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Cation–π interactions in CREBBP bromodomain inhibition: an electrostatic model for small-molecule binding affinity and selectivity

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Supporting Information

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1. DFT CALCULATIONS

1.1 Cartesian coordinates

The computational methodology is described in the main article text. Below, all species were optimized at the TPSS-D3/def2-TZVPP level of theory using *Gaussian 09*.[1] Boys-Bernadi counterpoise corrections were applied in the optimization of all complexes. Counterpoise-corrected complexation energies are used throughout, although the BSSE is small, typically in the region of 0.2 kcal/mol for all of the complexes studied. Grimme's D3 dispersion correction was applied with Becke-Johnson damping at short range using the functional-specific global parameters (S6 = 1.00, S8 = 1.9435, A1 = 0.4535, A2 = 4.4752) implemented through the use of the `empiricaldispersion=gd3bj` keyword in G09 rev. D.01. Energies below are quoted in Hartree per molecule unless otherwise stated. Since these complexes contain some atomic restraints to crystallographic positions we have not included zero-point energy corrections since they are not genuine stationary points on the Born-Oppenheimer potential energy surface. Effects of different levels of theory and basis set were marginal, as discussed in section **1.2**

Ligand 1: Arg complex

Counterpoise corrected energy = -516.9725

BSSE energy = 0.0003

Sum of monomers = -516.9547

Complexation energy = -11.41 kcal/mol (raw)

Complexation energy = -11.20 kcal/mol (corrected)

Atom	X	Y	Z
C	3.254757	-1.196359	-0.260889
N	2.760614	0.160226	-0.464438
C	1.863896	0.744207	0.319794
N	1.356313	0.091733	1.356060
N	1.460071	1.970973	0.052844
C	-1.147831	-1.407212	-1.268060
C	-1.332192	-2.118981	-0.081304
C	-1.839744	-1.461388	1.041383
C	-2.148519	-0.100506	0.975254
C	-1.461309	-0.047988	-1.330251
C	-1.970640	0.628007	-0.213451
C	-2.253308	2.091646	-0.249558
H	2.415105	-1.896804	-0.226695
H	3.855476	-1.277696	0.651073
H	3.286274	0.753771	-1.092933
H	1.661272	-0.854445	1.534927
H	0.399320	0.286437	1.638416
H	0.794882	2.439073	0.650695
H	1.670108	2.412151	-0.830149
H	-2.009768	-2.008861	1.963781
H	-2.557419	0.400382	1.850161
H	-1.318596	0.494510	-2.261763
H	-2.044402	2.568590	0.714235
H	-1.672656	2.597066	-1.027640
H	3.878224	-1.458990	-1.114187
H	-3.309925	2.288840	-0.468328
H	-1.105377	-3.179680	-0.037953
H	-0.772170	-1.913425	-2.152411

Ligand 2: Arg complex

Counterpoise corrected energy = -556.3155 (

BSSE energy = 0.0004

Sum of monomers = -556.2964

Complexation energy = -12.33 kcal/mol (raw)

Complexation energy = -12.06 kcal/mol (corrected)

Atom	X	Y	Z
C	3.388361	0.924579	0.699348
N	2.804280	-0.389883	0.460428
C	1.968574	-0.655771	-0.535171
N	1.612074	0.299673	-1.381970
N	1.474281	-1.871199	-0.668462
C	-1.074611	1.209204	1.298680
C	-1.048644	2.220615	0.336597
C	-1.448683	1.938075	-0.968984

C	-1.856173	0.641815	-1.295915
C	-1.490931	-0.090337	0.986215
C	-1.889551	-0.381543	-0.336065
C	-2.251371	-1.768685	-0.746518
H	2.595784	1.673694	0.784966
H	4.094224	1.205310	-0.089241
H	3.229100	-1.176059	0.934887
H	1.976766	1.231722	-1.244136
H	0.675061	0.275235	-1.778925
H	0.871079	-2.103084	-1.443889
H	1.585789	-2.568324	0.052416
H	-1.463386	2.719520	-1.722716
H	-2.184463	0.421236	-2.309442
H	-2.418762	-1.835248	-1.824432
H	-1.473808	-2.492543	-0.468867
H	3.920897	0.888491	1.648561
H	-3.165996	-2.115549	-0.250245
H	-0.744626	3.225763	0.612551
H	-0.783050	1.434289	2.321623
C	-1.521517	-1.157864	2.049743
H	-2.532824	-1.558428	2.180765
H	-0.883042	-2.011478	1.786599
H	-1.185913	-0.765210	3.011965

Ligand 3: Arg complex

Counterpoise corrected energy = -556.3155

BSSE energy = 0.0004

Sum of monomers = -556.2958

Complexation energy = -12.58 kcal/mol (raw)

Complexation energy = -12.35 kcal/mol (corrected)

Atom	X	Y	Z
C	-3.233765	1.116135	0.285129
N	-2.781468	-0.084026	-0.408461
C	-1.933693	-0.961671	0.112515
N	-1.439311	-0.773341	1.327873
N	-1.564754	-2.013619	-0.592213
C	1.115883	1.476361	-0.495752
C	1.310697	1.668536	0.877903
C	1.810986	0.636140	1.673139
C	2.106577	-0.606078	1.109042
C	1.418745	0.222068	-1.043606
C	1.918714	-0.828864	-0.265742
C	2.150411	-2.181573	-0.848885
H	-2.371230	1.710202	0.601042
H	-3.865408	0.874965	1.146450
H	-3.308001	-0.372158	-1.222985
H	-1.713183	0.050094	1.844891
H	-0.497076	-1.099573	1.529127
H	-0.926457	-2.695050	-0.208178
H	-1.752496	-2.073119	-1.581983
H	1.978408	0.801605	2.733485
H	2.502657	-1.403829	1.732951
H	1.855100	-2.977254	-0.155698
H	1.607952	-2.313835	-1.790120
H	-3.813979	1.712306	-0.417585
H	3.211924	-2.347315	-1.070065
H	1.262613	0.060971	-2.109066
H	1.089568	2.635778	1.321569
C	0.622564	2.599466	-1.374246
H	1.467746	3.151657	-1.800942
H	0.027645	2.222220	-2.211575
H	0.020232	3.316113	-0.808682

Ligand 4: Arg complex

Counterpoise corrected energy = -556.3151

BSSE energy = 0.0003 (Hartrees)

Sum of monomers = -556.2956

Complexation energy = -12.45 kcal/mol (raw)

Complexation energy = -12.24 kcal/mol (corrected)

Atom	X	Y	Z
C	-3.039264	1.607780	-0.257029
N	-2.861686	0.174835	-0.459681
C	-2.116237	-0.594205	0.323287
N	-1.472763	-0.070831	1.357324
N	-1.997816	-1.880476	0.057253
C	1.257563	0.830971	-1.254874
C	1.600716	1.506419	-0.076386
C	1.964545	0.731537	1.033509
C	1.981884	-0.662867	0.964885
C	1.278054	-0.562422	-1.325132
C	1.645656	-1.339327	-0.219365
C	1.593620	-2.829140	-0.253901
H	-2.063460	2.100706	-0.215878
H	-3.612562	1.822119	0.650906
H	-3.511420	-0.286601	-1.083186
H	-1.564223	0.918328	1.540058
H	-0.574462	-0.465693	1.625724
H	-1.440774	-2.480026	0.648559
H	-2.283590	-2.259035	-0.833609
H	2.249219	1.224286	1.960031
H	2.278882	-1.236374	1.840532
H	1.007062	-1.054229	-2.256560
H	1.284191	-3.246207	0.710817
H	0.911809	-3.191830	-1.029758
H	-3.581250	2.004372	-1.114253
H	2.577321	-3.261671	-0.474594
H	0.979603	1.404683	-2.135794
C	1.624111	3.013725	-0.017977

H	1.407971	3.380441	0.989664
H	2.614170	3.393754	-0.295143
H	0.903479	3.453465	-0.713893

Ligand 5: Arg complex

Counterpoise corrected energy = -631.5662

BSSE energy = 0.0004

Sum of monomers = -631.5455

Complexation energy = -13.23 kcal/mol (raw)

Complexation energy = -12.97 kcal/mol (corrected)

Atom	X	Y	Z
C	1.873828	-2.864558	-0.139980
N	2.486051	-1.589936	-0.495588
C	2.358077	-0.483453	0.225157
N	1.635960	-0.489611	1.336787
N	2.933737	0.632065	-0.179228
C	-1.480109	0.128878	-1.078950
Atom	X	Y	Z
C	-1.913165	-0.196327	0.212286
C	-1.612085	0.668431	1.276458
C	-0.878240	1.827075	1.042822
C	-0.740812	1.296992	-1.289581
C	-0.424190	2.169656	-0.245506
C	0.426465	3.377154	-0.449906
H	0.797783	-2.731474	0.006117
H	2.326844	-3.298360	0.757642
H	3.223122	-1.610677	-1.188574
H	1.196973	-1.351219	1.629606
H	1.115265	0.349014	1.586620
H	2.839361	1.482268	0.357342
H	3.283630	0.727294	-1.121217
H	-1.980372	0.426035	2.268400
H	-0.673008	2.496806	1.875619
H	-0.410953	1.530254	-2.299120
H	1.069590	3.570666	0.416315
H	1.058385	3.280954	-1.338657
H	2.019576	-3.551773	-0.972129
H	-0.177503	4.282185	-0.590369
H	-1.718097	-0.509309	-1.922070
O	-2.618093	-1.319162	0.534047
C	-3.078245	-2.144306	-0.546628
H	-3.664364	-2.934136	-0.079714
H	-3.706149	-1.568093	-1.234169
H	-2.234715	-2.582027	-1.094862

Ligand 6: Arg complex

Counterpoise corrected energy = -721.6023

BSSE energy = 0.0007

Sum of monomers = -721.5881

Complexation energy = -9.36 kcal/mol (raw)

Complexation energy = -8.93 kcal/mol (corrected)

Atom	X	Y	Z
C	-3.173837	0.031853	0.792022
N	-2.536290	-0.994099	-0.024692
C	-1.456455	-1.668628	0.348541
N	-0.887682	-1.424349	1.520634
N	-0.935421	-2.570294	-0.460629
C	0.653319	1.238951	-0.247430
C	1.254543	1.728255	0.907776
C	2.342469	1.021264	1.419775
C	2.799012	-0.136251	0.785864
C	1.111300	0.103604	-0.907906
C	2.194954	-0.610287	-0.390894
C	2.666655	-1.841564	-1.087259
H	-2.547353	0.924007	0.891700
H	-3.415571	-0.374997	1.777151
H	-2.747953	-0.984039	-1.014333
H	-1.103786	-0.581469	2.032455
H	-0.099169	-1.964758	1.843635
H	-0.043627	-3.000204	-0.266888
H	-1.454577	-2.925662	-1.250323
H	2.837830	1.375977	2.317418
H	3.646029	-0.673517	1.203935
H	2.806155	-2.675980	-0.389659
H	1.970454	-2.148587	-1.872445
H	-4.102524	0.320878	0.303242
H	3.639228	-1.678442	-1.565523
H	0.612798	-0.213894	-1.816164
H	0.875793	2.627117	1.378827
N	-0.562544	1.906294	-0.762581
O	-1.185213	1.334076	-1.669852
O	-0.911279	2.959365	-0.230784

Ligand 7: Arg complex

Counterpoise corrected energy = -721.5991

BSSE energy = 0.0005

Sum of monomers = -721.5866

Complexation energy = -8.13 kcal/mol (raw)

Complexation energy = -7.81 kcal/mol (corrected)

Atom	X	Y	Z
C	-1.239442	-3.100944	0.163147
N	-2.185846	-2.001103	0.306681
C	-2.179867	-0.917934	-0.459390
N	-1.275269	-0.782833	-1.418900

N	-3.064125	0.037765	-0.249589
C	0.763703	0.333406	1.268639
C	1.659890	0.298976	0.205104
C	1.688719	1.290700	-0.771980
C	0.727766	2.297850	-0.722442
C	-0.165675	1.367099	1.318070
C	-0.228872	2.339038	0.306945
C	-1.358028	3.311982	0.264151
H	-0.212089	-2.730096	0.237243
H	-1.388674	-3.637403	-0.779668
H	-3.005494	-2.163913	0.876461
H	-0.577452	-1.501303	-1.551225
H	-1.022404	0.139890	-1.749323
H	-3.161549	0.812627	-0.888487
H	-3.712185	-0.002630	0.522617
H	2.430208	1.244323	-1.561380
H	0.710725	3.055497	-1.500995
H	-0.873950	1.409403	2.140818
H	-1.811906	3.350473	-0.732633
H	-2.130836	3.061949	0.995268
H	-1.403121	-3.794015	0.986940
H	-1.020625	4.332012	0.483732
H	0.797648	-0.442021	2.024718
N	2.558456	-0.864826	0.068468
O	3.568013	-0.736946	-0.617546
O	2.199488	-1.910409	0.632024

Ligand 8: Arg complex

Counterpoise corrected energy = -616.2621

BSSE energy = 0.0005

Sum of monomers = -616.2459

Complexation energy = -10.51 kcal/mol (raw)

Complexation energy = -10.17 kcal/mol (corrected)

Atom	X	Y	Z
C	3.323259	1.171583	0.349475
N	2.805711	-0.190964	0.308827
C	1.921679	-0.617872	-0.583688
N	1.449905	0.209257	-1.505805
N	1.494644	-1.864806	-0.537824
C	-0.838998	1.212313	1.230964
C	-1.232683	2.185943	0.310337
C	-1.954687	1.816638	-0.825806
C	-2.290813	0.477013	-1.037087
C	-1.186010	-0.108057	0.984445
C	-1.923297	-0.525595	-0.127309
C	-2.226887	-1.968999	-0.346255
H	2.494002	1.883389	0.395489
H	3.963019	1.387953	-0.512432
H	3.297883	-0.891789	0.847535
H	1.786613	1.159915	-1.549480
H	0.525652	0.055800	-1.891799
H	0.848195	-2.214781	-1.229638
H	1.617722	-2.426463	0.292442
H	-2.272395	2.570564	-1.538333
H	-2.865142	0.196556	-1.916179
H	-2.553806	-2.150264	-1.372942
H	-1.362640	-2.604647	-0.127836
H	3.912656	1.281354	1.258513
H	-3.026143	-2.312296	0.320602
H	-0.990506	3.228025	0.492237
H	-0.291285	1.463655	2.133097
F	-0.765003	-1.062132	1.867988

Ligand 9

Counterpoise corrected energy = -616.2608

BSSE energy = 0.0006 (Hartrees)

Sum of monomers = -616.2450 (Hartrees)

Complexation energy = -10.24 kcal/mol (raw)

Complexation energy = -9.88 kcal/mol (corrected)

Atom	X	Y	Z
C	3.249932	-1.042566	0.233303
N	2.768271	0.221887	-0.310024
C	1.861129	0.983676	0.287575
N	1.330654	0.609660	1.443306
N	1.470228	2.106519	-0.283161
C	-0.897134	-1.381514	-0.666557
C	-1.295837	-1.875275	0.568187
C	-2.046728	-1.032086	1.391190
C	-2.366607	0.263958	0.983330
C	-1.217666	-0.101962	-1.104136
C	-1.963604	0.745197	-0.273767
C	-2.236478	2.154518	-0.677326
H	2.409827	-1.723491	0.398270
H	3.812422	-0.895038	1.160989
H	3.289280	0.627592	-1.076031
H	1.605432	-0.273036	1.849849
H	0.395806	0.919801	1.684811
H	0.814558	2.723970	0.172067
H	1.743793	2.342600	-1.225182
H	-2.387162	-1.394049	2.356186
H	-2.950192	0.904192	1.639014
H	-0.886432	0.223778	-2.085484
H	-2.038735	2.852910	0.143781
H	-1.638467	2.450082	-1.544006
H	3.907758	-1.496967	-0.505754
H	-3.288777	2.295216	-0.951120
F	-0.139087	-2.168797	-1.475481
H	-1.043435	-2.888528	0.860297

Ligand 10: Arg complex

Counterpoise corrected energy = -616.2592

BSSE energy = 0.0004

Sum of monomers = -616.2441

Complexation energy = -9.77 kcal/mol (raw)

Complexation energy = -9.50 kcal/mol (corrected)

Atom	X	Y	Z
C	-3.124544	1.455139	-0.250561
N	-2.860330	0.035469	-0.452483
C	-2.067574	-0.685793	0.329612
N	-1.455021	-0.123127	1.361691
N	-1.871630	-1.962732	0.064370
C	1.178855	0.932222	-1.272475
C	1.501938	1.580171	-0.086720
C	1.954401	0.888619	1.031067
C	2.060111	-0.502035	0.953071
C	1.294914	-0.457671	-1.326196
C	1.731451	-1.200535	-0.220849
C	1.770608	-2.690794	-0.254012
H	-2.182287	2.010054	-0.220564
H	-3.701109	1.634126	0.662904
H	-3.479478	-0.465064	-1.076827
H	-1.604826	0.857343	1.552898
H	-0.554677	-0.484532	1.660891
H	-1.306218	-2.539158	0.670083
H	-2.164682	-2.369365	-0.811426
H	2.226125	1.430104	1.930888
H	2.420556	-1.051824	1.819167
H	1.474510	-3.125407	0.707090
H	1.119421	-3.093032	-1.036054
H	-3.699694	1.814970	-1.102317
H	2.780670	-3.064166	-0.462227
H	0.854407	1.508568	-2.132251
H	1.043954	-0.972319	-2.250077
F	1.364580	2.927389	-0.016095

Ligand 11: Arg complex

Counterpoise corrected energy = -1091.2019

BSSE energy = 0.0007

Sum of monomers = -1091.1808

Complexation energy = -13.69 kcal/mol (raw)

Complexation energy = -13.25 kcal/mol (corrected)

Atom	X	Y	Z
C	-1.975456	-2.694968	-0.503301
N	-2.639045	-1.451879	-0.128570
C	-2.417333	-0.288213	-0.726130
N	-1.546108	-0.203126	-1.721485
N	-3.050760	0.791854	-0.311949
C	0.820459	0.001152	0.937344
C	1.762940	-0.071617	-0.105637
O	2.417336	-1.248566	-0.267693
C	3.487792	-1.287951	-1.228590
C	1.942978	1.065592	-0.905477
C	1.193483	2.222031	-0.679321
C	0.091231	1.162373	1.165301
C	0.255520	2.296511	0.358130
C	-0.622233	3.487464	0.544369
H	-0.890326	-2.578207	-0.429525
H	-2.265487	-3.016322	-1.508950
H	-3.420105	-1.511752	0.510379
H	-1.014375	-1.023124	-1.976930
H	-1.077438	0.679222	-1.892949
H	-2.889627	1.689659	-0.743754
H	-3.601925	0.785809	0.533085
H	3.911016	-2.287092	-1.143231
H	4.246308	-0.536242	-0.989010
H	3.107871	-1.127887	-2.243953
H	2.672800	1.051153	-1.706685
H	1.353319	3.082514	-1.323432
H	-0.617172	1.176130	1.988104
H	-1.078382	3.806414	-0.400805
H	-1.420773	3.286434	1.264465
C	0.552881	-1.393581	1.945275
H	-2.274722	-3.462102	0.208769
H	-0.063557	4.352623	0.920184

Ligand 12: Arg complex

Counterpoise corrected energy = -730.8504

BSSE energy = 0.0008

Sum of monomers = -730.8306

Complexation energy = -12.93 kcal/mol (raw)

Complexation energy = -12.45 kcal/mol (corrected)

Atom	X	Y	Z
C	-2.040209	-2.754727	-0.000375
N	-2.661495	-1.446518	0.168847
C	-2.371403	-0.389868	-0.579276
N	-1.466311	-0.481514	-1.543337
N	-2.970795	0.761643	-0.346741
C	0.838550	0.020495	1.123537
C	1.776571	-0.257487	0.115555
O	2.362618	-1.482872	0.144173
C	3.436810	-1.715067	-0.785053
C	2.007680	0.743493	-0.835971
C	1.307552	1.953146	-0.782599
C	0.156567	1.222632	1.189585

C	0.374026	2.220656	0.225924
C	-0.457395	3.458366	0.208099
H	-0.952730	-2.666927	0.082569
H	-2.318480	-3.212378	-0.955255
H	-3.482385	-1.393285	0.757093
H	-0.976014	-1.355124	-1.672647
H	-0.939521	0.344969	-1.805454
H	-2.761739	1.578859	-0.900938
H	-3.532152	0.903641	0.479573
H	3.809526	-2.710183	-0.549339
H	4.230146	-0.973631	-0.647520
H	3.072962	-1.687020	-1.818595
H	2.735430	0.584029	-1.623248
H	1.505331	2.702961	-1.543766
H	-0.549035	1.372029	2.001775
H	-0.868209	3.653825	-0.789592
H	-1.286456	3.394645	0.918959
H	-2.384501	-3.396775	0.808717
H	0.125130	4.347205	0.477792
F	0.576606	-0.940996	2.044284

Ligand 13: Arg complex

Counterpoise corrected energy = -837.7292

BSSE energy = 0.0004

Sum of monomers = -837.7121

Complexation energy = -11.02 kcal/mol (raw)

Complexation energy = -10.75 kcal/mol (corrected)

Atom	X	Y	Z
C	3.272676	-1.190683	-0.233070
N	2.729857	0.135766	-0.501046
C	1.870085	0.756027	0.296589
N	1.448156	0.170802	1.408660
N	1.416723	1.950340	-0.031105
C	-2.310264	1.965465	-0.094741
H	2.456625	-1.905596	-0.092487
H	3.933069	-1.190322	0.640363
H	3.190773	0.689921	-1.210885
H	1.785893	-0.753931	1.634036
H	0.509007	0.372618	1.739744
H	0.805780	2.461409	0.588555
H	1.566598	2.335769	-0.951558
H	-2.434213	2.395289	0.901857
H	-1.524398	2.508902	-0.627667
H	3.846473	-1.501997	-1.104629
H	-3.242349	2.114592	-0.647915
C	-2.080801	-0.327089	1.152974
C	-1.175056	-1.869397	-0.335704
C	-1.635852	-1.665800	0.939628
H	-2.501941	0.029436	2.087393
H	-1.680959	-2.447227	1.689436
S	-1.302592	-0.433592	-1.283990
C	-1.975708	0.467632	0.032384
H	-0.822519	-2.786675	-0.786307

Ligand 14: Arg complex

Counterpoise corrected energy = -1007.5333

BSSE energy = 0.0005

Sum of monomers = -1007.5137

Complexation energy = -12.57 kcal/mol (raw)

Complexation energy = -12.28 kcal/mol (corrected)

Atom	X	Y	Z
C	2.852846	-2.033901	0.163170
N	3.046038	-0.631908	-0.187520
C	2.452992	0.374417	0.441549
N	1.624138	0.137644	1.448626
N	2.672140	1.613749	0.047415
C	-0.544928	3.336064	-0.712813
H	1.787522	-2.282474	0.131877
H	3.273782	-2.264877	1.147351
H	3.809963	-0.405477	-0.810248
H	1.436820	-0.813233	1.732457
H	0.905610	0.811652	1.684565
H	2.225447	2.389832	0.512462
H	3.072452	1.804312	-0.859615
H	-0.092948	3.718089	0.208485
H	0.164947	3.387626	-1.538912
H	3.361994	-2.640167	-0.584414
H	-1.404381	3.972697	-0.941311
C	-0.974721	1.867245	-0.541145
C	-0.952251	-0.332773	-0.839358
C	-1.747768	-0.300402	0.335219
C	-0.642655	-1.564666	-1.432367
C	-2.232296	-1.472433	0.922455
C	-1.119675	-2.730618	-0.843785
H	-0.057148	-1.586266	-2.345785
C	-1.903497	-2.685176	0.322440
H	-2.852189	-1.443201	1.811898
H	-0.901220	-3.690881	-1.299784
H	-2.273059	-3.608763	0.755524
N	-0.520490	0.906945	-1.290803
S	-1.958666	1.357473	0.836202

Ligand 15: Arg complex

Counterpoise corrected energy = -648.6199

BSSE energy = 0.0005

Sum of monomers = -648.5963

Complexation energy = -15.10 kcal/mol (raw) Complexation energy = -14.77 kcal/mol (corrected)			
Atom	X	Y	Z
C	3.254473	0.006745	-0.623892
N	2.511800	-0.764395	0.365915
C	1.472069	-1.534594	0.072505
N	1.045482	-1.633511	-1.178602
N	0.847640	-2.186188	1.034184
C	-2.790916	-1.375244	1.017433
H	2.570053	0.664884	-1.166387
H	3.800171	-0.645747	-1.313156
H	2.920120	-0.859057	1.286014
H	1.518078	-1.089920	-1.887378
H	0.049973	-1.746297	-1.353870
H	0.183469	-2.913577	0.817896
H	1.041957	-2.004118	2.007019
H	-3.503720	-1.984536	0.464988
H	-1.986452	-1.992744	1.422853
H	3.968904	0.633941	-0.093215
H	-3.297005	-0.846081	1.824855
C	-1.232890	0.585953	0.355956
C	-2.306703	-0.426309	-1.343608
C	-0.750489	1.143170	-0.867068
C	-0.731687	0.973509	1.603387
C	-1.448321	0.478058	-1.930089
H	-3.032377	-1.089504	-1.793480
C	0.235184	2.145535	-0.811983
C	0.258980	1.950572	1.620009
H	-1.117902	0.554465	2.527695
H	-1.376386	0.683526	-2.988758
C	0.730739	2.535076	0.426416
H	0.588373	2.621626	-1.722492
H	0.653402	2.292799	2.571526
H	1.479124	3.319290	0.482780
N	-2.205267	-0.343588	0.035462

1.2 Binding energies: comparison of density functionals

QM-computed complexation energies between the guanidinium and **L1-L15** were evaluated with different functionals, and basis set size. Firstly, the effect of increasing the basis set size from valence triple-ζ to quadruple-ζ is negligible: the complexation energies are within 0.1 kcal/mol confirming that the def2-TZVPP values are essentially converged. Secondly, the effect of using a hybrid functional such as B3LYP, again with a Grimme-D3 correction for dispersion, or a hybrid meta-GGA functional (M06-2X) also has relatively little effect. The correlation against experimental binding affinities ranges from 0.57-0.63 for all levels of theory considered here, and so there is little quantitative difference associated with the level of theory. This is somewhat to be expected, since the intermolecular interaction is dominated by electrostatics: for all of the complexes the calculated extent of charge transfer (TPSS/def2-TZVPP) from arene to guanidinium is only 0.03e.

Table S1. Counterpoise-corrected complexation energies (kcal/mol^{-1}).

Ligand	TPSS-D3/def2-TZVPP (TPSS-D3/cc-pVQZ)	B3LYP-D3/def2-TZVPP	M06-2X/def2-TZVPP
1	-11.20 (-11.24)	-11.52	-11.10

2	-12.06 (-12.11)	-12.43	-11.93
3	-12.35 (-12.38)	-12.66	-12.26
4	-12.24 (-12.27)	-12.54	-12.14
5	-12.97 (-13.00)	-13.11	-12.54
6	-8.93 (-9.01)	-9.69	-9.57
7	-7.81 (-7.92)	-8.21	-7.87
8	-10.17 (-10.21)	-10.58	-10.36
9	-9.88 (-9.93)	-10.16	-9.92
10	-9.50 (-9.55)	-9.68	-9.24
11	-13.25 (-13.27)	-13.8	-13.3
12	-12.45 (-12.48)	-12.73	-12.54
13	-10.75 (-10.77)	-11.15	-10.67
14	-12.28 (-10.81)	-11.35	-10.39
15	-14.77 (-14.82)	-15.48	-15.12
	R^2 = 0.57 (0.63)	R^2 = 0.61	R^2 = 0.63

1.3 Molecular Electrostatic Potential Surfaces

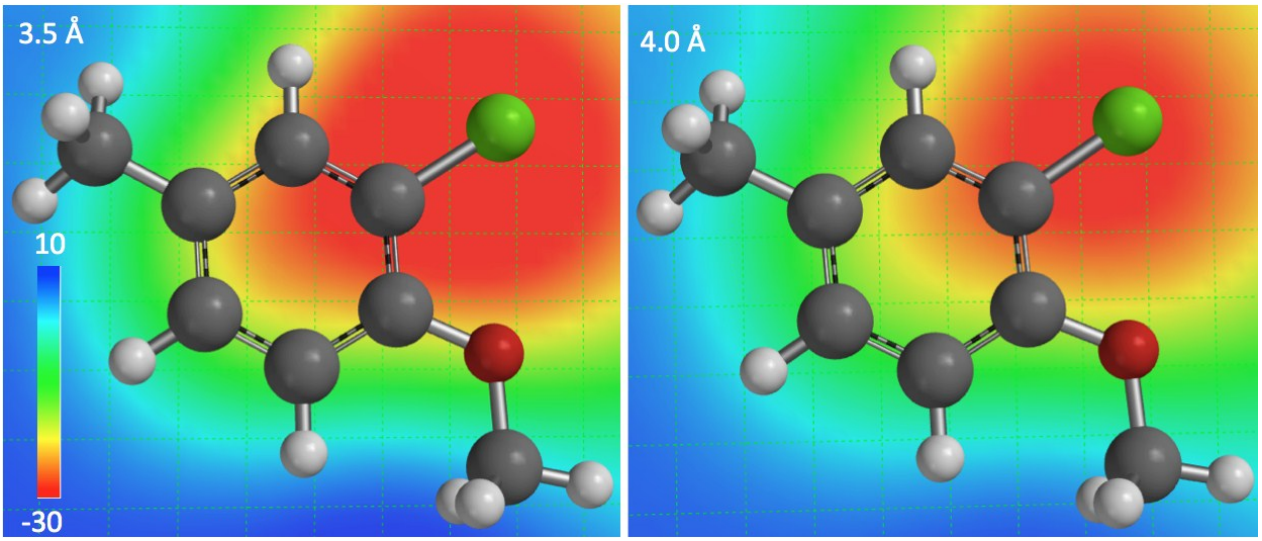
We constructed a bivariate model using the ESP evaluated at two different points in space for each aromatic group: above the aromatic ring, and secondly, above the substituent with the most negative ESP. ESP values were computed from B3LYP/6-31G(d,p) densities and correlated with the experimental binding affinities for ligands **L1**-**L15**. The coefficients were optimized by a linear regression using the experimental ΔT_m values. As shown below, there is little sensitivity to the QM level of theory used to generate the two molecular descriptors (i.e. the ESP values). The negative sign of the coefficients is a consequence of the negative ESP values used in the model (i.e. the coulombic potential energy at these points of a point-positive charge is negative, and hence favorable).

$$\Delta T_m = -307.70145*ESP_{cation} - 238.74216*ESP_{substituent} + 2.57912 \qquad \textbf{(Eq. 1)}$$

Qualitative comparison of ESP surfaces (**Figure S1**) evaluated at different distances from the arene indicate relatively little sensitivity to the choice of distance: a value of 3.5 Å was chosen since this is close to the separation between arene and guanidinium

in the X-ray structure used to initiate QM calculations.

Figure S1. 2D ESP isosurfaces were generated for planes 3.5 Å and 4.0 Å perpendicular distance above the aromatic systems. ESP values for **L1-L15** were used for model fitting. Color scale spans -30 to 10 kJ/mol.



Model S1. The data analysis for this paper was generated using the *Real Statistics Resource Pack* (Release 4.3). Copyright (2013 – 2015) Charles Zaiontz.

The bivariate model was constructed using the *Real Statistics* plugin for Microsoft Excel. Here the objective is to optimize coefficients (b_1, b_2 and c) to produce a linear model for experimental thermal shift data (y), given ESP values above the aromatic ring (x_1) and above the substituent (x_2) for each ligand **L1**-**L15**.

$$\hat{y} = b_1 x_1 + b_2 x_2 + c$$

By following the Method of Least Squares, we can rewrite this equation as:

$$\hat{y} - b_0 = b_1(x_1 - \bar{x}_1) + b_2(x_2 - \bar{x}_2)$$

The best correlation corresponds to finding the best-fit line to:

$$\hat{y} - \bar{y} = b_1(x_1 - \bar{x}_1) + b_2(x_2 - \bar{x}_2)$$

With b_1 and b_2 being calculated as the solutions of the following two equations system based on the covariance(cov):

$$cov(y,x_j) = \sum_{m=1}^{2} b_m \,.\, cov(x_m,x_j)$$

The quality of the model was then based on the analysis of the standard R^2 between the sum of squares of defined as follow:

$$R^2 = \frac{SS_{reg}}{SS_{reg} + SS_{res}}$$

where the sum of squares ($SS_{reg}\ and\ SS_{res}$) $are\ defined\ as$:

$$SS_{reg} = \sum (\hat{y} - \bar{y})^2$$

and

$$SS_{res} = \sum (y - \hat{y})^2$$

The choice of functional and basis set has a negligible effect on the correlation obtained constructing a model as outlined above. In each case the regression coefficients of the two ESP descriptors are very similar in magnitude (**Table S2**): the ratio of b_1:b_2 is in the narrow region of 55:45 – 57:43, showing the near equal significance of both ESP descriptors in the overall model performance. An alternative model, using the minimum value of the ESP (i.e. the most attractive part of the potential) rather than a value directly above one of the substituents led to a very small improvement (an increase in R^2 by 0.01). Based on the simplicity of the original model, there is no reason to adopt this more complex implementation.

Table S2. Theoretical ΔT_m calculated after using multiple linear regression with ESP values at 3.5 Å above the aromatic ring and above the substituent with the most negative ESP. Different methodologies were considered: 1) M06-2X/6-31G(d,p) in diethylether; 2) B3LYP/6-31G(d,p) in gas-phase; 3) B3LYP/6-311++G(d,p) in diethylether.

Ligand	**Expt. ΔT_m**	**Theoretical ΔT_m**			
		M06-2X	**Gas-phase**	**6-311++G(d,p)**	**Different ESP***
1	6.5	6.3	6.4	6.4	6.3

2	6.4	7.0	6.9	6.9	6.8
3	6.3	6.8	6.7	6.8	6.9
4	7.4	7.0	7.0	7.1	7.1
5	8.1	8.6	8.5	8.5	8.5
6	5.2	4.8	4.8	4.8	4.8
7	5.2	4.9	4.9	4.9	5.0
8	6.2	6.9	6.9	7.0	6.9
9	7.1	7.2	7.2	7.2	7.1
10	6.4	7.2	7.2	7.3	7.2
11	9.0	9.2	9.3	9.1	9.2
12	9.6	8.5	8.5	8.6	8.6
13	6.0	6.1	6.3	6.1	6.2
14	6.2	6.1	6.0	6.0	6.0
15	8.9	7.9	7.8	7.8	7.9
		R^2 = 0.83 (57/43)**	R^2 = 0.82 (56/44)	R^2 = 0.82 (55/45)	R^2 = 0.84 (55/45)

*Consideration of the most negative ESP value near the substituent.

**Ratio between the coefficients related to the ESP values above the π-system and the substituent, respectively.

Molecular dipole moments were also computed, however, the correlation between these values and ligand binding affinities are poor, and so this approach was not considered further.

Table S3. B3LYP/6-31G* dipole moment (Debye) of the aromatic/heteroarmatic groups of Ligands **L1-L15**.

Ligand	Dipole Moment
1	0.3447
2	2.4238
3	0.7305
4	0.5882
5	0.0827
6	0.7799
7	0.3544
8	1.1869
9	5.0183
10	1.6946

11	5.3473
12	1.1795
13	1.8249
14	2.4212
15	2.8971
	R^2 = 0.13

2. MOLECULAR DYNAMICS SIMULATIONS

The methodology is described in the main text and employs the ligand RESP charges below.

2.1 RESP Charges

Ligand 1				
Atom	X	Y	Z	RESP Charge
C	-2.06	2.75	2.47	-0.18
H	-1.42	2.60	3.31	0.13
C	-3.44	2.64	2.61	-0.08
H	-3.87	2.41	3.56	0.11
C	-4.25	2.85	1.51	-0.18
H	-5.32	2.78	1.61	0.13
C	-3.70	3.16	0.28	-0.10
H	-4.34	3.33	-0.57	0.11
C	-2.32	3.26	0.12	0.00
C	-1.51	3.06	1.23	-0.10
H	-0.44	3.14	1.13	0.11
C	-1.72	3.58	-1.24	-0.01
H	-0.78	4.10	-1.12	0.03
H	-2.39	4.24	-1.78	0.03
C	-1.48	2.33	-2.10	-0.02
H	-1.23	2.64	-3.11	0.04
H	-2.40	1.76	-2.17	0.04
C	-0.35	1.47	-1.60	0.33
N	-0.43	0.11	-1.47	-0.05
C	-1.57	-0.76	-1.67	-0.06
H	-2.19	-0.37	-2.47	0.08
H	-1.19	-1.72	-2.01	0.08
C	-2.41	-0.91	-0.40	-0.03
H	-2.73	0.08	-0.10	0.08
H	-1.78	-1.30	0.40	0.08
N	-3.58	-1.73	-0.64	-0.35
C	-3.28	-3.14	-0.82	-0.03
H	-2.50	-3.47	-0.13	0.08
H	-2.92	-3.33	-1.82	0.08
C	-4.52	-3.99	-0.58	0.09
H	-5.29	-3.71	-1.28	0.06

H	-4.29	-5.03	-0.73	0.06
O	-4.99	-3.87	0.74	-0.39
C	-4.80	-2.61	1.34	0.09
Ligand 2				
Atom	X	Y	Z	RESP Charge
H	-3.90	-2.63	1.95	0.06
C	-4.69	-1.51	0.29	-0.03
C	-2.30	3.47	2.20	-0.22
H	-4.57	-0.55	0.79	0.08
H	-1.77	3.74	3.09	0.14
H	-5.62	-1.46	-0.26	0.08
C	-3.60	3.00	2.29	-0.16
C	0.82	-0.30	-1.01	0.01
H	-4.07	2.92	3.26	0.13
C	1.34	-1.54	-0.69	-0.19
C	-4.29	2.66	1.14	-0.10
H	0.77	-2.45	-0.77	0.14
H	-5.31	2.32	1.19	0.11
C	2.65	-1.58	-0.27	-0.18
C	-3.65	2.78	-0.08	-0.18
H	3.10	-2.52	-0.03	0.14
H	-4.20	2.53	-0.98	0.12
C	3.44	-0.41	-0.15	-0.09
C	-2.34	3.23	-0.19	0.02
C	2.89	0.82	-0.47	-0.13
C	-1.65	3.59	0.97	0.10
H	3.46	1.72	-0.37	0.11
C	-0.24	4.15	0.94	-0.14
C	1.57	0.87	-0.91	0.30
H	0.43	3.51	0.40	0.05
N	0.80	1.95	-1.28	-0.61
H	-0.22	5.13	0.46	0.05
C	4.84	-0.51	0.32	-0.09
H	0.14	4.28	1.94	0.05
C	5.98	-0.21	-0.34	0.29
C	-1.73	3.32	-1.58	-0.01
C	6.27	0.28	-1.72	-0.30
H	-0.79	3.85	-1.56	0.03
H	6.74	1.25	-1.68	0.10
H	-2.40	3.90	-2.21	0.03
H	6.94	-0.41	-2.22	0.10
C	-1.51	1.96	-2.27	-0.05
H	5.35	0.36	-2.29	0.10
H	-1.28	2.13	-3.32	0.05
O	7.03	-0.43	0.44	-0.10
H	-2.43	1.39	-2.24	0.05
N	6.61	-0.89	1.66	-0.46
C	-0.37	1.17	-1.69	0.32
C	5.33	-0.94	1.60	0.35
N	-0.43	-0.18	-1.46	-0.05
C	4.53	-1.38	2.79	-0.18
C	-1.36	-1.08	-1.61	-0.04
H	5.19	-1.56	3.63	0.07
H	-2.19	-0.74	-2.42	0.07
H	3.80	-0.62	3.06	0.07
H	-1.17	-2.05	-1.91	0.07
H	3.98	-2.29	2.57	0.07
C	-2.38	-1.19	-0.32	-0.03
H	-2.71	-0.19	-0.06	0.08
H	-1.73	-1.54	0.49	0.08
N	-3.54	-2.03	-0.50	-0.36
C	-3.22	-3.45	-0.64	-0.02
H	-2.42	-3.74	0.05	0.07
H	-2.88	-3.67	-1.64	0.07
C	-4.44	-4.30	-0.34	0.10
H	-5.23	-4.06	-1.04	0.05
H	-4.20	-5.35	-0.47	0.05
O	-4.88	-4.14	0.98	-0.40
C	-4.70	-2.86	1.53	0.10

H	-5.53	-2.67	2.20	0.05
H	-3.78	-2.85	2.12	0.05
C	-4.63	-1.80	0.45	-0.02
H	-4.51	-0.82	0.91	0.07
H	-5.58	-1.78	-0.09	0.07
C	0.82	-0.54	-0.99	0.01
C	1.36	-1.76	-0.59	-0.20
H	0.80	-2.67	-0.60	0.14
C	2.68	-1.75	-0.17	-0.16
H	3.14	-2.67	0.13	0.13
C	3.45	-0.57	-0.14	-0.07
C	2.88	0.63	-0.54	-0.13
H	3.44	1.55	-0.51	0.11
C	1.56	0.63	-0.97	0.29
N	0.78	1.68	-1.42	-0.59
C	4.86	-0.62	0.32	-0.13
C	5.99	-0.36	-0.36	0.29
C	6.26	0.03	-1.78	-0.28
H	6.73	1.01	-1.81	0.10
H	6.94	-0.69	-2.23	0.10
H	5.34	0.06	-2.34	0.10
O	7.04	-0.51	0.42	-0.10
N	6.63	-0.88	1.68	-0.47
C	5.35	-0.95	1.63	0.39
C	4.56	-1.31	2.85	-0.18
Ligand 3				
Atom	X	Y	Z	RESP Charge
H	3.83	-0.54	3.07	0.06
H	4.03	-2.24	2.70	0.06
C	-2.06	2.90	1.98	0.03
C	-1.17	2.87	3.19	-0.20
H	-0.27	2.28	3.01	0.07
H	-0.85	3.87	3.47	0.07
H	-1.68	2.44	4.05	0.07
C	-3.44	2.78	2.10	-0.11
H	-3.89	2.65	3.07	0.11
C	-4.25	2.84	0.98	-0.18
H	-5.32	2.77	1.08	0.13
C	-3.69	3.01	-0.28	-0.11
H	-4.33	3.07	-1.15	0.11
C	-2.31	3.13	-0.43	-0.05
C	-1.52	3.07	0.71	-0.09
H	-0.45	3.16	0.60	0.12
C	-1.70	3.28	-1.80	0.00

H	-0.77	3.83	-1.74	0.04
H	-2.37	3.86	-2.43	0.04
C	-1.44	1.94	-2.51	-0.07
H	-1.17	2.13	-3.55	0.06
H	-2.35	1.35	-2.52	0.06
C	-0.31	1.16	-1.89	0.32
N	-0.37	-0.17	-1.59	-0.06
C	-1.51	-1.07	-1.70	-0.02
H	-2.12	-0.79	-2.54	0.07
H	-1.12	-2.06	-1.91	0.07
C	-2.36	-1.07	-0.43	-0.01
H	-2.70	-0.05	-0.26	0.07
H	-1.74	-1.35	0.43	0.07
N	-3.52	-1.92	-0.57	-0.36
C	-3.20	-3.35	-0.56	-0.02
H	-2.43	-3.58	0.18	0.07
H	-2.83	-3.66	-1.53	0.07
C	-4.44	-4.17	-0.23	0.09
H	-5.21	-3.99	-0.97	0.05
H	-4.19	-5.22	-0.25	0.05
O	-4.93	-3.88	1.06	-0.39
C	-4.76	-2.56	1.49	0.09
H	-5.61	-2.30	2.10	0.05
H	-3.87	-2.49	2.11	0.05
C	-4.65	-1.60	0.31	-0.02
H	-4.54	-0.58	0.68	0.07
H	-5.57	-1.63	-0.26	0.07
C	0.86	-0.51	-1.07	0.01
C	1.40	-1.70	-0.59	-0.18
H	0.83	-2.61	-0.56	0.13
C	2.70	-1.67	-0.15	-0.17
H	3.15	-2.57	0.21	0.13
C	3.48	-0.49	-0.18	-0.10
C	2.92	0.69	-0.66	-0.11
H	3.49	1.60	-0.67	0.10
C	1.61	0.67	-1.11	0.28
N	0.84	1.69	-1.63	-0.61
C	4.88	-0.52	0.31	-0.12
C	6.02	-0.30	-0.37	0.30
C	6.32	0.02	-1.80	-0.30
H	6.79	0.99	-1.88	0.10
H	7.00	-0.72	-2.20	0.10

H	5.41	0.02	-2.38	0.10
O	7.06	-0.41	0.44	-0.10
N	6.63	-0.71	1.70	-0.47
C	5.35	-0.78	1.64	0.37
C	4.54	-1.08	2.87	-0.19
H	5.20	-1.14	3.73	0.07
H	3.81	-0.29	3.04	0.07
H	4.01	-2.01	2.76	0.07

Ligand 4				
Atom	X	Y	Z	RESP Charge
C	2.09	-2.90	1.86	-0.20
H	1.47	-2.89	2.74	0.13
C	3.47	-2.76	1.99	0.15
C	4.11	-2.62	3.36	-0.18
H	5.10	-2.18	3.29	0.06
H	4.22	-3.60	3.83	0.06
H	3.51	-2.01	4.02	0.06
C	4.24	-2.78	0.84	-0.20
H	5.31	-2.68	0.90	0.13
C	3.64	-2.93	-0.41	-0.15
H	4.27	-2.95	-1.29	0.13
C	2.27	-3.07	-0.54	0.00
C	1.50	-3.06	0.62	-0.15
H	0.43	-3.16	0.55	0.13
C	1.63	-3.22	-1.91	0.01
H	0.71	-3.79	-1.83	0.03
H	2.30	-3.77	-2.56	0.03
C	1.31	-1.87	-2.58	-0.03
H	1.02	-2.05	-3.61	0.04
H	2.21	-1.26	-2.60	0.04
C	0.18	-1.13	-1.92	0.33
N	0.22	0.20	-1.61	-0.06
C	1.32	1.13	-1.74	-0.03
H	1.91	0.88	-2.61	0.07
H	0.90	2.11	-1.93	0.07
C	2.22	1.13	-0.50	-0.01
H	2.59	0.13	-0.36	0.07
H	1.62	1.39	0.37	0.07
N	3.35	2.02	-0.68	-0.36
C	3.00	3.44	-0.63	-0.03
H	2.24	3.63	0.13	0.07

H	2.58	3.75	-1.59	0.07
C	4.22	4.29	-0.33	0.10
H	4.96	4.14	-1.11	0.05
H	3.95	5.33	-0.33	0.05
O	4.76	4.00	0.93	-0.39
C	4.64	2.66	1.34	0.10
H	5.53	2.42	1.92	0.05
H	3.78	2.55	2.00	0.05
C	4.51	1.71	0.16	-0.03
H	4.45	0.69	0.51	0.07
H	5.42	1.78	-0.44	0.07
C	-1.01	0.49	-1.05	0.00
C	-1.57	1.66	-0.54	-0.19
H	-1.03	2.59	-0.52	0.14
C	-2.86	1.59	-0.07	-0.18
H	-3.32	2.48	0.32	0.14
C	-3.60	0.39	-0.08	-0.09
C	-3.02	-0.76	-0.58	-0.14
H	-3.56	-1.69	-0.59	0.11
C	-1.72	-0.70	-1.08	0.30
N	-0.94	-1.70	-1.62	-0.61
C	-4.98	0.38	0.45	-0.09
C	-6.14	0.13	-0.19	0.29
C	-6.47	-0.18	-1.61	-0.29
H	-6.92	-1.17	-1.69	0.10
H	-7.19	0.54	-1.99	0.10
H	-5.58	-0.15	-2.33	0.10
Ligand 5				
Atom	X	Y	Z	RESP Charge
N	-6.69	0.50	1.91	0.46
C	-5.42	-0.87	1.86	-0.25
H	-4.58	-0.92	2.07	0.18
C	-5.21	-0.96	1.49	0.07
H	-4.81	-0.76	1.67	0.07
H	-5.40	-1.87	2.89	0.07
H	5.58	-2.63	3.91	0.06
H	5.91	-3.45	2.37	0.06
H	5.79	-1.68	2.44	0.06
C	4.22	-2.61	0.26	-0.21
H	5.29	-2.50	0.28	0.12
C	3.57	-2.65	-0.97	-0.15
H	4.16	-2.57	-1.86	0.14
C	2.19	-2.79	-1.06	-0.04

C	1.47	-2.91	0.13	-0.15
H	0.41	-3.03	0.09	0.14
C	1.50	-2.81	-2.41	-0.02
H	0.62	-3.44	-2.37	0.04
H	2.17	-3.25	-3.15	0.04
C	1.09	-1.42	-2.91	-0.02
H	0.77	-1.50	-3.95	0.03
H	1.96	-0.77	-2.91	0.03
C	-0.04	-0.82	-2.13	0.34
N	-0.05	0.48	-1.67	-0.05
C	1.01	1.47	-1.74	-0.04
H	1.57	1.34	-2.66	0.07
H	0.53	2.44	-1.80	0.07
C	1.96	1.38	-0.55	-0.02
H	2.37	0.38	-0.53	0.07
H	1.39	1.50	0.37	0.07
N	3.04	2.33	-0.67	-0.36
C	2.63	3.71	-0.46	-0.04
H	1.90	3.79	0.36	0.08
H	2.16	4.11	-1.35	0.08
C	3.82	4.59	-0.11	0.10
H	4.54	4.56	-0.93	0.06
H	3.51	5.61	0.02	0.06
O	4.43	4.19	1.09	-0.40
C	4.39	2.81	1.36	0.10
H	5.30	2.55	1.89	0.06
H	3.55	2.60	2.03	0.06
C	4.25	1.99	0.09	-0.04
H	4.24	0.94	0.34	0.08
H	5.13	2.16	-0.53	0.08
C	-1.26	0.65	-1.04	0.00
C	-1.85	1.72	-0.38	-0.20
H	-1.35	2.67	-0.27	0.14
C	-3.11	1.54	0.14	-0.17
H	-3.59	2.36	0.64	0.14
C	-3.79	0.31	0.02	-0.08
C	-3.19	-0.75	-0.63	-0.14
H	-3.69	-1.70	-0.72	0.11
C	-1.92	-0.57	-1.17	0.32
N	-1.12	-1.46	-1.85	-0.63
C	-5.15	0.17	0.60	-0.10
C	-6.32	-0.06	-0.02	0.29

C	-6.71	-0.23	-1.45	-0.28
H	-7.11	-1.22	-1.62	0.10
H	-7.47	0.49	-1.71	0.10
H	-5.85	-0.08	-2.09	0.10
O	-7.30	-0.13	0.87	-0.10
N	-6.80	0.05	2.13	-0.47
C	-5.54	0.23	1.99	0.36
C	-4.66	0.44	3.18	-0.19
H	-5.24	0.35	4.09	0.07
H	-3.86	-0.29	3.20	0.07
H	-4.20	1.42	3.16	0.07

Ligand 6				
Atom	X	Y	Z	RESP Charge
C	-0.91	4.30	0.79	-0.01
N	0.23	4.62	1.64	0.72
O	0.01	5.11	2.70	-0.44
O	1.32	4.37	1.22	-0.44
C	-2.18	4.65	1.23	-0.13
H	-2.31	5.13	2.17	0.14
C	-3.25	4.34	0.41	-0.15
H	-4.25	4.61	0.71	0.14
C	-3.04	3.72	-0.81	-0.08
H	-3.89	3.50	-1.44	0.12
C	-1.77	3.37	-1.24	-0.01
C	-0.69	3.67	-0.42	-0.06
H	0.31	3.41	-0.72	0.11
C	-1.57	2.68	-2.58	-0.02

H	-0.58	2.89	-2.96	0.04
H	-2.29	3.08	-3.29	0.04
C	-1.77	1.15	-2.52	-0.03
H	-1.88	0.77	-3.53	0.05
H	-2.70	0.93	-2.01	0.05
C	-0.63	0.42	-1.87	0.29
N	-0.75	-0.86	-1.42	-0.05
C	-1.93	-1.70	-1.39	-0.03
H	-2.60	-1.41	-2.19	0.07
H	-1.62	-2.72	-1.60	0.07
C	-2.68	-1.60	-0.06	-0.04
H	-2.93	-0.56	0.11	0.08
H	-2.01	-1.90	0.75	0.08
N	-3.90	-2.37	-0.08	-0.37
C	-3.68	-3.82	-0.10	-0.02
H	-2.86	-4.11	0.56	0.08
H	-3.43	-4.15	-1.10	0.08
C	-4.93	-4.55	0.35	0.10
H	-5.76	-4.32	-0.32	0.05
H	-4.77	-5.62	0.30	0.05
O	-5.28	-4.24	1.67	-0.39
C	-4.96	-2.94	2.09	0.10
H	-5.73	-2.63	2.79	0.05
H	-4.01	-2.95	2.62	0.05
C	-4.90	-1.98	0.92	-0.02
H	-4.68	-0.98	1.28	0.08
H	-5.88	-1.93	0.45	0.08
C	0.50	-1.22	-0.94	0.02
C	1.00	-2.38	-0.36	-0.20
H	0.39	-3.25	-0.20	0.14
C	2.33	-2.38	-0.01	-0.15
H	2.76	-3.26	0.43	0.13
C	3.16	-1.26	-0.20	-0.07
C	2.64	-0.11	-0.77	-0.11
H	3.25	0.77	-0.92	0.11
C	1.30	-0.10	-1.15	0.21
N	0.56	0.91	-1.73	-0.53
C	4.59	-1.32	0.20	-0.14
C	5.70	-1.27	-0.56	0.29
C	5.92	-1.17	-2.03	-0.30
H	6.45	-0.25	-2.27	0.10
H	6.52	-2.00	-2.37	0.10

H	4.97	-1.18	-2.56	0.10
O	6.78	-1.35	0.20	-0.10
N	6.41	-1.45	1.51	-0.47
C	5.13	-1.43	1.54	0.38
C	4.38	-1.49	2.83	-0.17
H	5.08	-1.51	3.66	0.06
H	3.73	-0.63	2.94	0.06
H	3.77	-2.38	2.88	0.06

Ligand 7				
Atom	X	Y	Z	RESP Charge
C	1.89	-3.63	0.49	-0.17
H	1.26	-4.08	1.23	0.15
C	3.25	-3.49	0.72	0.04
C	4.09	-2.92	-0.22	-0.17
H	5.14	-2.84	-0.02	0.15
C	3.55	-2.48	-1.41	-0.08
H	4.20	-2.04	-2.15	0.12
C	2.18	-2.59	-1.67	0.01
C	1.37	-3.18	-0.71	-0.08
H	0.31	-3.26	-0.90	0.12
C	1.62	-2.08	-2.98	-0.02
H	0.70	-2.60	-3.22	0.04
H	2.33	-2.28	-3.77	0.04

C	1.34	-0.57	-2.96	0.01
H	1.15	-0.23	-3.98	0.04
H	2.22	-0.04	-2.61	0.04
C	0.14	-0.20	-2.13	0.30
N	0.00	1.03	-1.53	-0.08
C	0.96	2.11	-1.47	0.01
H	1.56	2.11	-2.37	0.06
H	0.40	3.04	-1.47	0.06
C	1.87	2.01	-0.25	-0.03
H	2.37	1.05	-0.28	0.07
H	1.26	2.02	0.66	0.07
N	2.88	3.05	-0.26	-0.37
C	2.35	4.38	-0.01	-0.02
H	1.57	4.37	0.76	0.07
H	1.90	4.78	-0.91	0.07
C	3.45	5.33	0.44	0.12
H	4.21	5.39	-0.33	0.05
H	3.05	6.32	0.60	0.05
O	4.02	4.92	1.66	-0.41
C	4.06	3.53	1.87	0.12
H	4.96	3.32	2.44	0.05
H	3.21	3.23	2.48	0.05
C	4.07	2.77	0.56	-0.02
H	4.12	1.70	0.77	0.07
H	4.96	3.03	0.00	0.07
C	-1.24	1.01	-0.92	0.02
C	-1.93	1.95	-0.16	-0.18
H	-1.52	2.92	0.07	0.14
C	-3.18	1.59	0.30	-0.18
H	-3.75	2.30	0.88	0.14
C	-3.74	0.33	0.02	-0.06
C	-3.04	-0.59	-0.73	-0.10
H	-3.44	-1.56	-0.94	0.10
C	-1.78	-0.24	-1.20	0.23
N	-0.88	-0.96	-1.97	-0.56
C	-5.09	0.00	0.54	-0.14
C	-6.23	-0.25	-0.14	0.30
C	-6.57	-0.28	-1.59	-0.30
H	-6.88	-1.27	-1.89	0.10
H	-7.39	0.40	-1.79	0.10
H	-5.71	0.02	-2.18	0.10
O	-7.21	-0.52	0.71	-0.10

N	-6.75	-0.45	1.99	-0.46
C	-5.51	-0.15	1.91	0.37
C	-4.68	0.00	3.15	-0.17
H	-5.27	-0.25	4.02	0.06
H	-3.82	-0.66	3.11	0.06
H	-4.31	1.01	3.25	0.06
N	3.80	-3.96	1.98	0.73
O	3.06	-4.47	2.76	-0.44
O	4.98	-3.81	2.16	-0.44

Ligand 8				
Atom	X	Y	Z	RESP Charge
C	-2.23	3.17	2.27	-0.23
H	-1.62	3.31	3.15	0.16
C	-3.57	2.84	2.35	-0.14
H	-4.03	2.71	3.32	0.14
C	-4.31	2.68	1.19	-0.12
H	-5.36	2.44	1.25	0.12
C	-3.71	2.86	-0.04	-0.19
H	-4.29	2.75	-0.94	0.14
C	-2.36	3.18	-0.16	0.00
C	-1.65	3.34	1.03	0.24
F	-0.37	3.68	0.98	-0.18
C	-1.71	3.36	-1.51	0.00
H	-0.76	3.88	-1.41	0.03

H	-2.35	3.99	-2.12	0.03
C	-1.48	2.04	-2.27	-0.04
H	-1.22	2.27	-3.30	0.05
H	-2.39	1.47	-2.29	0.05
C	-0.34	1.23	-1.70	0.35
N	-0.41	-0.12	-1.47	-0.09
C	-1.55	-1.02	-1.63	-0.02
H	-2.18	-0.67	-2.44	0.07
H	-1.16	-1.98	-1.93	0.07
C	-2.37	-1.13	-0.35	-0.03
H	-2.71	-0.13	-0.08	0.08
H	-1.73	-1.48	0.46	0.08
N	-3.54	-1.97	-0.54	-0.36
C	-3.21	-3.39	-0.69	-0.03
H	-2.41	-3.69	0.00	0.08
H	-2.86	-3.60	-1.69	0.08
C	-4.43	-4.25	-0.40	0.10
H	-5.22	-4.00	-1.10	0.05
H	-4.18	-5.29	-0.54	0.05
O	-4.88	-4.10	0.92	-0.39
C	-4.70	-2.82	1.48	0.10
H	-5.53	-2.64	2.15	0.05
H	-3.79	-2.81	2.08	0.05
C	-4.63	-1.75	0.41	-0.03
H	-4.51	-0.78	0.87	0.08
H	-5.57	-1.73	-0.13	0.08
C	0.83	-0.49	-1.00	0.01
C	1.37	-1.70	-0.59	-0.18
H	0.80	-2.61	-0.60	0.13
C	2.68	-1.70	-0.17	-0.18
H	3.13	-2.63	0.13	0.14
C	3.46	-0.53	-0.14	-0.06
C	2.90	0.67	-0.55	-0.13
H	3.47	1.59	-0.52	0.11
C	1.58	0.69	-0.98	0.29
N	0.81	1.74	-1.43	-0.62
C	4.87	-0.59	0.32	-0.16
C	6.00	-0.34	-0.37	0.31
C	6.28	0.04	-1.78	-0.29
H	6.75	1.01	-1.82	0.10
H	6.95	-0.68	-2.23	0.10
H	5.36	0.07	-2.35	0.10

O	7.05	-0.50	0.43	-0.10
N	6.64	-0.86	1.68	-0.47
C	5.36	-0.91	1.63	0.38
C	4.57	-1.26	2.85	-0.18
H	5.23	-1.38	3.70	0.07
H	3.84	-0.48	3.07	0.07
H	4.02	-2.19	2.71	0.07

Ligand 9				
Atom	X	Y	Z	RESP Charge
C	-2.01	3.06	1.91	0.15

F	-1.20	3.04	2.97	-0.18
C	-3.37	2.98	2.11	-0.11
H	-3.76	2.91	3.11	0.13
C	-4.19	2.99	1.00	-0.18
H	-5.26	2.94	1.13	0.14
C	-3.65	3.09	-0.27	-0.12
H	-4.31	3.11	-1.13	0.12
C	-2.27	3.16	-0.46	-0.05
C	-1.44	3.15	0.66	-0.09
H	-0.38	3.21	0.56	0.13
C	-1.69	3.24	-1.86	0.00
H	-0.75	3.77	-1.84	0.04
H	-2.37	3.80	-2.49	0.04
C	-1.47	1.86	-2.50	-0.06
H	-1.24	1.99	-3.55	0.06
H	-2.39	1.29	-2.45	0.06
C	-0.33	1.10	-1.88	0.31
N	-0.38	-0.23	-1.57	-0.05
C	-1.52	-1.14	-1.67	-0.04
H	-2.13	-0.87	-2.51	0.08
H	-1.12	-2.13	-1.87	0.08
C	-2.37	-1.12	-0.40	-0.04
H	-2.70	-0.10	-0.23	0.08
H	-1.74	-1.40	0.46	0.08
N	-3.53	-1.97	-0.53	-0.36
C	-3.22	-3.40	-0.52	-0.02
H	-2.44	-3.63	0.21	0.08
H	-2.85	-3.71	-1.50	0.08
C	-4.45	-4.21	-0.19	0.09
H	-5.23	-4.03	-0.93	0.06
H	-4.22	-5.27	-0.21	0.06
O	-4.94	-3.93	1.10	-0.39
C	-4.75	-2.61	1.54	0.09
H	-5.60	-2.35	2.16	0.06
H	-3.86	-2.55	2.15	0.06
C	-4.65	-1.64	0.36	-0.02
H	-4.53	-0.63	0.74	0.08
H	-5.58	-1.67	-0.19	0.08
C	0.86	-0.55	-1.06	0.02
C	1.40	-1.74	-0.57	-0.20
H	0.85	-2.65	-0.53	0.14
C	2.71	-1.69	-0.14	-0.17

H	3.17	-2.59	0.23	0.14
C	3.47	-0.51	-0.17	-0.07
C	2.91	0.66	-0.65	-0.12
H	3.46	1.58	-0.67	0.11
C	1.59	0.63	-1.10	0.27
N	0.81	1.64	-1.62	-0.59
C	4.87	-0.52	0.32	-0.13
C	6.02	-0.31	-0.37	0.30
C	6.31	-0.02	-1.80	-0.30
H	6.78	0.96	-1.90	0.10
H	7.00	-0.76	-2.19	0.10
H	5.40	-0.03	-2.38	0.10
O	7.06	-0.40	0.45	-0.10
N	6.63	-0.68	1.72	-0.47
C	5.35	-0.76	1.66	0.36
C	4.54	-1.03	2.89	-0.17
H	5.20	-1.09	3.75	0.06
H	3.81	-0.25	3.04	0.06
H	4.01	-1.97	2.79	0.06

Ligand 10				
Atom	X	Y	Z	RESP Charge
C	1.95	-3.10	1.84	-0.20
H	1.33	-3.14	2.71	0.15
C	3.31	-2.98	1.98	0.27
F	3.84	-2.90	3.20	-0.20
C	4.16	-2.93	0.89	-0.20
H	5.22	-2.84	1.04	0.15
C	3.60	-3.00	-0.38	-0.13
H	4.25	-2.97	-1.24	0.13
C	2.23	-3.12	-0.57	-0.02
C	1.41	-3.18	0.56	-0.13
H	0.35	-3.27	0.44	0.13
C	1.64	-3.18	-1.96	0.00
H	0.71	-3.74	-1.96	0.03
H	2.33	-3.70	-2.62	0.03
C	1.38	-1.79	-2.57	-0.02
H	1.13	-1.90	-3.62	0.04
H	2.28	-1.20	-2.53	0.04

C	0.24	-1.07	-1.91	0.33
N	0.26	0.26	-1.59	-0.06
C	1.37	1.20	-1.70	-0.02
H	1.97	0.95	-2.56	0.07
H	0.95	2.18	-1.88	0.07
C	2.25	1.19	-0.45	-0.02
H	2.61	0.18	-0.30	0.07
H	1.64	1.44	0.42	0.07
N	3.40	2.06	-0.60	-0.37
C	3.05	3.48	-0.58	-0.02
H	2.28	3.69	0.17	0.07
H	2.66	3.79	-1.54	0.07
C	4.27	4.32	-0.26	0.11
H	5.03	4.16	-1.02	0.05
H	4.01	5.37	-0.27	0.05
O	4.79	4.04	1.01	-0.40
C	4.64	2.71	1.44	0.11
H	5.51	2.47	2.05	0.05
H	3.76	2.63	2.08	0.05
C	4.53	1.75	0.27	-0.02
H	4.45	0.74	0.63	0.07
H	5.45	1.81	-0.31	0.07
C	-0.97	0.55	-1.04	0.01
C	-1.53	1.71	-0.52	-0.20
H	-1.00	2.64	-0.49	0.15
C	-2.83	1.63	-0.06	-0.17
H	-3.30	2.51	0.33	0.14
C	-3.56	0.43	-0.09	-0.07
C	-2.98	-0.72	-0.60	-0.12
H	-3.52	-1.65	-0.62	0.11
C	-1.68	-0.65	-1.08	0.28
N	-0.89	-1.64	-1.63	-0.61
C	-4.95	0.40	0.43	-0.12
C	-6.10	0.16	-0.23	0.30
C	-6.42	-0.14	-1.65	-0.28
H	-6.86	-1.13	-1.74	0.10
H	-7.14	0.57	-2.03	0.10
H	-5.53	-0.10	-2.26	0.10
O	-7.13	0.22	0.61	-0.10
N	-6.68	0.51	1.87	-0.46
C	-5.41	0.62	1.78	0.35
C	-4.58	0.92	2.99	-0.16

H	-5.21	0.95	3.87	0.06
H	-3.82	0.16	3.13	0.06
H	-4.08	1.88	2.89	0.06

Ligand 11				
Atom	X	Y	Z	RESP Charge
C	-2.08	-2.92	-0.51	-0.16
Cl	-1.14	-3.44	-1.87	-0.11
C	-3.46	-2.78	-0.63	0.38
O	-4.00	-3.06	-1.83	-0.29
C	-5.39	-3.00	-2.00	-0.01
H	-5.58	-3.29	-3.03	0.07
H	-5.90	-3.69	-1.34	0.07
H	-5.77	-2.00	-1.84	0.07
C	-4.18	-2.36	0.48	-0.18
H	-5.25	-2.26	0.42	0.12
C	-3.53	-2.10	1.68	-0.23
H	-4.12	-1.79	2.52	0.16
C	-2.16	-2.24	1.81	-0.03
C	-1.44	-2.65	0.69	-0.04
H	-0.38	-2.77	0.75	0.13
C	-1.47	-1.92	3.12	0.00
H	-0.58	-2.54	3.23	0.04

H	-2.13	-2.16	3.94	0.04
C	-1.05	-0.45	3.26	-0.05
H	-0.74	-0.26	4.28	0.05
H	-1.91	0.19	3.07	0.05
C	0.09	-0.07	2.35	0.31
N	0.15	1.10	1.64	-0.05
C	-0.88	2.12	1.50	-0.03
H	-1.43	2.21	2.43	0.07
H	-0.37	3.06	1.35	0.07
C	-1.84	1.81	0.36	-0.02
H	-2.28	0.83	0.55	0.08
H	-1.27	1.72	-0.58	0.08
N	-2.90	2.79	0.28	-0.36
C	-2.46	4.09	-0.20	-0.03
H	-1.73	3.99	-1.01	0.07
H	-1.98	4.64	0.60	0.07
C	-3.63	4.90	-0.71	0.09
H	-4.35	5.05	0.09	0.06
H	-3.30	5.88	-1.04	0.06
O	-4.26	4.30	-1.81	-0.39
C	-4.23	2.89	-1.82	0.09
H	-5.15	2.55	-2.29	0.06
H	-3.40	2.54	-2.43	0.06
C	-4.12	2.33	-0.41	-0.03
H	-4.13	1.25	-0.45	0.07
H	-4.99	2.63	0.16	0.07
C	1.36	1.08	0.98	0.02
C	1.97	1.97	0.11	-0.20
H	1.51	2.90	-0.19	0.15
C	3.22	1.63	-0.37	-0.17
H	3.73	2.31	-1.03	0.14
C	3.86	0.43	0.00	-0.08
C	3.22	-0.45	0.86	-0.13
H	3.68	-1.38	1.14	0.11
C	1.97	-0.11	1.36	0.27
N	1.14	-0.80	2.22	-0.59
C	5.20	0.12	-0.55	-0.12
C	6.38	-0.01	0.10	0.30
C	6.78	0.13	1.52	-0.30
H	7.16	-0.81	1.91	0.10
H	7.57	0.87	1.62	0.10
H	5.93	0.44	2.12	0.10

O	7.34	-0.31	-0.76	-0.10
N	6.82	-0.40	-2.03	-0.47
C	5.56	-0.15	-1.92	0.36
C	4.67	-0.18	-3.12	-0.17
H	5.24	-0.48	-3.99	0.07
H	3.85	-0.87	-2.97	0.07
H	4.24	0.80	-3.30	0.07

Ligand 12				
Atom	X	Y	Z	RESP Charge
C	2.09	-2.92	0.90	0.09
F	1.38	-3.17	1.99	-0.18
C	3.47	-2.79	1.02	0.28
O	3.98	-2.94	2.26	-0.28
C	5.36	-2.89	2.44	-0.01
H	5.53	-3.06	3.50	0.07
H	5.86	-3.67	1.87	0.07
H	5.77	-1.92	2.17	0.07
C	4.19	-2.53	-0.13	-0.19
H	5.26	-2.44	-0.09	0.13
C	3.55	-2.41	-1.35	-0.22

H	4.14	-2.21	-2.23	0.16
C	2.18	-2.53	-1.47	-0.06
C	1.45	-2.80	-0.30	-0.14
H	0.38	-2.91	-0.33	0.16
C	1.48	-2.37	-2.80	0.00
H	0.60	-3.00	-2.85	0.04
H	2.15	-2.70	-3.59	0.04
C	1.07	-0.92	-3.11	-0.07
H	0.76	-0.86	-4.15	0.06
H	1.94	-0.27	-3.01	0.06
C	-0.07	-0.44	-2.26	0.32
N	-0.10	0.80	-1.67	-0.05
C	0.93	1.81	-1.63	-0.02
H	1.49	1.80	-2.56	0.07
H	0.44	2.77	-1.57	0.07
C	1.89	1.61	-0.46	-0.02
H	2.32	0.62	-0.55	0.07
H	1.32	1.62	0.48	0.07
N	2.96	2.58	-0.47	-0.36
C	2.53	3.93	-0.12	-0.03
H	1.80	3.92	0.69	0.08
H	2.05	4.41	-0.97	0.08
C	3.71	4.78	0.31	0.09
H	4.43	4.85	-0.51	0.06
H	3.38	5.78	0.54	0.06
O	4.33	4.27	1.46	-0.39
C	4.30	2.87	1.60	0.09
H	5.22	2.57	2.09	0.06
H	3.47	2.59	2.24	0.06
C	4.17	2.18	0.25	-0.03
H	4.18	1.11	0.39	0.08
H	5.05	2.43	-0.35	0.08
C	-1.32	0.87	-1.01	0.02
C	-1.92	1.85	-0.24	-0.20
H	-1.44	2.79	-0.03	0.14
C	-3.17	1.58	0.26	-0.17
H	-3.68	2.33	0.85	0.14
C	-3.83	0.36	0.02	-0.07
C	-3.21	-0.61	-0.75	-0.12
H	-3.69	-1.56	-0.94	0.11
C	-1.95	-0.35	-1.27	0.27
N	-1.13	-1.13	-2.06	-0.60

C	-5.18	0.12	0.58	-0.12
C	-6.36	-0.05	-0.05	0.30
C	-6.75	-0.05	-1.49	-0.30
H	-7.14	-1.02	-1.77	0.10
H	-7.53	0.69	-1.66	0.10
H	-5.90	0.18	-2.11	0.10
O	-7.32	-0.25	0.83	-0.10
N	-6.81	-0.21	2.10	-0.47
C	-5.55	0.01	1.97	0.36
C	-4.67	0.09	3.17	-0.17
H	-5.24	-0.11	4.07	0.07
H	-3.86	-0.63	3.10	0.07
H	-4.22	1.07	3.26	0.07

Ligand 13				
Atom	X	Y	Z	RESP Charge
H	0.76	-4.03	-1.14	0.05
H	2.40	-4.17	-1.73	0.05
C	1.54	-2.23	-2.01	-0.11
H	1.35	-2.49	-3.05	0.08
H	2.45	-1.66	-1.99	0.08
C	0.38	-1.40	-1.52	0.32
N	0.41	-0.04	-1.42	-0.07
C	1.54	0.86	-1.62	-0.02
H	2.18	0.47	-2.40	0.07
H	1.14	1.80	-1.99	0.07
C	2.35	1.05	-0.34	-0.05
H	2.69	0.08	-0.01	0.08
H	1.70	1.45	0.44	0.08
N	3.51	1.89	-0.58	-0.36

C	3.18	3.29	-0.79	-0.03
H	2.39	3.62	-0.11	0.08
H	2.83	3.45	-1.80	0.08
C	4.40	4.17	-0.55	0.10
H	5.19	3.89	-1.24	0.05
H	4.15	5.21	-0.73	0.05
O	4.86	4.08	0.78	-0.39
C	4.69	2.83	1.39	0.10
H	5.53	2.68	2.06	0.05
H	3.78	2.84	2.00	0.05
C	4.61	1.71	0.37	-0.03
H	4.50	0.76	0.88	0.08
H	5.55	1.66	-0.17	0.08
C	-0.84	0.34	-0.98	0.03
C	-1.41	1.58	-0.69	-0.18
H	-0.86	2.50	-0.78	0.13
C	-2.73	1.59	-0.28	-0.19
H	-3.20	2.53	-0.06	0.14
C	-3.48	0.40	-0.15	-0.06
C	-2.89	-0.82	-0.44	-0.10
H	-3.44	-1.74	-0.33	0.10
C	-1.56	-0.84	-0.86	0.24
N	-0.77	-1.91	-1.21	-0.58
C	-4.89	0.47	0.30	-0.13
C	-6.01	0.13	-0.37	0.29
C	-6.27	-0.39	-1.74	-0.29
H	-6.72	-1.38	-1.69	0.10
H	-6.96	0.27	-2.26	0.10
H	-5.35	-0.45	-2.29	0.10
O	-7.07	0.34	0.40	-0.10
N	-6.68	0.82	1.62	-0.47
C	-5.40	0.91	1.57	0.37
C	-4.62	1.39	2.76	-0.15
H	-5.30	1.57	3.59	0.06
H	-3.88	0.66	3.05	0.06
H	-4.10	2.32	2.53	0.06
C	2.22	-3.28	0.20	-0.05
C	1.51	-3.12	1.34	-0.05
H	0.43	-3.17	1.36	0.13
C	2.32	-2.87	2.49	-0.32
H	1.92	-2.72	3.48	0.18
C	3.63	-2.85	2.21	-0.11

H	4.45	-2.71	2.89	0.17
S	3.92	-3.14	0.53	-0.05

Ligand 14				
Atom	X	Y	Z	RESP Charge
C	1.40	-3.00	-1.98	-0.04
H	0.54	-3.57	-1.64	0.07
H	1.96	-3.61	-2.68	0.07
C	0.90	-1.74	-2.71	-0.07
H	0.54	-2.03	-3.69	0.07
H	1.73	-1.06	-2.87	0.07
C	-0.24	-1.07	-2.00	0.31
N	-0.27	0.27	-1.68	-0.03
C	0.75	1.28	-1.87	-0.02
H	1.34	1.04	-2.74	0.07
H	0.24	2.21	-2.08	0.07
C	1.66	1.42	-0.65	0.00
H	2.13	0.46	-0.48	0.07
H	1.05	1.63	0.24	0.07
N	2.69	2.41	-0.87	-0.38
C	2.18	3.78	-0.85	-0.02
H	1.43	3.92	-0.07	0.07
H	1.71	4.02	-1.80	0.07
C	3.32	4.77	-0.61	0.12
H	4.06	4.68	-1.40	0.05

H	2.93	5.78	-0.62	0.05
O	3.92	4.57	0.65	-0.40
C	3.95	3.24	1.10	0.12
H	4.87	3.11	1.66	0.05
H	3.12	3.06	1.78	0.05
C	3.90	2.25	-0.06	-0.02
H	3.95	1.24	0.33	0.07
H	4.77	2.40	-0.69	0.07
C	-1.50	0.47	-1.08	0.01
C	-2.11	1.60	-0.54	-0.21
H	-1.63	2.56	-0.53	0.14
C	-3.38	1.45	-0.02	-0.14
H	-3.88	2.30	0.39	0.13
C	-4.04	0.20	-0.02	-0.08
C	-3.41	-0.91	-0.55	-0.12
H	-3.88	-1.87	-0.55	0.11
C	-2.13	-0.77	-1.09	0.28
N	-1.31	-1.70	-1.68	-0.61
C	-5.40	0.09	0.56	-0.14
C	-6.56	-0.21	-0.05	0.29
C	-6.93	-0.52	-1.46	-0.30
H	-7.31	-1.53	-1.54	0.11
H	-7.70	0.16	-1.80	0.11
H	-6.06	-0.43	-2.10	0.11
O	-7.55	-0.21	0.84	-0.10
N	-7.06	0.09	2.07	-0.47
C	-5.80	0.28	1.93	0.38
C	-4.94	0.62	3.11	-0.17
H	-5.53	0.61	4.01	0.07
H	-4.13	-0.10	3.20	0.07
H	-4.49	1.60	2.99	0.07
C	2.26	-2.69	-0.79	0.27
N	1.81	-2.49	0.39	-0.50
C	2.83	-2.18	1.28	0.25
C	4.11	-2.15	0.73	0.09
C	5.22	-1.85	1.51	-0.17
H	6.21	-1.83	1.08	0.17
C	5.03	-1.59	2.85	-0.18
H	5.87	-1.35	3.47	0.14
C	3.75	-1.62	3.40	-0.14
H	3.62	-1.41	4.45	0.14
C	2.65	-1.91	2.63	-0.16

H	1.66	-1.94	3.05	0.13
S	4.00	-2.53	-0.97	-0.13

Ligand 15				
Atom	X	Y	Z	RESP Charge
C	-1.72	2.89	-2.14	0.00
H	-0.82	3.46	-1.95	0.07
H	-2.32	3.45	-2.85	0.07
C	-1.35	1.54	-2.79	-0.10
H	-1.02	1.74	-3.81	0.07
H	-2.23	0.92	-2.85	0.07
C	-0.22	0.84	-2.09	0.33
N	-0.28	-0.45	-1.64	-0.05
C	-1.40	-1.38	-1.67	-0.01
H	-1.99	-1.20	-2.56	0.07
H	-0.99	-2.37	-1.77	0.07
C	-2.28	-1.26	-0.43	0.00
H	-2.66	-0.25	-0.38	0.07
H	-1.67	-1.41	0.46	0.07
N	-3.40	-2.18	-0.50	-0.38
C	-3.03	-3.57	-0.28	-0.02

H	-2.27	-3.66	0.50	0.07
H	-2.61	-4.00	-1.19	0.07
C	-4.24	-4.39	0.13	0.11
H	-4.99	-4.35	-0.66	0.05
H	-3.95	-5.43	0.26	0.05
O	-4.78	-3.95	1.34	-0.40
C	-4.69	-2.57	1.58	0.11
H	-5.58	-2.27	2.12	0.05
H	-3.83	-2.36	2.22	0.05
C	-4.57	-1.79	0.28	-0.02
H	-4.53	-0.73	0.50	0.07
H	-5.47	-1.95	-0.31	0.07
C	0.96	-0.71	-1.09	0.01
C	1.50	-1.84	-0.48	-0.18
H	0.95	-2.75	-0.35	0.13
C	2.81	-1.74	-0.04	-0.16
H	3.26	-2.60	0.43	0.14
C	3.57	-0.57	-0.18	-0.09
C	3.00	0.54	-0.79	-0.09
H	3.56	1.46	-0.90	0.10
C	1.69	0.46	-1.25	0.25
N	0.91	1.41	-1.88	-0.60
C	4.96	-0.52	0.31	-0.11
C	6.11	-0.37	-0.38	0.28
C	6.42	-0.21	-1.83	-0.28
H	6.88	0.75	-2.01	0.10
H	7.11	-0.98	-2.14	0.10
H	5.51	-0.29	-2.41	0.10
O	7.14	-0.38	0.45	-0.10
N	6.70	-0.54	1.74	-0.47
C	5.43	-0.63	1.67	0.36
C	4.61	-0.80	2.92	-0.15
H	5.25	-0.76	3.79	0.06
H	3.86	-0.01	2.99	0.06
H	4.09	-1.75	2.91	0.06
N	-2.48	2.76	-0.92	0.01
C	-2.00	2.83	0.38	0.07
C	-3.10	2.70	1.25	0.11
C	-4.27	2.55	0.42	-0.32
H	-5.28	2.45	0.74	0.18
C	-3.84	2.60	-0.86	-0.20
H	-4.41	2.55	-1.77	0.18

C	-2.89	2.75	2.63	-0.19
H	-3.72	2.66	3.31	0.13
C	-1.61	2.92	3.10	-0.17
H	-1.44	2.96	4.17	0.13
C	-0.53	3.04	2.22	-0.18
H	0.46	3.17	2.62	0.14
C	-0.70	3.00	0.86	-0.15
H	0.14	3.08	0.19	0.13

2.2 MM-PBSA and MM-GBSA analysis

The MM-PB(GB)SA analysis was performed with an internal dielectric constant (ε_{int}) of 1; the MM-PBSA analysis was also repeated with ε_{int}=4.0, giving worse results: the correlation coefficient drops from 0.59 to 0.38 with this change in dielectric constant. This change is due to the importance of electrostatics (and thus dielectric constant) for quantification of the strength of cation-π interactions.

Both PB and GB surface area models give similar levels of correlation with experimental binding affinities (**Table S4**), while consideration of just the electrostatic term improves this correlation. This observation is coherent with earlier attempts to use classical force fields to evaluate the interaction strength of cation-π interaction: the intermolecular electrostatic term tends to correlate more strongly with QM-computed results than does the total classical intermolecular energy.

Table S4. Binding free energies (kcal/mol) calculated for ligands **L1-L15**.

Ligand	MM-PBSA	MM-GBSA	Electrostatic	MM-PBSA ε_{int}=4.0
L1	-33.46 ± 2.73	-36.43 ± 4.63	-2.07 ± 1.08	-43.39 ± 2.58
L2	-35.90 ± 3.30	-38.83 ± 3.35	-1.81 ± 1.27	-48.05 ± 2.53
L3	-34.21 ± 3.07	-38.11 ± 2.59	-1.75 ± 1.26	-45.10 ± 2.75
L4	-33.00 ± 3.28	-37.01 ± 3.30	-1.30 ± 1.06	-46.40 ± 2.17
L5	-36.10 ± 2.73	-38.98 ± 2.82	-2.48 ± 1.44	-44.80 ± 2.56
L6	-34.15 ± 2.33	-37.77 ± 2.47	-1.14 ± 2.28	-47.27 ± 2.29
L7	-32.02 ± 2.47	-35.83 ± 2.60	0.13 ± 2.51	-46.38 ± 2.60
L8	-33.01 ± 2.78	-35.84 ± 3.35	-1.16 ± 0.91	-45.34 ± 2.71
L9	-34.64 ± 2.96	-36.90 ± 2.55	-1.58 ± 1.06	-44.42± 2.31
L10	-32.89 ± 2.52	-35.98 ± 2.62	-1.88 ± 1.22	-45.22 ± 2.16
L11	-37.13 ± 2.32	-40.15 ± 2.06	-2.97 ± 1.30	-43.92 ± 2.38
L12	-36.72 ± 2.45	-38.72 ± 2.36	-2.09 ± 1.16	-47.50 ± 2.42
L13	-33.72 ± 2.64	-36.23 ± 2.45	0.85 ± 1.18	-43.80 ± 2.19
L14	-35.24 ± 2.52	-37.77 ± 2.44	-2.52 ± 1.67	-46.60 ± 3.01
L15	-34.84 ± 2.37	-37.06 ± 2.38	-4.91 ± 2.11	-46.09 ± 2.40
	r_s = 0.59	r_s = 0.53	r_s = 0.72	r_s = 0.38

3. REFERENCES

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