Supplementary Materials

Bioactivity of Methoxylated and Methylated 1-Hydroxynaphthalene-2-Carboxanilides: Comparative Molecular Surface Analysis†

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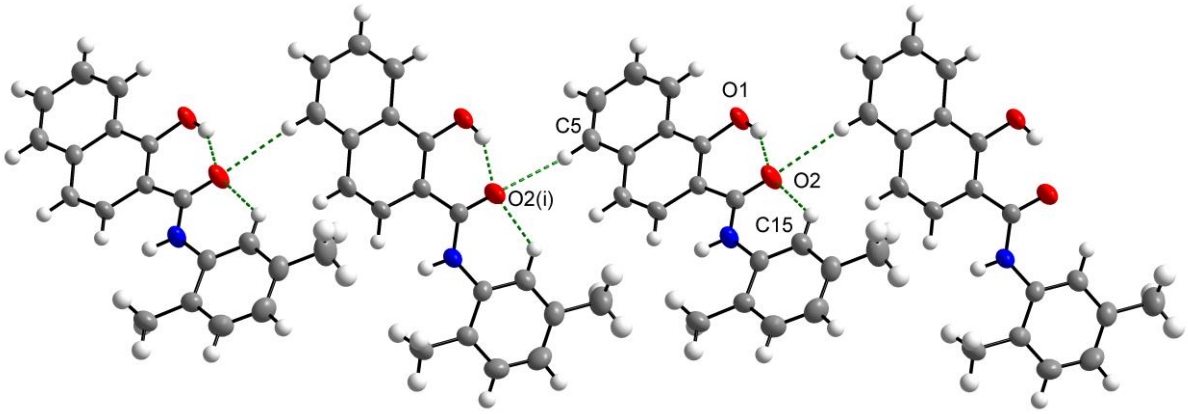

Figure S1. Part of the crystal structure of *N*-(2,5-dimethylphenyl)-1-hydroxynaphthalene-2-carboxamide (**11**), showing O–H···O and C–H···O non-covalent contacts (green dashed lines). Symmetry code: (i) x+1/2,-y+1/2,z-1/2.

Table S1. Selected bond lengths (Å) and angles (°) in **11**.

O(1)-C(1)	1.349(3)
O(2)-C(9)	1.249(3)
N(1)-C(9)	1.351(3)
N(1)-C(10)	1.418(3)
C(1)-C(2)	1.387(4)
C(1)-C(8A)	1.415(4)
C(2)-C(3)	1.429(3)
C(2)-C(9)	1.466(4)
C(9)-N(1)-C(10)	130.9(2)
O(1)-C(1)-C(2)	122.4(2)
O(1)-C(1)-C(8A)	116.6(2)
C(2)-C(1)-C(8A)	121.0(2)
C(1)-C(2)-C(3)	118.0(2)
C(1)-C(2)-C(9)	118.9(2)
C(3)-C(2)-C(9)	123.1(2)
C(4)-C(3)-C(2)	122.3(3)
O(2)-C(9)-N(1)	120.9(3)
O(2)-C(9)-C(2)	121.4(2)
N(1)-C(9)-C(2)	117.7(2)
C(15)-C(10)-C(11)	121.2(3)
C(15)-C(10)-N(1)	122.6(3)
C(11)-C(10)-N(1)	116.2(2)

Table S2. Parameters (in Å, °) of selected non-covalent contacts within crystal structure of **11**.

D-H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
O1-H1A...O2	0.84	1.78	2.524(3)	146.8
C15-H15A...O2	0.95	2.23	2.858(4)	122.6
C5-H5A...O2(i)	0.95	2.59	3.429(4)	146.8

Symmetry transformation used to generate equivalent atoms: (i) x+1/2,-y+1/2,z-1/2.

Table S3. Matrix of correlation coefficients (n=26, α=0.05) of linear relationships between particular partition coefficients and experimental lipophilicity data (log *k*) for *N*-(methoxy/methyl-phenyl)-1-hydroxynaphthalene-2-carboxamides **1**–**26**.

	log *k*	logP[a]	miLogP[b]	ClogP[c]	ClogP[d]	ClogP[e]	ClogP[f]	ClogP[g]	MlogP[h]	AlogP[i]	ClogP[j]	ClogP[k]
log*k*	1											
logP[a]	0.37	1										
miLogP[b]	0.59	0.78	1									
ClogP[c]	0.53	0.73	0.78	1								
ClogP[d]	0.49	0.67	0.68	0.97	1							
ClogP[e]	0.65	0.64	0.83	0.66	0.57	1						
ClogP[f]	0.40	0.76	0.75	0.89	0.85	0.65	1					
ClogP[g]	0.47	0.70	0.81	0.77	0.63	0.79	0.81	1				
MlogP[h]	0.44	0.81	0.76	0.82	0.80	0.70	0.93	0.74	1			
AlogP[i]	0.39	0.77	0.79	0.92	0.85	0.68	0.98	0.87	0.88	1		
ClogP[j]	0.58	0.65	0.79	0.64	0.56	0.97	0.72	0.77	0.75	0.73	1	
ClogP[k]	0.44	0.82	0.76	0.83	0.73	0.59	0.81	0.76	0.72	0.86	0.60	1

[a] clogPS, [b] Molinspirations, [c] OSIRIS property explorer, [d] HyperChem 7.0, [e] Sybyl X, [f] Marvin Sketch (ChemAxon) 15, [g] ChemSketch 2015, [h] Dragon 6.0, [i] Dragon 6.0, [j] Kowwin, [k] XlogP3.

Table S4. Physicochemical properties and calculated HAC, LE and LELP values of **1–26** analogues.

Comp.	R	log *k*	HAC	PET	LE[a]	LELP[a]
1	H[a]	0.6769	20	31.3	0.3153	2.1468
2	2-OCH_3[a]	0.8584	22	199	0.2355	3.6446
3	3-OCH_3[a]	0.6713	22	23.5	0.2946	2.2789
4	4-OCH_3[a]	0.6284	22	79.5	0.2609	2.4087
5	2,5-OCH_3[b]	0.8712	24	201	0.2156	4.0399
6	3,5-OCH_3[b]	0.7048	24	13.4	0.2651	2.6583
7	3,4,5-OCH_3[b]	0.5603	26	468	0.1793	3.1250
8	2-CH_3[a]	0.5650	21	62.8	0.2801	2.0169
9	3-CH_3[a]	0.8235	21	20.0	0.3133	2.6288
10	4-CH_3[a]	0.8294	21	28.7	0.3123	2.6560
11	2,5-CH_3[b]	0.7155	22	52.4	0.2724	2.6266
12	2,6-CH_3[b]	0.5990	22	60.3	0.2685	2.2307
13	3,5-CH_3[b]	1.0030	22	8.19	0.3047	3.2920
14	2,4,6-CH_3[b]	0.7477	23	295	0.2149	3.4796
15	2-OCH_3-5-CH_3[b]	1.0603	23	588	0.2575	4.1174
16	2-OCH_3-6-CH_3[b]	0.4574	23	747	0.1903	2.4033
17	2-CH_3-5-OCH_3[b]	0.5362	23	142	0.2342	2.2894
18	2-OCH_3-4-NO_2[b]	0.5434	25	495	0.1851	2.9357
19	2-OCH_3-5-NO_2[b]	0.4827	25	155	0.2133	2.2626
20	2-OCH_3-5-Br	1.0432	23	569	0.1975	5.2816
21	2-OCH_3-5-CF_3[b]	0.9428	26	26.4	0.2465	3.8243
22	3-CF_3-4-OCH_3[b]	0.8915	26	18.5	0.2739	3.2548
23	3-F-5-OCH_3	0.7629	23	10.1	0.2966	2.5721
24	2-Cl-5-OCH_3[b]	0.8130	23	60.9	0.2566	3.1685
25	2-CH_3-5-CF_3[b]	0.7479	25	36.7	0.2484	3.0111
26	3-CF_3-4-CH_3[b]	1.1411	25	16.3	0.2798	4.0789

[a] as described by Shultz [1], HAC – heavy atom count, LE – ligand efficiency (1.4×pIC_{50})/HAC, LELP – ligand efficiency dependent lipophilicity clogP/LE

[1] Shultz, M.D. Setting expectations in molecular optimizations: Strengths and limitations of commonly used composite parameters. *Bioorg. Med. Chem.* **2013**, *23*, 5980–5991.