Supplementary Material (ESI) for Chemical Communications

Supplementary information for:

Synthesis and study of a new diamidodipyrromethane macrocycle. An anion receptor with a high sulfate-to-nitrate binding selectivity.

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SYNTHESIS

General: All solvents were of reagent grade quality and purchased commercially. All starting materials were purchased from Aldrich Chemical Co. and used without further purification. NMR spectra used in the characterization of products were recorded on Varian INOVA 500, Varian Mercury 400 or Varian UNITY+ 300 instruments. The NMR spectra were referenced to solvent and the spectroscopic solvents were purchased from Cambridge Isotope Laboratories. All high-resolution (HR) chemical ionization (CI) mass spectra were recorded on a VG ZAB-2E instrument. Elemental analyses were performed by Atlantic Microlabs, Inc., Atlanta, GA, and are reported as percentages. TLC analyses were carried out using Baker-flex Silica gel IB-F sheets. Column chromatography was performed on Whatman silica gel 60Å (230 – 400 mesh). bis(2-aminophenyl)pyridine-2,6-dicarboxamide[1] **3** and diformyl dimethyldipyrrolmethane[2] **4** were prepared according to literature procedures.

Synthesis of macrocycle 1. Bis(2-aminophenyl)pyridine-2,6-dicarboxamide **3** (100 mg; 0.288 mmol) , diformyl dimethyldipyrrolmethane **4** (66.4 mg; 0.288 mmol), and TFA (82 mg; 0.72 mmol) were mixed in 50 ml of dry MeOH. The mixture was heated at reflux under Ar for 15 min. At this point, 2 ml of Et_3N was added to the solution, and the reaction mixture was allowed to cool to room temperature. The volatile components were removed at 40^0 C under reduced pressure and the residue was dissolved in ethyl acetate. The resulting ethyl acetate solution was passed through a small plug of alumina (to get remove the presumed TFA*Et_3N) and evaporated to dryness. The residue produced in this way was dissolved in 9 ml of $CHCl_3$, layered with 3 ml of Et_2O and put in a refrigerator overnight. The precipitate that results was filtered off to yield the desired product, while evaporation of the filtrate yielded addition material. The total yield of free receptor **1** obtained in this was 140 mg (90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 1.69 (s, 6H, CH_3), 6.16 (d, 2H, pyrrole H), 6.62 (d, 2H, pyrrole H), 7.08 (m, 2H, phenyl-CH). 7.23 (m, 4H, phenyl-CH), 7.67 (m, 2H, phenyl-CH), 8.06 (t, 1H, pyridine-CH), 8.19 (s, 2H, N=CH), 8.40 (d, 2H, pyridine-CH), 9.77 (br s, 2H, pyrrole-NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 30.89, 35.77,

106.82, 118.79, 119.42, 125.76, 126.09, 127.00, 127.24, 129.64, 130.44, 138.81, 144.86, 145.43, 149.69, 151.10, 163.71. HRMS (CI^+): calcd for $C_{32}H_{28}N_7O_2$ $[M + H]^+$ 542.2304; found *m/z*: 542.2299. Anal. calcd for $C_{32}H_{28}N_7 \bullet H_2O$: C: 68.68; H: 5.22; N: 17.52; found C: 68.32; H: 5.16; N: 17.25.

ANION BINDING STUDIES

UV-Vis Anion Recognition Study:

Stock solutions of the host molecule being studied were made up in acetonitrile with the final concentrations being between 1.750×10^{-5} M and 2.215×10^{-5} M. The host was synthesized using the procedure described in the Experimental Section. For instance, 1.2 mg of receptor **1** were dissolved in 10 mL of acetonitrile (spectrophotometric grade) yielding a 2.215×10^{-4} M stock solution. This first stock solution was then diluted 10 times to give the titration stock solution with a concentration of 2.215×10^{-5}.

Stock solutions of the guest were prepared by dissolving 10 - 100 equivalents of tetrabutylammonium salts of the anions used in this study in 1.5 - 2.5 ml of stock solution of the host, prepared as described above. Making up the anion source solutions in this way allowed the binding studies to be carried out without having to make mathematical corrections to account for the changes in host concentration.

The general procedure for the UV-Vis binding studies involved making sequential additions of titrant (anionic guest) using Hamilton® pipettes to a 2 mL aliquot of the host stock solution in the spectrometric cell. The data was then collated and combined to produce plots that showed the changes in host spectral features as a function of changes in the concentration of the guest.

Calculations of Equilibrium Constants, K_a:

Equilibrium constants were calculated using equation 4.5 of Connors[3] where [L] = [anion]. The resulting equation, of the form, $y = B \times K_a \times x / (1 + K_a \times x)$, was computer fit using Origin version 7.0, where x = [anion], y = ΔA, B = $\Delta\varepsilon \times b$, K_a = the equilibrium constant. The change in absorbance, ΔA, was calculated at a λ value where the spectral change was maximal.

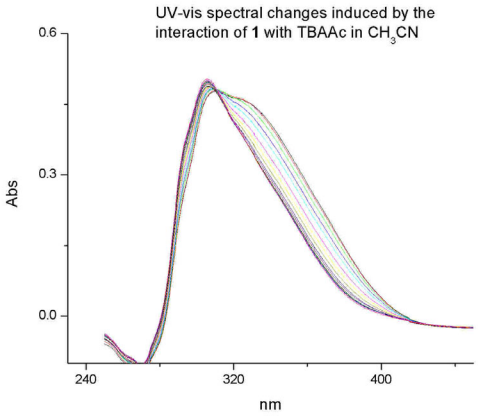
Job Plot Construction:

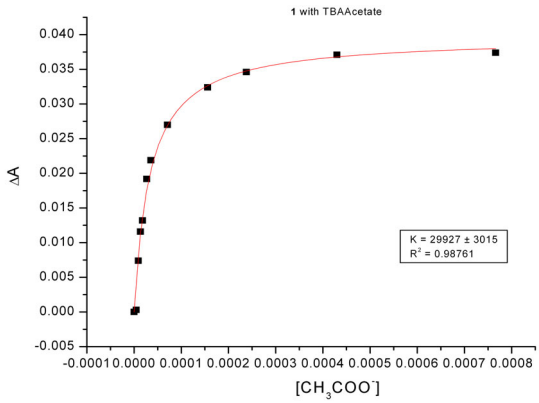
A stock solution of the host was prepared as described for the K_a determination experiments. The guest stock solution was prepared by dissolving 1 - 2 equivalents of the tetrabutylammonium salts of the studied anions is the same solvent (acetonitrile) as the one used for the host stock solution.

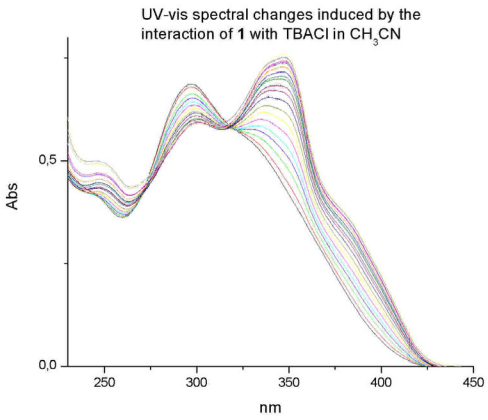
The general procedure for the UV-Vis Job titrations involved making sequential additions of titrant (anionic guest) using Hamilton® pipettes to a 1.5 ml aliquot of the host stock solution in a spectrometric cell. The data was then collated and combined to produce data files from which so-called Job plots could be constructed. These latter were

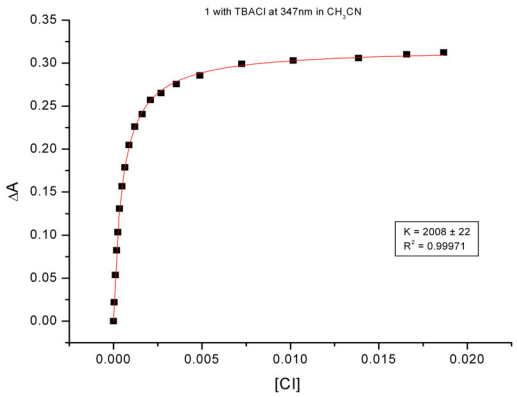
produced as described by Connors[4], namely by plotting the molar fraction of guest (X_G) as a function of [host] × ΔA. The plots themselves were generated using Kaleidagraph software version 3.5.2. The change in absorbance, ΔA, was calculated at a λ value where the spectral change was maximal. In accord with accepted practice, the maxima of the resulting graph was considered indicative of the stoichiometry of the host:guest complex, namely a maximum where X_G = 0.5 was considered indicative of a 1:1 host:guest complex stoichiometry.

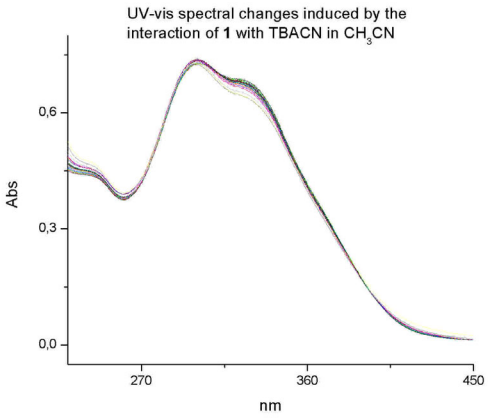
Representative plots and curve fits are given below.

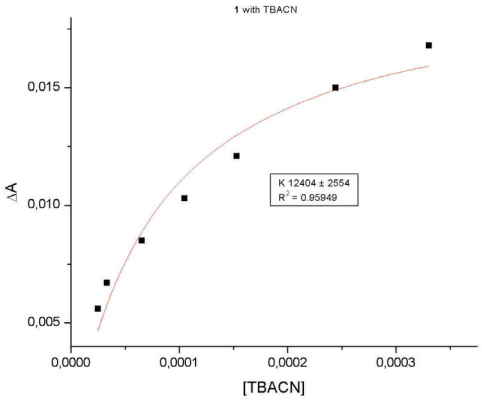


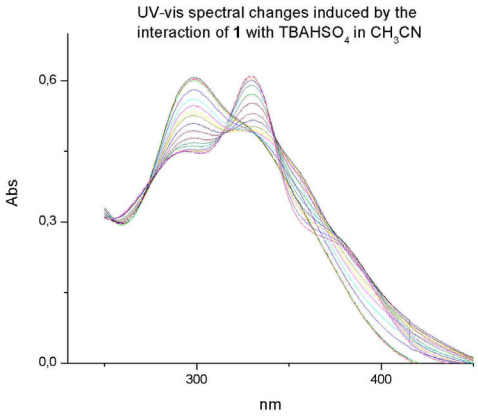


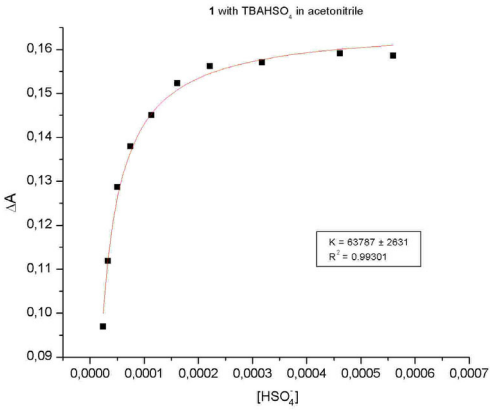


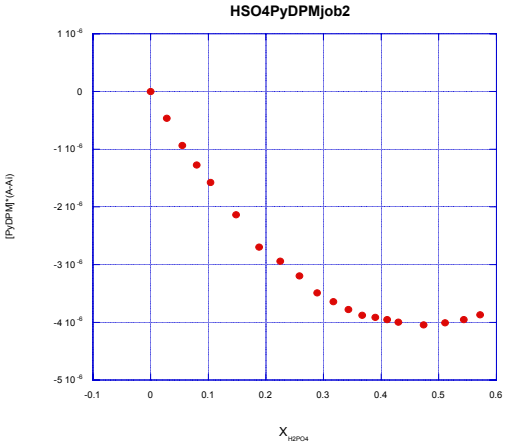


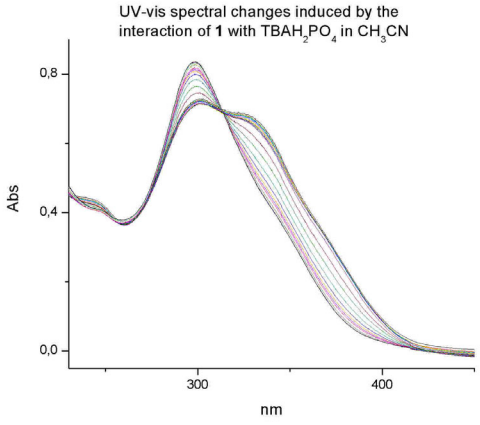


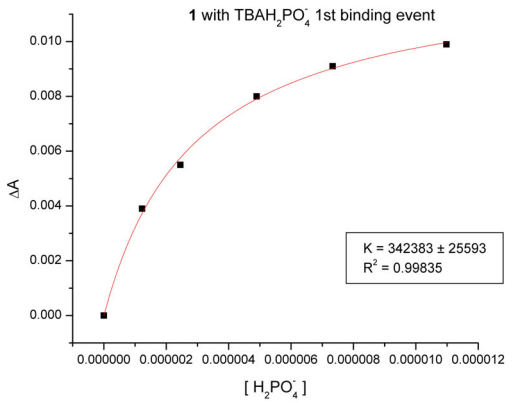


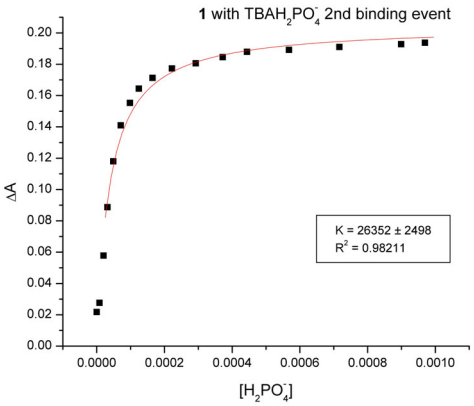


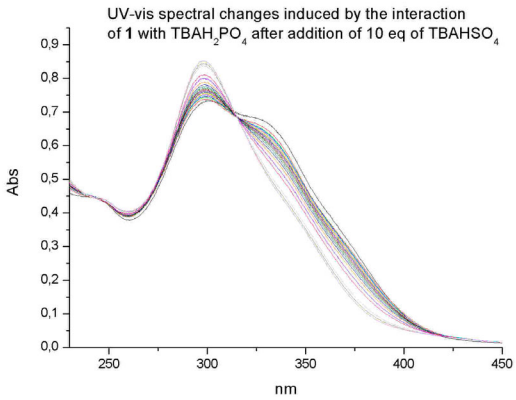


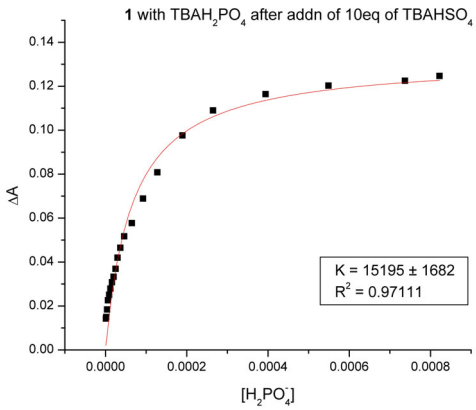


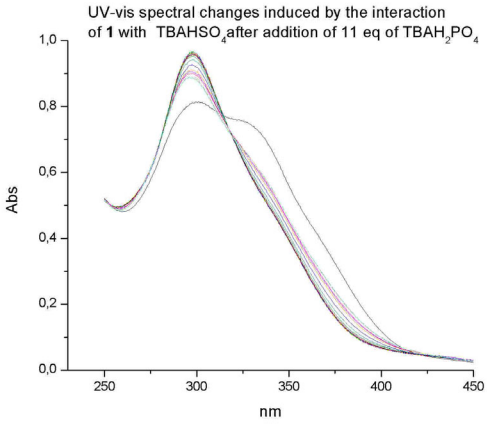


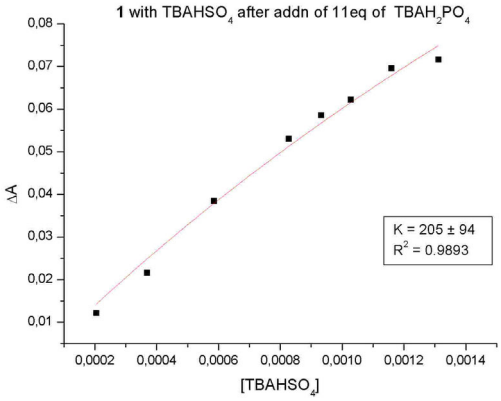










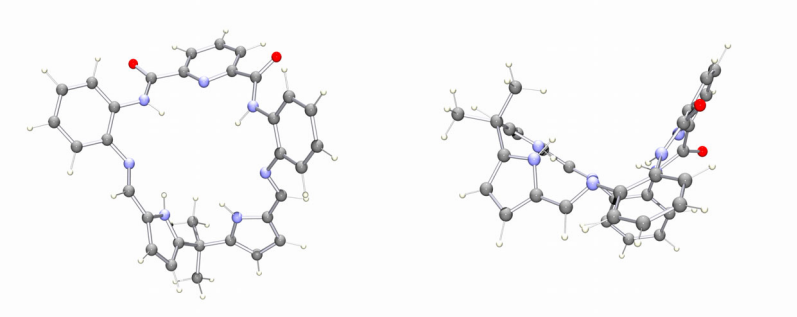


Molecular Modeling

Molecular modeling calculations were performed using the DFT program "PRIRODA" developed by Dmitri Laikov.[5,6] PBE functional that includes the electron density gradient was used. The TZ2p_atomic basis sets of grouped Gaussian functions were used to solve the Kohn—Sham equations. The criterion for convergence was a difference in energy between two sequential structures below 0.01 kcal/mol/Angstrom. The host-guest model structures were generated by combining a preoptimized structure of the receptor with a

preoptimized structure of the anion, followed by simultaneous optimization of the proposed structures. Searches for the relevant global minima were performed by calculating different anion-to-receptor coordination modes. Various stationary points on the potential energy surface (PES) were determined from analytical calculations of the second energy derivatives (Hessian matrixes).

Supplementary Figure 1. Structure of free receptor **1.**



Atomic Coordinates:

6	-0.65727812	3.78984363	0.59743480
6	0.14365279	4.85099838	1.03226808
6	1.43745549	4.66169535	0.49857911
6	1.41351613	3.48318669	-0.25608585
7	0.13517086	2.97246911	-0.16367462
6	-3.21052069	1.35670822	-2.00865899
6	-3.44986769	2.61597132	-2.57025350
6	-3.12911929	3.58469265	-1.59613820
6	-2.69877786	2.91476730	-0.44564424
7	-2.74845952	1.57179416	-0.72332647
6	-2.88369388	4.72778395	1.26981232
6	-3.41466575	0.03410706	-2.51550293
7	-3.10983327	-1.00963360	-1.80395583
6	-3.52083294	-2.28439984	-2.20604352
6	2.42948478	2.85630753	-1.04506791
7	2.24496891	1.71497726	-1.63710045
6	-2.78441196	-3.40680956	-1.74292592
6	-3.23400421	-4.70426228	-2.02810576
6	-4.39470528	-4.90277846	-2.77307005
6	-5.12768136	-3.80567077	-3.23823215
6	-4.69467139	-2.51433890	-2.95391731
6	3.24036384	1.23979155	-2.50182765
6	3.92064477	2.07334639	-3.40847319

6	4.90227394	1.56153071	-4.25520363
6	5.21825691	0.20068709	-4.20880095
6	4.54212347	-0.65015213	-3.33370901
6	3.54447294	-0.14704905	-2.48839370
7	2.82756866	-0.97525494	-1.60140324
7	-1.58323771	-3.19136361	-1.03520720
6	3.34896965	-2.04387560	-0.91613499
6	-1.09800746	-3.99112052	-0.03128630
8	-1.70721768	-4.94039215	0.46574029
6	0.31241442	-3.67145593	0.42347984
7	1.08236069	-2.84973277	-0.31818279
6	2.38861985	-2.77539491	-0.00099266
6	2.95047141	-3.44113357	1.09843674
6	2.12214063	-4.20970250	1.91117356
6	0.78379975	-4.35381357	1.55170440
8	4.51497525	-2.43295743	-1.00610511
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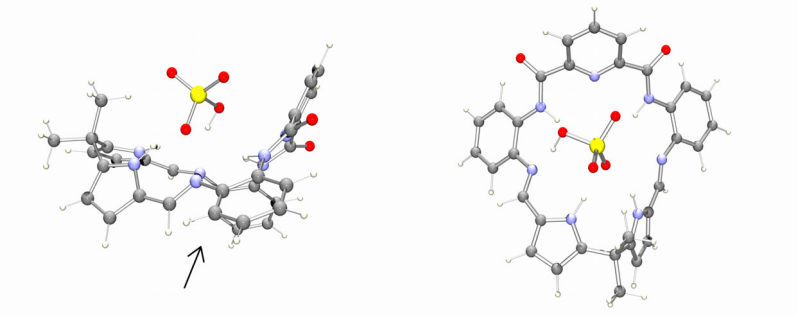
1	-2.56978588	0.80048558	-0.08647857
1	-3.85462874	-0.03789433	-3.52365438
1	3.38518013	3.40051667	-1.12180512
1	-2.66757653	-5.55227635	-1.65273615
1	-4.73202700	-5.91831278	-2.98043166
1	-6.04994018	-3.95740748	-3.79980448
1	-5.30109183	-1.66126591	-3.25896531
1	3.64354562	3.12702697	-3.45888438
1	5.41307839	2.22234285	-4.95607714
1	5.98518393	-0.20827473	-4.86657142
1	-3.94350504	4.49291992	1.43228022
1	1.91623604	-0.62540793	-1.30728203
1	-2.81350378	5.51327126	0.50742393
6	-2.22186764	2.41225079	1.98790730
1	-3.82041277	2.79680951	-3.57408945
1	-1.02417693	-2.37316438	-1.26994764
6	-2.11991297	3.45730023	0.84902634
1	-3.26806455	2.12067759	2.15895806

1	4.02117765	-3.35126596	1.27231506
1	2.52074966	-4.71900266	2.78907769
1	-1.82561257	2.84106931	2.91711657
1	-3.18643154	4.66105974	-1.71414630
1	0.09464455	-4.99956824	2.09285589
1	-2.47447139	5.12546700	2.20805728
1	-1.63235664	1.50892135	1.77629564
1	4.78697079	-1.70778451	-3.28932894

Table 1. Calculated thermochemical data for free receptor **1** (kcal/mol)

E	-1109386.76
E0	-1109059.65
G	-1109101.92
H	-1109037.09
S	217.45

Supplementary Figure 2. Structure of **1*HSO$_4^-$.**



Atomic Coordinates:

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6	1.28921529	3.64899330	0.62763118
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6	-2.90428261	3.11575192	0.56550942
7	-2.80677637	1.76226523	0.37590650

6	-2.95810601	5.19767067	1.93932829
6	-3.58077268	0.07815176	-1.31074215
7	-3.18451266	-1.00714560	-0.71676279
6	-3.59745225	-2.23803122	-1.23733508
6	2.36426252	2.96427283	-0.00778996
7	2.37580455	1.70651603	-0.36743236
6	-2.79944096	-3.39305132	-0.99235669
6	-3.22533125	-4.64047656	-1.48306255
6	-4.42648061	-4.76629303	-2.17909937
6	-5.23790802	-3.64787399	-2.38837474
6	-4.82214127	-2.40489923	-1.91973307
6	3.38970676	1.28116900	-1.24182652
6	4.04842110	2.16469167	-2.12553866
6	5.05993122	1.73325502	-2.97871238
6	5.42709312	0.38460309	-2.98772640
6	4.75545671	-0.52443827	-2.17320391
6	3.72433457	-0.10393567	-1.31544661
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7	-1.58082609	-3.25090623	-0.30316172
6	3.49037739	-2.20726802	-0.03369454
6	-0.96743094	-4.25010166	0.41904751
8	-1.44909003	-5.37497748	0.59655946
6	0.40742519	-3.95347940	0.97505974
7	1.21636054	-3.09077678	0.33686595
6	2.49474354	-3.03105669	0.75055685
6	2.99283970	-3.76646143	1.83304073
6	2.11986092	-4.59249690	2.53489946
6	0.81056142	-4.71301918	2.08148100
8	4.65019479	-2.61037020	-0.17133175
6	-2.34676759	3.03307381	3.03569516
6	-2.24367179	3.84921798	1.72437728
1	-0.45606410	6.29148423	1.61942112
1	2.04490808	5.73152233	0.73690134
1	-0.16500209	2.09606006	0.96535732
1	-4.53135952	2.62558960	-2.28968331
1	-3.90062469	4.68591966	-0.64278343
1	-2.19876113	1.11957720	0.91429337

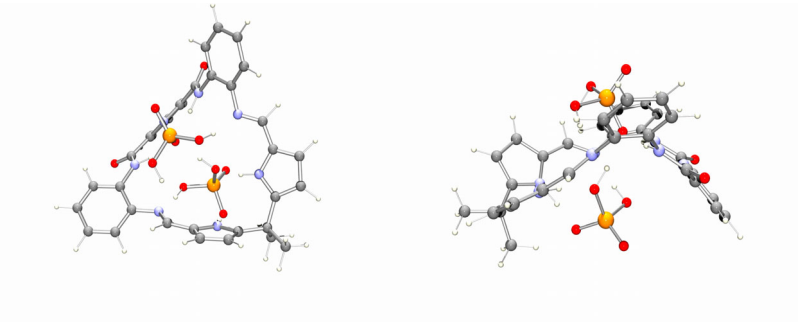
1	-4.01824583	5.02504631	2.16673894
1	-2.89217793	5.84820756	1.05746339
1	-2.50856410	5.72755395	2.78994772
1	-4.10681426	0.04054802	-2.28240092
1	3.22436310	3.61903289	-0.22725748
1	-2.60942761	-5.51264377	-1.28945320
1	-4.73515436	-5.74906586	-2.53802594
1	-6.20000267	-3.74589293	-2.89391332
1	-5.47656491	-1.54040452	-2.03267628
1	3.73005247	3.20634131	-2.16055360
1	5.54466518	2.44480672	-3.64897850
1	6.21594286	0.02942191	-3.65191630
1	5.01811689	-1.57815169	-2.18471241
1	2.09974964	-0.72714998	-0.17912128
1	-1.22848301	-2.29911462	-0.18313316
1	4.04448174	-3.66997274	2.09653742
1	2.46006972	-5.14799863	3.40971764
1	0.09070457	-5.38200997	2.54825675
1	-3.40200523	2.82082493	3.26099310
1	-1.91938584	3.61408846	3.86438077
1	-1.78825101	2.09156330	2.99402892
8	1.81099195	-0.04753234	2.01490224
16	0.22822453	-0.01219914	2.58027151
8	0.18848216	1.00399492	3.66050410
8	-0.03967978	-1.40890065	2.96576970
8	-0.54339175	0.44290110	1.33629856
1	1.90270208	0.68973999	1.35916717

Table 2. Calculated thermochemical data for **1***HSO_4^- (kcal/mol)

E	-1548312.99
E0	-1547969.06
G	-1548015.45
H	-1547942.89
S	243.36

Supplementary Material (ESI) for Chemical Communications

Supplementary Figure 3. Structure of **1*2$H_2PO_4^-$**.



Atomic Coordinates:

6	-0.37267819	3.99750823	1.14000608
6	0.48458684	5.09437853	1.34260698
6	1.78015087	4.70017059	0.97140670
6	1.70185479	3.37353853	0.51653612
7	0.38105604	2.97478556	0.63450423
6	-3.19555576	1.04899514	-0.43643377
6	-3.68114145	2.09519731	-1.27355758
6	-3.27507745	3.29263605	-0.69267524
6	-2.56475628	2.94078893	0.48866348
7	-2.52816031	1.59655200	0.64762731
6	-2.47776149	5.32063266	1.25576828
6	-3.35870758	-0.31490906	-0.81995204
7	-2.85775741	-1.42590014	-0.33033247
6	-3.26925452	-2.61364056	-0.96462616
6	2.77892187	2.65164904	-0.08933817
7	2.69312580	1.54980571	-0.77137956
6	-2.35928309	-3.68520450	-1.19344190
6	-2.81771075	-4.85151627	-1.82600764
6	-4.14738653	-4.99858095	-2.21815217
6	-5.05565369	-3.96605606	-1.97111715
6	-4.61439958	-2.79658384	-1.35654025
6	3.83416200	1.08281623	-1.44434103
6	4.66876218	1.97390817	-2.15110084
6	5.78666515	1.52878664	-2.85195470
6	6.08977477	0.16448248	-2.86756272
6	5.26422552	-0.73540602	-2.19615710

6	4.12931095	-0.30604240	-1.49226983
7	3.32786911	-1.25539175	-0.81324818
7	-1.00873252	-3.60843418	-0.77594737
6	3.88510768	-2.22136647	-0.02071763
6	-0.44610364	-4.61795964	-0.03879839
8	-0.99157955	-5.70800485	0.19216431
6	0.92082475	-4.34658082	0.55572684
7	1.71210354	-3.39680149	0.03947639
6	2.92603517	-3.22592978	0.58262917
6	3.38751484	-3.96974302	1.67720003
6	2.54804106	-4.93655147	2.22366387
6	1.30020072	-5.14636879	1.64428572
8	5.09707048	-2.31263404	0.23084648
6	-2.07394732	3.51090205	2.92505580
6	-1.86824064	3.91140901	1.44079635
1	0.18548067	6.06942767	1.71158560
1	2.68183414	5.30636680	0.97096044
1	0.09743160	1.97681292	0.55887053
1	-4.22740919	1.95920536	-2.20467070
1	-3.44902031	4.29318097	-1.07707207
1	-1.89867303	0.85601494	1.86854031
1	-3.56324545	5.27581968	1.42041706
1	-2.29242250	5.71904751	0.24982966
1	-2.05144007	6.02187223	1.98680877
1	-3.96528480	-0.39873711	-1.73825431
1	3.76005184	3.14243611	0.04531211
1	-2.10201257	-5.65033377	-2.00225270
1	-4.47020398	-5.92075062	-2.70461907
1	-6.10788323	-4.07276025	-2.24427585
1	-5.32652196	-2.00430276	-1.12335228
1	4.39166118	3.02869406	-2.17224511
1	6.40383947	2.24170200	-3.40251041
1	6.95318662	-0.20534689	-3.42324135
1	5.48612254	-1.79979088	-2.20946893
1	2.29432641	-1.23757180	-0.94607523
1	-0.50093484	-2.70626157	-0.86633335
1	4.38370241	-3.76318938	2.06388558

1	2.86169494	-5.51801062	3.09285941
1	0.59900939	-5.89601110	2.00581843
1	-3.15036437	3.45184051	3.14698582
1	-1.62238527	4.27430389	3.57707883
1	-1.62055881	2.54119552	3.15700328
8	0.63881540	1.21161476	-2.60500304
15	0.26753158	-0.38010805	-2.81561260
8	0.39978945	-1.04153250	-1.39877048
8	0.97634884	-1.03917644	-3.96489120
8	-1.33285199	-0.23552994	-3.20872318
1	1.29523419	1.29324607	-1.85607731
1	-1.76243950	0.32590195	-2.53322381
8	0.27830213	0.15197534	0.84873279
15	-0.27656391	-0.59531328	2.18587406
8	-1.40589274	0.42926544	2.70274340
8	0.75136907	-0.92556511	3.22295566
8	-1.05462990	-1.91070840	1.66046894
1	0.29105231	-0.37230220	-0.05708532
1	-1.75031184	-1.67060687	0.95291319

Table 2. Calculated thermochemical data for **1***$H_2PO_4^-$ (kcal/mol)

E	-1916782.816
E0	-1916411.126
G	-1916461.174
H	-1916381.163
S	268.3575

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