloride for a period of 4-16 hours. The

mixture was filtered to remove succinimide and the solvent removed *in vacuo*. The bromides were produced in good yields with high purity and generally used without further purification.

1-Bromomethylnaphthalene (method 2). 1-Methylnaphthalene (10 g, 0.0602 mol) was dissolved in carbon tetrachloride (70 ml) and to this was added *N*-bromosuccinimde (12.5 g, 0.0702 mol) and benzoyl peroxide (0.5 g) and the mixture heated under reflux for 16 hr. The reaction was cooled in ice and the solid succinimide removed via filtration. The solvent was removed under reduced pressure, affording the title compound as a heavy oil which was used without further purification (9.4g 64%). δ_H(300 MHz, $CDCl_3$) 5.01 (2H, s, CH_2Br), 7.45 (1H, t, Ar-H), 7.59 (2H, m, Ar-H), 7.68 (1H, t, Ar-H), 7.89 (1H, d, Ar-H), 7.94 (1H, d, Ar-H), 8.23 (1H, d, Ar-H); δ_C(75 MHz $CDCl_3$) 31.8 (t), 123.8 (d), 125.5 (d), 126.3 (d), 126.7 (d), 127.7 (d), 128.9 (d), 129.8 (d), 131.1 (s), 133.3 (s), 134.1 (s).

2-Bromomethylnaphthalene (method 2). 2-Methylnaphthalene (10.00 g, 0.0602 mol) was dissolved in carbon tetrachloride (70 ml) and to this was added *N*-bromosuccinimde (12.5 g, 0.0702 mol) and benzoyl peroxide (0.5 g) and the mixture heated under reflux for 16 hr. The reaction was cooled in ice and the solid succinimide removed via filtration. The solvent was removed under reduced pressure and the title compound solidified on cooling. Recrystallisation from ethanol afforded pure 2-bromomethylnaphthalene (10.6 g 72%). m.p. 55°C (lit[6] m.p. 56°C); δ_H(300 MHz, $CDCl_3$) 4.69 (2H, m, $\underline{CH_2}CH_2Br$), 7.52 (3H, m, Ar-H), 7.84 (4H, m, Ar-H); δ_C(75 MHz $CDCl_3$) 34.0 (t), 126.5 (d), 126.6 (d), 126.8 (d), 127.7 (d), 127.9 (d), 128.0 (d), 128.8 (d), 133.1 (s), 133.2 (s), 135.1 (s).

2-(2'-Naphthyl)ethyl bromide (method 1). 2-(2'-Naphthyl)ethyl alcohol (2.0 g, 0.012 mol) was added to 45 ml conc. HBr and refluxed for 3 hr. 2-(2'-Naphthyl)ethyl bromide was extracted with chloroform (3 x 30 ml) and successively washed with conc. HCl, H_2O and 10% Na_2CO_3. Drying over Na_2SO_4 and concentration under reduced pressure afforded 2-(2'-Naphthyl)ethyl bromide which was used without further purification (2.23 g, 82%). m.p. 62°C (lit [7]m.p. 64-65°C) δ_H(300 MHz, $CDCl_3$) 3.36 (2H, t, $ArCH_2$), 3.69 (2H, t, CH_2Br), 7.36 (1H, d, Ar-H), 7.49 (2H, m, Ar-H), 7.70 (1H, s, Ar-H), 7.78-7.87 (3H, m, Ar-H); δ_C(75 MHz $CDCl_3$) 32.8 (t), 39.6 (t), 125.7 (d), 126.2 (d), 126.9 (d), 127.3 (d), 127.6 (d), 127.7 (d), 128.3 (d), 132.5 (s), 133.5 (s), 136.3 (s).

3-(2'-Naphthyl)-1-propyl bromide (method 1). 3-(2'-Naphthyl)-1-propyl alcohol (1.21 g, 6.5 mmol) was added to 40ml conc. HBr and refluxed for 4 hours. 3-(2'-Naphthyl)-1-propyl bromide was extracted with chloroform (3 x 25 ml) and successively washed with conc. HCl, H_2O and 10% Na_2CO_3. Drying over Na_2SO_4 and concentration under reduced pressure afforded 3-(2'-naphthyl)-1-

propyl bromide (1.46 g, 90%) as a brown oil and this was used without further purification. δ_H(300 MHz, $CDCl_3$) 2.29 (2H, qui, $CH_2\underline{CH_2}CH_2$), 2.98 (2H, t, $ArCH_2$), 3.46 (2H, t, CH_2O), 7.35 (1H, d, Ar-H), 7.48 (2H, m, Ar-H), 7.68 (1H, s, Ar-H), 7.76-7.85 (3H, m, Ar-H); δ_C(75 MHz $CDCl_3$) 33.1 (t), 34.1 (t), 34.1 (t), 125.4 (d), 126.1 (d), 126.8 (d), 127.2 (d), 127.5 (d), 127.6 (d), 128.2 (d), 132.2 (s), 133.6 (s), 138.0 (s).

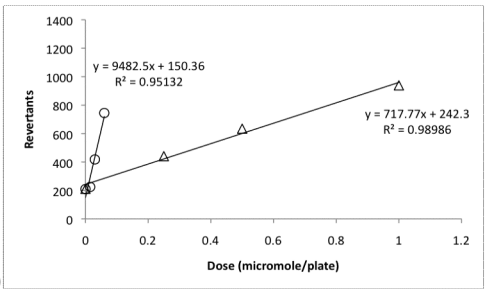
DNA Sequence plasmid pBR322:

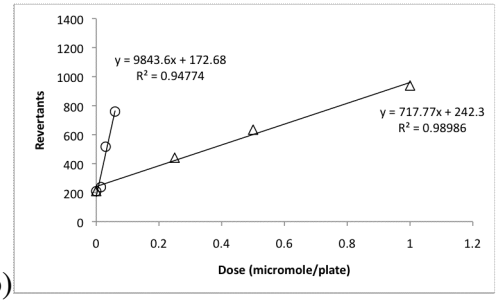
A partial sequence of the 375 base pair *EcoRI* to *BamHI* fragment of plasmid pBR322 DNA used in DNA damage studies is presented below.[8]

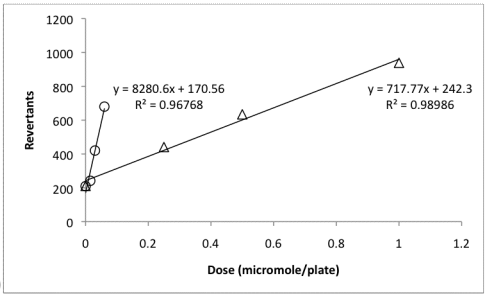
```
   31          41          51          61          71
   GCTTTAATGC  GGTAGTTTAT  CACAGTTAAA  TTGCTAACGC  AGTCAGGCAC
3'-CGAAATTACG  CCATCAAATA  GTGTCAATTT  AACGATTGCG  TCAGTCCGTG

   81          91          101         111         121
   CGTGTATGAA  ATCTAACAAT  GCGCTCATCG  TCATCCTCGG  CACCGTCACC
   GCACATACTT  TAGATTGTTA  CGCGAGTAGC  AGTAGGAGCC  GTGGCAGTGG

   131         141         151         161
   CTGGATGCTG  TAGGCATAGG  CTTGGGTTAT  GCCGGTACTG
   GACCTACGAC  ATCCGTATCC  GAACCCAATA  CGGCCATGAC-5'
```

Dose-response plots for mutagenicity in *S.typhimurium* TA100 and TA98

Dose response plots for mutagens **2**-**9** in *S*. *typhimurium* TA100:

a) 

b) 

c) 

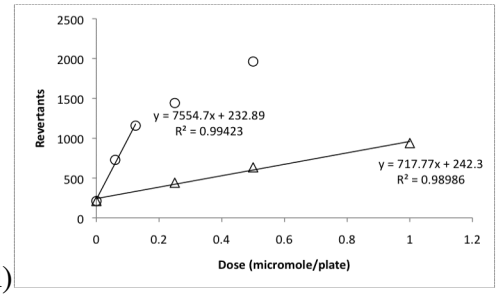
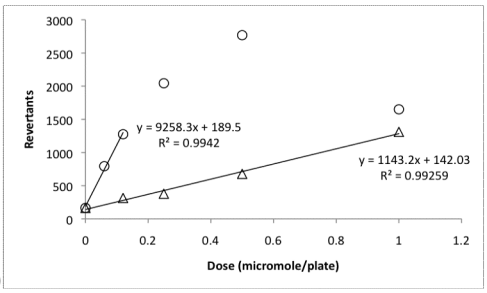
d) 

Figure S1. Dose-response (circles) for a) *N*-acetoxy-*N*-butoxy-2-naphthamide **2**, b) *N*-butoxy-*N*-2-naphthoyloxyacetamide **3**, c) *N*-acetoxy-*N*-(1-naphthylmethoxy)acetamide **6** and d) *N*-acetoxy-*N*-(2-naphthylmethoxy)acetamide **7** along with standard *N*-acetoxy-*N*-butoxybenzamide **14** (triangles) in *S. typhimurium* TA100; data from Table 2.

a) 

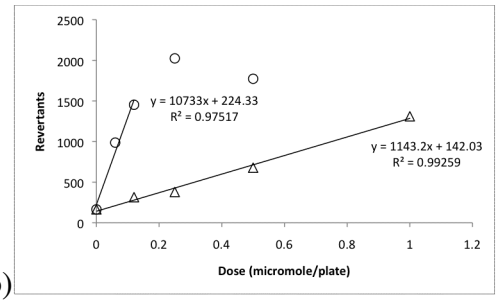
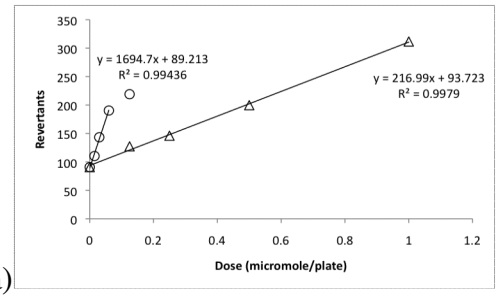
b) 

Figure S2. Dose-response (circles) for a) *N*-acetoxy-*N*-(2-(2'-naphthyl)ethoxy)acetamide **8** and b) *N*-acetoxy-*N*-(3-(2'-naphthyl)propyloxy)acetamide **9** along with standard *N*-acetoxy-*N*-butoxybenzamide **14** (triangles) in *S. typhimurium* TA100; data from Table 3.

a) 

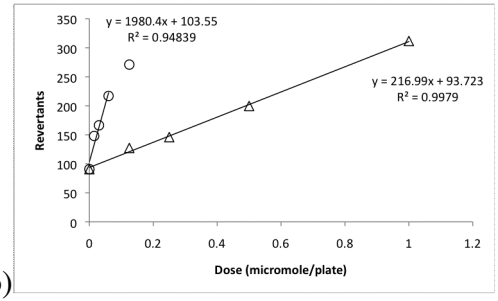
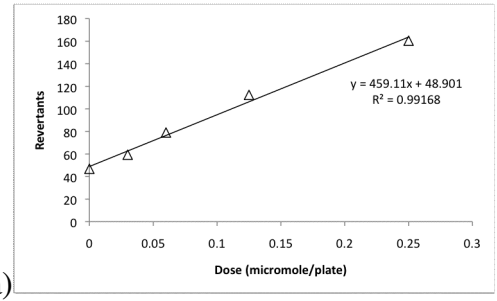
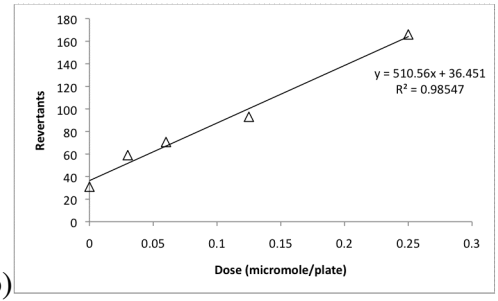
b) 

Figure S3. Dose-response (circles) for a) *N*-butoxy-*N*-(2-naphthylacetoxy)acetamide **4** and b) *N*-butoxy-*N*-(3-(2-naphthyl)propanoyloxy)acetamide **5** along with standard *N*-acetoxy-*N*-butoxybenzamide **14** (triangles) in *S. typhimurium* TA100; data from Table 4.

Dose response plots for mutagens in *S. typhimurium* TA98 (data from Table 6):

a) 

b) 

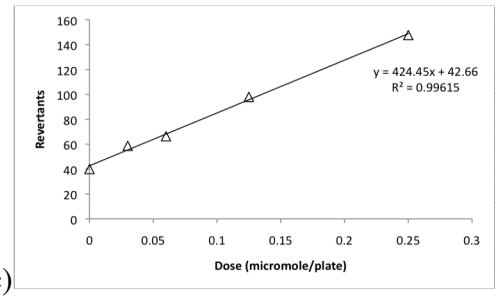
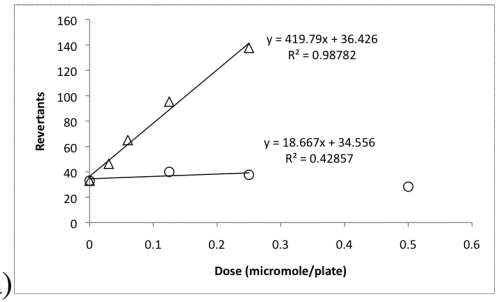
c) 

Figure S4. Mutagenic activity of *N*-acetoxy-*N*-butoxy-2-naphthamide **2**, a) test A, b) test B, c) test C in *S. typhimurium* TA98.

a)



b)

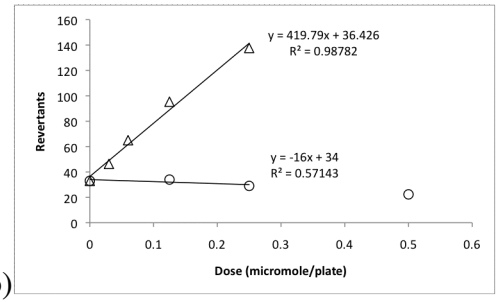
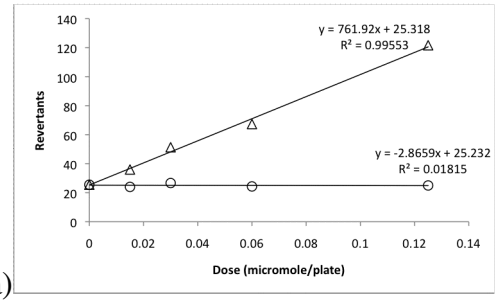


Figure S5. Test set D - Dose-response (circles) for a) *N*-acetoxy-*N*-butoxybenzamide **14** and b) *N*-benzoyloxy-*N*-butoxyacetamide **15** along with standard *N*-acetoxy-*N*-butoxy-2-naphthamide **2** (triangles) in *S. typhimurium* TA98

a)



b)

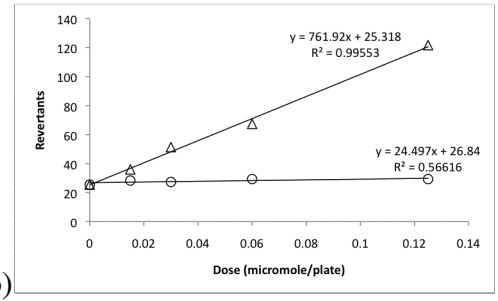
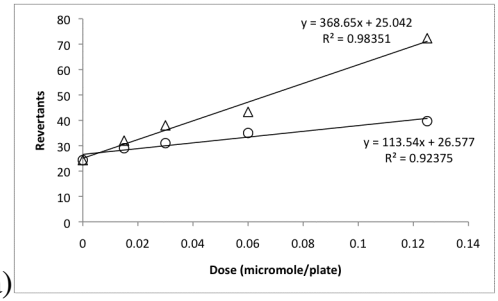
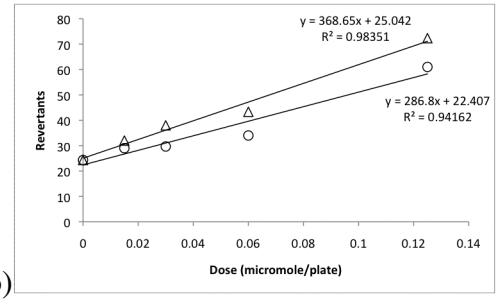


Figure S6. Test set E - Dose-response (circles) for a) *N*-butoxy-*N*-ethoxy-2-naphthamide **16** and b) *N*-butoxy-*N*-(2-naphthoyloxy)acetamide **3** along with standard *N*-acetoxy-*N*-butoxy-2-naphthamide **2** (triangles) in *S. typhimurium* TA98

a)



b)



c)

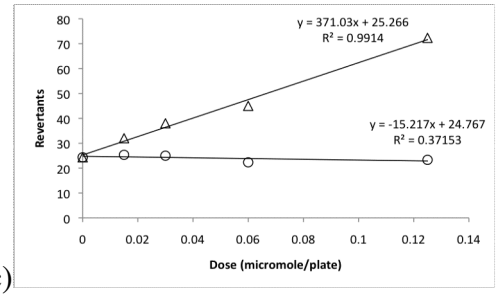


Figure S7. Test set F – Dose-response (circles) for a) *N*-acetoxy-*N*-(1-naphthylmethoxy)acetamide **6**, b) *N*-acetoxy-*N*-(2-naphthylmethoxy)acetamide **7** and c) *N*-butoxy-*N*-methyl-2-naphthamide **17** along with standard *N*-acetoxy-*N*-butoxy-2-naphthamide **2** (triangles) in *Salmonella typhimurium* TA98

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