Supporting Information for:

Predicting the phospholipophilicity of monoprotic positively charged amines

S.T.J. Droge*[a], J.L.M Hermens [a], S. Gutsell [b], J. Rabone [b], G. Hodges[b]

[a] Institute for Risk Assessment Sciences, Utrecht University, The Netherlands

[b] Safety and Environmental Assurance Centre, Unilever, Sharnbrook, Bedford, United Kingdom.

* Corresponding author, steven.droge@gmail.com

SI-Tables: 3

SI-Figures: 3

Pages: 10

Table S1. Suppliers and properties of tested amines.

#	Compound	Supplier	purity	Detection	CAS	Use
	halogenated/nonpolar amines					
1	R-(-) deprenyl HCl	Sigma	>98%	UV	14611-52-0	Antidepressant
2	4-fluoroaniline (f.b.)	Sigma	99%	UV	371-40-4	(Model structure)
3	3-chloroaniline (f.b.)	Sigma	99%	UV	108-42-9	(Model structure)
4	4-chlorobenzylamine (f.b.)	Alfa Aesa	97%	UV	104-86-9	(Model structure)
5	3,4-dichlorobenzylamine (f.b.)	Fluorochem Ltd	98%	UV	102-49-8	(Model structure)
6	sertraline HCl	Sigma	98%	UV	79559-97-0	Antidepressant
	simple monopolar amines					
7	diphenhydramine HCl	Sigma	>98%	UV	147-24-0	Antidepressant
8	tamoxifen (f.b.)	Sigma	>99%	LC-MS/MS	10540-29-1	SERM
9	fluoxetine HCl	Ehrenstorfer	99%	UV	54910-89-3	Antidepressant
10	duloxetine HCl	Eur.Ph.Ref.	CRS	LC-MS/MS	136434-34-9	Antidepressant
11	*N*-Benzylaminoacet-aldehydediethylacetal (f.b.)	Alfa Aesar	98%	UV	61190-10-1	(Model structure)
12	escitalopram oxalate	Sigma	>98%	LC-MS/MS	219861-08-2	Antidepressant
13	spiroxamine (f.b.)	Sigma	98.8%	LC-MS/MS	118134-30-8	Pesticide
14	MDMA HCl	Duchefa	99.7	UV	42542-10-9	Illicit drug
15	3-dimethylamino-propiophenone HCl	Alfa Aesar	99%	UV	879-72-1	(Model structure)
16	bupropion HCl	Sigma	>98%	UV	31677-93-7	Antidepressant
17	ketamine HCl	Sigma		UV	1867-66-9	Anaesthetic
18	ethyl3-(benzylamino)-propanoate f.b.	Alfa Aesar	96%	UV	23583-21-3	(Model structure)
19	butyrylcholine Cl	Sigma	>98%	UV	2963-78-2	(Model structure)
20	S-Butyrylthiocholine I	Fluka	>99%	UV	1866-16-6	(Model structure)
21	valethamate Br	Alfa Aesar	99%	UV	90-22-2	Spasmolytic
22	cocaine HCl	Spruyt hillen		UV	50-36-2	Illicit drug
	simple bipolar amines					
23	*N*-ethanolbenzylamine (f.b.)	Alfa Aesar	96%	UV	104-63-2	(Model structure)
24	methylephedrine (f.b.)	Alfa Aesar	98+%	UV	552-79-4	(Model structure)
25	benzyldimethylhydroxyethylamm. Cl	Sigma	≥97%	UV	7221-40-1	(Model structure)
26	2,2'-(benzylimino)-diethanol (f.b.)	Sigma	CPR>99%	UV	101-32-6	(Model structure)
27	dopamine HCl	Sigma	+98%	UV	62-31-7	Stimulant
28	albuterol sulfate	Sigma	Ph.std.	UV	51022-70-9	Bronchodilator
29	tramadol HCl	Sigma	>99%	UV	27203-92-5	Analgesic
30	alprenolol HCl	Sigma	>98%	UV	13655-52-2	Beta-blocker
31	nadolol (f.b.)	Ehrenstorfer	99.1%	UV	42200-33-9	Beta-blocker
32	metoprolol tartrate	Sigma	>98%	UV	37350-58-6	Beta-blocker
33	propranolol HCl	Promochem	99%	UV	525-66-6	Beta-blocker
34	atropine (f.b.)	Fluka	>95%	UV	51-55-8	Anticholinergic
35	scopolamine HCl	Fluka	99%	UV	51-34-3	Anticholinergic
	simple amines with polar N groups					
36	procaine HCl	Ehrenstorfer	99.3%	UV	59-46-1	Anaesthetic
37	4-amino-2-methylquinoline (f.b.)	Alfa Aesar	98%	UV	6628-04-2	(Model structure)
38	ropivacaine HCl	Molekula		UV	84057-95-4	Anaesthetic
39	bupivacaine HCl	Fluka	>99%	UV	2180-92-9	Anaesthetic
40	lidocaine (f.b.)	Sigma	>99%	UV	137-58-6	Anaesthetic
41	prilocaine HCl	Sigma	≥98%	UV	721-50-6	Anaesthetic
42	1-benzyl-3-acetamidopyrrolidine (f.b.)	Alfa Aesar	98%	UV	114636-30-5	(Model structure)
43	propamocarb HCl	Ehrenstorfer	99%	LC-MS/MS	24579-73-5	Pesticide
44	neostigmine Br	Sigma	>98%	UV	114-80-7	ACh inhibitor
45	pyridostigmine Br	Sigma	>98%	UV	101-26-8	Ch inhibitor
46	4-carbamoyl-1-pentylpyridinium Br	Sigma	CPR	UV	X-S400483-1EA	(Model structure)
47	4-carbamoyl-1-octylpyridinium Br	Sigma	CPR	UV	X-S421189-1EA	(Model structure)

#	Compound	Supplier	purity	Detection	CAS	Use
48	atenolol (f.b.)	Sigma	99%	UV	56715-13-0	Beta-blocker
49	tryptamine HCl	Sigma	99%	UV	61-54-1	(Model structure)
50	serotonin HCl	Alfa Aesar	99%	UV	50-67-9	(Model structure)
51	benzimidazole (f.b.)	Alfa Aesar	99%	UV	51-17-2	Fungicide
52	thiabendazole (f.b.)	Ehrenstorfer		UV	148-79-8	Fungicide
53	pindolol (f.b.)	Sigma	>98%	UV	13523-86-9	Beta-blocker
54	(S)-(-)nicotine (f.b.)	Alfa Aesar	99%	UV	54-11-5	Opioid
55	clonidine HCl	Fluka	An.std.	UV	4205-90-7	Antihypertensive
56	clotrimazole (f.b.)	Sigma	99.3%	UV	23593-75-1	Fungicide
57	timolol maleate	Ehrenstorfer	99%	LC-MS/MS	26921-17-5	Beta-blocker
58	1,3-diphenylguanidine (f.b.)	Alfa Aesar	99+%	UV	102-06-7	(Model structure)
59	sotalol HCl	Ehrenstorfer	98.5%	UV	959-24-0	Beta-blocker
60	S-sulpiride (f.b.)	Ehrenstorfer	98%	UV	23672-07-3	Antipsychotic
	polyaromatic amines					
61	morphine sulfate	Spruyt hillen	>98%	UV	6211-15-0	Analgesic
62	naloxone HCl	Alfa Aesar	98%	UV	357-08-4	Opioid antagonist
63	strychnine (f.b.)	Sigma	>98%	UV	57-24-9	Pesticide
64	harmine (f.b.)	Sigma	98%	UV	442-51-3	CNS stimulant
65	harmaline (f.b.)	Sigma	99.2	UV	304-21-2	CNS stimulant
66	promazine HCl	Sigma	99.9%	UV	58-40-2	Antidepressant
67	chlorpromazine HCl	Sigma	>98%	UV	50-53-3	Antidepressant
68	triflupromazine HCl	Sigma	99.7%	UV	146-54-3	Antidepressant
69	doxepin HCl	Alfa Aesar	99.2%	UV	1229-29-4	Antidepressant
70	difenzoquat hemisulfate	Ehrenstorfer		UV	43222-48-6	Pesticide
	complex amines (≥ 4 polar groups, and/or large rings, and/or Mw > 400)					
71	(±)-verapamil HCl	Sigma	98%	UV	52-53-9	Ca -channel bl.
72	trimethoprim (f.b.)	Ehrenstorfer	99.5%	UV	738-70-5	Antibiotic
73	loperamide HCl	Sigma	99.9%	UV	34552-83-5	Antiperistaltic
74	ketanserin tartrate	Janssen	>97%	UV	83846-83-7	Antihypertensive
75	amlodipine (f.b.)	Alfa Aesar	97%	UV	88150-42-9	Ca-channel bl.
76	nicardipine HCl	Alfa Aesar	98+%	UV	54527-84-3	Ca-channel bl.
77	acebutolol HCl	Sigma	An.std.	UV	34381-68-5	Beta-blocker
78	lincomycin HCl	Riedel deHaen	103%	UV	7179-49-9	Antibiotic
79	diltiazem ((+)-cis-) HCl	Sigma	>99%	UV	33286-22-5	Ca-channel bl.
80	amiodarone (f.b.)	Sigma	>98%	UV	19774-82-4	Antiarrhythmic
81	ergocornine	Sigma	≥95%	LC-MS/MS	564-36-3	Mycotoxin
82	nefopam HCl	Sigma	>98%	UV	23327-57-3	Analgesic
83	tiamulin fumarate	Riedel de Haen	99.9%	UV	55297-96-6	Antibiotic
84	clarithromycin (f.b.)	Sigma	>98%	LC-MS/MS	81103-11-9	Macrolide
85	erythromycin A (<12% B) (f.b.)	Sigma	>85%	LC-MS/MS	114-078	Macrolide
86	tylosin hemitartrate	Ehrenstorfer	91.4%	LC-MS/MS	1401-69-0	Antibiotic

Table S2. Uncorrected and corrected LogK_{IAM} and LogK_{DMPC} values

#	Name	amine type	logK_{IAM} pH5.0 [d] uncorrected	logK_{IAM} pH5.0 [d] δIAM-SSLM corrected	logK_{DMPC} [d] COSMO uncorrected	logK_{DMPC} [d] TUHH uncorrected	logK_{DMPC} COSMO-TUHH difference	logK_{DMPC} TUHH corrected
	halogenated/nonpolar amines							***+0.43***
1	deprenyl	3°	1.97	1.94	1.05	1.48	0.4	1.91
2	4-fluoroaniline	1°	1.05	1.83	1.50	2.01	0.5	2.44
3	3-chloroaniline	1°	1.97	2.75	1.87	2.34	0.5	2.77
4	4-chlorobenzylamine	1°	1.66	2.44	2.07	2.53	0.5	2.96
5	3,4-dichlorobenzylamine	1°	2.24	3.02	2.61	3.06	0.4	3.49
6	sertraline	2°	4.32	4.79	3.11	3.47	0.4	3.90
	simple monopolar amines							***+0.43***
7	diphenhydramine	3°	2.88	2.85	2.86	3.28	0.4	3.71
8	tamoxifen	3°	6.51	6.48	4.91	5.29	0.4	5.72
9	fluoxetine	2°	4.28	4.75	3.67	4.10	0.4	4.53
10	duloxetine	2°	3.93	4.40	3.52	3.93	0.4	4.36
11	escitalopram	3°	3.28	3.25	1.17	1.53	0.4	1.96
12	*N*-benzylaminoacet-aldehydediethylacetal	2°	1.85	2.32	1.86	2.16	0.3	2.59
13	spiroxamine	3°	3.30	3.27	3.02	3.23	0.2	3.66
14	MDMA	2°	1.74	2.21	1.19	1.63	0.4	2.06
15	3-dimethylamino-propiophenone	3°	1.33	1.30	0.45	0.83	0.4	1.26
16	bupropion	2°	2.42	2.89	1.69	2.00	0.3	2.43
17	ketamine	2°	1.88	2.35	0.93	1.23	0.3	1.66
18	ethyl-3-(benzylamino)propanoate	2°	1.27	1.74	1.22	1.60	0.4	2.03
19	butyrylcholine	4°	0.66	0.55	-0.02	0.41	0.4	0.84
20	butyrylthiocholine	4°	1.13	1.02	0.85	1.23	0.4	1.66
21	valethamate	4°	3.06	2.95	2.34	2.65	0.3	3.08
22	cocaine	3°	2.10	2.07	1.31	1.77	0.5	2.20
	simple dipolar amines							***+0.09***
23	*N*-ethanolbenzylamine	2°	0.97	1.44	0.93	1.42	0.5	1.51
24	methylephedrine	3°	1.35	1.32	1.00	1.44	0.4	1.53
25	benzyldimethylhydroxyethylamm.	4°	1.00	0.89	0.51	0.90	0.4	0.99
26	2,2'-(benzylimino)-diethanol	3°	1.01	0.98	0.50	0.99	0.5	1.08
27	dopamine	1°	0.96	1.74	1.99	2.64	0.6	2.73
28	albuterol	2°	1.23	1.70	1.33	1.83	0.5	1.92
29	tramadol	3°	2.01	1.98	1.48	1.76	0.3	1.85
30	alprenolol	2°	2.79	3.26	2.56	3.00	0.4	3.09
31	nadolol	2°	1.88	2.35	1.30	1.74	0.4	1.83
32	metoprolol	2°	2.06	2.53	2.13	2.57	0.4	2.66
33	propranolol	2°	3.12	3.59	2.66	3.11	0.4	3.20
34	atropine	3°	1.95	1.92	0.65	1.14	0.5	1.23
35	scopolamine	3°	1.42	1.39	0.84	1.39	0.5	1.48
	simple amines with polar N groups							***+0.54***
36	procaine	3°	1.57	1.54	0.67	0.99	0.3	1.53
37	4-amino-2-methylquinoline	3°	2.04	2.01	0.17	0.67	0.5	1.21
38	ropivacaine	3°	2.15	2.12	1.37	1.74	0.4	2.28
39	bupivacaine	3°	2.45	2.42	1.82	2.14	0.3	2.68
40	lidocaine	3°	1.66	1.63	1.13	1.58	0.4	2.12
41	prilocaine	2°	1.78	2.25	1.93	2.34	0.4	2.88
42	1-benzyl-3-acetamidopyrrolidine	3°	1.27	1.24	-0.17	0.23	0.4	0.77
43	propamocarb	3°	0.95	0.92	0.37	0.70	0.3	1.24
44	neostigmine	4°	1.19	1.08	0.09	0.45	0.4	0.99
45	pyridostigmine	4°	0.59	0.48	-0.40	-0.07	0.3	0.47
46	4-carbamoyl-1-pentylpyridinium	4°	1.12	1.01	0.41	0.75	0.3	1.29
47	4-carbamoyl-1-octylpyridinium	4°	2.52	2.41	2.10	2.40	0.3	2.94
48	atenolol	2°	1.26	1.73	2.12	0.70	0.5	1.24
49	tryptamine	1°	1.91	2.69	1.96	2.50	0.5	3.04
50	serotonin	1°	1.59	2.37	1.76	2.42	0.7	2.96
51	benzimidazole	3°	1.22	1.19	0.46	0.96	0.5	1.50
52	thiabendazole	3°	2.28	2.25	0.43	0.94	0.5	1.48
53	pindolol	2°	2.11	2.58	1.61	2.11	0.5	2.65
54	nicotine	3°	0.96	0.93	-0.72	-0.26	0.5	0.28
55	clonidine	3°	1.71	1.68	0.91	1.36	0.5	1.90
56	clotrimazole	3°	4.10	4.07	3.16	3.33	0.2	3.87
57	timolol	2°	1.98	2.45	1.44	1.89	0.5	2.43
58	1,3-diphenylguanidine	2°	2.05	2.52	1.79	2.17	0.4	2.71
59	sotalol	2°	1.33	1.80	0.66	1.22	0.6	1.76
60	sulpiride	3°	1.64	1.61	0.11	0.26	0.2	0.80

#	name	amine type	logK_{IAM} pH5.0 [d] uncorrected	logK_{IAM} pH5.0 [d] δIAM-SSLM corrected	logK_{DMPC} [d] COSMO uncorrected	logK_{DMPC} [d] TUHH uncorrected	logK_{DMPC} COSMO-TUHH difference	logK_{DMPC} COSMO-TUHH corrected
	polyaromatic amines							***+0.76***
61	morphine	3°	1.29	1.26	0.09	0.69	0.2	1.45
62	naloxone	3°	1.63	1.60	0.75	1.22	0.6	1.98
63	strychnine	3°	2.28	2.25	0.00	0.51	0.5	1.27
64	harmine	3°	3.08	3.05	1.08	1.48	0.5	2.24
65	harmaline	3°	2.78	2.75	0.86	1.21	0.4	1.97
66	promazine	3°	3.87	3.84	2.37	2.77	0.4	3.53
67	chlorpromazine	3°	4.34	4.31	2.82	3.21	0.4	3.97
68	triflupromazine	3°	4.58	4.55	3.05	3.45	0.4	4.21
69	doxepin	3°	3.31	3.28	2.32	2.73	0.4	3.49
70	difenzoquat	4°	2.56	2.45	1.55	1.67	0.4	2.43
	complex amines (≥ 4 polar groups, and/or large rings, and/or Mw > 400)							***+0.59***
71	verapamil	3°	4.08	4.05	0.63 $	1.08 $	0.5	2.29
72	trimethoprim	3°	2.14	2.11	0.97	1.51	0.5	2.10
73	loperamide	3°	4.44	4.41	4.21	4.23	0.0	4.82
74	ketanserin	3°	3.19	3.16	1.63	1.92	0.3	2.51
75	amlodipine	1°	4.15	4.93	3.93	4.44	0.5	5.03
76	nicardipine	3°	3.89	3.86	2.70	3.0	0.3	3.59
77	acebutolol	2°	2.40	2.87	2.16	2.62	0.5	3.21
78	lincomycin	3°	1.28	1.25	1.72	2.06	0.3	2.65
79	diltiazem	3°	3.26	3.23	1.89	2.24	0.4	2.83
80	amiodarone	3°	4.52	6.48	5.50	5.68	0.2	6.27
81	ergocornine	3°	4.30	4.27	1.46	2.03	0.6	2.62
82	nefopam	3°	2.52	2.49	1.55	1.91	0.4	2.50
83	tiamulin	3°	0.99	0.96	1.82	2.01	0.2	2.60
84	clarithromycin	3°	3.70	3.67	2.90	3.3	0.4	3.89
85	erythromycin	3°	3.38	3.35	3.46	3.86	0.4	4.45
86	tylosine	3°	3.40	3.37	1.99	2.48	0.5	3.07

Table S3A. LogK_{OW} values for primary and secondary amines

Amine type		#	Name	Experimental	EPISuite	ACD/Labs
1°	CxHyN		benzylamine	1.09	1.07	1.09
1°	CxHyN		4-methylbenzylamine	1.46	1.62	1.55
1°	CxHyN		4-butylbenzylamine		3.09	3.14
1°	CxHyN		4-octylbenzylamine		5.05	5.27
1°	CxHyN		2-phenylethylamine	1.41	1.34	1.46
1°	CxHyN		amphetamine	1.76	1.76	1.81
1°	CxHyN		3-phenylpropylamine	1.83	2.05	1.83
1°	CxHyN		4-phenylbutylamine	2.40	2.54	2.36
1°	CxHyN		4-t-butylcyclohexylamine		3.41	3.12
1°	CxHyN		1-hexylamine	2.06	1.82	1.99
1°	CxHyN		1-heptylamine	2.57	2.31	2.52
1°	CxHyN		1-octylamine	2.90	2.8	3.06
1°	CxHyN		1-decylamine		3.78	4.12
1°	CxHyN		tert-octylamine		2.58	2.32
1°	CxHyN		(±)-1-aminoindane		1.92	1.61
1°	CxHyN		amantadine	2.44	2.43	2.22
1°	CxHyN		1-naphthylmethylamine		2.25	2.32
1°	CxHyN		1-naphthylamine	2.25	2.25	2.17
1°	CxHyN		3,4-dimethylaniline	1.84	2.17	1.90
1°	CxHyN		2,4,6-trimethylaniline		2.72	2.30
1°	CxHyN		4-octylaniline		5.06	5.12
1°	polar	2	4-fluoroaniline	1.15	1.28	1.15
1°	polar	3	3-chloroaniline	1.88	1.72	1.81
1°	polar	4	4-chlorobenzylamine		1.71	1.68
1°	polar	5	3,4-dichlorobenzylamine		2.36	2.15
1°	polar	50	tryptamine	1.55	1.27	1.38
1°	polar	51	serotonin	0.21	0.79	0.21
1°	polar	28	dopamine	-0.98	0.38	0.12
1°	polar	75	amlodipine	3.00	2.07	4.16
2°	CxHyN		*N*-methylbenzylamine	1.52	1.54	1.52
2°	CxHyN		*N*-ethylbenzylamine	1.82	2.03	2.05
2°	CxHyN		*N*-butylbenzylamine	2.59	3.01	3.11
2°	CxHyN		*N*-hexylbenzylamine		3.99	4.18
2°	CxHyN		*N*-octylbenzylamine		4.97	5.24
2°	CxHyN		3-methyl-*N*-methylbenzylamine		2.08	1.98
2°	CxHyN		methamphetamine	2.07	2.22	1.94
2°	CxHyN		*N*-methylphenethylamine	1.91	1.80	1.60
2°	CxHyN		dibenzylamine	2.67	3.24	3.42
2°	CxHyN		dicyclohexylamine		4.37	3.69
2°	CxHyN		dihexylamine		4.74	4.88
2°	CxHyN		*N*-ethylcyclohexylamine		2.59	2.16
2°	CxHyN		*N*-methyloctylamine		3.27	3.29
2°	CxHyN		*N*-methyldodecylamine		5.23	5.41
2°	CxHyN		maprotiline		4.52	4.50
2°	CxHyN		*N*-methylaniline	1.66	1.62	1.60
2°	CxHyN		*N*-ethyl-*M*-toluidine		2.66	2.59
2°	polar	6	sertraline		5.29	4.81
2°	polar	9	fluoxetine	4.05	4.65	4.09
2°	polar	10	duloxetine		4.68	3.73
2°	polar	13	N-benzylaminoacet-aldehydediethylacetal		1.91	3.25
2°	polar	15	MDMA	2.15	2.28	1.81
2°	polar	17	bupropion		3.85	3.47
2°	polar	18	ketamine	2.18	3.12	2.18
2°	polar	19	ethyl 3-(benzylamino)-propanoate		2.06	2.41
2°	polar	24	N-ethanolbenzylamine	0.79	0.56	1.12
2°	polar	29	albuterol		0.64	0.01
2°	polar	31	alprenolol	3.10	2.81	2.88
2°	polar	32	nadolol	0.81	1.17	1.29
2°	polar	33	metoprolol	1.88	2.44	1.79
2°	polar	34	propranolol	3.48	2.60	3.10
2°	polar	42	prilocaine	2.11	1.88	1.74
2°	polar	49	atenolol	0.16	-0.03	0.10
2°	polar	54	pindolol	1.75	1.48	1.97
2°	polar	58	timolol	1.83	1.75	0.68
2°	polar	59	1,3-diphenylguanidine		2.89	2.36
2°	polar	61	sotalol	0.24	0.37	0.32
2°	polar	77	acebutolol	1.71	1.19	1.95

Table S3B. LogK_{OW} values for tertiary amines

Amine type		#	Name	Experimental	EPISuite	ACD/Labs
3°	CxHyN		pyridine	0.65	0.80	0.73
3°	CxHyN		quinoline	2.03	2.14	2.08
3°	CxHyN		acridine	3.40	3.32	3.40
3°	CxHyN		2-methylpyridine	1.11	1.35	1.19
3°	CxHyN		3,4-lutidine		1.90	1.65
3°	CxHyN		2,6-dimethylpyridine	1.68	1.90	1.65
3°	CxHyN		2,4,6-collidine	1.88	2.45	2.11
3°	CxHyN		N,N-dimethylbenzylamine	1.98	1.75	1.98
3°	CxHyN		N,N-diethylbenzylamine		2.73	3.04
3°	CxHyN		N,N-dimethyloctylamine		3.48	3.78
3°	CxHyN		N,N,N-tributylamine		4.46	4.84
3°	CxHyN		N,N,N-trihexylamine		7.41	8.03
3°	CxHyN		N,N-dimethylcyclohexylam.		2.31	2.12
3°	CxHyN		N,N-diethylaniline	3.31	3.15	3.39
3°	CxHyN		imipramine	4.80	5.01	4.80
3°	CxHyN		amitriptyline (HCl)	4.92	4.95	4.92
3°	CxHyN		fenpropidin		6.42	5.87
3°	polar	1	deprenyl	2.90	2.64	2.95
3°	polar	7	diphenhydramine	3.27	3.11	3.66
3°	polar	8	escitalopram		3.74	2.51
3°	polar	12	spiroxamine		5.51	4.88
3°	polar	14	3-dimethylamino-propiophenone		1.37	1.74
3°	polar	16	cocaine	2.30	2.17	3.08
3°	polar	23	methylephedrine	1.70	0.89	1.74
3°	polar	25	2,2'-(benzylimino)-diethanol		0.21	1.47
3°	polar	27	tramadol	2.63	3.01	2.51
3°	polar	30	atropine	1.83	1.91	1.53
3°	polar	35	scopolamine	0.98	0.39	0.76
3°	polar	36	procaine	2.14	1.99	2.36
3°	polar	37	4-amino-2-methylquinoline		1.77	2.09
3°	polar	38	ropivacaine	2.90	2.95	4.39
3°	polar	39	bupivacaine	3.41	3.44	3.64
3°	polar	40	lidocaine	2.44	1.66	3.63
3°	polar	41	S-(-)-1-benzyl-3-acetamidopyrrolidine		1.01	0.88
3°	polar	43	propamocarb	1.12	1.13	1.80
3°	polar	44	benzimidazole	1.32	1.23	1.38
3°	polar	52	thiabendazole	2.47	2.00	2.47
3°	polar	53	(S)-(-)nicotine	1.17	1.00	0.72
3°	polar	55	clonidine	1.59	1.45	1.41
3°	polar	56	clotrimazole	6.26	6.26	5.44
3°	polar	57	sulpiride	0.57	0.65	0.45
3°	polar	62	morphine	0.89	0.72	0.43
3°	polar	63	naloxone	2.09	0.95	1.45
3°	polar	64	strychnine	1.93	1.85	1.74
3°	polar	65	harmine	3.56	2.83	3.17
3°	polar	66	harmaline		4.64	1.02
3°	polar	67	promazine	4.55	3.79	4.63
3°	polar	68	chlorpromazine	5.41	5.20	5.20
3°	polar	69	triflupromazine	5.54	5.52	5.70
3°	polar	70	doxepin	4.36	3.99	3.86
3°	polar	71	(±)-verapamil	3.79	4.80	3.9
3°	polar	11	trimethoprim	0.91	0.73	0.38
3°	polar	60	loperamide		5.15	4.26
3°	polar	73	ketanserin	3.29	3.02	3.21
3°	polar	74	nicardipine	3.82	3.9	5.13
3°	polar	76	lincomycin	0.20	0.29	1.82
3°	polar	78	diltiazem	2.70	2.79	3.63
3°	polar	79	amiodarone	7.57	8.81	8.89
3°	polar	80	ergocornine		2.64	4.51
3°	polar	81	nefopam	3.05	3.05	3.44
3°	polar	82	tiamulin		4.75	5.93
3°	polar	83	clarithromycin	3.16	3.18	3.16
3°	polar	84	erythromycin	3.06	2.48	2.83
3°	polar	85	tylosine	1.63	1.05	3.27

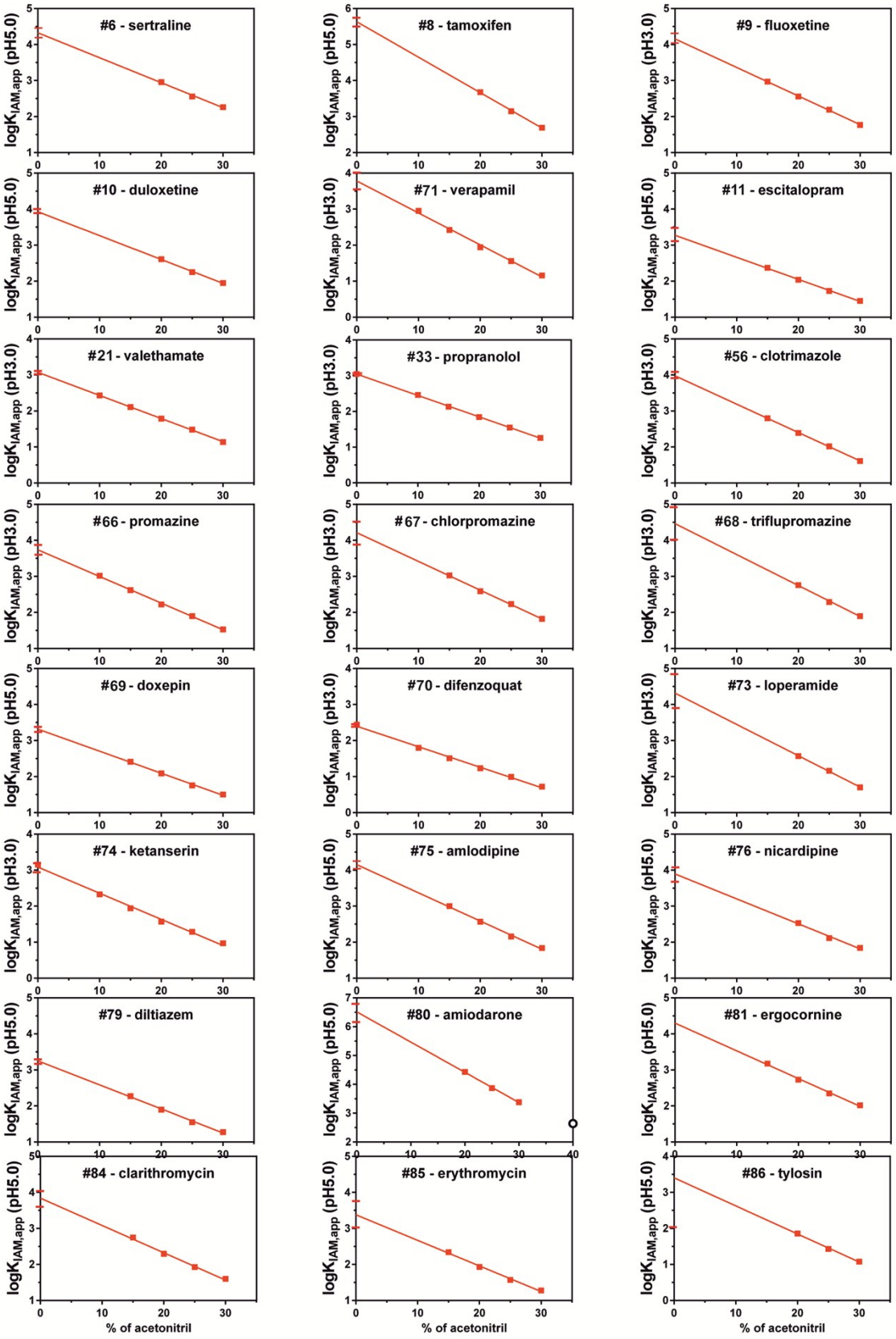


Figure S1. Apparent sorption coefficients to IAM column material at various acetonitrile mixtures with 10mM pH5.0 buffer (UV-HPLC or LC-MS/MS detection). Red bars on the y-axis represent 95% confidence intervals for the extrapolated log$K_{IAM,aq}$ value.

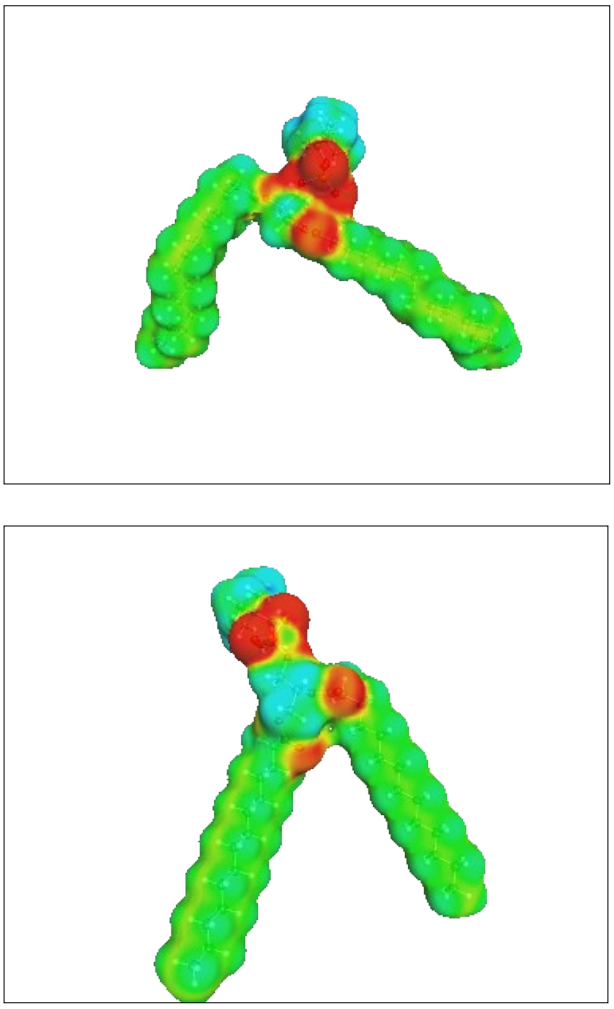


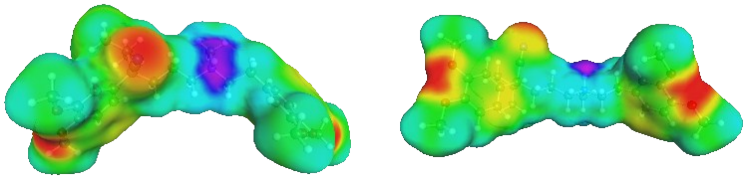
Figure S2. Surface charge density profiles of TZVP molecules

Top: DMPC-long.cosmo used in the COSMOmic example file

Bottom: DMPC-TZVP structure used in the Bittermann et al. 2014 study (1)

Difference between the two DMPC bilayer input systems for acids:

	From Bittermann et al. 2014: TUHH-DMPC (1 Gauss potential) - model M2 (logK L/kg) (no offset used, recommended to be even 0.37 log units lower)	COSMOmic DMPC V15 (logK L/kg)	difference (log units)
dinoseb	2.87	3.69	0.82
pentachlorophenol	3.58	4.38	0.80
2346-tetrachlorophenol	3.36	4.19	0.83
diclofenac	2.94	3.74	0.80



logK_{DMPC-W} = 1.717

Figure S3A. verapamil stretched TZVP conformation, from 2 different angles

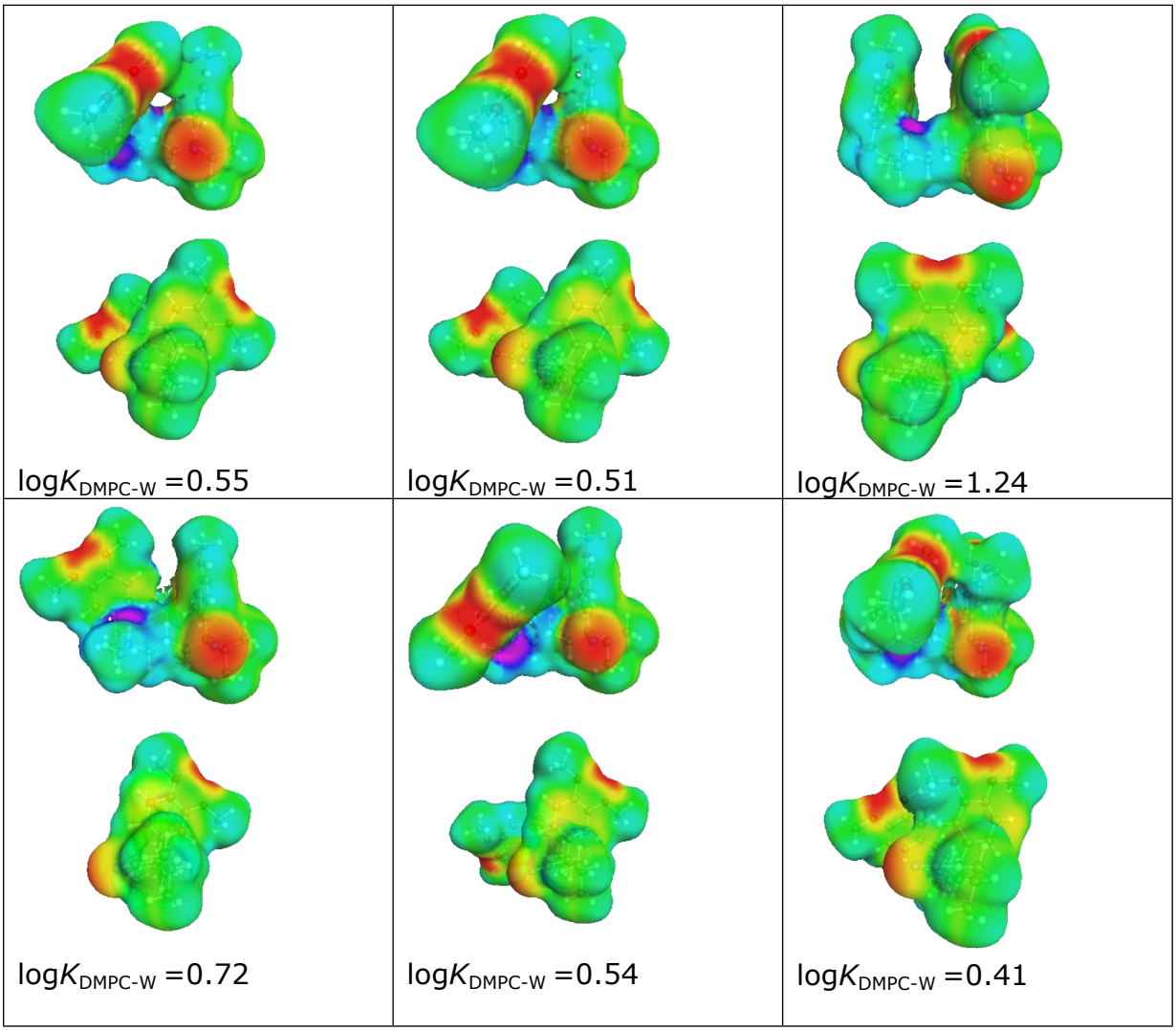


Figure S3B. verapamil 6 optimized TZVP configurations via COSMO*conf*, each from 2 different angles

weighted logK_{DMPC-W} = 0.63