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Supplementary Material

The Utility of Calculated Proton Affinities in Drug Design: A DFT Study

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Content of Supplementary Material

Table S1. Calculated and experimental proton affinity using RB3LYP/6-311+G (2df, p) // RB3LYP/6-31+G (d, p) model chemistry

Name	Energy	ZPE	Cal.PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-193.226784	0.083377		
Protonated Acetone	-193.5493135	0.096149	194.536315	194.07612
p-anisidine	-402.2628273	0.14926		
Protonared p-anisidine	-402.6177831	0.163817	213.7863965	215.180703
Methyl nicotinate	-476.3046815	0.131049		
Protonated Methyl nicotinate	-476.6621687	0.144716	215.9223974	221.227656
1,3-Diazine	-264.4086891	0.07703		
Protonated 1,3-Diazine	-264.7597266	0.09054	211.9717193	211.715058
1H-Imidazole	-226.2949996	0.071146		
Protonated 1H-Imidazole	-226.6675658	0.085242	225.1208624	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.879924	0.082659		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1061.222288	0.091934	209.1342123	217.833714
2-Propenamide	-247.389348	0.0789		
Protonated 2-Propenamide	-247.7325366	0.09244	207.0278817	208.106007
3-Aminopyrazole	-281.6536389	0.087805		
Protonated 3-Aminopyrazole	-282.0251087	0.100464	225.316933	220.247715
Acetamide, N-hydroxy-N-methyl	-323.8057951	0.105542		
Protonated Acetamide, N-hydroxy-N-methyl	-324.1525881	0.118541	209.6225435	209.420562

Aziridine, 2-methyl	-173.3018323	0.09811		
Protonated Aziridine, 2-methyl	-173.6664159	0.112504	219.9282704	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-173.2902393	0.097745		
Protonated Aziridine, 1-methyl	-173.6580199	0.112813	221.5198509	223.426548
1H-Pyrazole	-226.278128	0.071267		
Protonated 1H-Pyrazole	-226.6316513	0.08429	213.8312131	213.698841
Isoxazole	-246.1189148	0.0579		
Protonated Isoxazole	-246.454218	0.071205	202.2241853	202.823886
L-Cysteine	-722.084362	0.10754		
Protonated L-Cysteine	-722.4422123	0.122156	215.5664083	215.873832
N-Methylglycine	-323.8548311	0.107751		
Protonated N-Methylglycerine	-324.2195523	0.122881	219.5618501	220.176012
Oxazole	-246.1551916	0.058555		
Protonated Oxazole	-246.5008437	0.07196	208.6568472	209.468364
Propylen oxide (2-Methyloxirane)	-193.1781927	0.085389		
Protonated Propylen oxide (2-Methyloxirane)	-193.492321	0.097787	189.4944861	191.996733
1H-Imidazole,1-methyl-	-265.6162193	0.098958		
Protonated 1H-Imidazole,1-methyl-	-265.9964041	0.112923	229.982291	229.353996

1H-Imidazole,2-methyl	-265.6293186	0.098581		
Protonated 1H-Imidazole,2-methyl	-266.0106678	0.112567	230.700054	230.262234
1H-Pyrazole, 3-methyl	-265.6107137	0.098689		
Protonated 1H-Pyrazole, 3-methyl	-265.972662	0.111551	219.2171387	216.54306
1-methyl-5-aminopyrazole	-320.9773189	0.115581		
Protonated 1-methyl-5-aminopyrazole	-321.3538303	0.128007	228.6239844	226.939995
1-methylcyclopropene	-155.9971711	0.08422		
Protonated 1-methylcyclopropene	-156.3328205	0.096036	203.3575076	204.59256
1-methylpyrazol-3-amine	-320.9645423	0.115609		
Protonated 1-methylpyrazol-3-amine	-321.3337484	0.130439	222.5607354	224.047974
2-butenamide	-286.7225783	0.106885		
Protonated 2-butenamide	-287.0729802	0.12026	211.6558912	212.025771
Asparagine	-492.6341792	0.13546		
Protonated Asparagine	-493.0048559	0.149596	223.9105995	222.04029
Butyrolactone	-306.5849454	0.098417		
Protonated Butyrolactone	-306.9275356	0.111317	207.0461125	200.7684
cyclobutanone	-231.308162	0.090568		
Protonated cyclobutanone	-231.6138662	0.103149	184.0956563	191.805525
cyclobutene	-156.0244484	0.086367		

Protonated cyclobutene	-156.3191501	0.093694	180.4237109	187.479444
cyclopropanecarboxylic	-306.5847318	0.096909		
Protonated cyclopropanecarboxylic	-306.9092821	0.109366	195.9982162	196.322814
Cytosine	-395.0752371	0.098193		
Protonated Cytosine	-395.4513658	0.112433	227.2677818	227.035599
Furan, 2,3-dihydro-	-231.3028141	0.09257		
Protonated Furan, 2,3-dihydro-	-231.6444875	0.105419	206.5021928	207.197769
Methacrylamide	-286.7186776	0.107138		
Protonated Methacrylamide	-287.0648617	0.120672	208.9112902	210.424404
Pyrrolidine	-212.6545199	0.129452		
Protonated Pyrrolidine	-213.0283363	0.144821	225.1221963	226.653183
1,2-Diamethylimidazole	-304.9493514	0.126462		
Protonated 1,2-Diamethylimidazole	-305.3374081	0.140412	234.9312742	235.353147
1,5-dimethylimidazole	-304.9476232	0.126731		
Protonated 1,5-dimethylimidazole	-305.3342948	0.140657	234.0768875	233.656176
2-Aminopyridine	-303.7545327	0.105453		
Protonated 2-Aminopyridine	-304.1303099	0.119	227.4736163	226.390272
2-bromo-pyridine	-2821.907939	0.078881		
Protonated 2-bromo-pyridine	-2822.266507	0.092843	216.4193801	216.256248

2-chloro-pyridine	-707.9946675	0.079088		
Protonated 2-chloro-pyridine	-708.3518263	0.092908	215.6221732	215.324109
2-fluoro-pyridine	-347.6467313	0.080693		
Protonated 2-fluoro-pyridine	-347.9902411	0.094269	207.2072765	211.428246
3-bromo-pyridine	-2821.90488	0.079066		
Protonated 3-bromo-pyridine	-2822.264938	0.09303	217.3529422	217.4991
3-fluoro-pyridine	-347.636329	0.080506		
Protonated 3-fluoro-pyridine	-347.9939551	0.094526	215.792429	215.58702
4-aminopyridine	-303.7487018	0.10537		
Protonated 4-aminopyridine	-304.1385172	0.119867	235.6983865	234.158097
4-Bromo-pyridine	-2821.90572	0.079068		
Protonated 4-Bromo-pyridine	-2822.269617	0.093049	219.751749	219.363378
4-fluoro-pyridine	-347.6393863	0.080612		
Protonated 4-fluoro-pyridine	-348.0012646	0.09467	218.4373535	218.240031
Acetamide,N-ethyl	-287.9458655	0.130524		
Protonated Acetamide,N-ethyl	-288.2997852	0.144056	213.7667789	214.63098
Cyclobutane carboxylic acid	-345.9001578	0.125497		
Protonated Cyclobutane carboxylic	-346.2261633	0.138594	196.517693	195.366774

Morpholine	-287.8940871	0.134964		
Protonated Morpholine	-288.2597954	0.15023	220.0975662	220.916943
Piperazine	-268.0228145	0.147848		
Protonated Piperazine	-268.3964007	0.162944	225.1457624	225.553737
Purine	-412.0734785	0.094907		
Protonated Purine	-412.4368426	0.108408	219.7123953	219.913101
Threonine	-438.4451965	0.141703		
Protonated Threonine	-438.8062728	0.155325	218.2022883	220.486725
(E)-Dimethylamino acrylonitirle	-304.9191653	0.124704		
Protonated (E)-Dimethylamino acrylonitrile	-305.2775756	0.1366	217.5912371	214.344168
1-hexyne	-234.676218	0.141414		
Protonated 1-hexyne	-234.9866667	0.150889	188.9837245	191.160198
1-Methylcyclopentene	-234.7222738	0.144091		
Protonated 1-Methylcyclopentane	-235.0491031	0.153729	199.1626538	195.151665
2-hexyne	-234.6861644	0.141442		
Protonated 2-hexyne	-234.9967076	0.15156	188.6475069	192.665961
2-propenamide N,N-dimethyl	-326.0212347	0.135312		
Protonated 2-propenamide	-326.381523	0.148912	217.7213776	216.136743
3-pyridinecarbonitrile	-340.6343915	0.087228		

Protonated 3-pyridinecarbonitrile	-340.9807229	0.101012	208.8498847	209.61177
4-pyridinecarbonitrile	-340.6331026	0.087225		
Protonated 4-pyridinecarbonitrile	-340.9820442	0.101017	210.4829773	210.472206
cyclohexanone	-309.9852038	0.150473		
Protonated cyclohexanone	-310.3215961	0.162917	203.4373607	201.00741
Cyclohexene oxide	-309.9490651	0.151397		
Protonated Cyclohexene oxide	-310.2788106	0.1635	199.4761161	202.704381
Isoquinoline	-402.0522091	0.13563		
Protonated Isoquinoline	-402.4312247	0.149694	229.1877207	227.465817
L-proline	-401.3013178	0.145078		
Protonated L-proline	-401.6639863	0.159366	218.7917277	220.008705
nicotinamide	-417.1070043	0.115532		
Protonated nicotinamide	-417.4740535	0.128788	222.1756226	219.482883
N-Methylpyrrolidine	-251.9703898	0.157047		
Protonated N-Methylpyrrolidine	-252.3531242	0.172949	230.3905116	230.788056
p-benzoquinone	-381.5822631	0.08493		
Protonated p-benzoquinone	-381.8995508	0.097507	191.3669775	190.992891
1-methylbenzotriazole	-435.3195006	0.133674		
Protonated 1-methylbenzotriazole	-435.6893411	0.147814	223.3833624	222.566112

2,2-dimethyltetrahydrofuran	-311.1900306	0.172039		
Protonated 2,2-dimethyltetrahydrofuran	-311.5266493	0.184637	203.4846472	202.608777
3-aminobenzoic acid	-476.349743	0.132059		
Protonated 3-aminobenzoic acid	-476.6889855	0.14624	204.1573123	206.671947
Acetylpyrrolidine	-365.3767084	0.167055		
Protonated Acetylpyrrolidine	-365.7380049	0.180419	218.4992519	221.179854
benzimidazole	-379.9889916	0.11821		
Protonated benzimidazole	-380.3657412	0.132251	227.7798604	227.967738
benzoxazole	-399.8516418	0.105754		
Protonated benzoxazole	-400.2048062	0.119065	213.4287714	213.101316
Cinnoline	-418.060543	0.122899		
Protonated Cinniloine	-418.4344812	0.13721	225.8495332	223.785063
Hexahydroazepine	-291.2987342	0.187559		
Protonated Hexahydroazepine	-291.6772313	0.203226	227.876098	228.660867
Quinoxaline	-418.0933667	0.123494		
Protonated Quinoxaline	-418.4535049	0.137051	217.653667	216.017238
Triglycine	-700.714787	0.190551		
Protonated Triglycine	-701.0866161	0.205037	224.4183322	231.074868

2,3-Cyclopentenopyridine	-365.1381013	0.152536		
Protonated 2,3-Cyclopentenopyridine	-365.5177662	0.166643	229.5687116	228.852075
2,3-Dihydroindole	-365.1362018	0.152981		
Protonated 2,3-Dihydroindole	-365.4985954	0.16794	218.2064137	228.756471
Benzoic acid, 2-methyl	-460.2853237	0.142824		
Protonated Benzoic acid, 2-methyl	-460.6294331	0.155462	208.1606143	200.481588
Benzoic acid, 3-methyl	-460.2901813	0.142344		
Protonated Benzioc acid, 3-methyl	-460.6316399	0.155037	206.463347	198.330498
o-Xylene	-310.9815756	0.155672		
Protonated o-Xylene	-311.2973588	0.165612	192.0452106	190.25196
P-Xylene	-310.9820623	0.154995		
Protonated P-Xylene	-311.2989681	0.165349	192.4949983	189.869544
2,2,6,6-Tetramethyl-piperidine	-409.2910655	0.269577		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.679705	0.284906	234.4485974	235.90287
cyclooctanone	-388.6300017	0.208476		
Protonated cyclooctanoone	-388.9666859	0.221376	203.3399617	203.015094
Cytidine	-891.4631644	0.237264		
Protonated Cytidine	-891.8447968	0.2511	230.9700787	234.827325
Deoxycytidine	-816.2170986	0.232682		

Protonated Deoxycytidine	-816.5980977	0.246548	230.5541479	236.237484
N,3,5-Trimethylpiperidine	-369.9632026	0.241771		
Protonated N,3,5-Trimethylpiperidine	-370.3471174	0.257718	231.1035766	233.775681
Naphthalene	-386.0107373	0.14736		
Protonated Naphthalene	-386.3287251	0.157888	193.066899	191.901129
1,8-Diaminonaphthalene	-496.7638424	0.181694		
Protonated 1,8-Diaminonaphthalene	-497.1321099	0.194636	223.1332981	225.744945
1-methyl-3-phenylpyrazole	-496.7305816	0.179693		
Protonated 1-methyl-3-phenylpyrazole	-497.1019719	0.19288	224.9422107	222.900726
Acridine	-555.7369344	0.182009		
Protonated Acridine	-556.1262906	0.195968	235.7411979	232.461126
Anthracene	-539.6915191	0.193912		
Protonated Anthracene	-540.0414302	0.205817	212.2522738	209.683473
Coronene	-922.1495897	0.279903		
Protonated Coronene	-922.4960557	0.291253	210.4318894	205.859313
Phenazine	-571.7785618	0.170011		
Protonated Phenazine	-572.1520167	0.183449	226.083372	224.286984
Picene	-847.0732358	0.287868		
Protonated Picene	-847.414436	0.298946	207.2947674	203.469213

Piperidine, 1-phenyl	-483.1024779	0.239478		
Protonated Piperidine, 1-phenyl	-483.4762436	0.254555	225.2700508	227.752629
Pyrene	-615.9524869	0.2069		
Protonated Pyrene	-616.2829243	0.217823	200.6362639	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.6356534	0.172827		
Protonated 2,3-Dimethylimodazole	-459.030692	0.186644	239.3944379	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.637477	0.172973		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-459.0317117	0.186672	238.3226652	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.6341424	0.172538		
Protonated 2,7-Dimethylimidazole	-459.0295218	0.186281	239.6538083	239.129505
2-Methylbiphenyl	-502.7736779	0.208798		
Protonated 2-Methylbiphenyl	-503.0976211	0.22016	196.2909296	195.008259
3-Methylbiphenyl	-502.7776973	0.208558		
Protonated 3-Methylbiphenyl	-503.1054046	0.219747	193.8751066	197.90028
Benzoquinuclidine	-481.883697	0.218152		
Protonated Benzoquinuclidine	-482.2683437	0.233341	232.029183	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.4910957	0.278158		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.8699453	0.294295	227.8081721	232.293819

N,N- diethylnicotinamide	-574.4167797	0.228705		
Protonated N,N- diethylnicotinamide	-574.7792163	0.242055	219.223319	224.884509
3-hexen-2-one	-309.9772575	0.145935		
Protonated 3-hexen-2-one	-310.322671	0.15865	208.9316197	206.887056
3-chloro-pyridine-1-oxide	-783.1826399	0.083157		
Protonated 3-chloro-pyridine	-783.5340648	0.095024	213.2255467	215.634822
Niacinamide	-417.1318655	0.115531		
Protonated Niacinamide	-417.4934623	0.129457	218.3419025	219.482883
1-methyl-3,5-dinitropyrazole	-674.7358051	0.103925		
Protonated 1-methyl-3,5-dinitropyrazole	-675.0453838	0.115946	186.8714762	188.531088
Piperidine	-251.9873113	0.158748		
Protonated Piperidine	-252.3643608	0.174378	226.9904201	228.01554

Table S2. Calculated and experimental proton affinity using RB3PW91/6-311+G (2df, p) // RB3PW91/6-31+G (d, p) model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-193.1483495	0.083769		
Protonated Acetone	-193.4740127	0.096426	196.57359	194.07612
p-anisidine	-402.1018684	0.149816		
Protonared p-anisidine	-402.4590856	0.164449	215.1586969	215.180703
Methyl nicotinate	-476.11068	0.131524		
Protonated Methyl nicotinate	-476.4458648	0.144525	202.3369204	221.227656
1,3-Diazine	-264.2996628	0.077284		
Protonated 1,3-Diazine	-264.6526302	0.090873	213.1341591	211.715058
1H-Imidazole	-226.2058523	0.071551		
Protonated 1H-Imidazole	-226.5805716	0.08569	226.4455002	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.673156	0.083096		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1061.017197	0.092446	210.1405736	217.833714
2-Propenamide	-247.286932	0.079203		
Protonated 2-Propenamide	-247.6328088	0.092908	208.6132985	208.106007
3-Aminopyrazole	-281.5448557	0.088386		
Protonated 3-Aminopyrazole	-281.9183242	0.100987	226.606792	220.247715
Acetamide, N-hydroxy-N-methyl	-323.6772523	0.106014		
Protonated Acetamide, N-hydroxy-N-methyl	-324.0272315	0.119038	211.6065439	209.420562

Aziridine, 2-methyl	-173.2371097	0.098535		
Protonated Aziridine, 2-methyl	-173.6035374	0.113015	221.032568	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-173.2248164	0.098112		
Protonated Aziridine, 1-methyl	-173.5941356	0.113278	222.4249899	223.426548
1H-Pyrazole	-226.1895192	0.0717		
Protonated 1H-Pyrazole	-226.545061	0.08477	215.0689346	213.698841
Isoxazole	-246.0201821	0.058272		
Protonated Isoxazole	-246.3582278	0.071646	203.9027276	202.823886
L-Cysteine	-721.9070621	0.108154		
Protonated L-Cysteine	-722.2687223	0.122694	218.0039483	215.873832
N-Methylglycine	-323.7253298	0.108338		
Protonated N-Methylglycine	-324.0942354	0.123423	222.2153631	220.176012
Oxazole	-246.0564639	0.058894		
Protonated Oxazole	-246.4044079	0.072371	210.0507585	209.468364
Propylen oxide (2-Methyloxirane)	-193.1041109	0.085745		
Protonated Propylen oxide (2-Methyloxirane)	-193.4186596	0.098353	189.6291564	191.996733
1H-Imidazole,1-methyl-	-265.5117565	0.099368		
Protonated 1H-Imidazole,1-methyl-	-265.8938506	0.113382	231.1502956	229.353996

1H-Imidazole,2-methyl	-265.5257935	0.09905		
Protonated 1H-Imidazole,2-methyl	-265.9094145	0.113156	232.0518335	230.262234
1H-Pyrazole, 3-methyl	-265.5077039	0.099197		
Protonated 1H-Pyrazole, 3-methyl	-265.8717569	0.112088	220.5199618	216.54306
1-methyl-5-aminopyrazole	-320.8532256	0.116169		
Protonated 1-methyl-5-aminopyrazole	-321.2315804	0.128498	229.8403912	226.939995
1-methylcyclopropene	-155.9360425	0.084546		
Protonated 1-methylcyclopropene	-156.2770958	0.096054	206.9380552	204.59256
1-methylpyrazol-3-amine	-320.8573731	0.116193		
Protonated 1-methylpyrazol-3-amine	-321.2122303	0.131065	213.5307376	224.047974
2-butenamide	-286.6059334	0.107262		
Protonated 2-butenamide	-286.9590069	0.120695	213.2966841	212.025771
Asparagine	-492.439758	0.13597		
Protonated Asparagine	-492.8178907	0.150313	228.4620108	222.04029
Butyrolactone	-306.4817781	0.098844		
Protonated Butyrolactone	-306.8110318	0.111841	198.6175324	200.7684
cyclobutanone	-231.2185852	0.091036		
Protonated cyclobutanone	-231.5389026	0.103636	193.2540333	191.805525
cyclobutene	-155.9642978	0.086668		

Protonated cyclobutene	-156.2606039	0.094451	181.1499592	187.479444
cyclopropanecarboxylic acid	-306.465926	0.097369		
Protonated cyclopropanecarboxylic acid	-306.7645491	0.104633	182.923224	196.322814
Cytosine	-394.9182926	0.098646		
Protonated Cytosine	-395.2967961	0.113032	228.6682265	227.035599
Furan, 2,3-dihydro-	-231.2120716	0.093143		
Protonated Furan, 2,3-dihydro-	-231.5207966	0.105731	185.9869256	207.197769
Methacrylamide	-286.6021736	0.107469		
Protonated Methacrylamide	-286.9464189	0.120906	207.7543175	210.424404
Pyrrolidine	-212.5760269	0.129947		
Protonated Pyrrolidine	-212.9528503	0.145283	227.0294711	226.653183
1,2-Dimethylimidazole	-304.8305599	0.126944		
Protonated 1,2-Dimethylimidazole	-305.2206184	0.140967	236.1425674	235.353147
1,5-dimethylimidazole	-304.8288932	0.127197		
Protonated 1,5-dimethylimidazole	-305.2175183	0.141155	235.2830497	233.656176
2-Aminopyridine	-303.6320646	0.105857		
Protonated 2-Aminopyridine	-304.0098706	0.119493	228.6919142	226.390272
2-bromo-pyridine	-2821.790339	0.079183		
Protonated 2-bromo-pyridine	-2822.150817	0.093186	217.5926704	216.256248

2-chloro-pyridine	-707.8400218	0.079396		
Protonated 2-chloro-pyridine	-708.1992208	0.093267	216.8710522	215.324109
2-fluoro-pyridine	-347.5074049	0.081013		
Protonated 2-fluoro-pyridine	-347.8599068	0.09477	212.7386866	211.428246
3-bromo-pyridine	-2821.78725	0.079344		
Protonated 3-bromo-pyridine	-2822.149192	0.093379	218.4917679	217.4991
3-fluoro-pyridine	-347.4965326	0.080802		
Protonated 3-fluoro-pyridine	-347.8564162	0.094894	217.1647586	215.58702
4-aminopyridine	-303.6320646	0.105857		
Protonated 4-aminopyridine	-304.0098706	0.119493	228.6919142	234.158097
4-Bromo-pyridine	-2821.788117	0.079352		
Protonated4-Bromo-pyridine	-2822.153977	0.09341	220.9359617	219.363378
4-fluoro-pyridine	-347.499706	0.080912		
Protonated 4-fluoro-pyridine	-347.8638937	0.095044	219.8410437	218.240031
Acetamide,N-ethyl	-287.8321519	0.130943		
Protonated Acetamide,N-ethyl	-288.1887389	0.144571	215.3815069	214.63098
Cyclobutane carboxylic acid	-345.7754705	0.126613		
Protonated Cyclobutane carboxylic acid	-346.1010492	0.139073	196.6417713	195.366774

Morpholine	-287.7840491	0.135446		
Protonated Morpholine	-288.1520785	0.150807	221.49569	220.916943
Piperazine	-267.9224472	0.148391		
Protonated Piperazine	-268.2983661	0.163543	226.5750775	225.553737
Purine	-411.9107951	0.095463		
Protonated Purine	-412.2730014	0.108992	218.9686105	219.913101
Threonine	-438.2664257	0.141743		
Protonated Threonine	-438.6380269	0.155986	224.424915	220.486725
(E)-Dimethylamino acrylonitirle	-304.7916065	0.124995		
Protonated (E)-Dimethylamino acrylonitrile	-305.1526678	0.136968	219.2074301	214.344168
1-hexyne	-234.5795769	0.141767		
Protonated 1-hexyne	-234.8920999	0.15124	190.286625	191.160198
1-Methylcyclopentene	-234.6337588	0.144699		
Protonated 1-Methylcyclopentene	-234.9625139	0.154105	200.5138992	195.151665
2-hexyne	-234.5902526	0.141774		
Protonated 2-hexyne	-234.9009138	0.151648	188.8716037	192.665961
2-propenamide N,N-dimethyl	-325.8888807	0.135666		
Protonated 2-propenamide N,N-dimethyl	-326.2477315	0.149154	216.8882106	216.136743
3-pyridinecarbonitrile	-340.489484	0.087517		

Protonated 3-pyridinecarbonitrile	-340.8081671	0.097918	193.5813467	209.61177
4-pyridinecarbonitrile	-340.4881114	0.087513		
Protonated 4-pyridinecarbonitrile	-340.8004955	0.097978	189.5892036	210.472206
cyclohexanone	-309.8693793	0.150936		
Protonated cyclohexanone	-310.206212	0.163422	203.6878176	201.00741
Cyclohexene oxide	-309.8371381	0.151987		
Protonated Cyclohexene oxide	-310.1648529	0.164274	198.0886284	202.704381
Isoquinoline	-401.8882972	0.136022		
Protonated Isoquinoline	-402.2690473	0.150207	230.2016691	227.465817
L-proline	-401.142225	0.145218		
Protonated L-proline	-401.5123952	0.160065	223.1552876	220.008705
nicotinamide	-416.962329	0.115976		
Protonated nicotinamide	-417.3071394	0.129338	208.1550955	219.482883
N-Methylpyrrolidine	-251.8768106	0.15755		
Protonated N-Methylpyrrolidine	-252.2611845	0.173513	231.3817852	230.788056
p-benzoquinone	-381.4232708	0.085163		
Protonated p-benzoquinone	-381.7425433	0.097846	192.5472334	190.992891
1-methylbenzotriazole	-435.1484837	0.134305		
Protonated 1-methylbenzotriazole	-435.5206335	0.148485	224.8078778	222.566112

2,2-dimethyltetrahydrofuran	-311.0724308	0.172535		
Protonated 2,2-dimethyltetrahydrofuran	-311.4099102	0.185309	203.9164559	202.608777
3-aminobenzoic acid	-476.1584443	0.132634		
Protonated 3-aminobenzoic acid	-476.4998594	0.146849	205.4996804	206.671947
Acetylpyrrolidine	-365.2371055	0.167586		
Protonated Acetylpyrrolidine	-365.6042001	0.181116	222.035547	221.179854
benzimidazole	-379.8389598	0.118769		
Protonated benzimidazole	-380.2176257	0.132836	228.9664216	227.967738
benzoxazole	-399.692049	0.106235		
Protonated benzoxazole	-400.0472606	0.119608	214.6752624	213.101316
Cinnoline	-417.8904735	0.123332		
Protonated Cinniloine	-418.2664708	0.137715	227.0973765	223.785063
Hexahydroazepine	-291.1908065	0.188054		
Protonated Hexahydroazepine	-291.57163	0.203754	229.3157146	228.660867
Quinoxaline	-417.9228471	0.123957		
Protonated Quinoxaline	-418.284788	0.137581	218.743655	216.017238
Triglycine	-700.7147882	0.190551		
Protonated Triglycine	-701.0866158	0.205037	224.4174518	231.074868

2,3-Cyclopentenopyridine	-364.9962463	0.153056		
Protonated 2,3-Cyclopentenopyridine	-365.3779323	0.16722	230.8018754	228.852075
2,3-Dihydroindole	-364.9945678	0.153532		
Protonated 2,3-Dihydroindole	-365.3583804	0.16858	219.0420878	228.756471
Benzoic acid, 2-methyl	-460.1090461	0.143861		
Protonated Benzoic acid, 2-methyl	-460.4439184	0.156094	202.6133164	200.481588
Benzoic acid, 3-methyl	-460.1048418	0.14281		
Protonated Benzioc acid, 3-methyl	-460.4214968	0.150883	193.7409272	198.330498
o-Xylene	-310.8570611	0.15602		
Protonated o-Xylene	-311.1761145	0.165877	194.1483522	190.25196
P-Xylene	-310.8574826	0.155271		
Protonated P-Xylene	-311.1753896	0.165611	193.1318281	189.869544
2,2,6,6-Tetramethyl-piperidine	-409.1396314	0.270128		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.5306778	0.285523	235.9183788	235.90287
cyclooctanone	-388.4815285	0.209023		
Protonated cyclooctanone	-388.8211239	0.222013	205.1113857	203.015094
Cytidine	-891.1156727	0.238352		
Protonated Cytidine	-891.5001636	0.252401	232.6327381	234.827325
Deoxycytidine	-815.8991135	0.233561		

Protonated Deoxycytidine	-816.2828469	0.247603	232.1617322	236.237484
N,3,5-Trimethylpiperidine	-369.825481	0.242282		
Protonated N,3,5-Trimethylpiperidine	-370.2113881	0.258328	232.2929113	233.775681
Naphthalene	-385.8535547	0.147727		
Protonated Naphthalene	-386.1719016	0.158177	193.3402679	191.901129
1,8-Diaminonaphthalene	-496.5670895	0.182302		
Protonated 1,8-Diaminonaphthalene	-496.9384117	0.194991	225.2058706	225.744945
1-methyl-3-phenylpyrazole	-496.5330893	0.180285		
Protonated 1-methyl-3-phenylpyrazole	-496.9060411	0.193574	225.8593418	222.900726
Acridine	-555.5118986	0.18255		
Protonated Acridine	-555.9028267	0.19656	236.6962447	232.461126
Anthracene	-539.4731638	0.194396		
Protonated Anthracene	-539.8037022	0.20522	200.7605693	209.683473
Coronene	-921.7924535	0.279689		
Protonated Coronene	-922.1362642	0.290754	208.9409396	205.859313
Phenazine	-571.5467232	0.170563		
Protonated Phenazine	-571.9218647	0.18407	227.0992832	224.286984
Picene	-846.7333916	0.288462		
Protonated Picene	-847.0661447	0.298976	202.3410813	203.469213

Piperidine, 1-phenyl	-482.9162008	0.240152		
Protonated Piperidine, 1-phenyl	-483.2905353	0.255215	225.635604	227.752629
Pyrene	-615.705828	0.207435		
Protonated Pyrene	-616.036443	0.21828	200.7957372	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.456313	0.173421		
Protonated 2,3-Dimethylimodazole	-458.8531423	0.187305	240.4768988	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.4580566	0.173562		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-458.854161	0.187336	240.0896582	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.4546983	0.17315		
Protonated 2,7-Dimethylimidazo-1,2-a,pyridine	-458.8519097	0.186955	240.7652813	239.129505
2-Methylbiphenyl	-502.570502	0.209348		
Protonated 2-Methylbiphenyl	-502.8948317	0.220507	196.6583513	195.008259
3-Methylbiphenyl	-502.5742705	0.209041		
Protonated 3-Methylbiphenyl	-502.8866775	0.218964	189.9370733	197.90028
Benzoquinuclidine	-481.7017659	0.218823		
Protonated Benzoquinuclidine	-482.0876681	0.234089	232.7696802	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.328157	0.278859		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.7100377	0.294731	229.873228	232.293819

N,N- diethylnicotinamide	-574.1880585	0.229317		
Protonated N,N- diethylnicotinamide	-574.5467541	0.242522	216.9649346	224.884509
3-hexen-2-one	-309.8513746	0.146291		
Protonated 3-hexen-2-one	-310.1953226	0.158813	208.1307038	206.887056
3-chloro-pyridine-1-oxide	-783.0001305	0.083569		
Protonated 3-chloro-pyridine	-783.3541007	0.095842	214.5730148	215.634822
Niacinamide	-416.962329	0.115976		
Protonated Niacinamide	-417.326006	0.129958	219.6128596	219.482883
1-methyl-3,5-dinitropyrazole	-674.4745701	0.104769		
Protonated 1-methyl-3,5-dinitropyrazole	-674.7684589	0.116065	177.4717763	188.531088
Piperidine	-251.894053	0.159257		
Protonated Piperidine	-252.2732761	0.174961	228.308925	228.01554

Table S3. Calculated and experimental proton affinity using RwB97XD/6-311+G (2df, p) // RwB97XD/6-31+G (d, p) model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-193.1574817	0.084714		
Protonated Acetone	-193.4838491	0.097408	196.9926937	194.07612
p-anisidine	-402.1187648	0.150979		
Protonared p-anisidine	-402.4774534	0.165958	215.8691424	215.180703
Methyl nicotinate	-476.1363097	0.132927		
Protonated Methyl nicotinate	-476.4719073	0.146	202.5516663	221.227656
1,3-Diazine	-264.3080779	0.07793		
Protonated 1,3-Diazine	-264.6626054	0.091623	214.049116	211.715058
1H-Imidazole	-226.2130415	0.072207		
Protonated 1H-Imidazole	-226.5895222	0.086463	227.4788569	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.74301	0.084009		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1061.087974	0.093383	210.7048844	217.833714
2-Propenamide	-247.2990083	0.07976		
Protonated 2-Propenamide	-247.6455592	0.093721	208.8787684	208.106007
3-Aminopyrazole	-281.5548756	0.089163		
Protonated 3-Aminopyrazole	-281.9293874	0.101575	227.3777524	220.247715
Acetamide, N-hydroxy-N-methyl	-323.6962497	0.107096		
Protonated Acetamide, N-hydroxy-N-methyl	-324.0469729	0.120466	211.8605439	209.420562

Aziridine, 2-methyl	-173.2420028	0.099388		
Protonated Aziridine, 2-methyl	-173.6107684	0.113828	222.5242501	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-173.2297902	0.098969		
Protonated Aziridine, 1-methyl	-173.6018457	0.114161	224.1261062	223.426548
1H-Pyrazole	-226.1958755	0.072333		
Protonated 1H-Pyrazole	-226.5530072	0.085414	216.059816	213.698841
Isoxazole	-246.0293162	0.058798		
Protonated Isoxazole	-246.3688303	0.072376	204.698625	202.823886
L-Cysteine	-721.9612722	0.109361		
Protonated L-Cysteine	-722.3227489	0.124228	217.6876221	215.873832
N-Methylglycine	-323.7451115	0.109522		
Protonated N-Methylglycine	-324.0639764	0.122466	192.1309007	220.176012
Oxazole	-246.0667842	0.059604		
Protonated Oxazole	-246.4164595	0.07311	211.1192974	209.468364
Propylen oxide (2-Methyloxirane)	-193.1115518	0.086376		
Protonated Propylen oxide (2-Methyloxirane)	-193.4275912	0.099339	190.3461673	191.996733
1H-Imidazole,1-methyl-	-265.5213041	0.100172		
Protonated 1H-Imidazole,1-methyl-	-265.9051371	0.114207	232.2285059	229.353996

1H-Imidazole,2-methyl	-265.5349329	0.099949		
Protonated 1H-Imidazole,2-methyl	-265.9204293	0.114162	233.1628434	230.262234
1H-Pyrazole, 3-methyl	-265.5160021	0.100005		
Protonated 1H-Pyrazole, 3-methyl	-265.8816415	0.113001	221.4509321	216.54306
1-methyl-5-aminopyrazole	-320.8662699	0.117161		
Protonated 1-methyl-5-aminopyrazole	-321.2459746	0.129377	230.7569908	226.939995
1-methylcyclopropene	-155.9367738	0.085068		
Protonated 1-methylcyclopropene	-156.2814075	0.096699	209.1091771	204.59256
1-methylpyrazol-3-amine	-320.8694831	0.117333		
Protonated 1-methylpyrazol-3-amine	-321.2258079	0.132485	214.2793944	224.047974
2-butenamide	-286.6193443	0.10793		
Protonated 2-butenamide	-286.9741387	0.121966	214.0055966	212.025771
Asparagine	-492.476166	0.137661		
Protonated Asparagine	-492.8533179	0.152179	227.7388308	222.04029
Butyrolactone	-306.4994631	0.099799		
Protonated Butyrolactone	-306.8301516	0.112773	199.5320198	200.7684
Cyclobutanone	-231.2298605	0.092168		
Protonated Cyclobutanone	-231.5510398	0.104615	193.8889878	191.805525
cyclobutene	-155.9678435	0.087724		

Protonated cyclobutene	-156.265494	0.095648	181.9068092	187.479444
cyclopropanecarboxylic acid	-306.4827111	0.098317		
Protonated cyclopropanecarboxylic acid	-306.7818999	0.105864	183.1041162	196.322814
Cytosine	-394.9368474	0.099399		
Protonated Cytosine pn ring free	-395.317212	0.114036	229.6816666	227.035599
Furan, 2,3-dihydro-	-231.2215294	0.093907		
Protonated Furan, 2,3-dihydro-	-231.5320708	0.106793	186.943397	207.197769
Methacrylamide	-286.6169445	0.108429		
Protonated Methacrylamide	-286.9617856	0.122073	208.0008749	210.424404
Pyrrolidine	-212.5850412	0.13124		
Protonated Pyrrolidine	-212.9636478	0.146592	228.1386126	226.653183
1,2-Diamethylimidazole	-304.8433126	0.128091		
Protonated 1,2-Diamethylimidazole	-305.2351246	0.142279	237.1414298	235.353147
1,5-dimethylimidazole	-304.8414803	0.128111		
Protonated 1,5-dimethylimidazole	-305.2317242	0.142136	236.2577188	233.656176
2-Aminopyridine	-303.6415882	0.106703		
Protonated 2-Aminopyridine	-304.0209896	0.120521	229.5811187	226.390272
2-bromo-pyridine	-2821.841127	0.079937		
Protonated 2-bromo-pyridine	-2822.20319	0.093988	218.557892	216.256248

2-chloro-pyridine	-707.8833845	0.080117		
Protonated 2-chloro-pyridine	-708.2437129	0.094032	217.55269	215.324109
2-fluoro-pyridine	-347.5244463	0.081717		
Protonated 2-fluoro-pyridine	-347.8786036	0.095532	213.7417338	211.428246
3-bromo-pyridine	-2821.838224	0.080093		
Protonated 3-bromo-pyridine	-2822.201592	0.094223	219.3273883	217.4991
3-fluoro-pyridine	-347.5133804	0.081519		
Protonated 3-fluoro-pyridine	-347.8746516	0.095722	217.967198	215.58702
4-aminopyridine	-303.6415882	0.106703		
Protonated 4-aminopyridine	-304.0209875	0.120521	229.5798041	234.158097
4-Bromo-pyridine	-2821.839209	0.080167		
Protonated4-Bromo-pyridine	-2822.206052	0.094217	221.5576736	219.363378
4-fluoro-pyridine	-347.5168039	0.081685		
Protonated 4-fluoro-pyridine	-347.8825595	0.095847	220.8064837	218.240031
Acetamide,N-ethyl	-287.847457	0.132107		
Protonated Acetamide,N-ethyl	-288.2007051	0.145808	213.2413448	214.63098
Cyclobutane carboxylic acid	-345.7974005	0.128098		
Protonated Cyclobutane carboxylic	-346.1153761	0.14034	192.0047859	195.366774

Morpholine	-287.8005837	0.136743		
Protonated Morpholine	-288.170595	0.152224	222.6655393	220.916943
Piperazine	-267.9368884	0.14989		
Protonated Piperazine	-268.3148495	0.165125	227.8055432	225.553737
Purine	-411.9255404	0.09634		
Protonated Purine	-412.2895666	0.110032	220.0103732	219.913101
Threonine	-438.2992972	0.143335		
Protonated Threonine	-438.6129656	0.154644	189.875866	220.486725
(E)-Dimethylamino acrylonitirle	-304.8044175	0.126191		
Protonated (E)-Dimethylamino acrylonitrile	-305.1634387	0.13781	218.1449863	214.344168
1-hexyne	-234.5889296	0.142648		
Protonated 1-hexyne free	-234.8960094	0.151206	187.4338698	191.160198
1-Methylcyclopentene	-234.6418002	0.145934		
Protonated 1-Methylcyclopentene	-234.9724795	0.155502	201.6216648	195.151665
2-hexyne	-234.5977374	0.143254		
Protonated 2-hexyne pctome	-234.9081204	0.153101	188.7136591	192.665961
2-propenamide N,N-dimethyl	-325.9060716	0.137365		
Protonated 2-propenamide N,N-dimethyl	-326.2695631	0.150966	219.7308143	216.136743
3-pyridinecarbonitrile	-340.5014918	0.0883		

Protonated 3-pyridinecarbonitrile	-340.818968	0.09892	192.6892465	209.61177
4-pyridinecarbonitrile	-340.5001305	0.088354		
Protonated 4-pyridinecarbonitrile	-340.851809	0.102257	212.1321662	210.472206
cyclohexanone	-309.887767	0.152483		
Protonated cyclohexanone	-310.224844	0.165142	203.7347001	201.00741
Cyclohexene oxide	-309.8538724	0.153391		
Protonated Cyclohexene oxide	-310.1827389	0.165726	198.7817909	202.704381
Isoquinoline	-401.8994396	0.137122		
Protonated Isoquinoline	-402.2810054	0.151374	230.672338	227.465817
L-proline	-401.1688015	0.146865		
Protonated L-proline pn	-401.5486177	0.161763	229.1769665	220.008705
nicotinamide	-416.9818507	0.117166		
Protonated nicotinamide	-417.3270618	0.130646	208.3339187	219.482883
N-Methylpyrrolidine	-251.8900712	0.159173		
Protonated N-Methylpyrrolidine	-252.2770901	0.175156	233.0293089	230.788056
p-benzoquinone	-381.4417009	0.086011		
Protonated p-benzoquinone	-381.7611814	0.09881	192.6064391	190.992891
1-methylbenzotriazole	-435.1626462	0.13532		
Protonated 1-methylbenzotriazole	-435.5357597	0.149473	225.4292394	222.566112

2,2-dimethyltetrahydrofuran	-311.0914859	0.173906		
Protonated 2,2-dimethyltetrahydrofuran	-311.4304266	0.186881	204.7098282	202.608777
3-aminobenzoic acid	-476.1822337	0.133725		
Protonated 3-aminobenzoic acid	-476.5257961	0.148349	206.5955371	206.671947
Acetylpyrrolidine	-365.2590442	0.169233		
Protonated Acetylpyrrolidine	-365.6238668	0.182848	220.557558	221.179854
benzimidazole	-379.8505521	0.119724		
Protonated benzimidazole	-380.2308172	0.133909	229.8973146	227.967738
benzoxazole	-399.7066909	0.107193		
Protonated benzoxazole	-400.0631409	0.120668	215.3896705	213.101316
Cinnoline	-417.9020924	0.124411		
Protonated Cinniloine	-418.2785896	0.138795	227.4104175	223.785063
Hexahydroazepine	-291.2089883	0.189866		
Protonated Hexahydroazepine	-291.5916655	0.205641	230.4327819	228.660867
Quinoxaline	-417.9350906	0.125101		
Protonated Quinoxaline	-418.2972933	0.138749	218.8931965	216.017238
Triglycine	-700.4870678	0.193451		
Protonated Triglycine	-700.8615774	0.208052	226.0297295	231.074868

2,3-Cyclopentenopyridine	-365.0097676	0.154257		
Protonated 2,3-Cyclopentenopyridine	-365.3927958	0.168512	231.5881838	228.852075
2,3-Dihydroindole	-365.0070678	0.154868		
Protonated 2,3-Dihydroindole	-365.3734471	0.170081	220.5512589	228.756471
Benzoic acid, 2-methyl	-460.132784	0.145393		
Protonated Benzoic acid, 2-methyl	-460.4630749	0.157782	199.6423913	200.481588
Benzoic acid, 3-methyl	-460.1277785	0.144255		
Protonated Benzioc acid, 3-methyl	-460.4652897	0.157653	203.552555	198.330498
o-Xylene	-310.8674633	0.157046		
Protonated o-Xylene	-311.1867897	0.167348	194.0459201	190.25196
P-Xylene	-310.8667773	0.156759		
Protonated P-Xylene	-311.1850596	0.167104	193.3643019	189.869544
2,2,6,6-Tetramethyl-piperidine	-409.1729201	0.273167		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.566133	0.288853	237.0988995	235.90287
cyclooctanone	-388.5105663	0.211246		
Protonated cyclooctanoone	-388.8504433	0.224374	205.2032031	203.015094
Cytidine	-891.1812207	0.241061		
Protonated Cytidine	-891.5663531	0.255373	232.8735233	234.827325
Deoxycytidine	-815.9566736	0.236465		

Protonated Deoxycytidine	-816.3410306	0.250488	232.5647716	236.237484
N,3,5-Trimethylpiperidine	-369.8501777	0.244142		
Protonated N,3,5-Trimethylpiperidine	-370.2388247	0.260364	233.9039237	233.775681
Naphthalene	-385.8630326	0.148901		
Protonated Naphthalene	-386.181491	0.159277	193.4557045	191.901129
1,8-Diaminonaphthalene	-496.5846485	0.184311		
Protonated 1,8-Diaminonaphthalene	-496.9567405	0.197361	225.4667928	225.744945
1-methyl-3-phenylpyrazole	-496.5512097	0.182011		
Protonated 1-methyl-3-phenylpyrazole	-496.9256357	0.195382	226.7339609	222.900726
Acridine	-555.5270455	0.184092		
Protonated Acridine	-555.9194396	0.198063	237.6401738	232.461126
Anthracene	-539.4869085	0.195923		
Protonated Anthracene	-539.8167021	0.206689	200.3288634	209.683473
Coronene	-921.8217037	0.281485		
Protonated Coronene	-922.1639702	0.293338	207.4871151	205.859313
Phenazine	-571.5628364	0.172057		
Protonated Phenazine	-571.938205	0.185581	227.2313218	224.286984
Picene	-846.7616115	0.291377		
Protonated Picene	-847.0927942	0.301714	201.4645219	203.469213

Piperidine, 1-phenyl	-482.9419644	0.242591		
Protonated Piperidine, 1-phenyl	-483.3202092	0.257971	227.8943745	227.752629
Pyrene	-615.7228098	0.209444		
Protonated Pyrene	-616.0541583	0.220258	201.2750541	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.4725661	0.174802		
Protonated 2,3-Dimethylimodazole	-458.8719474	0.188673	242.0862964	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.474401	0.175205		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-458.8728937	0.188981	241.5871639	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.4702449	0.174482		
Protonated 2,7-Dimethylimidazole	-458.8698458	0.188295	242.2597796	239.129505
2-Methylbiphenyl	-502.5900358	0.211195		
Protonated 2-Methylbiphenyl	-502.9124457	0.222575	195.3176711	195.008259
3-Methylbiphenyl	-502.591956	0.211339		
Protonated 3-Methylbiphenyl	-502.9038497	0.220861	189.8616764	197.90028
Benzoquinuclidine	-481.7263382	0.220788		
Protonated Benzoquinuclidine	-482.1148108	0.236192	234.2977596	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.3577795	0.28197		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.7406557	0.298137	230.3164779	232.293819

N,N- diethylnicotinamide	-574.2217474	0.231459		
Protonated N,N- diethylnicotinamide	-574.5871465	0.245196	220.8442115	224.884509
3-hexen-2-one	-309.8659001	0.147369		
Protonated 3-hexen-2-one	-310.2132022	0.160708	209.732782	206.887056
3-chloro-pyridine-1-oxide	-783.0457689	0.084372		
Protonated 3-chloro-pyridine	-783.404386	0.096901	217.3315456	215.634822
Niacinamide	-416.9818507	0.117166		
Protonated Niacinamide	-417.3466965	0.13123	220.2958476	219.482883
1-methyl-3,5-dinitropyrazole	-674.5070422	0.105905		
Protonated 1-methyl-3,5-dinitropyrazole	-674.7983564	0.117808	175.4827182	188.531088
Piperidine	-251.907456	0.160584		
Protonated Piperidine	-252.2886599	0.17646	229.4461151	228.01554

Table S4. Calculated and experimental proton affinity using RPBEPBE/6-311+G (2df, p) // RPBEPBE/6-31+G (d, p) model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-192.9765578	0.081313		
Protonated Acetone	-193.2988517	0.093604	194.6844522	194.07612
p-anisidine	-401.756875	0.145295		
Protonared p-anisidine	-402.1102455	0.159393	213.0738903	215.180703
Methyl nicotinate	-475.7389098	0.127217		
Protonated Methyl nicotinate	-476.0702262	0.139847	200.1376687	221.227656
1,3-Diazine	-264.0837211	0.074744		
Protonated 1,3-Diazine	-264.4326074	0.088006	210.7742862	211.715058
1H-Imidazole	-226.021235	0.069183		
Protonated 1H-Imidazole	-226.3909941	0.083048	223.5014462	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.198266	0.08034		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1060.539051	0.089428	208.258372	217.833714
2-Propenamide	-247.0886526	0.076628		
Protonated 2-Propenamide	-247.4300121	0.089958	206.0092762	208.106007
3-Aminopyrazole	-281.3208628	0.085476		
Protonated 3-Aminopyrazole	-281.6895208	0.098086	223.5826172	220.247715
Acetamide, N-hydroxy-N-methyl	-323.4270493	0.102439		
Protonated Acetamide, N-hydroxy-N-methyl	-323.7727761	0.115265	209.0599192	209.420562

Aziridine, 2-methyl	-173.0661419	0.095557		
Protonated Aziridine, 2-methyl	-173.4273591	0.109777	217.9227973	223.426548
Aziridine, 1-methyl (N-Methyl aziridine)	-173.0541749	0.095179		
Protonated Aziridine, 1-methyl (N-Methyl aziridine)	-173.4178086	0.110012	219.0621239	223.426548
1H-Pyrazole	-226.0063194	0.069318		
Protonated 1H-Pyrazole	-226.3570632	0.082077	212.2493987	213.698841
Isoxazole	-245.839188	0.056184		
Protonated Isoxazole	-246.1723238	0.069197	201.0437634	202.823886
L-Cysteine	-721.522929	0.104544		
Protonated L-Cysteine	-721.8420414	0.115661	193.410261	215.873832
N-Methylglycine	-323.4724192	0.104868		
Protonated N-Methylglycine	-323.8263453	0.118962	213.4250018	220.176012
Oxazole	-245.8719499	0.056807		
Protonated Oxazole	-246.201983	0.069989	198.9927955	209.468364
Propylen oxide (2-Methyloxirane)	-192.9331511	0.083111		
Protonated Propylen oxide (2-Methyloxirane)	-193.2443118	0.095216	187.8125656	191.996733
1H-Imidazole,1-methyl-	-265.2837959	0.096242		
Protonated 1H-Imidazole,1-methyl-	-265.6609104	0.109966	228.203888	229.353996

1H-Imidazole,2-methyl	-265.2975961	0.095919		
Protonated 1H-Imidazole,2-methyl	-265.6762172	0.109793	229.0570307	230.262234
1H-Pyrazole, 3-methyl	-265.2810505	0.069318		
Protonated 1H-Pyrazole, 3-methyl	-265.6402915	0.108641	201.2388445	216.54306
1-methyl-5-aminopyrazole	-320.5862052	0.11252		
Protonated 1-methyl-5-aminopyrazole	-320.9596029	0.124904	226.6958665	226.939995
			0	0
1-methylcyclopropene	-155.7761986	0.082073	0	0
Protonated 1-methylcyclopropene	-156.1120642	0.093252	203.8850754	204.59256
1-methylpyrazol-3-amine	-320.5902564	0.112562		
Protonated 1-methylpyrazol-3-amine	-320.9412871	0.126989	211.4032835	224.047974
2-butenamide	-286.3643947	0.10386		
Protonated 2-butenamide	-286.7150769	0.116932	212.0181522	212.025771
Asparagine	-492.07598	0.131338		
Protonated Asparagine	-492.4519184	0.145175	227.3963245	222.04029
Butyrolactone	-306.2384429	0.095702		
Protonated Butyrolactone	-306.563225	0.108343	196.0304711	200.7684
cyclobutanone	-231.0173407	0.088215		
Protonated cyclobutanone	-231.3341777	0.100483	191.2742567	191.805525
cyclobutene	-155.8037664	0.08412		

Protonated cyclobutene	-156.0978547	0.091192	180.1956955	187.479444
cyclopropanecarboxylic acid	-306.2235264	0.094292		
Protonated cyclopropanecarboxylic acid	-306.5203687	0.101645	181.7509885	196.322814
Cytosine	-394.6230098	0.095494		
Protonated Cytosine	-394.996818	0.109372	226.0343921	227.035599
Furan, 2,3-dihydro-	-231.0099723	0.090244		
Protonated Furan, 2,3-dihydro-	-231.3144358	0.102416	183.5686899	207.197769
Methacrylamide	-286.360899	0.104203		
Protonated Methacrylamide	-286.7055918	0.1174	208.1828112	210.424404
Pyrrolidine	-212.3602018	0.126182		
Protonated Pyrrolidine	-212.7322324	0.141065	224.300573	226.653183
1,2-Diamethylimidazole	-304.5592906	0.123138		
Protonated 1,2-Diamethylimidazole	-304.9443744	0.136811	233.2361259	235.353147
1,5-dimethylimidazole	-304.5577686	0.123335		
Protonated 1,5-dimethylimidazole	-304.9416205	0.136979	232.4809634	233.656176
2-Aminopyridine	-303.3735362	0.102687		
Protonated 2-Aminopyridine	-303.7469416	0.115935	226.1691378	226.390272
2-bromo-pyridine	-2821.186485	0.076696		
Protonated 2-bromo-pyridine	-2821.543287	0.090371	215.4876403	216.256248

2-chloro-pyridine	-707.4824419	0.076914		
Protonated 2-chloro-pyridine	-707.8379103	0.090466	214.7263504	215.324109
2-fluoro-pyridine	-347.2426968	0.078439		
Protonated 2-fluoro-pyridine	-347.5912847	0.091902	210.4633927	211.428246
3-bromo-pyridine	-2821.183264	0.076773		
Protonated 3-bromo-pyridine	-2821.541654	0.090499	216.4531246	217.4991
3-fluoro-pyridine	-347.2322176	0.078209		
Protonated 3-fluoro-pyridine	-347.5884715	0.092009	215.0666943	215.58702
4-aminopyridine	-303.3735363	0.102687		
Protonated 4-aminopyridine	-303.7469416	0.115935	226.1691321	234.158097
4-Bromo-pyridine	-2821.183966	0.076828		
Protonated4-Bromo-pyridine	-2821.546583	0.0906	219.0765201	219.363378
4-fluoro-pyridine	-347.2350727	0.078327		
Protonated 4-fluoro-pyridine	-347.5954743	0.092173	217.6411651	218.240031
Acetamide,N-ethyl	-287.5767865	0.127081		
Protonated Acetamide,N-ethyl	-287.9286393	0.14038	212.6130677	214.63098
Cyclobutane carboxylic acid	-345.48958	0.12265		
Protonated Cyclobutane carboxylic acid	-345.8037203	0.134494	189.8428578	195.366774

Morpholine	-287.5272593	0.131161		
Protonated Morpholine	-287.8907227	0.146154	218.8568066	220.916943
Piperazine	-267.6659132	0.143812		
Protonated Piperazine	-268.0374192	0.158599	224.0303961	225.553737
Purine	-411.5992528	0.092111		
Protonated Purine	-411.9568377	0.10531	216.271611	219.913101
Threonine	-437.9295777	0.137012		
Protonated Threonine	-438.242066	0.147482	189.6515515	220.486725
(E)-Dimethylamino acrylonitirle	-304.5210538	0.121254		
Protonated (E)-Dimethylamino acrylonitrile	-304.8807978	0.13301	218.5143377	214.344168
1-hexyne	-234.3312755	0.137745		
Protonated 1-hexyne	-234.6446667	0.146967	190.9859049	191.160198
1-Methylcyclopentene	-234.3851941	0.140575		
Protonated 1-Methylcyclopentene	-234.7113107	0.149699	199.0316975	195.151665
2-hexyne	-234.341959	0.137804		
Protonated 2-hexyne	-234.6524469	0.147342	188.9695838	192.665961
2-propenamide N,N-dimethyl	-325.6050777	0.131403		
Protonated 2-propenamide N,N-dimethyl	-325.9591777	0.144663	214.0472341	216.136743
3-pyridinecarbonitrile	-340.2136566	0.084678		

Protonated 3-pyridinecarbonitrile	-340.530513	0.09446	192.8158728	209.61177
4-pyridinecarbonitrile	-340.2124332	0.084705		
Protonated 4-pyridinecarbonitrile	-340.5228468	0.094637	188.6806145	210.472206
cyclohexanone	-309.5800542	0.146488		
Protonated cyclohexanone	-309.9138523	0.158584	202.0235152	201.00741
Cyclohexene oxide	-309.548645	0.147392		
Protonated Cyclohexene oxide	-309.8733647	0.159171	196.5216157	202.704381
Isoquinoline	-401.5366515	0.131891		
Protonated Isoquinoline	-401.9136765	0.145782	228.0449472	227.465817
L-proline	-400.8150308	0.140618		
Protonated L-proline	-401.1897247	0.155112	226.2111413	220.008705
nicotinamide	-416.6334128	0.112219		
Protonated nicotinamide	-416.974222	0.125144	205.9131005	219.482883
N-Methylpyrrolidine	-251.6180841	0.152908		
Protonated N-Methylpyrrolidine	-251.9972896	0.168514	228.3581842	230.788056
p-benzoquinone	-381.1359625	0.082348		
Protonated p-benzoquinone	-381.4521558	0.094679	190.8315545	190.992891
1-methylbenzotriazole	-434.7945049	0.12996		
Protonated 1-methylbenzotriazole	-435.1624172	0.143824	222.3432106	222.566112

2,2-dimethyltetrahydrofuran	-310.769613	0.167424		
Protonated 2,2-dimethyltetrahydrofuran	-311.1040423	0.179859	202.2110619	202.608777
3-aminobenzoic acid	-475.7852073	0.127626		
Protonated 3-aminobenzoic acid	-476.1232996	0.142181	203.2053347	206.671947
Acetylpyrrolidine	-364.9077894	0.162553		
Protonated Acetylpyrrolidine	-365.2703025	0.175834	219.3137577	221.179854
benzimidazole	-379.5206425	0.115032		
Protonated benzimidazole	-379.8948011	0.128815	226.3126737	227.967738
benzoxazole	-399.3737232	0.102785		
Protonated benzoxazole	-399.7251301	0.115832	212.4883409	213.101316
Cinnoline	-417.5446492	0.119388		
Protonated Cinniloine	-417.9170069	0.133516	224.9703234	223.785063
Hexahydroazepine	-290.8889639	0.182658		
Protonated Hexahydroazepine	-291.2652092	0.197828	226.7688244	228.660867
Quinoxaline	-417.5749588	0.120055		
Protonated Quinoxaline	-417.9339964	0.133374	217.1093983	216.017238
Triglycine	-699.9194559	0.184894		
Protonated Triglycine	-700.2944061	0.198271	227.0592241	231.074868

2,3-Cyclopentenopyridine	-364.6602742	0.148505		
Protonated 2,3-Cyclopentenopyridine	-365.0379856	0.162324	228.5199897	228.852075
2,3-Dihydroindole	-364.6588626	0.148987		
Protonated 2,3-Dihydroindole	-365.0179002	0.163571	216.3312073	228.756471
Benzoic acid, 2-methyl	-459.7337784	0.139449		
Protonated Benzoic acid, 2-methyl	-460.065531	0.151286	200.8992575	200.481588
Benzoic acid, 3-methyl	-459.7295137	0.138341		
Protonated Benzioc acid, 3-methyl	-460.0635111	0.150301	202.2322665	198.330498
o-Xylene	-310.5491987	0.151654		
Protonated o-Xylene	-310.8667963	0.161232	193.4064819	190.25196
P-Xylene	-310.5492912	0.150914		
Protonated P-Xylene pc close to me	-310.8658269	0.160898	192.490386	189.869544
2,2,6,6-Tetramethyl-piperidine	-408.7089679	0.262426		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.0959745	0.277359	233.6676073	235.90287
cyclooctanone	-388.1067357	0.202945		
Protonated cyclooctanoone	-388.4438115	0.215525	203.7825872	203.015094
Cytidine	-890.4526522	0.230053		
Protonated Cytidine	-890.8312606	0.243557	229.2766479	234.827325
Deoxycytidine	-815.2772092	0.225712		

Protonated Deoxycytidine	-815.6560851	0.239113	229.5079227	236.237484
N,3,5-Trimethylpiperidine	-369.437432	0.235309		
Protonated N,3,5-Trimethylpiperidine	-369.8181065	0.250972	229.2449138	233.775681
Naphthalene	-385.4985871	0.14346		
Protonated Naphthalene	-385.8153149	0.153623	192.5008019	191.901129
1,8-Diaminonaphthalene	-496.1338753	0.176922		
Protonated 1,8-Diaminonaphthalene	-496.5013644	0.188286	223.6157161	225.744945
1-methyl-3-phenylpyrazole	-496.0999076	0.174838		
Protonated 1-methyl-3-phenylpyrazole	-496.468298	0.187754	223.226455	222.900726
Acridine	-555.0280574	0.177106		
Protonated Acridine	-555.4146159	0.190852	234.1166341	232.461126
Anthracene	-538.986007	0.18875		
Protonated Anthracene	-539.3149695	0.199246	199.9734494	209.683473
Coronene	-920.9904077	0.271959		
Protonated Coronene	-921.3326986	0.282221	208.4812218	205.859313
Phenazine	-571.0666694	0.165352		
Protonated Phenazine	-571.4386202	0.178596	225.2588559	224.286984
Picene	-845.9792056	0.280139		
Protonated Picene	-846.3198357	0.290838	207.1701522	203.469213

Piperidine, 1-phenyl	-482.4517218	0.2332		
Protonated Piperidine, 1-phenyl	-482.8205853	0.247856	222.4527853	227.752629
Pyrene	-615.1578439	0.201405		
Protonated Pyrene	-615.4865893	0.211945	199.8101361	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.0535888	0.168256		
Protonated 2,3-Dimethylimodazole	-458.4446177	0.181834	237.0252883	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.0550014	0.16837		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-458.4454073	0.181854	236.6921554	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.0514338	0.167919		
Protonated 2,7-Dimethylimidazole	-458.4428867	0.181456	237.3165115	239.129505
2-Methylbiphenyl	-502.0989992	0.203355		
Protonated 2-Methylbiphenyl	-502.4233839	0.214141	196.9223462	195.008259
3-Methylbiphenyl	-502.1026154	0.203039		
Protonated 3-Methylbiphenyl	-502.4145271	0.212595	189.852004	197.90028
Benzoquinuclidine	-481.2486112	0.212302		
Protonated Benzoquinuclidine	-481.6298633	0.227197	230.0798598	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-425.8886523	0.270804		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.2663367	0.286082	227.6054236	232.293819

N,N- diethylnicotinamide	-573.6875157	0.222391		
Protonated N,N- diethylnicotinamide	-574.0476498	0.235468	217.9463746	224.884509
3-hexen-2-one	-309.5636274	0.142018		
Protonated 3-hexen-2-one	-309.9050819	0.154149	206.8064802	206.887056
3-chloro-pyridine-1-oxide	-782.6097386	0.080819		
Protonated 3-chloro-pyridine	-782.9546834	0.092429	209.3172883	215.634822
Niacinamide	-416.6334128	0.112219		
Protonated Niacinamide	-416.9939131	0.125864	217.8267176	219.482883
1-methyl-3,5-dinitropyrazole	-674.0564376	0.10055		
Protonated 1-methyl-3,5-dinitropyrazole	-674.3512076	0.111282	178.3717864	188.531088
Piperidine	-251.6346967	0.1546		
Protonated Piperidine	-252.0092462	0.169919	225.6130406	228.01554

Table S5. Calculated and experimental proton affinity using RMP2/6-311+G (2df, p) // RMP2/6-31+G (d, p) model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-192.0250417	0.085677		
Protonated Acetone	-192.3569161	0.098743	200.2195957	194.07612
p-anisidine	-399.7357513	0.150756		
Protonared p-anisidine	-400.0977654	0.165399	218.1626494	215.180703
Methyl nicotinate	-473.462547	0.132669		
Protonated Methyl nicotinate	-473.8059999	0.145985	207.3314867	221.227656
1,3-Diazine	-262.7696429	0.077628		
Protonated 1,3-Diazine	-263.1287803	0.091422	216.8798223	211.715058
1H-Imidazole	-224.885851	0.07166		
Protonated 1H-Imidazole	-225.2663063	0.086034	229.9004663	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1057.872375	0.082542		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1058.21901	0.091763	211.8474687	217.833714
2-Propenamide	-245.9059097	0.08036		
Protonated 2-Propenamide	-246.2585389	0.093661	213.0990783	208.106007
3-Aminopyrazole	-279.9141648	0.088909		
Protonated 3-Aminopyrazole	-280.2970475	0.101911	232.2677487	220.247715
Acetamide, N-hydroxy-N-methyl	-321.9093613	0.108075		
Protonated Acetamide, N-hydroxy-N-methyl	-322.2649555	0.120992	215.1959531	209.420562

Aziridine, 2-methyl	-172.1352441	0.100851		
Protonated Aziridine, 2-methyl	-172.5101913	0.115594	226.2169775	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-172.1231568	0.100601		
Protonated Aziridine, 1-methyl	-172.5022415	0.115845	228.505108	223.426548
1H-Pyrazole	-224.8634772	0.071695		
Protonated 1H-Pyrazole	-225.2268305	0.085177	219.7173236	213.698841
Isoxazole	-244.6621173	0.058233		
Protonated Isoxazole	-245.0093147	0.072037	209.3810309	202.823886
L-Cysteine	-719.5185137	0.11015		
Protonated L-Cysteine	-719.878787	0.124905	217.0013665	215.873832
N-Methylglycine	-321.9653669	0.11053		
Protonated N-Methylglycine	-322.2834534	0.123202	191.8098239	220.176012
Oxazole	-244.7087664	0.058927		
Protonated Oxazole	-245.0622798	0.072651	213.3937104	209.468364
Propylen oxide (2-Methyloxirane)	-191.972154	0.087706		
Protonated Propylen oxide (2-Methyloxirane)	-192.2952311	0.100602	194.8036592	191.996733
1H-Imidazole,1-methyl-	-263.926484	0.100264		
Protonated 1H-Imidazole,1-methyl-	-264.3147237	0.11443	234.9132648	229.353996

1H-Imidazole,2-methyl	-263.9403406	0.099873		
Protonated 1H-Imidazole,2-methyl	-264.3302229	0.114428	235.7046509	230.262234
1H-Pyrazole, 3-methyl	-263.9158418	0.099822		
Protonated 1H-Pyrazole, 3-methyl	-264.2880391	0.113368	225.227775	216.54306
1-methyl-5-aminopyrazole	-318.9563474	0.117459		
Protonated 1-methyl-5-aminopyrazole	-319.3432669	0.130503	234.775067	226.939995
1-methylcyclopropene	-154.9153337	0.086279		
Protonated 1-methylcyclopropene	-155.2815547	0.098357	222.3806563	204.59256
1-methylpyrazol-3-amine	-318.9620126	0.117356		
Protonated 1-methylpyrazol-3-amine	-319.3191259	0.132295	214.9051965	224.047974
2-butenamide	-284.9583646	0.10927		
Protonated 2-butenamide	-285.3186259	0.122274	218.0711165	212.025771
Asparagine	-489.824648	0.137903		
Protonated Asparagine	-490.1973402	0.152554	224.8584915	222.04029
Butyrolactone	-304.8014584	0.100636		
Protonated Butyrolactone	-305.1392574	0.113831	203.8580736	200.7684
cyclobutanone	-229.8678492	0.092928		
Protonated cyclobutanone	-230.1916625	0.106399	194.9118959	191.805525
cyclobutene	-154.9457933	0.088137		

Protonated cyclobutene	-155.2443814	0.098439	181.0322209	187.479444
cyclopropanecarboxylic acid	-304.7836705	0.099122		
Protonated cyclopropanecarboxylic acid	-305.0878085	0.106413	186.3673041	196.322814
Cytosine	-392.746664	0.099213		
Protonated Cytosine	-393.1318348	0.112421	233.5768653	227.035599
Furan, 2,3-dihydro-	-229.8621942	0.094845		
Protonated Furan, 2,3-dihydro-	-230.1790313	0.107592	190.9796435	207.197769
Methacrylamide	-284.9536695	0.109358		
Protonated Methacrylamide	-285.3047333	0.122851	211.9985796	210.424404
Pyrrolidine	-211.2102627	0.132802		
Protonated Pyrrolidine	-211.5938004	0.148259	231.1684271	226.653183
1,2-Diamethylimidazole	-302.9793871	0.12876		
Protonated 1,2-Diamethylimidazole	-303.375899	0.142859	240.1454423	235.353147
1,5-dimethylimidazole	-302.9770165	0.128647		
Protonated 1,5-dimethylimidazole	-303.3711706	0.142774	238.6486772	233.656176
2-Aminopyridine	-301.830542	0.106427		
Protonated 2-Aminopyridine	-302.2131107	0.119642	231.9396575	226.390272
2-bromo-pyridine	-2818.549097	0.079156		
Protonated 2-bromo-pyridine	-2818.91279	0.093284	219.5330023	216.256248

2-chloro-pyridine	-705.6976251	0.0794		
Protonated 2-chloro-pyridine	-706.0602037	0.09332	218.961683	215.324109
2-fluoro-pyridine	-345.6619268	0.081073		
Protonated 2-fluoro-pyridine	-346.0191377	0.094983	215.5995322	211.428246
3-bromo-pyridine	-2818.546697	0.079259		
Protonated 3-bromo-pyridine	-2818.91111	0.093433	219.9561468	217.4991
3-fluoro-pyridine	-345.6496519	0.080828		
Protonated 3-fluoro-pyridine	-346.0127082	0.095077	219.0590463	215.58702
4-aminopyridine	-301.830542	0.106427		
Protonated 4-aminopyridine	-302.2131048	0.119648	231.9322663	234.158097
4-Bromo-pyridine	-2818.547799	0.079337		
Protonated4-Bromo-pyridine	-2818.915799	0.093473	222.2309128	219.363378
4-fluoro-pyridine	-345.6543729	0.08107		
Protonated 4-fluoro-pyridine	-346.0226223	0.095264	222.3516483	218.240031
Acetamide,N-ethyl	-286.1384349	0.133662		
Protonated Acetamide,N-ethyl	-286.4972648	0.147358	216.7470968	214.63098
Cyclobutane carboxylic acid	-343.8275047	0.128677		
Protonated Cyclobutane carboxylic acid	-344.1587631	0.141798	199.799207	195.366774

Morpholine	-286.0892444	0.138289		
Protonated Morpholine	-286.4632881	0.15367	225.2575075	220.916943
Piperazine	-266.2556965	0.151618		
Protonated Piperazine	-266.6372401	0.166794	230.0899099	225.553737
Purine	-409.5834842	0.094569		
Protonated Purine	-409.9521221	0.108492	222.762214	219.913101
Threonine	-435.9084503	0.144063		
Protonated Threonine	-436.2809181	0.158451	224.8794904	220.486725
(E)-Dimethylamino acrylonitirle	-302.9518368	0.127036		
Protonated (E)-Dimethylamino acrylonitrile	-303.3106624	0.138997	217.8118206	214.344168
1-hexyne	-233.0392955	0.144092		
Protonated 1-hexyne free	-233.3492352	0.155109	187.715711	191.160198
1-Methylcyclopentene	-233.0854617	0.147863		
Protonated 1-Methylcyclopentene	-233.4226815	0.157592	205.6269294	195.151665
2-hexyne	-233.047684	0.144467		
Protonated 2-hexyne pctome	-233.3544751	0.15347	186.9788997	192.665961
2-propenamide N,N-dimethyl	-323.9737016	0.138373		
Protonated 2-propenamide N,N-dimethyl	-324.343573	0.152056	223.6839115	216.136743
3-pyridinecarbonitrile	-338.5195385	0.086558		

Protonated 3-pyridinecarbonitrile	-338.8405449	0.097442	194.7421313	209.61177
4-pyridinecarbonitrile	-338.5162934	0.086686		
Protonated 4-pyridinecarbonitrile	-338.8291486	0.097521	189.6572174	210.472206
cyclohexanone	-307.9900926	0.154102		
Protonated cyclohexanone	-308.3320306	0.166978	206.6515868	201.00741
Cyclohexene oxide	-307.9500591	0.155173		
Protonated Cyclohexene oxide	-308.2852922	0.167775	202.6126879	202.704381
Isoquinoline	-399.4573272	0.13629		
Protonated Isoquinoline	-399.841129	0.150719	231.9665916	227.465817
L-proline	-398.8928841	0.147711		
Protonated L-proline pn	-399.274619	0.16275	230.2942971	220.008705
nicotinamide	-414.6096295	0.116619		
Protonated nicotinamide	-414.9605276	0.130148	211.8725016	219.482883
N-Methylpyrrolidine	-250.2455118	0.16127		
Protonated N-Methylpyrrolidine	-250.6377048	0.1772	236.3087174	230.788056
p-benzoquinone	-379.3472745	0.084266		
Protonated p-benzoquinone	-379.6715012	0.097089	195.5700128	190.992891
1-methylbenzotriazole	-432.57634	0.134231		
Protonated 1-methylbenzotriazole	-432.9501358	0.148175	225.9860075	222.566112

2,2-dimethyltetrahydrofuran	-309.148792	0.176589		
Protonated 2,2-dimethyltetrahydrofuran	-309.4916597	0.189643	207.1255167	202.608777
3-aminobenzoic acid	-473.5063123	0.132018		
Protonated 3-aminobenzoic acid	-473.8533565	0.146632	208.7865754	206.671947
Acetylpyrrolidine	-363.0534606	0.170977		
Protonated Acetylpyrrolidine	-363.4235313	0.184589	223.8526514	221.179854
benzimidazole	-377.5855703	0.118423		
Protonated benzimidazole	-377.9689073	0.132451	231.9216538	227.967738
benzoxazole	-397.411607	0.105563		
Protonated benzoxazole	-397.7705005	0.119049	216.9162362	213.101316
Cinnoline	-415.4134643	0.123225		
Protonated Cinniloine	-415.7913011	0.137964	228.0326853	223.785063
Hexahydroazepine	-289.292676	0.192287		
Protonated Hexahydroazepine	-289.6789299	0.208099	232.6544628	228.660867
Quinoxaline	-415.4520956	0.123982		
Protonated Quinoxaline	-415.8146047	0.13805	218.8270301	216.017238
Triglycine	-696.7020519	0.193983		
Protonated Triglycine	-697.0710871	0.208028	222.9364597	231.074868

2,3-Cyclopentenopyridine	-362.7427209	0.154781		
Protonated 2,3-Cyclopentenopyridine	-363.1283808	0.16908	233.2125623	228.852075
2,3-Dihydroindole	-362.7386467	0.154643		
Protonated 2,3-Dihydroindole	-363.1096526	0.169842	223.4631545	228.756471
Benzoic acid, 2-methyl	-457.4970153	0.144136		
Protonated Benzoic acid, 2-methyl	-457.8363869	0.157381	204.8141015	200.481588
Benzoic acid, 3-methyl	-457.4920174	0.143469		
Protonated Benzioc acid, 3-methyl	-457.841126	0.156347	211.1500692	198.330498
o-Xylene	-308.8642954	0.158008		
Protonated o-Xylene	-309.1896641	0.168765	197.5576486	190.25196
P-Xylene	-308.8655763	0.156315		
Protonated P-Xylene pc close to me	-309.1890203	0.168067	195.7377506	189.869544
2,2,6,6-Tetramethyl-piperidine	-406.4446184	0.276288		
Protonated 2,2,6,6-Tetramethyl-piperidine	-406.8400539	0.291611	238.7169468	235.90287
cyclooctanone	-386.0696879	0.213646		
Protonated cyclooctanoone	-386.4140884	0.226897	207.9661279	203.015094
Cytidine	-886.3332515	0.242051		
Protonated Cytidine	-886.7257554	0.25436	238.7315778	234.827325
Deoxycytidine	-811.4476486	0.2367		

Protonated Deoxycytidine	-811.8408222	0.249796	238.6676675	236.237484
N,3,5-Trimethylpiperidine	-367.3982933	0.247949		
Protonated N,3,5-Trimethylpiperidine	-367.791328	0.26383	236.8670889	233.775681
Naphthalene	-383.4598153	0.148091		
Protonated Naphthalene	-383.7855647	0.15912	197.6292156	191.901129
1,8-Diaminonaphthalene	-493.5553349	0.183057		
Protonated 1,8-Diaminonaphthalene	-493.9261032	0.196336	224.4953414	225.744945
1-methyl-3-phenylpyrazole	-493.5220112	0.181012		
Protonated 1-methyl-3-phenylpyrazole	-493.9033343	0.194749	230.8368608	222.900726
Acridine	-552.1428503	0.182023		
Protonated Acridine	-552.5407672	0.197104	240.4229735	232.461126
Anthracene	-536.1409922	0.194471		
Protonated Anthracene	-536.4803532	0.206111	205.7948995	209.683473
Coronene	-916.1819338	0.282197		
Protonated Coronene	-916.5306741	0.294159	211.482498	205.859313
Phenazine	-568.1377035	0.169786		
Protonated Phenazine	-568.5153903	0.184197	228.1403473	224.286984
Picene	-841.5361169	0.275582		
Protonated Picene	-841.8672648	0.300776	185.0511378	203.469213

Piperidine, 1-phenyl	-479.8617545	0.243241		
Protonated Piperidine, 1-phenyl	-480.2444601	0.258673	230.6616118	227.752629
Pyrene	-611.9267866	0.208554		
Protonated Pyrene	-612.2652474	0.220223	197.4742275	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-455.6636466	0.173689		
Protonated 2,3-Dimethylimodazole	-456.0706837	0.187552	246.895421	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-455.6673541	0.173154		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-456.0727792	0.187603	245.5233278	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-455.6646265	0.173299		
Protonated 2,7-Dimethylimidazole	-456.0714615	0.18747	246.5790958	239.129505
2-Methylbiphenyl	-499.4256612	0.210214		
Protonated 2-Methylbiphenyl	-499.7524857	0.222024	197.8233991	195.008259
3-Methylbiphenyl	-499.4296717	0.210023		
Protonated 3-Methylbiphenyl	-499.7687277	0.221685	205.5899695	197.90028
Benzoquinuclidine	-478.6918003	0.220653		
Protonated Benzoquinuclidine	-479.0838236	0.236033	236.540656	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-423.5519082	0.285829		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-423.9394925	0.301562	233.5378963	232.293819

N,N- diethylnicotinamide	-570.7689089	0.232689		
Protonated N,N- diethylnicotinamide	-571.1406946	0.246172	225.008247	224.884509
3-hexen-2-one	-307.9773296	0.149205		
Protonated 3-hexen-2-one	-308.3254011	0.162443	210.2778022	206.887056
3-chloro-pyridine-1-oxide	-780.4980938	0.082807		
Protonated 3-chloro-pyridine	-780.8740934	0.095731	227.9964221	215.634822
Niacinamide	-414.6096296	0.116619		
Protonated Niacinamide	-414.9753297	0.130737	220.7987518	219.482883
1-methyl-3,5-dinitropyrazole	-670.9516382	0.104718		
Protonated 1-methyl-3,5-dinitropyrazole	-671.240529	0.115622	174.576637	188.531088
Piperidine	-250.2639974	0.162843		
Protonated Piperidine	-250.649298	0.1785	232.1516097	228.01554

Table S6. Calculated and experimental proton affinity using RHF/6-311+G (2df, p) // RHF/6-31+G (d, p) model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-192.02838	0.089129		
Protonated Acetone	-192.3588987	0.102853	198.9640451	194.07612
p-anisidine	-399.7400886	0.159894		
Protonared p-anisidine	-400.1020914	0.175704	217.4376033	215.180703
Methyl nicotinate	-473.4939918	0.141533		
Protonated Methyl nicotinate	-473.8274635	0.154205	201.4642847	221.227656
1,3-Diazine	-262.7740241	0.082855		
Protonated 1,3-Diazine	-263.1326814	0.097204	216.2371137	211.715058
1H-Imidazole	-224.8900304	0.076787		
Protonated 1H-Imidazole	-225.2705678	0.091615	229.6725975	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1057.876711	0.089067		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1058.221696	0.098865	210.4573654	217.833714
2-Propenamide	-245.9104505	0.084842		
Protonated 2-Propenamide	-246.2622885	0.09962	211.6939239	208.106007
3-Aminopyrazole	-279.9186004	0.093121		
Protonated 3-Aminopyrazole	-280.3013561	0.107902	231.093524	220.247715
Acetamide, N-hydroxy-N-methyl	-321.9157411	0.113982		
Protonated Acetamide, N-hydroxy-N-methyl	-322.2700693	0.12768	213.9209819	209.420562

Aziridine, 2-methyl	-172.1366719	0.105173		
Protonated Aziridine, 2-methyl	-172.5111873	0.1203	225.7097439	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-172.124727	0.104834		
Protonated Aziridine, 1-methyl	-172.5032436	0.120639	227.8034072	223.426548
1H-Pyrazole	-224.8685411	0.076855		
Protonated 1H-Pyrazole	-225.2302264	0.090519	218.5586775	213.698841
Isoxazole	-244.669304	0.062864		
Protonated Isoxazole	-245.0137688	0.076863	207.5463365	202.823886
L-Cysteine	-719.524502	0.116489		
Protonated L-Cysteine	-719.8443655	0.12822	193.5038165	215.873832
N-Methylglycine	-321.9713711	0.116439		
Protonated N-Methylglycine	-322.2920548	0.129342	193.2974815	220.176012
Oxazole	-244.7144362	0.063523		
Protonated Oxazole	-245.062208	0.077636	209.5514457	209.468364
Propylen oxide (2-Methyloxirane)	-191.9749397	0.091581		
Protonated Propylen oxide (2-Methyloxirane)	-192.2974663	0.104989	194.1432458	191.996733
1H-Imidazole,1-methyl-	-263.9306899	0.106309		
Protonated 1H-Imidazole,1-methyl-	-264.319029	0.121025	234.6372353	229.353996

1H-Imidazole,2-methyl	-263.9446741	0.105868		
Protonated 1H-Imidazole,2-methyl	-264.3345133	0.120647	235.5398397	230.262234
1H-Pyrazole, 3-methyl	-263.9210211	0.105959		
Protonated 1H-Pyrazole, 3-methyl	-264.2914661	0.119388	224.2001142	216.54306
1-methyl-5-aminopyrazole	-318.963798	0.124216		
Protonated 1-methyl-5-aminopyrazole	-319.3490802	0.137358	233.6873745	226.939995
1-methylcyclopropene	-154.9172649	0.090113		
Protonated 1-methylcyclopropene	-155.3009477	0.102476	233.1628811	204.59256
1-methylpyrazol-3-amine	-318.9679502	0.124254		
Protonated 1-methylpyrazol-3-amine	-319.3252452	0.14021	214.3935758	224.047974
2-butenamide	-284.9627963	0.11459		
Protonated 2-butenamide	-285.3218276	0.128934	216.4748756	212.025771
Asparagine	-489.8345381	0.146288		
Protonated Asparagine pnmiddle	-490.2081585	0.162416	224.5322173	222.04029
Butyrolactone	-304.8070269	0.105789		
Protonated Butyrolactone	-305.1437764	0.119531	202.8629262	200.7684
cyclobutanone	-229.8714723	0.097265		
Protonated cyclobutanone	-230.1975041	0.110787	196.2727183	191.805525
cyclobutene	-154.9471019	0.092507		

Protonated cyclobutene	-155.253004	0.101906	186.1774187	187.479444
cyclopropanecarboxylic acid	-304.7889843	0.104379		
Protonated cyclopropanecarboxylic acid	-305.0967487	0.111732	188.6048612	196.322814
Cytosine	-392.7538551	0.105874		
Protonated Cytosine po	-393.1409965	0.121283	233.4592921	227.035599
Furan, 2,3-dihydro-	-229.8654914	0.099719		
Protonated Furan, 2,3-dihydro-	-230.1820888	0.112976	190.5154105	207.197769
Methacrylamide	-284.9585773	0.114998		
Protonated Methacrylamide	-285.3086281	0.129352	210.8332463	210.424404
Pyrrolidine	-211.2111619	0.138422		
Protonated Pyrrolidine	-211.5947538	0.154676	230.7120464	226.653183
1,2-Diamethylimidazole	-302.9837734	0.135446		
Protonated 1,2-Diamethylimidazole	-303.3802897	0.150164	239.7674203	235.353147
1,5-dimethylimidazole	-302.9814704	0.135866		
Protonated 1,5-dimethylimidazole	-303.3757204	0.150577	238.3495464	233.656176
2-Aminopyridine	-301.834202	0.112998		
Protonated 2-Aminopyridine	-302.21708	0.127397	231.4053213	226.390272
2-bromo-pyridine	-2818.552184	0.084551		
Protonated 2-bromo-pyridine	-2818.915556	0.099333	218.9292133	216.256248

2-chloro-pyridine	-705.7008124	0.08485		
Protonated 2-chloro-pyridine	-706.0630966	0.099489	218.3346344	215.324109
2-fluoro-pyridine	-345.6668947	0.086614		
Protonated 2-fluoro-pyridine	-346.0239109	0.101085	215.1322254	211.428246
3-bromo-pyridine	-2818.549913	0.084813		
Protonated 3-bromo-pyridine	-2818.914082	0.099568	219.445996	217.4991
3-fluoro-pyridine	-345.6543157	0.086415		
Protonated 3-fluoro-pyridine	-346.0168599	0.101202	218.40669	215.58702
4-aminopyridine	-301.834202	0.112998		
Protonated 4-aminopyridine	-302.21708	0.127397	231.4053213	234.158097
4-Bromo-pyridine	-2818.551011	0.084791		
Protonated4-Bromo-pyridine	-2818.918499	0.099539	221.533295	219.363378
4-fluoro-pyridine	-345.6592835	0.086564		
Protonated 4-fluoro-pyridine	-346.0272995	0.101377	221.82442	218.240031
Acetamide,N-ethyl	-286.1422203	0.139356		
Protonated Acetamide,N-ethyl	-286.5046848	0.154139	218.3592084	214.63098
Cyclobutane carboxylic acid	-343.8331281	0.135236		
Protonated Cyclobutane carboxylic	-344.1629265	0.148692	198.6769495	195.366774

Morpholine	-286.0917071	0.145014		
Protonated Morpholine	-286.4658267	0.161219	224.7981801	220.916943
Piperazine	-266.2573635	0.158645		
Protonated Piperazine	-266.6388071	0.174707	229.482036	225.553737
Purine	-409.5913512	0.102575		
Protonated Purine	-409.9597704	0.116992	222.3209957	219.913101
Threonine	-435.9160279	0.152336		
Protonated Threonine	-436.2588032	0.166009	206.6867525	220.486725
(E)-Dimethylamino acrylonitirle	-302.9605136	0.133541		
Protonated (E)-Dimethylamino acrylonitrile	-303.3160092	0.145535	215.7019	214.344168
1-hexyne	-233.0431139	0.151008		
Protonated 1-hexyne free	-233.3533299	0.16075	188.6735078	191.160198
1-Methylcyclopentene	-233.0869536	0.154029		
Protonated 1-Methylcyclopentane	-233.4233521	0.164332	204.7583631	195.151665
2-hexyne	-233.0518239	0.150917		
Protonated 2-hexyne pctome	-233.3641064	0.161297	189.5777808	192.665961
2-propenamide N,N-dimethyl	-323.978766	0.144914		
Protonated 2-propenamide N,N-dimethyl	-324.3477782	0.159602	222.5264626	216.136743
3-pyridinecarbonitrile	-338.5301575	0.09382		

Protonated 3-pyridinecarbonitrile	-338.848365	0.105262	192.6424354	209.61177
4-pyridinecarbonitrile	-338.5277278	0.093748		
Protonated 4-pyridinecarbonitrile	-338.8380579	0.105187	187.7010573	210.472206
cyclohexanone	-307.9938807	0.160821		
Protonated cyclohexanone	-308.3349874	0.174305	205.755861	201.00741
Cyclohexene oxide	-307.9531904	0.162162		
Protonated Cyclohexene oxide	-308.2879713	0.175377	201.9517691	202.704381
Isoquinoline	-399.4634626	0.145227		
Protonated Isoquinoline	-399.8469383	0.160011	231.5435303	227.465817
L-proline	-398.8999103	0.155188		
Protonated L-proline	-399.2725788	0.171329	223.9269545	220.008705
nicotinamide	-414.6169013	0.124359		
Protonated nicotinamide	-414.9668231	0.138645	210.7941161	219.482883
N-Methylpyrrolidine	-250.2467027	0.167993		
Protonated N-Methylpyrrolidine	-250.6387649	0.184803	235.6853176	230.788056
p-benzoquinone	-379.3588663	0.09178		
Protonated p-benzoquinone	-379.6813715	0.105069	194.2030565	190.992891
1-methylbenzotriazole	-432.5876488	0.143767		
Protonated 1-methylbenzotriazole	-432.9622215	0.158688	225.8724201	222.566112

2,2-dimethyltetrahydrofuran	-309.1510015	0.183811		
Protonated 2,2-dimethyltetrahydrofuran	-309.4942402	0.197238	207.1288625	202.608777
3-aminobenzoic acid	-473.5140303	0.141929		
Protonated 3-aminobenzoic acid	-473.8611783	0.157378	208.338006	206.671947
Acetylpyrrolidine	-363.0574364	0.17875		
Protonated Acetylpyrrolidine	-363.4303593	0.193207	225.1226286	221.179854
benzimidazole	-377.5913237	0.126883		
Protonated benzimidazole	-377.9743286	0.141696	231.2302326	227.967738
benzoxazole	-397.4183277	0.113815		
Protonated benzoxazole	-397.7768521	0.127862	216.3394753	213.101316
Cinnoline	-415.4230216	0.132028		
Protonated Cinniloine	-415.8003859	0.146894	227.6580298	223.785063
Hexahydroazepine	-289.2938524	0.200344		
Protonated Hexahydroazepine	-289.6803616	0.217114	232.2252723	228.660867
Quinoxaline	-415.4604293	0.132641		
Protonated Quinoxaline	-415.8218219	0.14679	218.0766211	216.017238
Triglycine	-696.715532	0.205891		
Protonated Triglycine	-697.0854575	0.222126	222.1477659	231.074868

2,3-Cyclopentenopyridine	-362.7463058	0.163075		
Protonated 2,3-Cyclopentenopyridine	-363.1317092	0.1781	232.6049418	228.852075
2,3-Dihydroindole	-362.7415198	0.163705		
Protonated 2,3-Dihydroindole	-363.1125143	0.179758	222.930613	228.756471
Benzoic acid, 2-methyl	-457.5045382	0.153829		
Protonated Benzoic acid, 2-methyl	-457.8423777	0.16692	203.9473934	200.481588
Benzoic acid, 3-methyl	-457.4992576	0.152795		
Protonated Benzioc acid, 3-methyl	-457.8419204	0.165578	207.1636464	198.330498
o-Xylene	-308.8665977	0.165873		
Protonated o-Xylene	-309.1926096	0.176715	197.908963	190.25196
P-Xylene	-308.8675019	0.165157		
Protonated P-Xylene	-309.1920931	0.175486	197.3330616	189.869544
2,2,6,6-Tetramethyl-piperidine	-406.4462505	0.28762		
Protonated 2,2,6,6-Tetramethyl-piperidine	-406.8416069	0.304136	237.9333257	235.90287
cyclooctanone	-386.0744341	0.222799		
Protonated cyclooctanoone	-386.4177829	0.236706	206.9026501	203.015094
Cytidine	-886.3463771	0.257168		
Protonated Cytidine	-886.7347892	0.272126	234.5341614	234.827325
Deoxycytidine	-811.4602195	0.251715		

Protonated Deoxycytidine	-811.8479001	0.266571	234.1379064	236.237484
N,3,5-Trimethylpiperidine	-367.3995994	0.258148		
Protonated N,3,5-Trimethylpiperidine	-367.7925172	0.274993	236.2006665	233.775681
Naphthalene	-383.4647987	0.157417		
Protonated Naphthalene	-383.7957561	0.168826	200.6635433	191.901129
1,8-Diaminonaphthalene	-493.5618374	0.194651		
Protonated 1,8-Diaminonaphthalene	-493.9339926	0.209731	224.2575409	225.744945
1-methyl-3-phenylpyrazole	-493.5298968	0.192538		
Protonated 1-methyl-3-phenylpyrazole	-493.909164	0.206466	229.4292204	222.900726
Acridine	-552.1524203	0.194754		
Protonated Acridine	-552.5478699	0.209197	239.2671959	232.461126
Anthracene	-536.1495069	0.207228		
Protonated Anthracene	-536.4884015	0.218808	205.5391484	209.683473
Coronene	-916.1966243	0.298055		
Protonated Coronene	-916.5446373	0.309137	211.5675126	205.859313
Phenazine	-568.1495124	0.182064		
Protonated Phenazine	-568.524751	0.195971	226.9140855	224.286984
Picene	-841.5448378	0.308071		
Protonated Picene	-841.8808528	0.319153	204.0384759	203.469213

Piperidine, 1-phenyl	-479.8656664	0.255818		
Protonated Piperidine, 1-phenyl	-480.2489116	0.272257	230.3806552	227.752629
Pyrene	-611.9363841	0.22122		
Protonated Pyrene	-612.2738768	0.232611	204.7756976	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-455.6719941	0.185236		
Protonated 2,3-Dimethylimodazole	-456.0769938	0.199679	245.2600499	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-455.6747956	0.18524		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-456.0786455	0.199535	244.6296194	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-455.6721595	0.184921		
Protonated 2,7-Dimethylimidazole	-456.0774217	0.199198	245.5268945	239.129505
2-Methylbiphenyl	-499.4296817	0.222707		
Protonated 2-Methylbiphenyl	-499.757314	0.234988	198.0405186	195.008259
3-Methylbiphenyl	-499.4334947	0.222543		
Protonated 3-Methylbiphenyl	-499.7496701	0.233529	191.6478423	197.90028
Benzoquinuclidine	-478.6947528	0.233486		
Protonated Benzoquinuclidine	-479.086742	0.249598	236.0689017	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-423.554667	0.297134		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-423.9420278	0.314125	232.6237465	232.293819

N,N- diethylnicotinamide	-570.7771944	0.244722		
Protonated N,N- diethylnicotinamide	-571.148095	0.259031	223.9446022	224.884509
3-hexen-2-one	-307.9815522	0.155943		
Protonated 3-hexen-2-one	-308.3282515	0.169347	209.3145595	206.887056
3-chloro-pyridine-1-oxide	-780.50368	0.08931		
Protonated 3-chloro-pyridine	-780.8721894	0.103677	222.4084212	215.634822
Niacinamide	-414.6169013	0.124359		
Protonated Niacinamide	-414.9827011	0.139025	220.5241084	219.482883
1-methyl-3,5-dinitropyrazole	-670.9819186	0.113853		
Protonated 1-methyl-3,5-dinitropyrazole	-671.2894555	0.126719	185.0703762	188.531088
Piperidine	-250.2648754	0.169635		
Protonated Piperidine	-250.6502696	0.186163	231.674479	228.01554

Table S7. Calculated and experimental proton affinity using RB3LYP/6-311 +G (2df, p) // RB3LYP/6-311+G (2df, p) model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-193.2269841	0.083228		
Protonated Acetone	-193.5494541	0.095837	194.5993069	194.07612
p-anisidine	-402.2631778	0.148839		
Protonared p-anisidine	-402.6181449	0.163378	213.8045276	215.180703
Methyl nicotinate	-476.3051773	0.130711		
Protonated Methyl nicotinate	-476.6381166	0.143665	200.9567298	221.227656
1,3-Diazine	-264.4089774	0.076796		
Protonated 1,3-Diazine	-264.7600066	0.090397	211.9104981	211.715058
1H-Imidazole	-226.2951979	0.070976		
Protonated 1H-Imidazole	-226.6677595	0.085101	225.1001544	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.880236	0.082652		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1061.222602	0.091873	209.1687771	217.833714
2-Propenamide	-247.3896322	0.07868		
Protonated 2-Propenamide	-247.7327829	0.092331	206.9358192	208.106007
3-Aminopyrazole	-281.6538808	0.087504		
Protonated 3-Aminopyrazole	-282.0253408	0.1001	225.3495491	220.247715
Acetamide, N-hydroxy-N-methyl	-323.8060538	0.105208		
Protonated Acetamide, N-hydroxy-N-methyl	-324.1527932	0.118226	209.5772161	209.420562

Aziridine, 2-methyl	-173.30194	0.097875		
Protonated Aziridine, 2-methyl	-173.6665271	0.112066	220.0553128	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-173.2903511	0.097447		
Protonated Aziridine, 1-methyl	-173.6581343	0.112389	221.5989081	223.426548
1H-Pyrazole	-226.2783259	0.071064		
Protonated 1H-Pyrazole	-226.6318328	0.084147	213.7839684	213.698841
Isoxazole	-246.1191302	0.057785		
Protonated Isoxazole	-246.4544015	0.071119	202.1862977	202.823886
L-Cysteine	-722.0846495	0.107084		
Protonated L-Cysteine	-722.4425154	0.121638	215.6143476	215.873832
N-Methylglycine	-323.8550764	0.107384		
Protonated N-Methylglycine	-324.219858	0.122561	219.5708345	220.176012
Oxazole	-246.1553901	0.058405		
Protonated Oxazole	-246.5010372	0.071863	208.6210928	209.468364
Propylen oxide (2-Methyloxirane)	-193.1783139	0.08514		
Protonated Propylen oxide (2-Methyloxirane)	-193.4924428	0.097462	189.5416326	191.996733
1H-Imidazole,1-methyl-	-265.6164354	0.098701		
Protonated 1H-Imidazole,1-methyl-	-265.9966178	0.112656	229.9869014	229.353996

1H-Imidazole,2-methyl	-265.6295366	0.098328		
Protonated 1H-Imidazole,2-methyl	-266.0109196	0.112359	230.6935648	230.262234
1H-Pyrazole, 3-methyl	-265.6109331	0.098396		
Protonated 1H-Pyrazole, 3-methyl	-265.9728669	0.11129	219.1883306	216.54306
1-methyl-5-aminopyrazole	-320.9775827	0.115229		
Protonated 1-methyl-5-aminopyrazole	-321.3540945	0.127462	228.7429562	226.939995
1-methylcyclopropene	-155.9974012	0.084015		
Protonated 1-methylcyclopropene	-156.34458	0.095591	210.7401135	204.59256
1-methylpyrazol-3-amine	-320.9818533	0.115284		
Protonated 1-methylpyrazol-3-amine	-321.3339731	0.130042	211.8829921	224.047974
2-butenamide	-286.722886	0.106591		
Protonated 2-butenamide	-287.0747337	0.120075	212.4960577	212.025771
Asparagine	-492.6345967	0.134843		
Protonated Asparagine pnmiddle	-493.00839	0.149482	225.5568153	222.04029
Butyrolactone	-306.6011235	0.098151		
Protonated Butyrolactone	-306.9277367	0.111027	197.0350201	200.7684
cyclobutanone	-231.3084065	0.090327		
Protonated cyclobutanone	-231.6254831	0.102754	191.326761	191.805525
cyclobutene	-156.0246038	0.086134		

Protonated cyclobutene	-156.3193176	0.09361	180.3396428	187.479444
cyclopropanecarboxylic acid	-306.5850119	0.09667		
Protonated cyclopropanecarboxylic acid	-306.8867811	0.103773	184.9965089	196.322814
Cytosine	-395.0756288	0.097955		
Protonated Cytosine	-395.4517189	0.112452	227.085457	227.035599
Furan, 2,3-dihydro-	-231.3030454	0.092535		
Protonated Furan, 2,3-dihydro-	-231.6113797	0.104943	185.8525502	207.197769
Methacrylamide	-286.7189836	0.106775		
Protonated Methacrylamide	-287.0651357	0.120441	208.8100091	210.424404
Pyrrolidine	-212.6546362	0.129103		
Protonated Pyrrolidine	-213.0294909	0.144269	225.8986593	226.653183
1,2-Diamethylimidazole	-304.9495902	0.126086		
Protonated 1,2-Diamethylimidazole	-305.3376448	0.140013	234.9441486	235.353147
1,5-dimethylimidazole	-304.947858	0.126374		
Protonated 1,5-dimethylimidazole	-305.3345295	0.140292	234.0817114	233.656176
2-Aminopyridine	-303.7548445	0.105147		
Protonated 2-Aminopyridine	-304.130625	0.118806	227.4067553	226.390272
2-bromo-pyridine	-2821.908238	0.07828		
Protonated 2-bromo-pyridine	-2822.266785	0.092233	216.4117078	216.256248

2-chloro-pyridine	-707.9949942	0.078913		
Protonated 2-chloro-pyridine	-708.35215	0.092873	215.5341716	215.324109
2-fluoro-pyridine	-347.6471061	0.080555		
Protonated 2-fluoro-pyridine	-347.9974898	0.094373	211.3719555	211.428246
3-bromo-pyridine	-2821.905159	0.078424		
Protonated 3-bromo-pyridine	-2822.265209	0.092399	217.3409412	217.4991
3-fluoro-pyridine	-347.636687	0.080351		
Protonated 3-fluoro-pyridine	-347.9943157	0.094485	215.7239454	215.58702
4-aminopyridine	-303.7548445	0.105147		
Protonated 4-aminopyridine	-304.130625	0.118806	227.4067553	234.158097
4-Bromo-pyridine	-2821.905992	0.078434		
Protonated4-Bromo-pyridine	-2822.269884	0.092459	219.7212404	219.363378
4-fluoro-pyridine	-347.6397395	0.080433		
Protonated 4-fluoro-pyridine	-348.0016265	0.094631	218.356729	218.240031
Acetamide,N-ethyl	-287.9460969	0.130057		
Protonated Acetamide,N-ethyl	-288.2999856	0.143562	213.7639581	214.63098
Cyclobutane carboxylic acid	-345.9084409	0.12566		
Protonated Cyclobutane carboxylic	-346.2307031	0.138139	194.5488493	195.366774

Morpholine	-287.8942139	0.134547		
Protonated Morpholine	-288.2599268	0.149694	220.1736679	220.916943
Piperazine	-268.0229552	0.147388		
Protonated Piperazine	-268.396531	0.16238	225.2031966	225.553737
Purine	-412.073836	0.094672		
Protonated Purine	-412.4340905	0.108165	217.7659998	219.913101
Threonine	-438.4387721	0.140592		
Protonated Threonine	-438.7534709	0.152145	190.3724121	220.486725
(E)-Dimethylamino acrylonitirle	-304.9196687	0.12428		
Protonated (E)-Dimethylamino acrylonitrile	-305.2780235	0.136106	217.5994821	214.344168
1-hexyne	-234.676573	0.141088		
Protonated 1-hexyne free	-234.9869426	0.150283	189.1063866	191.160198
1-Methylcyclopentene	-234.7229466	0.14391		
Protonated 1-Methylcyclopentene	-235.0492772	0.153203	199.0619556	195.151665
2-hexyne	-234.6865193	0.14113		
Protonated 2-hexyne pctome	-234.995728	0.150722	188.1336982	192.665961
2-propenamide N,N-dimethyl	-326.0215733	0.134819		
Protonated 2-propenamide N,N-dimethyl	-326.3782789	0.148336	215.5242663	216.136743
3-pyridinecarbonitrile	-340.6349958	0.087109		

Protonated 3-pyridinecarbonitrile	-340.981319	0.100931	208.8213883	209.61177
4-pyridinecarbonitrile	-340.6337081	0.087081		
Protonated 4-pyridinecarbonitrile	-340.9436123	0.097537	188.0385305	210.472206
cyclohexanone	-309.9881984	0.150088		
Protonated cyclohexanone	-310.3218051	0.162426	201.7545662	201.00741
Cyclohexene oxide	-309.9516758	0.151038		
Protonated Cyclohexene oxide	-310.2790045	0.163058	198.010603	202.704381
Isoquinoline	-402.0525649	0.135339		
Protonated Isoquinoline	-402.4316945	0.149538	229.1761329	227.465817
L-proline	-401.2963828	0.144118		
Protonated L-proline pn	-401.6720231	0.159091	226.5103522	220.008705
nicotinamide	-417.1323199	0.115218		
Protonated nicotinamide	-417.4716687	0.128234	204.940664	219.482883
N-Methylpyrrolidine	-251.9705587	0.156551		
Protonated N-Methylpyrrolidine	-252.3532634	0.1723	230.4660144	230.788056
p-benzoquinone	-381.5830071	0.08484		
Protonated p-benzoquinone	-381.8999873	0.097469	191.1420516	190.992891
1-methylbenzotriazole	-435.319908	0.133357		
Protonated 1-methylbenzotriazole	-435.6897417	0.147415	223.4295278	222.566112

2,2-dimethyltetrahydrofuran	-311.1901974	0.17151		
Protonated 2,2-dimethyltetrahydrofuran	-311.5268235	0.184036	203.5335874	202.608777
3-aminobenzoic acid	-476.3502152	0.13174		
Protonated 3-aminobenzoic acid	-476.6894702	0.145811	204.2327616	206.671947
Acetylpyrrolidine	-365.3769942	0.166599		
Protonated Acetylpyrrolidine	-365.7382554	0.179851	218.5459739	221.179854
benzimidazole	-379.9893787	0.117874		
Protonated benzimidazole	-380.3661214	0.131879	227.7977093	227.967738
benzoxazole	-399.8520342	0.105545		
Protonated benzoxazole	-400.2051913	0.118862	213.4205023	213.101316
Cinnoline	-418.0610202	0.122771		
Protonated Cinniloine	-418.4349579	0.137105	225.8350524	223.785063
Hexahydroazepine	-291.2988864	0.187014		
Protonated Hexahydroazepine	-291.677386	0.202566	227.9484399	228.660867
Quinoxaline	-418.0938509	0.123289		
Protonated Quinoxaline	-418.4539765	0.136926	217.5965613	216.017238
Triglycine	-700.7153722	0.189966		
Protonated Triglycine	-701.0871945	0.204603	224.3212557	231.074868

2,3-Cyclopentenopyridine	-365.1384644	0.152151		
Protonated 2,3-Cyclopentenopyridine	-365.5181239	0.166293	229.5438016	228.852075
2,3-Dihydroindole	-365.1365687	0.152592		
Protonated 2,3-Dihydroindole	-365.4989664	0.167535	218.218832	228.756471
Benzoic acid, 2-methyl	-460.2951148	0.143018		
Protonated Benzoic acid, 2-methyl	-460.6275134	0.155454	200.9361334	200.481588
Benzoic acid, 3-methyl	-460.2906893	0.142075		
Protonated Benzioc acid, 3-methyl	-460.626398	0.154274	203.1591437	198.330498
o-Xylene	-310.9819332	0.155211		
Protonated o-Xylene	-311.2999387	0.165246	193.3812927	190.25196
P-Xylene	-310.98242	0.154573		
Protonated P-Xylene pc close to me	-311.2993068	0.164852	192.5291681	189.869544
2,2,6,6-Tetramethyl-piperidine	-409.291296	0.268665		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.6799648	0.28388	234.5371542	235.90287
cyclooctanone	-388.6303119	0.207914		
Protonated cyclooctanoone	-388.9669369	0.220752	203.340965	203.015094
Cytidine	-891.4637489	0.236711		
Protonated Cytidine	-891.8453099	0.250592	230.8975392	234.827325
Deoxycytidine	-816.2176729	0.232153		

Protonated Deoxycytidine	-816.5986004	0.246065	230.4809379	236.237484
N,3,5-Trimethylpiperidine	-369.9634128	0.240946		
Protonated N,3,5-Trimethylpiperidine	-370.347333	0.256829	231.1463789	233.775681
Naphthalene	-386.0112296	0.146999		
Protonated Naphthalene	-386.3291912	0.157602	193.004312	191.901129
1,8-Diaminonaphthalene	-496.7643578	0.181213		
Protonated 1,8-Diaminonaphthalene	-497.132624	0.194168	223.1244806	225.744945
1-methyl-3-phenylpyrazole	-496.731103	0.179224		
Protonated 1-methyl-3-phenylpyrazole	-497.1024868	0.192498	224.8845787	222.900726
Acridine	-555.7375979	0.181624		
Protonated Acridine	-556.126927	0.1957	235.6521811	232.461126
Anthracene	-539.6921883	0.193486		
Protonated Anthracene	-540.0420837	0.205477	212.1895535	209.683473
Coronene	-922.1579258	0.278723		
Protonated Coronene	-922.5019033	0.290175	208.8075288	205.859313
Phenazine	-571.7792233	0.169608		
Protonated Phenazine	-572.1526807	0.183158	226.0160047	224.286984
Picene	-847.0742406	0.287369		
Protonated Picene	-847.4071313	0.29826	202.1954559	203.469213

Piperidine, 1-phenyl	-483.1029427	0.238845		
Protonated Piperidine, 1-phenyl	-483.4766863	0.253881	225.2813884	227.752629
Pyrene	-615.9532367	0.206542		
Protonated Pyrene	-616.2836705	0.217576	200.5657391	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.6360772	0.17239		
Protonated 2,3-Dimethylimodazole	-459.0310989	0.186225	239.3726973	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.6379031	0.172552		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-459.0321407	0.186238	238.9723859	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.6345694	0.172153		
Protonated 2,7-Dimethylimidazole	-459.0299502	0.185888	239.6596218	239.129505
2-Methylbiphenyl	-502.7743168	0.208347		
Protonated 2-Methylbiphenyl	-503.0983347	0.219563	196.4276672	195.008259
3-Methylbiphenyl	-502.7783278	0.208126		
Protonated 3-Methylbiphenyl	-503.1060121	0.219235	198.7942192	197.90028
Benzoquinuclidine	-481.884134	0.217647		
Protonated Benzoquinuclidine	-482.2687901	0.232811	232.0504654	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.4913249	0.277081		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.8713118	0.292766	228.7999214	232.293819

N,N- diethylnicotinamide	-574.4173349	0.228038		
Protonated N,N- diethylnicotinamide	-574.7797175	0.241382	219.1930834	224.884509
3-hexen-2-one	-309.9775891	0.145451		
Protonated 3-hexen-2-one	-310.3187778	0.157965	206.4040981	206.887056
3-chloro-pyridine-1-oxide	-783.183019	0.083151		
Protonated 3-chloro-pyridine	-783.5360407	0.095311	214.0473408	215.634822
Niacinamide	-417.1323199	0.115218		
Protonated Niacinamide	-417.4939256	0.129233	218.2927327	219.482883
1-methyl-3,5-dinitropyrazole	-674.736485	0.103715		
Protonated 1-methyl-3,5-dinitropyrazole	-675.0289145	0.11492	176.6120474	188.531088
Piperidine	-251.9874475	0.158322		
Protonated Piperidine	-252.3644987	0.173836	227.062931	228.01554

Table S8. Calculated and experimental proton affinity using RB3LYP/6-31 +G (d, p) // RB3LYP/6-31G model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-193.1737914	0.084537		
Protonated Acetone	-193.4958298	0.096678	194.6164114	194.07612
p-anisidine	-402.1539159	0.150508		
Protonared p-anisidine	-402.5113533	0.165571	215.0322904	215.180703
Methyl nicotinate	-476.1715417	0.131835		
Protonated Methyl nicotinate	-476.5038752	0.144081	201.0121644	221.227656
1,3-Diazine	-264.3398892	0.077512		
Protonated 1,3-Diazine	-264.6905837	0.091513	211.4543514	211.715058
1H-Imidazole	-226.2346114	0.071967		
Protonated 1H-Imidazole	-226.6076426	0.086788	224.9666291	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.746492	0.084053		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1061.085505	0.092795	207.3590459	217.833714
2-Propenamide	-247.3185101	0.080542		
Protonated 2-Propenamide	-247.6595081	0.093521	205.9983903	208.106007
3-Aminopyrazole	-281.5743008	0.087867		
Protonated 3-Aminopyrazole	-281.9476502	0.102457	225.3083966	220.247715
Acetamide, N-hydroxy-N-methyl	-323.710808	0.105749		
Protonated Acetamide, N-hydroxy-N-methyl	-324.0566649	0.118363	209.2719477	209.420562

Aziridine, 2-methyl	-173.258458	0.098759		
Protonated Aziridine, 2-methyl	-173.6256556	0.113812	221.1631625	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-173.2470687	0.098432		
Protonated Aziridine, 1-methyl	-173.6174294	0.113921	222.8798457	223.426548
1H-Pyrazole	-226.2180832	0.072105		
Protonated 1H-Pyrazole	-226.5715666	0.085889	213.3379119	213.698841
Isoxazole	-246.0474846	0.057798		
Protonated Isoxazole	-246.3827278	0.07163	201.8623393	202.823886
L-Cysteine	-721.9575492	0.107187		
Protonated L-Cysteine	-722.2676036	0.117494	188.2244709	215.873832
N-Methylglycine	-323.7578735	0.107517		
Protonated N-Methylglycine	-324.1250325	0.123526	220.5508357	220.176012
Oxazole	-246.0837886	0.05837		
Protonated Oxazole	-246.429584	0.072447	208.3333673	209.468364
Propylen oxide (2-Methyloxirane)	-193.123645	0.085884		
Protonated Propylen oxide (2-Methyloxirane)	-193.4393343	0.097526	190.9392261	191.996733
1H-Imidazole,1-methyl-	-265.5474019	0.09982		
Protonated 1H-Imidazole,1-methyl-	-265.928102	0.114491	229.8712911	229.353996

1H-Imidazole,2-methyl	-265.5604244	0.0999		
Protonated 1H-Imidazole,2-methyl	-265.9421591	0.11456	230.5273166	230.262234
1H-Pyrazole, 3-methyl	-265.5421566	0.099974		
Protonated 1H-Pyrazole, 3-methyl	-265.9040207	0.113535	218.7341783	216.54306
1-methyl-5-aminopyrazole	-320.8894945	0.115859		
Protonated 1-methyl-5-aminopyrazole	-321.268257	0.130455	228.7015529	226.939995
1-methylcyclopropene	-155.9595213	0.085402		
Protonated 1-methylcyclopropene	-156.3093885	0.097127	212.3354862	204.59256
1-methylpyrazol-3-amine	-320.894043	0.116146		
Protonated 1-methylpyrazol-3-amine	-321.2502281	0.13202	213.7474665	224.047974
2-butenamide	-286.6433338	0.109021		
Protonated 2-butenamide	-286.9931241	0.121726	211.6842872	212.025771
Asparagine	-492.4863385	0.136343		
Protonated Asparagine	-492.861869	0.151406	226.3860918	222.04029
Butyrolactone	-306.5123503	0.098867		
Protonated Butyrolactone	-306.8431912	0.111229	200.0042203	200.7684
cyclobutanone	-231.2472758	0.091771		
Protonated cyclobutanone	-231.5641803	0.103492	191.6531473	191.805525
cyclobutene	-155.9884149	0.087462		

Protonated cyclobutene	-156.2856958	0.095388	181.6737149	187.479444
cyclopropanecarboxylic acid	-306.4962607	0.097434		
Protonated cyclopropanecarboxylic acid	-306.7886519	0.10574	178.3715344	196.322814
Cytosine	-394.9620811	0.09997		
Protonated Cytosine	-395.3380233	0.114789	226.7945906	227.035599
Furan, 2,3-dihydro-	-231.2396173	0.093341		
Protonated Furan, 2,3-dihydro-	-231.5480907	0.105224	186.2627391	207.197769
Methacrylamide	-286.6390526	0.108916		
Protonated Methacrylamide	-286.9849255	0.121983	209.0033141	210.424404
Pyrrolidine	-212.6036683	0.130586		
Protonated Pyrrolidine	-212.9807372	0.146186	227.0210814	226.653183
1,2-Diamethylimidazole	-304.8720534	0.127798		
Protonated 1,2-Diamethylimidazole	-305.2605263	0.14234	234.8283082	235.353147
1,5-dimethylimidazole	-304.8703794	0.127974		
Protonated 1,5-dimethylimidazole	-305.2573872	0.142561	233.8812075	233.656176
2-Aminopyridine	-303.6755798	0.106783		
Protonated 2-Aminopyridine	-304.0517956	0.121591	226.9729912	226.390272
2-bromo-pyridine	-2819.427759	0.079467		
Protonated 2-bromo-pyridine	-2819.786836	0.094003	216.3852997	216.256248

2-chloro-pyridine	-707.8981245	0.079842		
Protonated 2-chloro-pyridine	-708.2545178	0.094337	214.7265561	215.324109
2-fluoro-pyridine	-347.5501167	0.08144		
Protonated 2-fluoro-pyridine	-347.8998018	0.09572	210.6493134	211.428246
3-bromo-pyridine	-2819.425319	0.079664		
Protonated 3-bromo-pyridine	-2819.785763	0.094193	217.2475149	217.4991
3-fluoro-pyridine	-347.5402306	0.081291		
Protonated 3-fluoro-pyridine	-347.8971633	0.095847	215.0275594	215.58702
4-aminopyridine	-303.6755798	0.106783		
Protonated 4-aminopyridine	-304.0517956	0.121591	226.972985	234.158097
4-Bromo-pyridine	-2819.426145	0.079641		
Protonated4-Bromo-pyridine	-2819.790449	0.094254	219.6178908	219.363378
4-fluoro-pyridine	-347.5431732	0.081335		
Protonated 4-fluoro-pyridine	-347.9040948	0.095986	217.4722001	218.240031
Acetamide,N-ethyl	-287.8681167	0.132162		
Protonated Acetamide,N-ethyl	-288.2217683	0.145239	213.8784714	214.63098
Cyclobutane carboxylic acid	-345.8121647	0.126699		
Protonated Cyclobutane carboxylic acid	-346.1332871	0.138552	194.2187598	195.366774

Morpholine	-287.8168142	0.135613		
Protonated Morpholine	-288.1841023	0.151107	220.9486725	220.916943
Piperazine	-267.9557982	0.148726		
Protonated Piperazine	-268.3308338	0.164017	225.9353172	225.553737
Purine	-411.9631974	0.095556		
Protonated Purine	-412.3230588	0.109645	217.1526257	219.913101
Threonine	-438.3059114	0.140582		
Protonated Threonine	-438.6769757	0.156119	223.2919045	220.486725
(E)-Dimethylamino acrylonitirle	-304.8384616	0.125862		
Protonated (E)-Dimethylamino acrylonitrile	-305.1955625	0.137845	216.7159957	214.344168
1-hexyne	-234.6194438	0.143228		
Protonated 1-hexyne	-234.9320351	0.152793	190.2729609	191.160198
1-Methylcyclopentene	-234.6693712	0.146152		
Protonated 1-Methylcyclopentene	-234.9975058	0.155682	200.048225	195.151665
2-hexyne	-234.6291835	0.143407		
Protonated 2-hexyne	-234.9409679	0.153343	189.5383679	192.665961
2-propenamide N,N-dimethyl	-325.9335487	0.136889		
Protonated 2-propenamide N,N-dimethyl	-326.2937094	0.149965	217.9636788	216.136743
3-pyridinecarbonitrile	-340.5447521	0.088029		

Protonated 3-pyridinecarbonitrile	-340.859561	0.099091	190.7435695	209.61177
4-pyridinecarbonitrile	-340.5434679	0.088029		
Protonated 4-pyridinecarbonitrile	-340.852062	0.099117	186.8276076	210.472206
cyclohexanone	-309.9101242	0.152211		
Protonated cyclohexanone	-310.2432741	0.164177	201.6967538	201.00741
Cyclohexene oxide	-309.872235	0.152701		
Protonated Cyclohexene oxide	-310.2009613	0.163903	199.3908307	202.704381
Isoquinoline	-401.9542558	0.1373		
Protonated Isoquinoline	-402.3336372	0.152042	229.0001276	227.465817
L-proline	-401.1824869	0.144503		
Protonated L-proline	-401.5531053	0.160199	222.9141681	220.008705
nicotinamide	-417.0184525	0.117275		
Protonated nicotinamide	-417.3570373	0.129662	204.8481854	219.482883
N-Methylpyrrolidine	-251.9114025	0.158472		
Protonated N-Methylpyrrolidine	-252.2985127	0.17434	233.1573118	230.788056
p-benzoquinone	-381.4749077	0.085838		
Protonated p-benzoquinone	-381.7914849	0.098134	191.0940326	190.992891
1-methylbenzotriazole	-435.2079342	0.134811		
Protonated 1-methylbenzotriazole	-435.5780076	0.149511	223.1850025	222.566112

2,2-dimethyltetrahydrofuran	-311.1125067	0.173801		
Protonated 2,2-dimethyltetrahydrofuran	-311.4505358	0.18582	204.7259056	202.608777
3-aminobenzoic acid	-476.2153721	0.132962		
Protonated 3-aminobenzoic acid	-476.5565458	0.147552	205.1175071	206.671947
Acetylpyrrolidine	-365.2825624	0.168911		
Protonated Acetylpyrrolidine	-365.6473662	0.18193	220.9123773	221.179854
benzimidazole	-379.8925444	0.119815		
Protonated benzimidazole	-380.2693411	0.134495	227.4162664	227.967738
benzoxazole	-399.7440091	0.106342		
Protonated benzoxazole	-400.0970943	0.120347	212.952127	213.101316
Cinnoline	-417.9561667	0.12426		
Protonated Cinniloine	-418.3299831	0.139051	225.4777968	223.785063
Hexahydroazepine	-291.2310667	0.189183		
Protonated Hexahydroazepine	-291.6116709	0.20538	228.872259	228.660867
Quinoxaline	-417.9890859	0.125023		
Protonated Quinoxaline	-418.3490034	0.139108	217.1902967	216.017238
Triglycine	-700.5064316	0.191722		
Protonated Triglycine	-700.8798146	0.207124	224.8299918	231.074868

2,3-Cyclopentenopyridine	-365.051391	0.15433		
Protonated 2,3-Cyclopentenopyridine	-365.4311932	0.168932	229.3502918	228.852075
2,3-Dihydroindole	-365.0464565	0.154411		
Protonated 2,3-Dihydroindole	-365.4117686	0.169927	219.6951265	228.756471
Benzoic acid, 2-methyl	-460.1696699	0.144596		
Protonated Benzoic acid, 2-methyl	-460.4952434	0.155904	197.347203	200.481588
Benzoic acid, 3-methyl	-460.1638248	0.143338		
Protonated Benzioc acid, 3-methyl	-460.4993384	0.155391	203.1265317	198.330498
o-Xylene	-310.9094091	0.157806		
Protonated o-Xylene	-311.2290445	0.168146	194.2164456	190.25196
P-Xylene	-310.9097757	0.157065		
Protonated P-Xylene pc close to me	-311.2284928	0.1677	193.4586735	189.869544
2,2,6,6-Tetramethyl-piperidine	-409.1991282	0.272564		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.5895553	0.287952	235.5340693	235.90287
cyclooctanone	-388.5351191	0.211043		
Protonated cyclooctanoone	-388.87144	0.223323	203.4934508	203.015094
Cytidine	-891.2044383	0.238201		
Protonated Cytidine	-891.5860023	0.251517	231.24703	234.827325
Deoxycytidine	-815.9838928	0.234021		

Protonated Deoxycytidine	-816.3647888	0.247507	230.7232491	236.237484
N,3,5-Trimethylpiperidine	-369.8792374	0.24435		
Protonated N,3,5-Trimethylpiperidine	-370.2649262	0.260185	232.2856856	233.775681
Naphthalene	-385.9194758	0.1494		
Protonated Naphthalene	-386.2391314	0.160191	193.9516341	191.901129
1,8-Diaminonaphthalene	-496.6382286	0.183831		
Protonated 1,8-Diaminonaphthalene	-497.0106301	0.196057	226.1679341	225.744945
1-methyl-3-phenylpyrazole	-496.6078335	0.181841		
Protonated 1-methyl-3-phenylpyrazole	-496.9789011	0.195694	224.3299723	222.900726
Acridine	-555.6035154	0.18448		
Protonated Acridine	-555.9924552	0.199014	235.1261956	232.461126
Anthracene	-539.5643153	0.196597		
Protonated Anthracene	-539.8961669	0.207742	201.3870927	209.683473
Coronene	-921.941304	0.283137		
Protonated Coronene	-922.286562	0.294616	209.5944262	205.859313
Phenazine	-571.6386322	0.172201		
Protonated Phenazine	-572.0116495	0.186237	225.4408383	224.286984
Picene	-846.8742068	0.291895		
Protonated Picene	-847.2082863	0.302902	202.8700649	203.469213

Piperidine, 1-phenyl	-482.9914709	0.242198		
Protonated Piperidine, 1-phenyl	-483.3725608	0.256943	230.0703836	227.752629
Pyrene	-615.8078103	0.209858		
Protonated Pyrene	-616.1399156	0.221058	201.5124619	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.5219406	0.174789		
Protonated 2,3-Dimethylimodazole	-458.9169869	0.189468	238.8688994	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.523694	0.174975		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-458.9179987	0.189509	238.4927378	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.5202704	0.17453		
Protonated 2,7-Dimethylimidazole	-458.9157138	0.189125	239.1697609	239.129505
2-Methylbiphenyl	-502.6558086	0.211736		
Protonated 2-Methylbiphenyl	-502.9815992	0.223251	197.3561215	195.008259
3-Methylbiphenyl	-502.6597677	0.211514		
Protonated 3-Methylbiphenyl	-502.9729275	0.221662	190.2710148	197.90028
Benzoquinuclidine	-481.7715761	0.220585		
Protonated Benzoquinuclidine	-482.1572499	0.235839	232.6337359	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.3912228	0.280807		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.7723472	0.29652	229.4964925	232.293819

N,N- diethylnicotinamide	-574.2696275	0.231334		
Protonated N,N- diethylnicotinamide	-574.631972	0.243952	219.6158526	224.884509
3-hexen-2-one	-309.8976573	0.147831		
Protonated 3-hexen-2-one	-310.2429989	0.160249	209.0691765	206.887056
3-chloro-pyridine-1-oxide	-783.0592778	0.083725		
Protonated 3-chloro-pyridine	-783.4117343	0.09565	213.8372155	215.634822
Niacinamide	-417.0184526	0.117275		
Protonated Niacinamide	-417.3795696	0.131635	217.773864	219.482883
1-methyl-3,5-dinitropyrazole	-674.5273649	0.103304		
Protonated 1-methyl-3,5-dinitropyrazole	-674.8182469	0.114037	175.9313404	188.531088
Piperidine	-251.9283119	0.160297		
Protonated Piperidine	-252.3073106	0.17608	228.1195012	228.01554

Table S9. Calculated and experimental proton affinity using RB3LYP/6-31G // RB3LYP/3-21G model chemistry

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. PA (kcal/mol)
Acetone	-193.0993357	0.084521		
Protonated Acetone	-193.4200074	0.096236	194.0208556	194.07612
p-anisidine	-402.0173285	0.150044		
Protonared p-anisidine	-402.3792924	0.164827	218.0450577	215.180703
Methyl nicotinate	-476.0145049	0.132158		
Protonated Methyl nicotinate	-476.338158	0.143154	196.3340813	221.227656
1,3-Diazine	-264.2336909	0.077162		
Protonated 1,3-Diazine	-264.5944932	0.090956	217.9245414	211.715058
1H-Imidazole	-226.1415607	0.071292		
Protonated 1H-Imidazole	-226.5297714	0.085836	234.6624948	225.338628
2,4(1H,3H)-Pyrimidinedithione (Dithiouracil)	-1060.610545	0.083544		
Protonated 2,4(1H,3H)-Pyrimidinedithione	-1060.937585	0.092125	199.9450917	217.833714
2-Propenamide	-247.2247002	0.080108		
Protonated 2-Propenamide	-247.5695893	0.092646	208.7113949	208.106007
3-Aminopyrazole	-281.4605638	0.086534		
Protonated 3-Aminopyrazole	-281.8480433	0.100942	234.2873355	220.247715
Acetamide, N-hydroxy-N-methyl	-323.5786068	0.105389		
Protonated Acetamide, N-hydroxy-N-methyl	-323.9243246	0.117582	209.443733	209.420562

Aziridine, 2-methyl	-173.1777664	0.098015		
Protonated Aziridine, 2-methyl	-173.561251	0.112693	231.6143274	223.426548
Aziridine, 1-methyl (N-Methylaziridine)	-173.1682246	0.097844		
Protonated Aziridine, 1-methyl	-173.5517348	0.112971	231.354167	223.426548
1H-Pyrazole	-226.12651	0.071145		
Protonated 1H-Pyrazole	-226.4922843	0.084651	221.2217923	213.698841
Isoxazole	-245.9487277	0.057503		
Protonated Isoxazole	-246.2889801	0.070767	205.3551677	202.823886
L-Cysteine	-721.7888937	0.106506		
Protonated L-Cysteine	-722.0854516	0.116893	179.7059551	215.873832
N-Methylglycine	-323.6185035	0.107332		
Protonated N-Methylglycine	-323.9943178	0.122359	226.5863389	220.176012
Oxazole	-245.9780368	0.058118		
Protonated Oxazole	-246.3333341	0.071887	214.4854886	209.468364
Propylen oxide (2-Methyloxirane)	-193.043083	0.085564		
Protonated Propylen oxide (2-Methyloxirane)	-193.3631626	0.097329	193.6185169	191.996733
1H-Imidazole,1-methyl-	-265.4408226	0.09923		
Protonated 1H-Imidazole,1-methyl-	-265.836366	0.113649	239.340844	229.353996

1H-Imidazole,2-methyl	-265.4555065	0.099324		
Protonated 1H-Imidazole,2-methyl	-265.8520649	0.113683	240.0146362	230.262234
1H-Pyrazole, 3-methyl	-265.4383328	0.099122		
Protonated 1H-Pyrazole, 3-methyl	-265.8122809	0.112409	226.4857574	216.54306
1-methyl-5-aminopyrazole	-320.7626766	0.114901		
Protonated 1-methyl-5-aminopyrazole	-321.1547562	0.129057	237.3290308	226.939995
1-methylcyclopropene	-155.899368	0.085286		
Protonated 1-methylcyclopropene	-156.262394	0.096718	220.7731379	204.59256
1-methylpyrazol-3-amine	-320.7665251	0.11485		
Protonated 1-methylpyrazol-3-amine	-321.127427	0.1304	216.9066988	224.047974
2-butenamide	-286.5370466	0.108661		
Protonated 2-butenamide	-286.8902297	0.12095	214.0692754	212.025771
Asparagine	-492.2797987	0.135263		
Protonated Asparagine pnmiddle	-492.6694615	0.149653	235.6684781	222.04029
Butyrolactone	-306.3909774	0.098806		
Protonated Butyrolactone	-306.7125138	0.110703	194.4514993	200.7684
cyclobutanone	-231.1593411	0.091471		
Protonated cyclobutanone	-231.4740479	0.102893	190.4579579	191.805525
cyclobutene	-155.931857	0.08718		

Protonated cyclobutene	-156.2322443	0.094992	183.6931969	187.479444
cyclopropanecarboxylic acid	-306.3686757	0.096969		
Protonated cyclopropanecarboxylic acid	-306.6671541	0.105366	182.1353879	196.322814
Cytosine	-394.8056465	0.099105		
Protonated Cytosine	-395.1961746	0.113866	235.983177	227.035599
Furan, 2,3-dihydro-	-231.1542529	0.093197		
Protonated Furan, 2,3-dihydro-	-231.4724842	0.104871	192.5146598	207.197769
Methacrylamide	-286.5324437	0.108268		
Protonated Methacrylamide	-286.8750231	0.120823	207.2516061	210.424404
Pyrrolidine	-212.5205427	0.130299		
Protonated Pyrrolidine	-212.9087659	0.145583	234.2150731	226.653183
1,2-Diamethylimidazole	-304.753857	0.127252		
Protonated 1,2-Diamethylimidazole	-305.1568081	0.141623	244.0188331	235.353147
1,5-dimethylimidazole	-304.7519074	0.127474		
Protonated 1,5-dimethylimidazole	-305.1534106	0.141777	243.1521129	233.656176
2-Aminopyridine	-303.5665044	0.106174		
Protonated 2-Aminopyridine	-303.9172316	0.120383	211.3469291	226.390272
2-bromo-pyridine	-2819.187772	0.07958		
Protonated 2-bromo-pyridine	-2819.557335	0.093881	223.1101284	216.256248

2-chloro-pyridine	-707.7924112	0.079763		
Protonated 2-chloro-pyridine	-708.1573235	0.09397	220.2496049	215.324109
2-fluoro-pyridine	-347.4338699	0.081665		
Protonated 2-fluoro-pyridine	-347.7950133	0.095673	218.0069891	211.428246
3-bromo-pyridine	-2819.186413	0.079865		
Protonated 3-bromo-pyridine	-2819.557419	0.094008	224.1132725	217.4991
3-fluoro-pyridine	-347.4260853	0.081656		
Protonated 3-fluoro-pyridine	-347.7936431	0.095918	221.8758745	215.58702
4-aminopyridine	-303.5665044	0.106174		
Protonated 4-aminopyridine	-303.9562574	0.120826	235.5638554	234.158097
4-Bromo-pyridine	-2819.186716	0.079875		
Protonated4-Bromo-pyridine	-2819.561592	0.094134	226.4699038	219.363378
4-fluoro-pyridine	-347.4284271	0.081645		
Protonated 4-fluoro-pyridine	-347.7998982	0.096026	224.2583269	218.240031
Acetamide,N-ethyl	-287.7571712	0.131781		
Protonated Acetamide,N-ethyl	-288.1123881	0.144767	214.9166978	214.63098
Cyclobutane carboxylic acid	-345.6738927	0.126197		
Protonated Cyclobutane carboxylic	-345.984214	0.13727	187.9207004	195.366774

Morpholine	-287.7020083	0.13508		
Protonated Morpholine	-288.0776901	0.150359	226.3481378	220.916943
Piperazine	-267.8449998	0.148006		
Protonated Piperazine	-268.2321051	0.162987	233.7000055	225.553737
Purine	-411.7919035	0.094973		
Protonated Purine	-412.1646775	0.108915	225.3460147	219.913101
Threonine	-438.1207413	0.140481		
Protonated Threonine	-438.432235	0.150677	189.1959656	220.486725
(E)-Dimethylamino acrylonitirle	-304.7277774	0.125966		
Protonated (E)-Dimethylamino acrylonitrile	-305.0925887	0.137097	222.0786235	214.344168
1-hexyne	-234.5411419	0.143729		
Protonated 1-hexyne free	-234.8574157	0.152769	192.9067772	191.160198
1-Methylcyclopentene	-234.5915613	0.146059		
Protonated 1-Methylcyclopentene	-234.9217204	0.155363	201.4576576	195.151665
2-hexyne	-234.5521502	0.143754		
Protonated 2-hexyne pctome	-234.8668109	0.15323	191.6263378	192.665961
2-propenamide N,N-dimethyl	-325.8145725	0.136773		
Protonated 2-propenamide N,N-dimethyl	-326.1759209	0.149252	219.0763225	216.136743
3-pyridinecarbonitrile	-340.4244783	0.088307		

Protonated 3-pyridinecarbonitrile	-340.7452519	0.099041	194.6882524	209.61177
4-pyridinecarbonitrile	-340.4232326	0.088336		
Protonated 4-pyridinecarbonitrile	-340.7390723	0.099301	191.4500467	210.472206
cyclohexanone	-309.7981108	0.152229		
Protonated cyclohexanone	-310.1298858	0.163891	201.0210122	201.00741
Cyclohexene oxide	-309.7551961	0.152559		
Protonated Cyclohexene oxide	-310.0890659	0.16387	202.5514371	202.704381
Isoquinoline	-401.8253416	0.136839		
Protonated Isoquinoline	-402.2174543	0.151175	237.2390487	227.465817
L-proline	-401.0183641	0.144606		
Protonated L-proline poan	-401.4010941	0.159257	231.1573729	220.008705
nicotinamide	-416.8660854	0.116654		
Protonated nicotinamide	-417.2084976	0.128982	207.2863411	219.482883
N-Methylpyrrolidine	-251.816662	0.158423		
Protonated N-Methylpyrrolidine	-252.2111313	0.17416	237.8559283	230.788056
p-benzoquinone	-381.3408864	0.086189		
Protonated p-benzoquinone	-381.657475	0.098038	191.37612	190.992891
1-methylbenzotriazole	-435.0441137	0.134132		
Protonated 1-methylbenzotriazole	-435.4241625	0.148346	229.7437668	222.566112

2,2-dimethyltetrahydrofuran	-311.0015555	0.173896		
Protonated 2,2-dimethyltetrahydrofuran	-311.3481271	0.185894	210.0994809	202.608777
3-aminobenzoic acid	-476.04426	0.132103		
Protonated 3-aminobenzoic acid	-476.3910669	0.146305	208.8911334	206.671947
Acetylpyrrolidine	-365.148073	0.168557		
Protonated Acetylpyrrolidine	-365.5143353	0.181274	222.0134509	221.179854
benzimidazole	-379.7584952	0.119391		
Protonated benzimidazole	-380.1506215	0.133869	237.1601895	227.967738
benzoxazole	-399.5977693	0.106279		
Protonated benzoxazole	-399.9613335	0.120033	219.6823363	213.101316
Cinnoline	-417.8101429	0.12359		
Protonated Cinniloine	-418.1945368	0.138072	232.3055229	223.785063
Hexahydroazepine	-291.1244153	0.189397		
Protonated Hexahydroazepine	-291.5133276	0.204926	234.4967841	228.660867
Quinoxaline	-417.8434898	0.124712		
Protonated Quinoxaline	-418.215009	0.138644	224.5647689	216.017238
Triglycine	-700.2184392	0.190182		
Protonated Triglycine	-700.6046756	0.204361	233.6481332	231.074868

2,3-Cyclopentenopyridine	-364.9274994	0.15408		
Protonated 2,3-Cyclopentenopyridine	-365.3194083	0.168401	237.1203927	228.852075
2,3-Dihydroindole	-364.9282287	0.153836		
Protonated 2,3-Dihydroindole	-365.3005909	0.168971	224.35364	228.756471
Benzoic acid, 2-methyl	-460.0086175	0.144204		
Protonated Benzoic acid, 2-methyl	-460.3392722	0.155378	200.6181886	200.481588
Benzoic acid, 3-methyl	-459.9997969	0.142733		
Protonated Benzioc acid, 3-methyl	-460.3369463	0.154522	204.3154009	198.330498
o-Xylene	-310.8146243	0.157596		
Protonated o-Xylene	-311.137495	0.167596	196.4558011	190.25196
P-Xylene	-310.8149108	0.156883		
Protonated P-Xylene pc close to me	-311.1368228	0.167088	195.7281619	189.869544
2,2,6,6-Tetramethyl-piperidine	-409.0546149	0.272699		
Protonated 2,2,6,6-Tetramethyl-piperidine	-409.4540038	0.287827	241.3177794	235.90287
cyclooctanone	-388.3966663	0.211753		
Protonated cyclooctanoone	-388.7326958	0.223398	203.701226	203.015094
Cytidine	-890.8464721	0.236541		
Protonated Cytidine	-891.2287384	0.249684	231.7941705	234.827325
Deoxycytidine	-815.6599722	0.232901		

Protonated Deoxycytidine	-816.042097	0.245893	231.7982571	236.237484
N,3,5-Trimethylpiperidine	-369.7450548	0.244493		
Protonated N,3,5-Trimethylpiperidine	-370.1397729	0.260024	238.1388087	233.775681
Naphthalene	-385.807579	0.148826		
Protonated Naphthalene	-386.1364529	0.15975	199.6545326	191.901129
1,8-Diaminonaphthalene	-496.4793462	0.182449		
Protonated 1,8-Diaminonaphthalene	-496.8646121	0.194762	234.1871048	225.744945
1-methyl-3-phenylpyrazole	-496.4395406	0.180955		
Protonated 1-methyl-3-phenylpyrazole	-496.8223183	0.194309	231.9852277	222.900726
Acridine	-555.4330824	0.184109		
Protonated Acridine	-555.8352231	0.198556	243.4635191	232.461126
Anthracene	-539.4102699	0.195591		
Protonated Anthracene	-539.7461076	0.206457	204.0601576	209.683473
Coronene	-921.6884272	0.281091		
Protonated Coronene	-922.0381666	0.292355	212.5388565	205.859313
Phenazine	-571.4515878	0.171887		
Protonated Phenazine	-571.8373638	0.185882	233.4724535	224.286984
Picene	-846.6367234	0.290254		
Protonated Picene	-846.9775535	0.301165	207.1652483	203.469213

Piperidine, 1-phenyl	-482.832606	0.242309		
Protonated Piperidine, 1-phenyl	-483.2139019	0.256959	230.2581021	227.752629
Pyrene	-615.6346813	0.208606		
Protonated Pyrene	-615.9638796	0.218986	200.1927939	207.747492
2,3-Dimethylimidazo-1,2-a,pyridine	-458.3612849	0.174503		
Protonated 2,3-Dimethylimodazole	-458.7719031	0.189141	248.6658353	238.579782
2,5-Dimethylimidazo-1,2-a,pyridine	-458.3626505	0.174561		
Protonated 2,5-Dimethylimidazole-1,2-a,pyridine	-458.7727607	0.189079	248.4208725	238.149564
2,7-Dimethylimidazo-1,2-a,pyridine	-458.3590824	0.174021		
Protonated 2,7-Dimethylimidazole	-458.7701785	0.188577	249.0161254	239.129505
2-Methylbiphenyl	-502.5081248	0.210884		
Protonated 2-Methylbiphenyl	-502.8383379	0.222032	200.3571164	195.008259
3-Methylbiphenyl	-502.5124694	0.21073		
Protonated 3-Methylbiphenyl	-502.8287639	0.22056	192.4337972	197.90028
Benzoquinuclidine	-481.613621	0.220446		
Protonated Benzoquinuclidine	-482.0094142	0.235451	239.137057	234.181998
Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.2320287	0.280944		
Protonated Hydrazine, 1,2- dimethyl-1,2-dipropyl	-426.6171649	0.296577	232.0631986	232.293819

N,N- diethylnicotinamide	-574.0644717	0.231055		
Protonated N,N- diethylnicotinamide	-574.4281518	0.243363	220.6446402	224.884509
3-hexen-2-one	-309.78836	0.148027		
Protonated 3-hexen-2-one	-310.1283104	0.159672	206.1616885	206.887056
3-chloro-pyridine-1-oxide	-782.9265795	0.083282		
Protonated 3-chloro-pyridine	-783.2777873	0.095154	213.0863067	215.634822
Niacinamide	-416.8660854	0.116654		
Protonated Niacinamide	-417.2390137	0.130534	225.4810137	219.482883
1-methyl-3,5-dinitropyrazole	-674.2420312	0.10155		
Protonated 1-methyl-3,5-dinitropyrazole	-674.5443503	0.112431	183.0173021	188.531088
Piperidine	-251.8335027	0.160072		
Protonated Piperidine	-252.2218326	0.175533	234.1731442	228.01554

Table S10. Calculated proton affinity and experimental pK_as of violuric acid using RB3LYP/6-311+G (2df, p) // RB3LYP/6-31+G (d, p) model chemistry

Name	**Energy**	**ZPE**	**PA (Kcal/mol)**	**Exp. pKa**
violuric acid	-619.5817535	0.088984		
1st	-619.0657791	0.074864	315.0977328	4.23
2nd	-618.3759174	0.061287	424.5496551	9.62
3rd	-617.524315	0.0483	526.4083064	13.1

Table S11. Calculated proton affinity and experimental pK_as of amiloride and its derivatives using RB3LYP/6-311+G (2df, p) // RB3LYP/6-31+G (d, p) model chemistry

No	R^1	R^2	Energy	ZPE	Cal. PA (Kcal/mol)	Exp. pK_a
1	NH_2	H	-692.8287897	0.175745		
			-693.2160242	0.189644	234.4466822	9.3
2	NH_2	SC_6H_5	-1322.170704	0.257356		
			-1322.559733	0.270776	235.8670056	9
3	$N(CH_3)_2$	Cl	-1231.082568	0.222434		
			-1231.467848	0.236056	233.3905321	8.76
4	NH_2	F	-792.1084056	0.167438		
			-792.4919386	0.181695	231.9036869	9
5	NH_2	Cl	-1152.460399	0.165747		
			-1152.842674	0.180078	231.0690356	8.7
6	NH_2	SCF_3	-1428.203405	0.181176		
			-1428.593066	0.195043	235.9892725	8.22
7	CH_3O	Cl	-1211.628146	0.181344		
			-1212.005619	0.195425	228.2090533	8.25
8	SCH_3	Cl	-1534.607465	0.177697		
			-1534.985119	0.19161	228.4260482	8.05
9	H	Cl	-1097.065203	0.149248		

			-1097.43609	0.163211	224.1488416	7.01
10	OH	Cl	-1172.329023	0.153879		
			-1172.702314	0.167801	225.6827385	5.45
11	SH	Cl	-1495.289624	0.148201		
			-1495.663241	0.162133	225.8807565	4
12	Cl	Cl	-1556.691701	0.13935		
			-1557.059429	0.153328	222.1577333	6.6

Table S12. Experimental pK_a and calculated proton affinities of carboxylic acid molecules

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp. pKa
2-Acetylbenzoic acid	-573.6556038	0.152076		
	-573.1187034	0.138706	328.6906193	4.13
2,2-Dibromopropanoic acid	-5415.568153	0.070573		
	-5415.037054	0.056999	324.9247752	1.48
2,2-Dimethylpropanoic acid	-347.1424481	0.146178		
	-346.592779	0.132241	336.3544293	5.031
2,3-Dimethylbenzoic acid	-499.6218847	0.171032		
	-499.0691228	0.156469	337.9100392	3.771
2,4-Dichlorophenoxyacetic acid	-1454.763857	0.127988		
	-1454.240805	0.1152	320.3585165	2.64
2,4-Dinitrobenzoic acid	-830.0998586	0.119563		
	-829.5830859	0.105924	315.8945991	1.43
2,5-Dimethylbenzoic acid	-499.6257357	0.170564		
	-499.0714416	0.156308	339.0604685	3.99
2,5-Dinitrobenzoic acid	-830.0937374	0.119731		
	-829.5806888	0.105869	313.4204565	1.62
2,6-Dimethylbenzoic acid	-499.619272	0.17073		
	-499.0713253	0.156296	334.9678188	3.362

2,6-Dimethylphenoxyacetic acid	-614.1681822	0.202324		
	-613.6333395	0.189353	327.6448826	3.356
2,6-Dinitrobenzoic acid	-830.0928349	0.119497		
	-829.5679971	0.105638	320.8202222	1.14
(E)-2-Methylcinnamic acid	-537.7136724	0.17661	0	
	-537.167075	0.162985	334.6188204	4.5
(E)-3-Methylcinnamic acid	-537.7274834	0.17619		
	-537.1712613	0.161939	340.2734009	4.442
(E)-4-Methylcinnamic acid	-537.7167652	0.175581		
	-537.170946	0.161898	334.0947952	4.564
trans-cinnamic acid	-498.3979129	0.148917		
	-497.8426415	0.134755	339.7315515	4.438
2-Allylpropionic acid	-385.2430905	0.152069		
	-384.6845356	0.137873	341.7711159	4.72
2-Benzoylbenzoic acid	-765.4508539	0.205617		
	-764.9130845	0.191868	329.0027621	3.54
2-Biphenylcarboxylic acid	-652.08542	0.195939		
	-651.5379335	0.182101	335.0456787	3.46

2-Bromo-2-phenylacetic acid	-3033.826861	0.134744		
	-3033.290316	0.120948	328.2056427	2.21
2-Bromobenzoic acid	-2994.499897	0.107051		
	-2993.956834	0.092108	331.5897437	2.85
2-Chloro-3-nitrobenzoic acid	-1085.147025	0.107697		
	-1084.618374	0.093848	323.2191424	2.02
2-Chloro-4-nitrobenzoic acid	-1085.15796	0.107789		
	-1084.634734	0.093921	319.8035673	1.96
2-Chloro-5-nitrobenzoic acid	-1085.159152	0.10789		
	-1084.631808	0.094055	322.4075796	2.17
2-Chloroisocrotonic acid	-766.2147685	0.085913		
	-765.672833	0.07222	331.6515156	2.8
2-Chlorophenoxyacetic acid	-995.1465741	0.138238		
	-994.6050029	0.124673	331.5016939	3.05
2-Chlorophenylacetic acid	-919.9101116	0.133614		
	-919.3692227	0.120123	331.1190967	4.066
2-Chloropropanoic acid	-728.1222996	0.081575		
	-727.5785745	0.067867	332.7652965	2.84

2-Ethylbenzoic acid	-499.6204472	0.171928		
	-499.0690122	0.157799	337.3444903	3.79
2-Fluoroacrylic acid	-366.5344265	0.059309		
	-365.9910614	0.045809	332.6673814	2.55
2-Fluorobenzoic acid	-520.2379858	0.107294		
	-519.6885564	0.093122	336.0594356	3.27
2-Fluorophenoxyacetic acid	-634.7911041	0.139376		
	-634.2540264	0.126196	328.9187494	3.08
2-Hydroxy-3-methylbenzoic acid	-535.5560589	0.147823		
	-535.0275581	0.13239	322.1504748	2.99
2-Hydroxy-5-methylbenzoic acid	-535.5346539	0.146245		
	-534.9862892	0.132211	335.4762549	4.08
2-Hydroxy-6-methylbenzoic acid	-535.5504518	0.147819		
	-535.0222757	0.1319	321.6477156	3.32
2-Methylbutanoic acid	-347.1420342	0.146963		
	-346.5910681	0.13305	337.1831186	4.761
2-Methylpentanoic acid	-386.4678519	0.175438		
	-385.9171482	0.161347	336.9089439	4.782

2-Nitrobenzoic acid	-625.5315126	0.117535		
	-624.9945595	0.103657	328.4111841	2.18
2-Phenoxybenzoic acid	-727.3236458	0.199924		
	-726.7761544	0.185664	334.7892155	3.53
2-tert-Butylbenzoic acid	-578.2570095	0.227833		
	-577.7106588	0.213746	334.1798195	3.57
3-Acetoxybenzoic acid	-648.9272825	0.156741		
	-648.3802548	0.142984	334.8076076	4
3-Aminobenzoic acid	-476.3497451	0.132063		
	-475.795113	0.11834	339.6004327	4.79
3-Bromomandelic acid	-3109.07105	0.138253		
	-3108.52847	0.124455	331.9909855	3.13
3-Bromopropanoic acid	-2842.039899	0.08159		
	-2841.498449	0.067792	331.2827216	3.992
3-Butenoic acid	-306.5848217	0.095449		
	-306.0364239	0.081496	335.5467754	4.68
3-Chlorobenzoic acid	-880.5964652	0.105889		
	-880.0527554	0.09208	332.6936227	3.83
3-Chlorolactic acid	-803.3645582	0.086384		

	-802.8236961	0.072803	331.0468691	3.12
3-Chloromandelic acid	-995.1630829	0.138418	0	
	-994.636784	0.125377	322.2403884	3.237
3-Chlorophenoxyacetic acid	-995.1511001	0.138171	0	
	-994.6109583	0.124463	330.5167208	3.07
3,4-Dinitrobenzoic acid	-830.096978	0.119695		
	-829.5785456	0.106107	316.967481	2.82
3,5-Dimethylbenzoic acid	-499.6293537	0.17003		
	-499.0749211	0.156056	339.3208569	4.302
3,5-Dinitrobenzoic acid	-830.1114345	0.119748		
	-829.5930593	0.106118	316.9057167	2.85
3-Chloropropanoic acid	-728.1181282	0.081607		
	-727.5810422	0.068183	328.7739091	3.992
3-Fluorobenzoic acid	-520.2432416	0.107225		
	-519.6976686	0.093414	333.8615174	3.865
3-Fluorophenoxyacetic acid	-634.7979481	0.139502		
	-634.2570779	0.12584	331.0021021	3.08
3-Hydroxybenzoic acid	-496.2114162	0.119063		
	-495.6690706	0.105487	331.9808716	4.076

3-Methylpentanoic acid	-386.4776467	0.175416		
	-385.9179758	0.161376	342.5674187	4.766
3-Phenoxybenzoic acid	-727.3204087	0.199493		
	-726.7841774	0.18607	328.2381403	3.95
4-Chlorobutanoic acid	-767.452954	0.110476		
	-766.9023305	0.096619	337.0025516	4.5
4-Chlorophenoxyacetic acid	-995.1504927	0.138072		
	-994.6105944	0.124456	330.4205739	3.1
4-Ethylbenzoic acid	-499.6246258	0.17174		
	-499.07001	0.15774	339.4198436	4.35
4-Fluorobenzoic acid	-520.2337179	0.106792		
	-519.6971693	0.093464	328.4956817	4.14
4-Fluorophenoxyacetic acid	-634.7968337	0.139541		
	-634.2543297	0.125748	331.9467346	3.13
4-Fluorophenylacetic acid	-559.5655009	0.135046		
	-559.0177358	0.12147	335.3817172	4.25
2,4-Dimethylbenzoic acid	-499.6267188	0.170532		
	-499.0712688	0.156228	339.7563149	4.217

4-Hydroxybenzoic acid	-496.2242747	0.119633		
	-495.6700197	0.105671	339.2168138	4.582
4-Nitrobenzoic acid	-625.5434512	0.117848		
	-625.0118054	0.104159	325.1970094	3.441
4-Phenoxybenzoic acid	-727.332749	0.199915		
	-726.7841221	0.186062	335.7521296	4.52
4-tert-Butylbenzoic acid	-578.2728767	0.227667		
	-577.7192469	0.21369	338.8152564	4.389
Acetic acid	-229.1668181	0.061322		
	-228.6125793	0.047929	339.5566725	4.756
Acrylic acid	-267.2664267	0.06736		
	-266.7086694	0.053574	341.5228681	4.26
Allylacetic acid	-345.9169808	0.124075		
	-345.3612764	0.109842	339.9595797	4.68
Benzilic acid	-766.6428561	0.227982		
	-766.098604	0.214134	333.0099273	3.09
Benzoic acid	-420.9704261	0.115566		
	-420.4182797	0.101712	337.9600756	4.204
Bromopropynoic acid	-2840.790137	0.057182		

	-2840.261626	0.044109	323.609197	1.855
Butyric acid	-307.8191887	0.118479		
	-307.2655556	0.104797	338.9988206	4.817
Chloroacetic acid	-688.7900727	0.053263		
	-688.2510911	0.039811	329.9461642	2.867
cis-2-Butenoic acid	-306.5952364	0.095507		
	-306.0369299	0.081628	341.8102744	4.44
cis-3-Methyl-2-pentenoic acid	-385.2454701	0.151823		
	-384.6920382	0.138107	338.8516164	5.15
cis-cinnamic acid	-498.3862063	0.148965		
	-497.8395704	0.135186	334.5482578	3.879
Cyclohexanecarboxylic acid	-424.595913	0.185027		
	-424.0355044	0.170675	342.8383471	4.9
Heptanoic acid	-425.8049497	0.204133		
	-425.2436639	0.190039	343.5475637	4.893
Propanoic acid	-268.4934338	0.090029		
	-267.9392101	0.076463	339.4407492	4.874

Table S13. Experimental pK_a and calculated proton affinities of phenolic molecules

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp.pKa
2-Bromophenol	-2881.118668	0.095378		
	-2880.563634	0.081286	339.6257245	8.452
2-Chlorophenol	-767.2043029	0.095231		
	-766.64757	0.08127	340.772305	8.55
2-Ethoxyphenol	-461.4712866	0.165624		
	-460.8974715	0.150858	350.9965533	10.109
2-Fluorophenol	-406.8483017	0.096562		
	-406.2875401	0.082362	343.1533687	8.73
2-Methoxyphenol	-422.1400125	0.137471		
	-421.5665418	0.122837	350.8616181	9.99
2-Phenylphenol	-538.6999923	0.185628		
	-538.1430541	0.171463	340.7757114	9.55
3-(Diethoxyphosphinyl)phenol	-1032.704352	0.242604		
	-1032.15434	0.228668	336.5702898	8.66
3-(S-Methylthio)phenol	-745.1193183	0.132934		
	-744.5620701	0.11906	341.149212	9.53
2,3-Dimethylphenol	-386.232166	0.159663		
	-385.6660275	0.145255	346.3996037	10.5

2,4-Dichlorophenol	-1226.829473	0.08556		
	-1226.282653	0.071862	334.7138357	7.85
2,4-Dimethylphenol	-386.233644	0.1594		
	-385.6666021	0.144945	346.9375416	10.58
2,5-Dimethylphenol	-386.2343298	0.15933		
	-385.6684957	0.145082	346.3069553	10.22
2,6-Dimethyl-4-cyanophenol	-478.5088208	0.158431		
	-477.9735898	0.144809	327.4880298	8.27
2,6-Dimethyl-4-nitrophenol	-590.8139924	0.162367		
	-590.2879476	0.14896	321.8557512	7.19
2,6-Dimethylphenol	-386.2340045	0.159717		
	-385.6701628	0.145403	345.0160696	10.59
3-Bromophenol	-2881.116539	0.095106		
	-2880.565675	0.081152	337.0939953	9.031
3-Chlorophenol	-767.2026117	0.094933		
	-766.6501237	0.081081	338.1756546	9.1
3-Ethoxyphenol	-461.4693897	0.16505		
	-460.9056612	0.151012	345.1148221	9.655

3-Fluorophenol	-406.8492459	0.096343		
	-406.2934408	0.082358	340.1754018	9.29
3-Methoxyphenol	-422.1381889	0.136912		
	-421.5749202	0.122886	344.8337071	9.652
3-Methylsulfonylphenol	-895.5941968	0.14224		
	-895.0508974	0.128344	332.3825652	9.33
3-Phenylphenol	-538.700105	0.185399		
	-538.1405491	0.171385	342.5112157	9.63
4-(Diethoxyphosphinyl)phenol	-1032.70618	0.242613		
	-1032.16328	0.229043	332.3321818	8.28
4-(S-Methylthio)phenol	-745.1196212	0.133012		
	-744.5660116	0.119148	338.8720998	9.53
3,4-Dimethylphenol	-386.2325409	0.159499		
	-385.6641417	0.145048	347.7917051	10.32
3,4-Dinitrophenol	-716.707652	0.109144		
	-716.2008093	0.096032	309.9875578	5.424
3,5-Dibromophenol	-5454.656227	0.085511		
	-5454.117931	0.071851	329.3878883	8.056
3,5-Dichlorophenol	-1226.828365	0.085267		

	-1226.28741	0.071599	331.0518831	8.179
3,5-Dimethoxyphenol	-536.7017775	0.1692		
	-536.135341	0.154732	346.5496082	9.345
3,5-Dimethyl-4-cyanophenol	-478.5098526	0.15805	0	
	-477.9705445	0.144748	330.2433636	8.21
3,5-Dimethyl-4-nitrophenol	-590.8049941	0.162558		
	-590.27202	0.149685	326.5325301	8.245
3,5-Dimethylphenol	-386.2341783	0.159028		
	-385.6669153	0.144846	347.2442745	10.15
3,5-Dinitrophenol	-716.7207554	0.109172		
	-716.2022689	0.095695	317.0697332	6.732
4-Bromophenol	-2881.115914	0.094984		
	-2880.563125	0.081263	338.4451687	9.34
4-Chloro-3-methylphenol	-806.5316268	0.122449		
	-805.9753075	0.108577	340.5675616	9.549
4-Chlorophenol	-767.2018554	0.094905		
	-766.6472888	0.081096	339.5065139	9.43
4-Cyano-2,6-dimethylphenol	-478.5088208	0.158431		
	-477.9735898	0.144809	327.4880348	8.27

4-Cyano-3,5-dimethylphenol	-478.5098526	0.15805		
	-477.9705445	0.144748	330.2433636	8.21
4-Fluorophenol	-406.8472872	0.096156		
	-406.2863947	0.082275	343.4317919	9.89
4-Hydroxypteridine	-525.4446213	0.105126		
	-524.9137391	0.091252	324.6040261	7.89
4-Methoxyphenol	-422.1357991	0.136732		
	-421.5664929	0.122505	348.4986446	10.2
4-Methylsulfonyl-3,5-dimethylphenol	-974.2423133	0.197971		
	-973.7031337	0.184445	330.0249026	8.13
4-Methylsulfonylphenol	-895.5956506	0.14234		
	-895.0599086	0.128822	327.8726898	7.83
4-Nitrosophenol	-436.9138511	0.101401		
	-436.3885164	0.088466	321.7005652	6.48
4-Phenylphenol	-538.6999647	0.185395		
	-538.1462386	0.171508	338.9309925	9.55
m-Cresol	-346.9048413	0.131725		
	-346.3383812	0.117685	346.8277619	10

o-Cresol	-346.9051385	0.13214		
	-346.3401023	0.11798	345.8603558	10.26
p-Cresol	-346.903863	0.131654		
	-346.3362815	0.117423	347.4139545	10.26

Table S14. Experimental pK_a and calculated proton affinities of nitrogen base molecules

Name	Energy	ZPE	Cal. PA (kcal/mol)	Exp.pKa
2-Hydroxypyrimidine	-339.6772624	0.081883		
	-339.9657552	0.092861	174.2812952	2.24
3-Hydroxypyridine	-327.2337424	0.163324		
	-327.5485045	0.174428	190.688329	4.8
3-Methoxycarbonylpyridine	-476.3046822	0.131049		
	-476.6165589	0.141632	189.1981764	3.13
4-Ethoxypyridine	-402.2627649	0.149611		
	-402.5637302	0.160903	181.9148815	6.67
4-Hydroxypteridine	-525.4446173	0.105126		
	-525.7236647	0.115425	168.7718836	1.3
4-Methoxycarbonylpyridine	-476.3037279	0.131016		
	-476.6079137	0.141663	184.3326763	2.38
Ethyl-3-pyridinecarboxylate	-515.6361186	0.159333		
	-515.9498088	0.170234	190.1405726	3.35
Glycine	-284.5402063	0.079576		
	-284.8335037	0.086086	180.0451431	2.341
2-aminobiphenyl	-518.8259864	0.198038		
	-519.1821611	0.212294	214.7364776	3.78

2-benzylpyridine	-518.8152634	0.197859		
	-519.1940768	0.211653	229.226905	5.13
Benzimidazole	-379.9889986	0.118212		
	-380.3657412	0.132251	227.7767026	5.53
2-tert-Butylpyridine	-405.6705841	0.200487		
	-406.0520163	0.214825	230.5355402	5.76
4-tert-Butylpyridine	-405.6684343	0.200992		
	-406.0481245	0.215028	229.6282228	5.99
2,3-Butanediamine	-269.250344	0.166715		
	-269.6313742	0.181457	230.0347807	6.91
2-bromoaniline	-2861.245421	0.107893		
	-2861.588414	0.122212	206.4256899	2.53
3-Aminobiphenyl	-518.8276696	0.197894		
	-519.177755	0.212164	210.9066804	4.18
4-Aminobenzonitrile	-379.9785882	0.115553		
	-380.3242362	0.127183	209.7463136	1.74
2-Chloroaniline	-747.3307555	0.106786		
	-747.6732249	0.121903	205.606339	2.64

2-Chloropyridine	-707.9946709	0.07909		
	-708.3518263	0.092908	215.62125	0.49
3-Chloropyridine	-707.9907949	0.079162		
	-708.350038	0.093081	216.8692341	2.84
4-Chloropyridine	-707.9919963	0.079193		
	-708.355271	0.093159	219.3702647	3.83
6-Chloro-o-toludine	-786.6607739	0.135544		
	-787.0056843	0.149433	207.8936454	3.62
5-Desoxypyridoxal	-515.6295011	0.157207		
	-515.9771433	0.170403	210.0342387	4.17
N,N-Dimethylglycine	-363.1650482	0.135003		
	-363.5141509	0.140756	215.5297763	2.146
N,N-Diethylaniline	-444.9833725	0.230427		
	-445.3601636	0.245214	227.3469958	6.56
N,N-Diethyl-o-toluidine	-484.3063946	0.25789		
	-484.689729	0.272784	231.3871565	7.18
2-Cyclohexyl-2-pyrroline	-446.1952521	0.255879		
	-446.5844783	0.270184	235.4467919	7.91
4-amino-3-bromomethylpyridine	-2916.621549	0.125007		

	-2917.00538	0.139099	232.1927593	7.47
2-Amino-3-mercapto-3-methylbutanoic acid	-800.728325	0.163367		
	-801.0684671	0.174397	206.6602964	1.8
DL-2-Amino-4-hydroxybutanoic acid	-438.4315921	0.141092		
	-438.7903917	0.155609	216.2230709	2.265
2-Amino-2-methylpropanoic acid	-363.197652	0.135974		
	-363.5519484	0.149855	213.7884682	2.357
2-Amino-5-methylpyridine	-343.0833301	0.132861		
	-343.4638964	0.146372	230.5010076	7.22
2-Amino-6-methylpyridine	-343.0873258	0.132764		
	-343.4686775	0.146284	230.9883367	7.41
2-Amino-3-hydroxybenzoic acid	-551.6023256	0.136078		
	-551.9527833	0.150631	210.9661655	2.5
2-Amino-4-methylpyridine	-343.0853985	0.132828		
	-343.4672691	0.146267	231.3638265	7.48
2-aminobenzoic acid	-476.3511782	0.13213		
	-476.6953404	0.146325	207.2358565	2.09
2-Aminopyridine	-303.7545317	0.105454		
	-304.130311	0.118999	227.4761507	6.71

4-Aminobenzoic acid	-476.353541	0.132003		
	-476.6975809	0.144249	208.3581721	2.41
2-aminobutanoic acid	-363.1916598	0.136232		
	-363.5454579	0.150879	213.0045307	2.286
Acridine	-555.7369344	0.182009		
	-556.1262906	0.195967	235.7418113	5.6
8-Aminoquinaldine	-496.7707627	0.179468		
	-497.1529051	0.193299	231.2931565	4.86
2-Ethoxyaniline	-441.5971121	0.177935		
	-441.9563036	0.192429	216.4831369	4.47
N-Ethylaniline	-366.3476242	0.173512		
	-366.7109024	0.188352	218.8346992	5.11
N,N-Dimethyl-o-toluidine	-405.6571039	0.200989		
	-406.0318888	0.215892	226.0166697	5.86
N,N-Dimethyl-p-toluidine	-405.6614869	0.200512		
	-406.0340653	0.215425	224.6258823	7.24
N-Ethylglycine	-363.1863695	0.136803		
	-363.546275	0.151046	217.0855778	2.34

S-Ethyl-L-cysteine	-800.7342106	0.166036		
	-801.0949323	0.179862	217.8543195	2.03
3Fluoropyridine	-347.6363255	0.080502		
	-347.9939551	0.094526	215.7921531	2.97
4-Fluorophenylalanine	-654.2561327	0.18107		
	-654.6084413	0.19523	212.3693848	2.13
Glycylalanylalanine	-779.3610537	0.247415		
	-779.710466	0.258401	212.5046818	3.38
L-Glutamine	-531.960262	0.163593		
	-532.3099075	0.17699	211.1676978	2.17
Glyoxaline	-226.2950066	0.071147		
	-226.6675657	0.085242	225.117068	7.03
Histidylhistidine	-1021.44247	0.296861		
	-1021.801029	0.308011	218.1431951	6.8
Homocysteine	-761.4069517	0.136143		
	-761.7487417	0.140729	211.6589163	2.523
N-Glycylsarcosine	-531.9356337	0.163891		
	-532.2863719	0.176792	212.1584987	2.98
2-Methoxyaniline	-402.2660216	0.149783		

	-402.6233362	0.164294	215.2948173	4.53
			0	
4-Methoxycarbonylaniline	-515.6466793	0.159341	0	
	-515.9928327	0.169186	211.1615781	2.38
8-Hydroxyquinazoline	-493.3574159	0.128666		
	-493.7190442	0.141579	218.9848936	3.41
Imidazole	-226.2950066	0.071147		
	-226.6675657	0.085242	225.117068	6.993
Isoasparagine	-492.6325969	0.135642		
	-492.9876694	0.148968	214.6169506	2.97
L-Leucine	-441.8440552	0.193231		
	-442.199771	0.207265	214.5850442	2.33
			0	
N-Isopropylaniline	-405.6746175	0.201483	0	
	-406.0418664	0.216223	221.3879638	5.5
4-Aminopyridine	-303.7487028	0.105374		
	-304.1385172	0.119867	235.7002092	9.114
1-Ethyl-2-methylpiperidine	-369.958809	0.242471		
	-370.3478135	0.258234	234.4106383	10.66
4-amino-3-methylpyridine	-343.0783784	0.133238		
	-343.4722742	0.147663	238.3032005	9.43

N,N-Diethylethylenediamine	-347.8788837	0.223173		
	-348.2645618	0.238554	232.558271	7.7
1-Butylpiperidine	-409.2803239	0.271637		
	-409.6703123	0.28769	234.8496738	10.43
2-Cyclohexylpyrrolidine	-447.4028328	0.279911		
	-447.7876792	0.295261	232.0554426	10.76
Di-sec-butylamine	-371.1722823	0.262093		
	-371.559725	0.277254	233.8009754	10.91
Dicyclohexylamine	-526.0625533	0.337548		
	-526.4529411	0.353526	235.1464403	11.25
3-Methoxyaniline	-402.2660783	0.14945		
	-402.5836037	0.160972	192.1651601	4.2
Aniline	-287.7028701	0.11693		
	-288.0492804	0.131354	208.505704	4.6
Dibutylamine	-371.1749737	0.262901		
	-371.5557768	0.278577	229.317654	11.25
Dipropylamine	-292.5235257	0.205989		
	-292.9022266	0.221668	227.9965821	10.91

2-Bromopyridine	-2821.907937	0.078881			
	-2822.266507	0.092843	216.4203527		0.71
2-chloro-6-nitroaniline	-951.9099229	0.109996			
	-952.2387409	0.123655	197.9368482	_2.41	
4-Chloro-2-nitroaniline	-951.9085882	0.10968			
	-952.2434844	0.122653	202.1730096	-1.11	
Acetamide	-209.298014	0.073433			
	-209.6355311	0.087133	203.3704705	_0.37	
2,4-Dichloro-6-nitroaniline	-1411.533069	0.100196			
	-1411.862725	0.112854	199.0788114	-3.00	
2,5-Dichloro-4-nitroaniline	-1411.522738	0.099303			
	-1411.839448	0.113832	189.8035599	-1.74	

Table S15. Calculated proton affinities use to predict experimental pK_a of carboxylic acid drugs

Name	Energy	ZPE	Cal. PA (kcal/mol)	Energy *slope	cal pka	Exp. pKa
Nalidixic	-800.000923	0.227737				
	-799.4304222	0.213004	348.9370128	38.38307141	5.653071405	5.94
Flumequine	-921.337044	0.240173				
	-920.7654327	0.225206	349.4899253	38.44389179	5.713891786	6.38
trans-Cinnamicacid	-498.3979127	0.148917				
	-497.8426421	0.134754	339.7304173	37.37034591	4.640345905	4.44
Naproxen	-767.8650547	0.250694				
	-767.3149659	0.236564	336.499025	37.01489276	4.284892755	4.2
Flurbiprofen	-830.0126682	0.24427				
	-829.4683688	0.230178	332.8894568	36.61784024	3.887840244	3.8
Probenecid	-1260.978884	0.312102				
	-1260.441041	0.298215	328.963985	36.18603835	3.456038349	3.4
Chlorambucil	-1670.860098	0.313418				
	-1670.304169	0.299274	340.1550378	37.41705416	4.687054155	5.75
Nicotinic acid (Niacin)	-437.010079	0.103725				
	-436.4655867	0.090166	333.3384442	36.66722886	3.937228865	4.76
Sulindac	-1496.432862	0.3216				
	-1495.893948	0.307194	329.3166657	36.22483323	3.494833228	4.03

Ethacrynic acid	-1724.201669	0.227239				
	-1723.667636	0.213902	326.9118541	35.96030395	3.230303947	3.5
Ketoprofen	-844.101262	0.262104				
	-843.5605531	0.248393	330.870751	36.39578261	3.665782608	4.02
Indomethacin	-1549.909582	0.313542				
	-1549.369895	0.300136	330.4169355	36.34586291	3.615862905	4.3
Hippuricacid	-629.0415355	0.170902				
	-628.5111344	0.157519	324.6041776	35.70645954	2.976459538	3.65
Salicylic acid	-496.2230035	0.11958				
	-495.6982639	0.105137	320.3993706	35.24393077	2.513930769	3.01
p-Aminohippuricacid	-684.4172282	0.187002				
	-683.8888594	0.174156	323.6592103	35.60251313	2.872513133	3.83
Diflunisal	-925.8954468	0.184318				
	-925.3752579	0.168597	316.7574095	34.84331504	2.113315042	3
Flufenamic acid	-1044.621538	0.216897				
	-1044.103753	0.203059	316.4078529	34.80486382	2.074863822	6.38
Furosemide *	-1808.247075	0.228609				
Furosemidedo	-1807.735631	0.213941	311.9178528	34.31096381	1.58096381	3.9
Furosemidedn	-1807.702669	0.215166	333.3562146	36.66918361	3.939183607	3.9

Table S16. Calculated proton affinities use to predict experimental pK_a of phenols, sulphonamide and amide

Name	Energy	ZPE	Cal. PA(kcal/mol)	Energy *slope	cal pka	Exp. pKa
Sulfamethoxazole	-1176.026242	0.210042				
	-1175.48163	0.196198	333.2385793	36.65624372	7.336243725	5.81
Dimethadione	-475.3830733	0.123794				
	-474.8388864	0.110178	333.111701	36.64228711	7.322287112	6.11
Sulfadiazine	-1154.988173	0.201098				
	-1154.440955	0.187195	334.837023	36.83207253	7.512072533	6.56
Sulfameter	-1269.546723	0.233435				
	-1268.996395	0.219492	336.7640727	37.044048	7.724048002	7
Sulfamethazine	-1233.657729	0.255757				
	-1233.106692	0.241629	337.0958279	37.08054107	7.76054107	7.38
Sulfadimethoxine	-1384.142539	0.266182				
	-1383.605255	0.252442	328.703287	36.15736157	6.837361572	6.2
Sulfachloropyridazine	-1614.575387	0.190739				
	-1614.040311	0.176731	327.1534255	35.9868768	6.666876801	6.1
Warfarin	-1034.904581	0.306179				
	-1034.39091	0.293312	314.4233364	34.586567	5.266567	5.03
Ranitidine	-1351.702968	0.35614				
	-1351.16504	0.342413	329.1160107	36.20276117	6.882761175	8.18

Bendroflumethiazide	-2141.53744	0.291544				
Bendroflumethiazide 1	-2140.996154	0.278557	331.678439	36.48462829	7.164628287	8.53
Bendroflumethiazide 2	-2141.014888	0.278647	319.9780861	35.19758947	5.877589468	
4-Hydroxybenzonitrile	-399.848909	0.103176				
	-399.3136075	0.089742	327.6479034	36.04126937	6.721269375	7.95
Acetaminophen	-515.6604846	0.158723				
	-515.1117726	0.144998	335.88429	36.9472719	7.627271903	9.7
Sulfathiazole	-1459.705301	0.179073				
	-1459.17237	0.165759	326.2339303	35.88573234	6.565732338	7.23
Phenolphthalein	-1071.813668	0.290934				
	-1071.26535	0.276894	335.4434435	36.89877879	7.578778787	9.71
4-Hydroxybenzaldehyde	-420.9416037	0.113925				
	-420.4051734	0.100535	328.383382	36.12217202	6.802172015	7.61
Nitrofurantoin	-903.7609084	0.154964				
	-903.2261243	0.140846	326.9024272	35.95926699	6.639266992	7.2
4-hydroxybenzamide	-476.3443122	0.131481				
	-475.7989912	0.118077	333.9538237	36.73492061	7.414920608	8.6
Uracil	-414.9689031	0.086962				
	-414.4254983	0.073288	332.5852053	36.58437259	7.264372587	9.45

4-Bromophenol	-2881.115913	0.094983				
	-2880.563125	0.08126	338.4435492	37.22879041	7.908790413	9.24
4-Chlorophenol	-767.2018475	0.094901				
	-766.6472884	0.081095	339.5035948	37.34539543	8.025395428	9.37
1-Naphthol	-461.2622058	0.151532				
	-460.7081342	0.137438	339.0204602	37.29225062	7.972250618	9.3
Sulpiride	-1449.124872	0.381936				
	-1448.571242	0.367768	338.6980792	37.25678871	7.936788708	9.12
Ethosuximide	-478.7743926	0.17641				
	-478.2171636	0.162415	341.0627105	37.51689816	8.196898158	9.5
Allopurinol	-487.316494	0.099807				
	-486.7763404	0.086279	330.6348573	36.3698343	7.0498343	9.4
Phenindione	-728.2993855	0.207315				
	-727.7809401	0.194538	317.4746203	34.92220823	5.602208229	4.1
Piroxicam	-1443.105086	0.268467				
	-1442.602585	0.255343	307.2556043	33.79811647	4.478116471	4.6
3-Chlorophenol	-767.2025612	0.094919				
	-766.6501259	0.081081	338.1511522	37.19662674	7.876626737	9.02

4-Chloro-2-nitrophenol	-971.7824385	0.09793				
	-971.2432249	0.083824	329.6894093	36.26583502	6.94583502	6.45
2,6-Dinitrophenol	-716.7191606	0.10981				
	-716.197429	0.095896	318.8372171	35.07209388	5.752093878	3.71
Pyridoxine	-592.0841541	0.186142				
	-591.5437389	0.172319	330.6176061	36.36793667	7.047936671	8.81

Table S17. Calculated proton affinities use to predict experimental pK_b /pK_a using protonated nitrogen base equation

Name	Energy	ZPE	Cal. PA (kcal/mol)	Energy *slope	Cal. pka	Cal. pkb	Exp. pka
1,10-Phenanthroline	-571.7811861	0.170332					
	-572.1771572	0.184727	239.6239974	62.30223933	9.432239	4.56776067	4.86
Isoquinoline	-402.0520809	0.135644					
	-402.4312248	0.149694	229.2768127	59.61197131	6.741971	7.25802869	5.4
Codeine	-979.211488	0.361663					
	-979.5725617	0.375518	218.0573491	56.69491075	3.824911	10.1750892	8.21
Dibucaine	-1094.67291						
	-1095.037097	0.479772	220.4611757	57.31990569	4.449906	9.55009431	8.85
Quinine	-1036.810106	0.409608					
	-1037.20535	0.424523	238.8476551	62.10039033	9.23039	4.76960967	4.1
2-Benzylaniline	-558.1483893	0.226365					
	-558.4998957	0.240434	211.922055	55.09973431	2.229734	11.7702657	4.29
2-Benzylpyridine	-518.8152634	0.197859					
	-519.1940768	0.211653	229.226905	59.5989953	6.728995	7.2710047	5.13
2-Fluoroaniline	-386.9765278	0.108923					
	-387.3171049	0.123437	204.7898687	53.24536587	0.375366	13.6246341	3.2
2-Methylbenzimidazole	-419.3248039	0.145503					
	-419.7088204	0.159541	232.3418499	60.40888096	7.538881	6.46111904	6.29

3,4-Lutidine	-327.0250866	0.144002					
	-327.4054651	0.15794	230.1204634	59.83132049	6.96132	7.03867951	6.47
4-Chloroaniline	-747.3299986	0.107391					
	-747.6704236	0.121665	204.842054	53.25893404	0.388934	13.611066	3.99
Acridine	-555.7369344	0.182009					
	-556.1262906	0.195967	235.7418132	61.29287142	8.422871	5.57712858	5.6
Aminopyrine	-745.2992343	0.28463					
	-745.6900154	0.296188	238.1125245	61.90925636	9.039256	4.96074364	5
Diclofenacsodium	-1827.787483	0.210253					
	-1828.180867	0.222948	239.0458939	62.15193242	9.281932	4.71806758	4.01
Methylnicotinate	-476.3046822	0.131049					
	-476.662169	0.144716	215.9221063	56.13974763	3.269748	10.7302524	3.13
N,N-Dimethyl nicotinamide	-495.7619554	0.171677					
	-496.1204854	0.185097	216.7286931	56.3494602	3.47946	10.5205398	3.92
Nicotinamide	-417.1318658	0.115531					
	-417.4934617	0.129459	218.3401562	56.76844062	3.898441	10.1015594	3.56
N-Methylaniline	-327.019202	0.14522					
	-327.3774827	0.160229	215.5946937	56.05462036	3.18462	10.8153796	4.85

Quinoline	-402.0538998	0.135532					
	-402.4321966	0.149579	228.7470617	59.47423604	6.604236	7.39576396	4.97
Tolmetin sodium	-1023.119933	0.260578					
	-1023.512556	0.273805	238.2414921	61.94278796	9.072788	4.92721204	3.5
Triamterene	-847.4977409	0.231107					
	-847.8566149	0.245632	216.2647864	56.22884448	3.358844	10.6411555	6.2
2-Aminopyrimidine	-319.8067303	0.093696					
	-320.1696121	0.107237	219.3851683	57.04014376	4.170144	9.82985624	3.46
8-Chlorotheophylline	-1100.902279	0.150774					
	-1101.246926	0.163535	208.422124	54.18975225	1.319752	12.6802477	5.2
2,4-Lutidine	-327.0284789	0.14337					
	-327.4104671	0.157268	231.1551736	60.10034514	7.230345	6.76965486	6.74
2,5-Lutidine	-327.0273037	0.143347					
	-327.4076692	0.157462	230.003414	59.80088763	6.930888	7.06911237	6.43
Aniline	-287.7028701	0.11693					
	-288.0492804	0.131354	208.505704	54.21148305	1.341483	12.658517	4.6
2,4,6-Collidine	-366.3610986	0.17051					
	-366.7488357	0.184485	234.7154027	61.0260047	8.156005	5.8439953	7.43
panisidine	-402.2628282	0.14926					

	-402.6177832	0.163817	213.7858336	55.58431674	2.714317	11.2856833	5.58
Papaverine	-1130.739513	0.37381					
	-1131.138541	0.387562	241.9375455	62.90376182	10.03376	3.96623818	6.39
1-Phenylpiperazine	-499.1389538	0.228119					
	-499.5132184	0.242477	226.0254506	58.76661716	5.896617	8.10338284	8.71
2-Methoxybenzylamine	-441.5827279	0.178903					
	-441.9599804	0.193822	227.5552606	59.16436776	6.294368	7.70563224	9.92
Tranylcypromine	-404.4264329	0.179375					
	-404.786698	0.194262	216.9150518	56.39791347	3.527913	10.4720865	8.2
pyrimethamine	-1144.607808	0.237819					
pyrimethaminep1	-1144.98439	0.250217	228.6852682	59.45816974	6.58817	7.41183026	7.34
pyrimethaminep2	-1144.999517	0.25125	237.5422448	61.76098364	8.890984	5.10901636	7.34
Atenolol	-882.2240067	0.351205					
	-882.5790833	0.364422	214.6865342	55.8184989	2.948499	11.0515011	9.58
Metoprolol	-867.3326158	0.384531					
	-867.7263112	0.400564	237.1882234	61.66893808	8.798938	5.20106192	9.75
Cimetidine	-1117.632329	0.267221					
	-1118.006775	0.275153	230.0926068	59.82407776	6.954078	7.04592224	6.7
Lindocaine	-731.7115878	0.339572					

	-732.1151026	0.35548	243.4269833	63.29101566	10.42102	3.57898434	7.9
Phenylbutazone	-996.3329984	0.353656					
	-996.6851273	0.36574	213.5339086	55.51881624	2.648816	11.3511838	4.4
Pindolol	-805.7397949	0.325385					
	-806.1165265	0.340261	227.2549054	59.08627542	6.216275	7.78372458	9.7
Metronidazole	-624.0916122	0.162948					
	-624.450957	0.176043	217.4400217	56.53440565	3.664406	10.3355943	2.55
Nadolol	-1020.043697	0.425124					
	-1020.425997	0.440424	230.4879152	59.92685796	7.056858	6.94314204	9.39
Azathioprine	-1279.284696	0.178268					
	-1279.652404	0.190747	223.0665902	57.99731345	5.127313	8.87268655	7.99

Table S18. Predicted ChemAxon pK_b and pK_a values

	Name	Exp.pKa	Marvin
1	Probenecid	3.4	3.53
2	Naproxen	4.2	4.19
3	Flurbiprofen	3.8	4.42
4	trans-Cinnamic acid	4.44	4.51
5	Ethacrynic acid	3.5	2.8
6	Nalidixic	5.94	5.95
7	Ketoprofen	4.02	3.88
8	Salicylic acid	3.01	2.79
9	Sulindac	4.03	4.09
10	Flumequine	6.38	6
11	Hippuric acid	3.65	3.59
12	Indomethacin	4.3	3.8
13	Nicotinic acid (Niacin)	4.76	2.79
14	Diflunisal	3	2.69
15	p-Aminohippuric acid	3.83	2.7
16	Chlorambucil	5.75	4.46
17	Furosemide	3.9	4.25
18	Flufenamic acid	6.38	3.88
19	Piroxicam	4.6	4.76
20	Warfarin	5.03	5.56
21	Sulfamethazine	7.38	6.99
22	Nitrofurantoin	7.2	8.23
23	Sulfathiazole	7.23	6.93
24	Sulfachloropyridazine	6.1	6.6
25	Sulfadimethoxine	6.2	6.91
26	4Hydroxybenzaldehyde	7.61	7.32

27	Sulfameter	7	7.09
28	Sulfadiazine	6.56	6.99
29	3-Chlorophenol	9.02	8.79
30	Sulpiride	9.12	10.24
31	4-hydroxybenzamide	8.6	8.49
32	4-Hydroxybenzonitrile	7.95	7.81
33	Ranitidine	8.18	7.12
34	Ethosuximide	9.5	10.73
35	1-Naphthol	9.3	9.6
36	4-Bromophenol	9.24	9.09
37	4-Chlorophenol	9.37	8.96
38	Dimethadione	6.11	6.91
39	Bendroflumethiazide	8.53	9.04
40	Phenindione	4.1	4.88
41	Sulfamethoxazole	5.81	6.16
42	Pyridoxine	8.81	9.4
43	Acetaminophen	9.7	9.46
44	Phenolphthalein	9.7	9.76
45	2,6-Dinitrophenol	3.71	4.14
46	Uracil	9.45	9.35
47	Allopurinol	9.4	7.19
48	4-Chloro-2-nitrophenol	9.37	6.14
49	Acridine	5.6	6.15
50	Aminopyrine	5	3.46
51	pyrimethamine	7.34	7.77
52	Methylnicotinate	3.13	1.89
53	Cimetidine	6.7	6.91
54	1,10-Phenanthroline	4.86	4.8

55	Nicotinamide	3.56	3.63
56	N,N-Dimethyl nicotinamide	3.92	3.61
57	2,4-Lutidine	6.74	6.58
58	3,4-Lutidine	6.47	6.33
59	2,5-Lutidine	6.43	6.24
60	1-Phenylpiperazine	8.71	8.89
61	Quinine	4.1	4.02
62	Dibucaine	8.85	9.04
63	Diclofenac sodium	4.01	4
64	2-Aminopyrimidine	3.46	3.62
65	2,4,6-Collidine	7.43	7.31
66	Metoprolol	9.75	9.67
67	Metronidazole	2.55	2.57
68	2-Methylbenzimidazole	6.29	6.33
69	Isoquinoline	5.4	5.26
70	Tolmetin sodium	3.5	3.96
71	Atenolol	9.58	9.67
72	2-Benzylpyridine	5.13	4.86
73	Quinoline	4.97	4.5
74	N-Methylaniline	4.85	4.68
75	Phenylbutazone	4.4	5.13
76	Pindolol	9.7	9.67
77	Codeine	8.21	9.19
78	2-Benzylaniline	4.29	4
79	2-Methoxybenzylamine	9.92	8.75
80	Tranylcypromine	8.2	9.62
81	Lidocaine	7.9	7.75
82	2-Fluoroaniline	3.2	2.98

83	p-anisidine	5.58	5.11
84	Aniline	4.6	4.64
85	4-Chloroaniline	3.99	3.49
86	Papaverine	6.39	6.03
87	8-Chlorotheophylline	5.2	5.14
88	Triamterene	6.2	1.86
89	Nadolol	9.39	9.76
90	Azathioprine	7.99	9.84

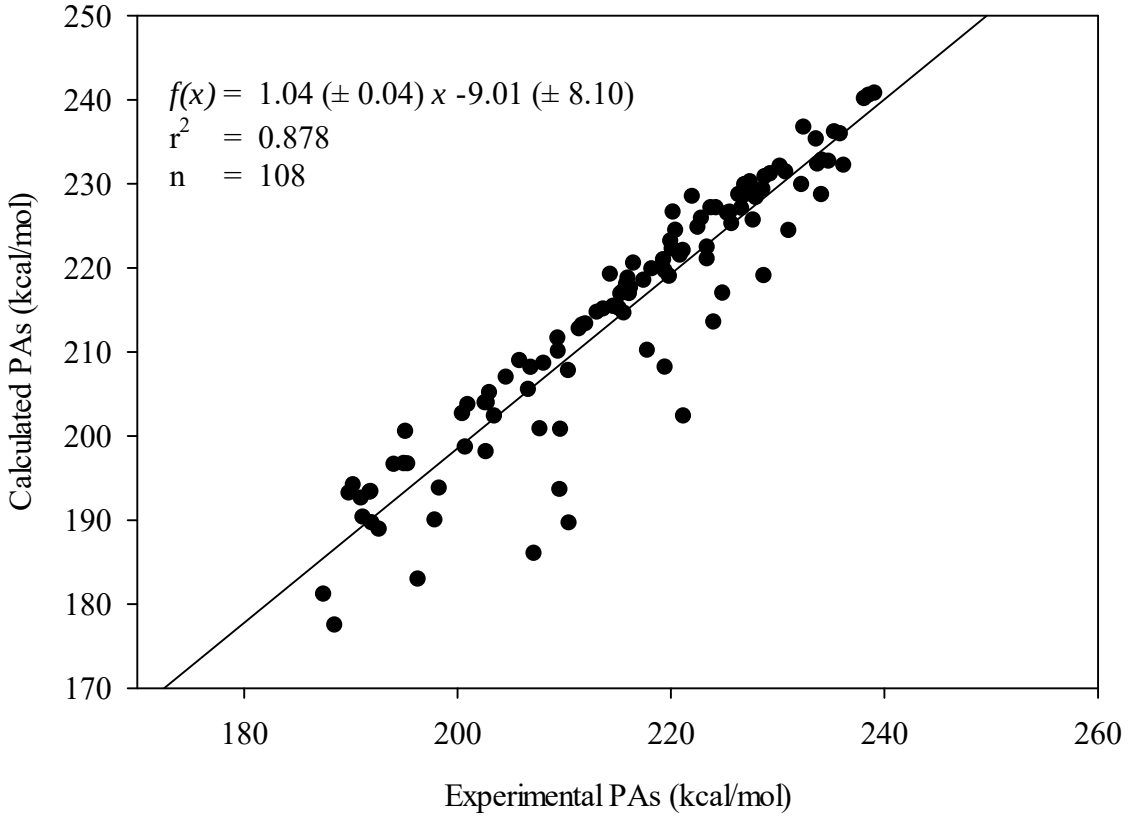

Figure. S1. Experimentally derived PAs plotted against their calculated counterparts using the B3PW91/6-311+G(2df,p)//6-31+G(d,p) method

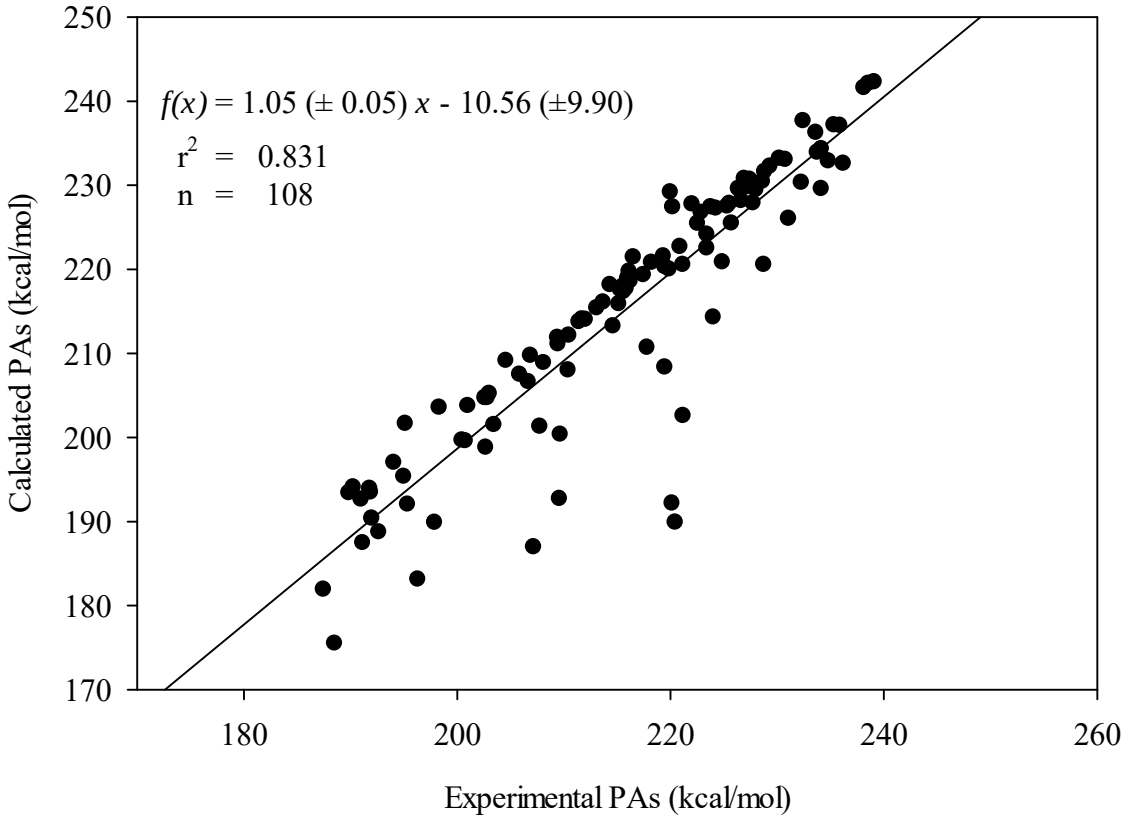

Figure. S2. Experimentally derived PAs plotted against their calculated counterparts using the wB97XD /6-311+G(2df,p)//6-31+G(d,p) method

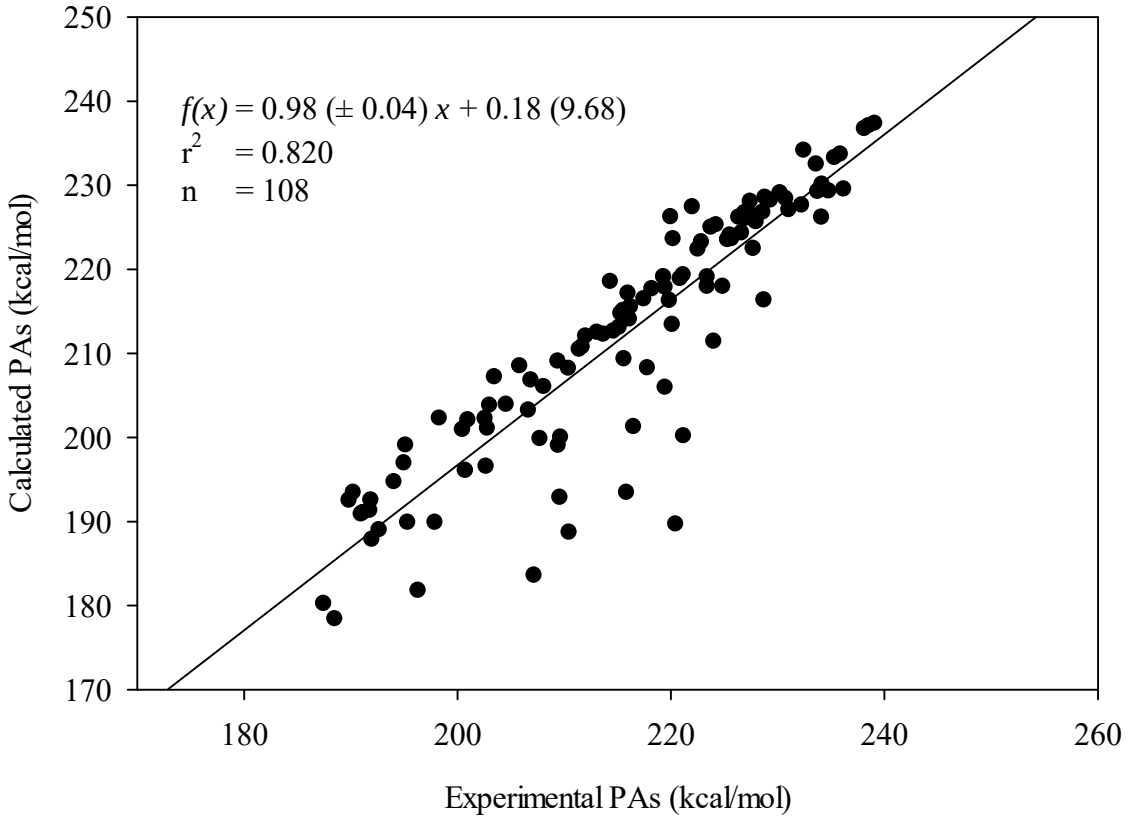

Figure. S3. Experimentally derived PAs plotted against their calculated counterparts using the PBEPBE /6-311+G (2df,p)//6-31+G(d,p) method

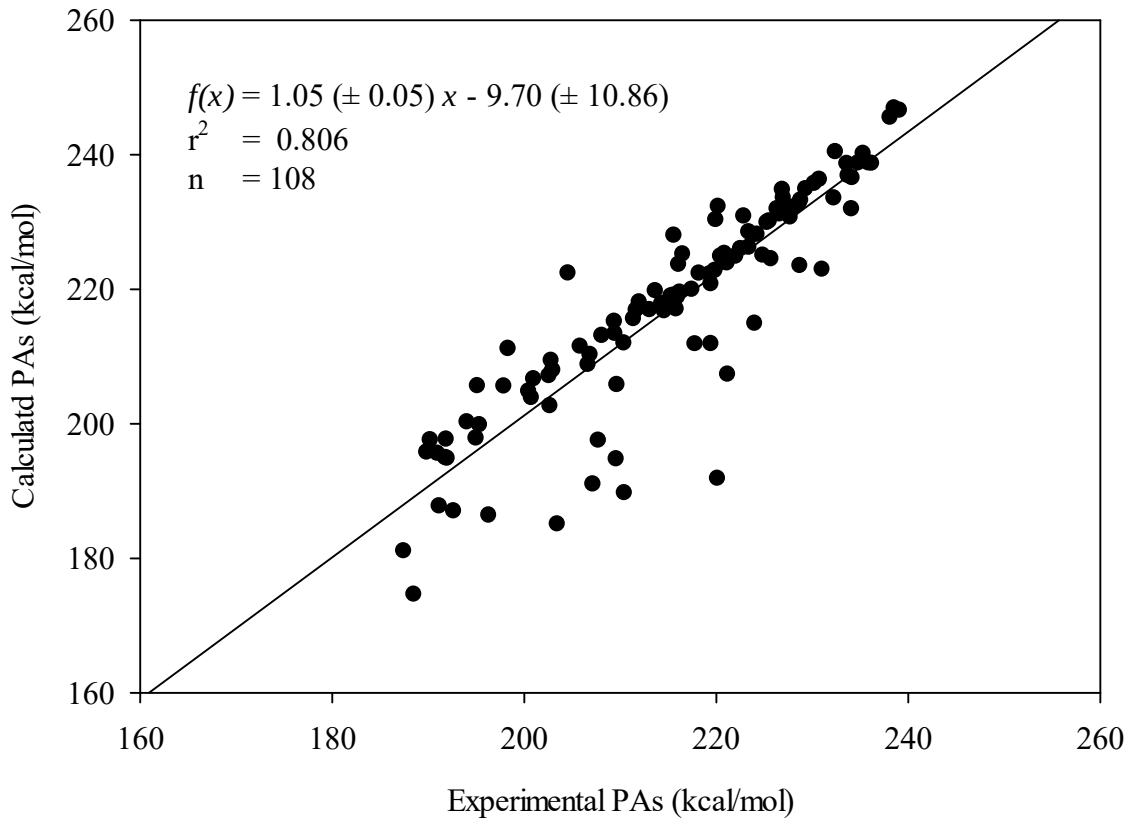

Figure. S4. Experimentally derived PAs plotted against their calculated counterparts using the MP2 /6-311+G (2df,p)//6-31+G(d,p) method

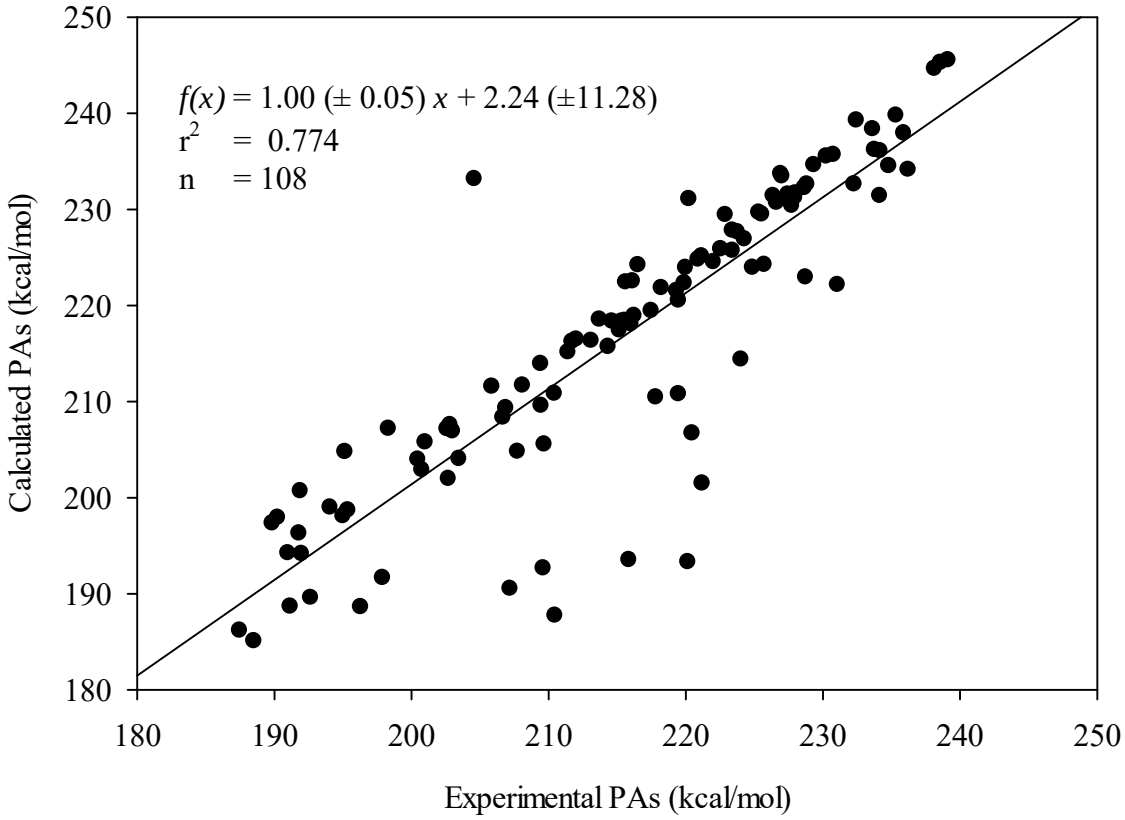
f(x) = 1.00 (± 0.05) x + 2.24 (±11.28)
r2 = 0.774
n = 108
Calculated PAs (kcal/mol)
Experimental PAs (kcal/mol)
180
190
200
210
220
230
240
250

Figure. S5. Experimentally derived PAs plotted against their calculated counterparts using the HF/6-311+G (2df,p)//6-31+G(d,p) method

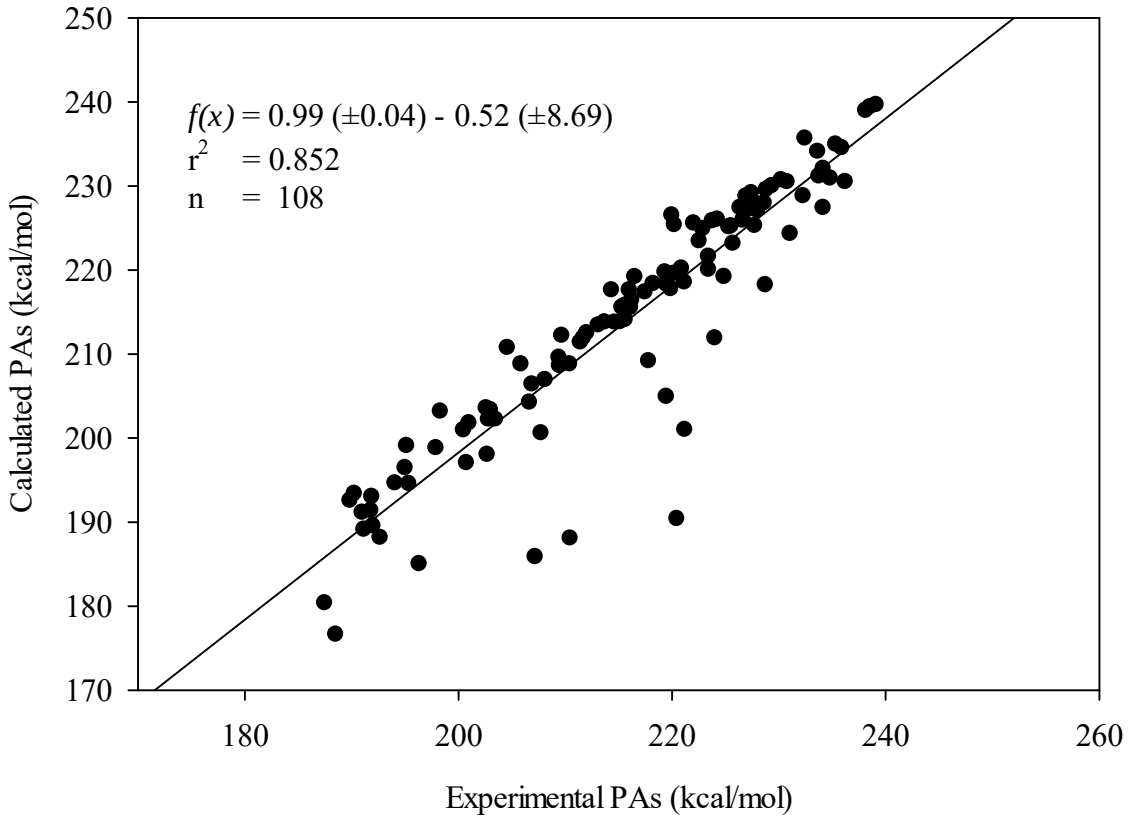

Figure. S6. Experimentally derived PAs plotted against their calculated counterparts using the B3LYP/6-311+G (2df, p) // 6-311+G (2df, p) method

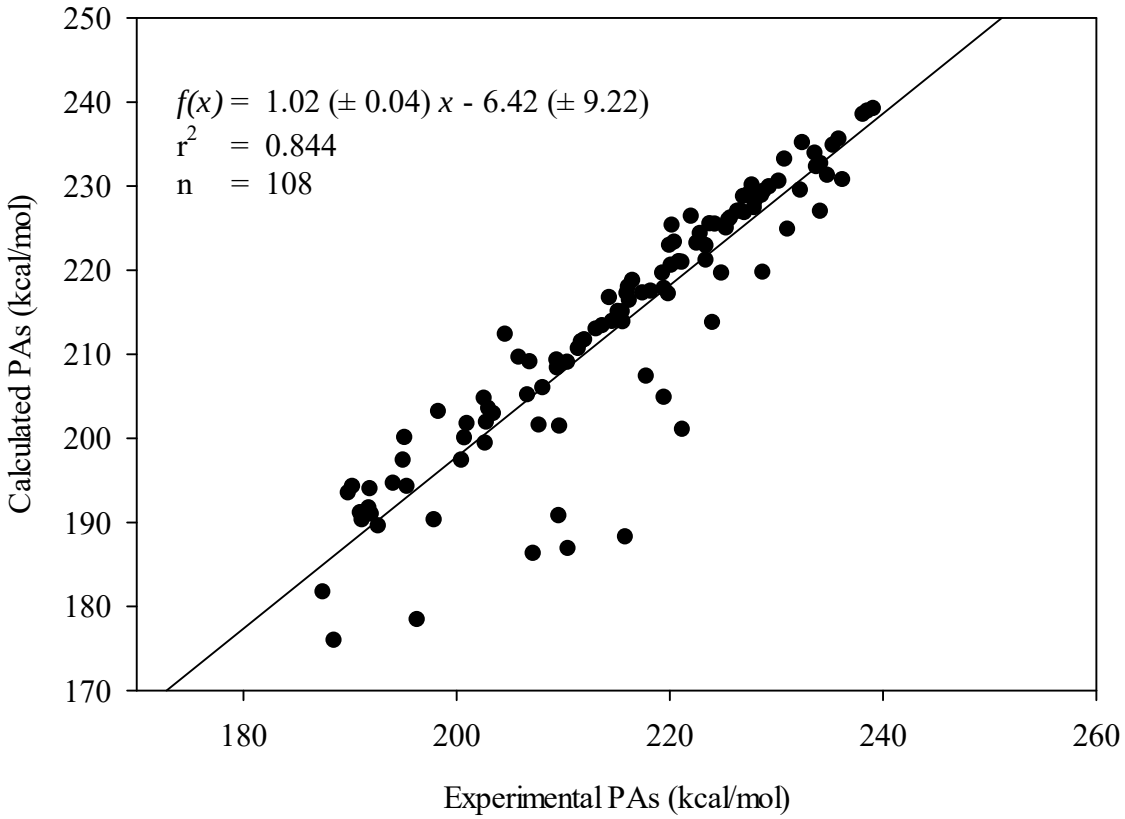

Figure. S7. Experimentally derived PAs plotted against their calculated counterparts using the B3LYP/6-31 +G (d, p) // 6-31G method

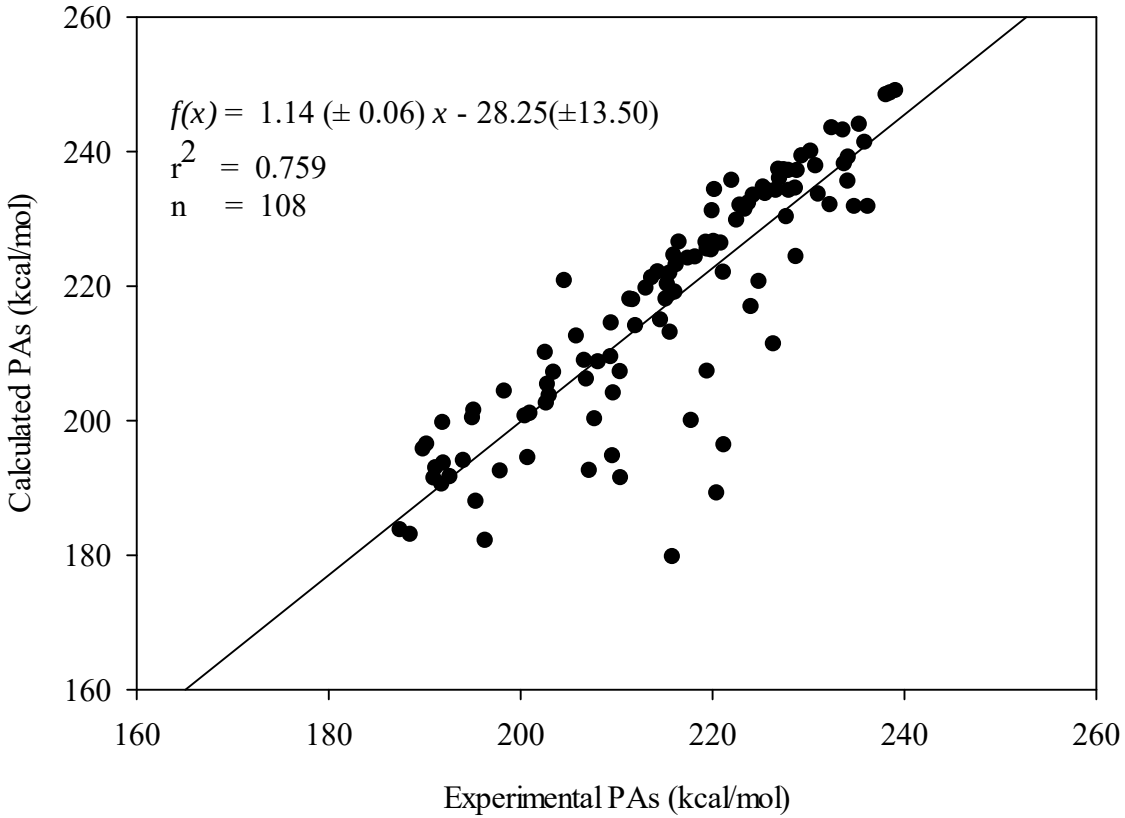

Figure. S8. Experimentally derived PAs plotted against their calculated counterparts using the B3LYP/6-31G // 3-21G method