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Controlling microenvironments and modifying anion binding selectivities using core functionalised hyperbranched polymers

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Supporting Information

Experimental

Instrumentation

Infrared (IR) Spectroscopy. IR spectra were recorded using a Perkin-Elmer UATR infrared spectrometer. Spectra were analysed with Spectrum100 software and positions of peaks are stated as wave numbers (cm^{-1}).

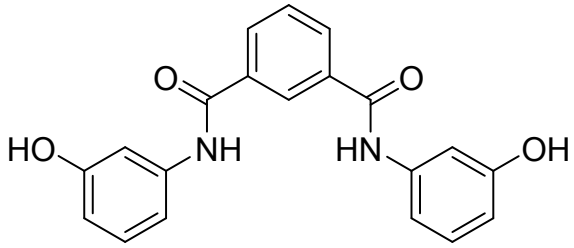
NMR Spectroscopy All NMR samples were prepared using deuterated solvents supplied by Sigma Aldrich. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Brucker AV1400 MHz machine. Chemical shifts are quoted using ppm, coupling constants are quoted in Hertz and anomalous impurity and solvent peaks are labelled and referenced to residual solvent signals, with Tetramethylsilane δ=0 at =0 as the reference. The NMR spectra were analysed using Topspin 3.0 NMR software.

Mass Spectrometry. The form of ionisation used was dependent on the molecular weight of the sample in question. For samples with a low molecular weight, an Electrospray ionisation (ES) was used to record spectra. The instrument used was a WATERS LCT mass spectrometer. For samples with a high molecular weight, matrix assisted laser desorption ionisation (MALDI) was required. The instrumentation used was a BRUKER REFLEX III MALDI-ToF mass spectrometer.

Gel Permeation Chromatography. Analytical THF GPC data was obtained at room temperature using either a high molecular weight column (3x300 mm PL gel 10 μm mixed-B), or a low molecular weight column (2x600 mm PL gel 5um (500 Å)). Calibration was achieved by using polystyrene standards (Mn 220-1, 1,000,000 Da) and molecular weights are thus reported relative to these specific standards used. The samples were run using Fisher GPC grade THF as a solvent stabilised with 0.025 % BHT (which was supplied to the columns by a Waters 515 HPLC Pump at 1.00 $mLmin^{-1}$). Toluene was added to prepared sample as a flow marker, before injection through a 200 μL sample loop with a Gilson 234 Auto Injector. The concentration of a sample was studied using an Erma ERC-7512 refractive index detector. The data attained was then analysed using cirrus GPC-online software. Samples were filtered using Whatman® GD/X syringe filters with a pore size of 0.45 μm prior to analysis.

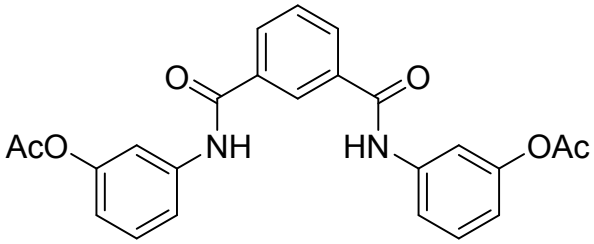
UV/Vis spectroscopy. The ultraviolet absorbance was recorded on an Analytik Jena AG Specord s600 UV/Vis Spectrometer and analysed using its attached Software (WinASPECT).

Synthesis of N, N'- Bis-(3-hydroxy-phenyl)-isophthalamide



3-Aminophenol (13.10 g, 0.119 mol) and anhydrous N, N'-Dimethylacetamide (75 mL) was added to a 250 mL round bottom flask under an inert atmosphere of argon. Isophthaloyl chloride (12.18 g, 0.060 mol) was added after cooling the solution to 0 ºC. The reaction was stirred for 6 hours, during which the temperature was allowed to rise to room temperature. The reaction mixture was then poured into 1 L of ice cold distilled water and filtered. The filtrate was washed several times with distilled water and the pH of the filtrate was monitored using litmus paper. Purification was achieved by dissolving the crude product in a minimum amount of hot ethanol followed by a hot filtration. The filtrate was subsequently added to an excess of ice cold distilled water and filtered. The crystals were dried under vacuum at 100 ºC. Yield 11.14 g, 64% ^{1}HNMR (CD_3SOCD_3, 400 MHz) δ_H 10.31 (s, 2H, OH) 9.47 (s, 2H, NH) 8.47 (s, 1H, *Ar*-OCCCHCCO) 8.11 (dd, 2H, *Ar*-COCCH, J=8.0, 2.0) 7.68 (t, 1H, *Ar*-COCCHCH, J=8.0) 7.39 (m, 2H, *Ar*-NHCCHCOH) 7.20-7.12 (bm, 4H, *Ar*-NHCCHCH) 6.53 (bm, 2H, *Ar*-NHCCHCOHCH) ^{13} CNMR (CD_3SOCD_3, 400 MHz) δ_c 107.9, 111.4, 111.6, 127.4, 129.0, 129.8, 131.1, 135.7, 140.5, 158.0, 165.5 FTIR (cm^{-1}) 3364 (N-H stretch), 3188 (OH stretch), 1646, 1604 (amide C=O stretch), 1547, 1489, 1450, 1266, 683 EA %: Carbon (Expected value: 68.96 %) Found: 68.53 % Hydrogen (Expected value: 4.63 %) Found: 4.81 % Nitrogen (Expected value: 8.04%) Found: 7.89 % ES-MS 349.1 (MH^+) m.p. 247-249 ˚C

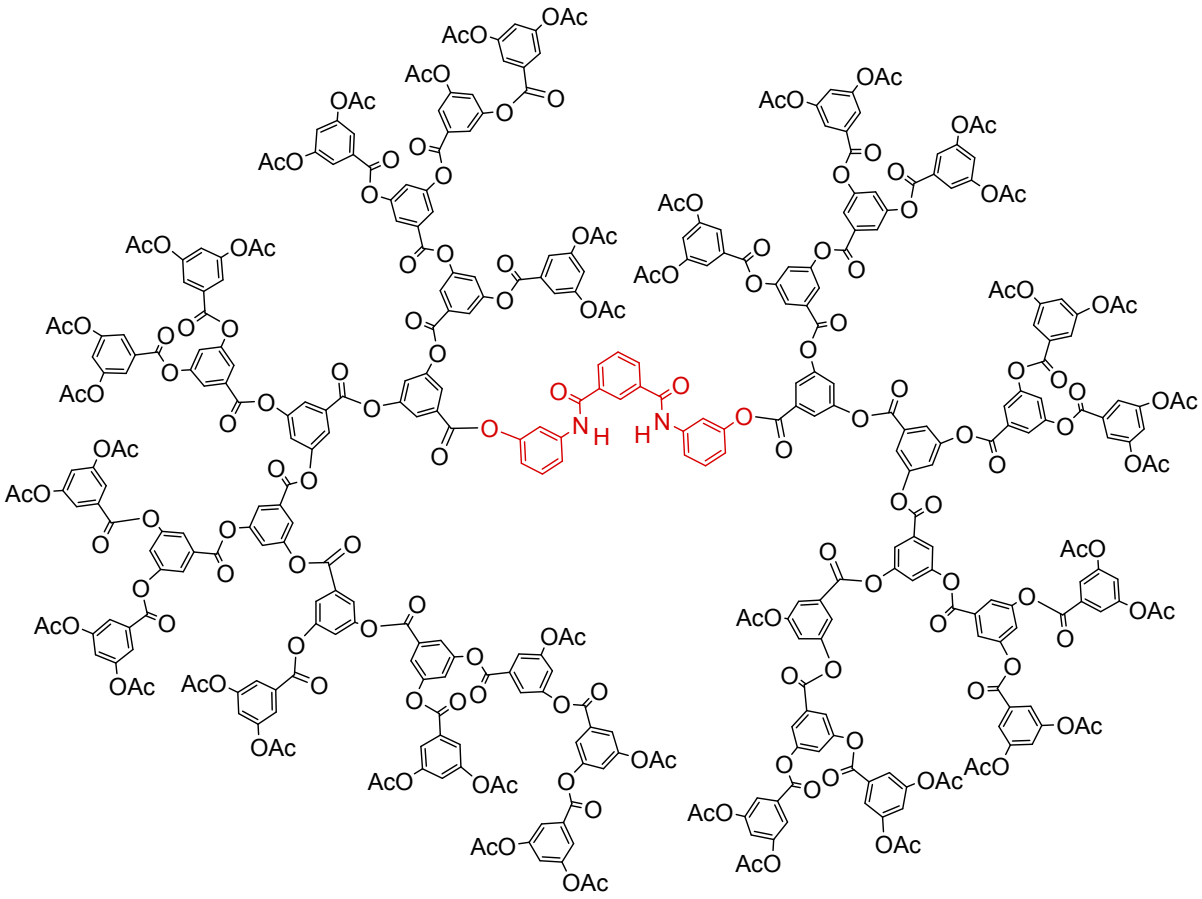
Synthesis of N, N'- Bis-(3-hydroxy-phenyl)-isophthalamide (1)



An oven dried round bottom flask was charged with N, N'- Bis-(3-hydroxy-phenyl)-isophthalamide (1.0 g, 2.9 mmol) and dissolved in anhydrous pyridine (75 mL). The flask was degassed with Argon before addition of acetyl chloride (1.22 mL, 17.2 mmol). The mixture was then stirred at room temperature for a period of 4 hours. Pyridine was then removed via vacuum distillation and dissolved in dichloromethane. This was followed by washings with saturated sodium hydrogen carbonate solution and distilled water to remove any trace amounts of acid. The organic layer was then reduced down and dissolved again in chloroform and filtered by gravity. A cream solid was collected and purified by recrystalisation. The crude cream solid was dissolved in a minimum amount of hot dichloromethane. Petroleum ether (40:60) was then added drop wise until the yellow solution remained cloudy. The solvent was left to evaporate slowly yielding cream coloured crystals. Yield 800 mg, 65% ^{1}HNMR ($(CD_3)_2CO$, 400 MHz) δ_H 9.86 (s, 2H, NH) 8.55 (s, 1H, *Ar*-OCCCHCCO) 8.20 (dd, 2H, *Ar*-COCCH, J=8.0, 2.0) 7.81 (t, 1H, *Ar*-COCCHCHCHCCO J=2.0) 7.70-7.66 (bm, 4H, *Ar*-CONHCCHCHCHCO, *Ar*-CONHCCHCO) 7.40-7.38 (bm, 2H, *Ar*-CONHCCHCHCHCO) 6.92 (dd, 2H, *Ar*-CONHCCHCHCHCO, J=8.0, 1.0) 2.30 (s, 6H, OCH_3) 13 CNMR ($(CD_3)_2CO$, 400 MHz) δ_c 168.8, 164.9, 151.3, 140.3, 135.4, 130.6, 129.3, 128.8, 126.5, 117.2, 117.2, 117.0, 113.6, 20.1 FTIR (cm^{-1}) 3050-3100 (aromatic C-H stretch), 1764 (acetate C=O stretch), 1646, 1603 (amide C=O), 1543, 1483,

1433, 1196, 681 EA %: Carbon (Expected value: 66.66 %) Found: 65.88 % Hydrogen (Expected value: 4.66 %) Found: 4.45 % Nitrogen (Expected value: 6.48%) Found: 6.40 % ES-MS 433.1406 (MH^+) m.p. 178-180 ˚C

General procedure for the preparation of isophthalamide cored HBPs



3, 5-Diacetoxy benzoic acid, N, N'- Bis-(3-acetoxy-phenyl)-isophthalamide **1** and diphenyl ether were dispensed into a 250 mL round bottom flask, which was then thoroughly degassed and flushed with nitrogen. The mixture was heated to 225 °C and stirred for a period of 45 minutes. The temperature was reduced to 180 °C and the reaction was subsequently placed under reduced pressure for 4 hours. The crude mixture was dissolved in refluxing THF and precipitated into ice cold methanol (800 mL) and placed in a freezer overnight to maximise precipitation. The resulting solid was filtered off and washed with ice cold methanol, yielding the polymer.

Polymerisation of 3, 5-diacetoxybenzoic acid with N, N'- Bis-(3-acetoxy-phenyl)-isophthalamide core using a 1:5 ratio (2)

The general procedure was followed where 3, 5-Diacetoxy benzoic acid (688 mg, 2.89 mmol), 4- N, N'- Bis-(3-acetoxy-phenyl)-isophthalamide (0.25 g, 0.72 mmol) and diphenyl ether (0.95 g, 5.58 mmol) were reacted together, yielding the polymer, which was a light brown/grey solid powder in appearance. Yield 488.2 mg, 71 % (by mass) ^{1}HNMR ($CDCl_3$, 400 MHz) δ_H 8.55-8.67 (bm, 2H, [Core] N<u>H</u>) 8.20-8.33 (bm, 1H, [Core] *Ar*-OCCC<u>H</u>CCO, 2H, [Core] *Ar*-COCC<u>H</u>) 7.65-8.08 (bm, 1H [Core] *Ar*-COCCHC<u>H</u>CHCCO, 2H [Polymer] *Ar p*-C<u>H</u>) 7.40-7.64 (bm, 4H, [Core] *Ar*-CONHCC<u>H</u>CHCHCO, *Ar* -CONHCC<u>H</u>CO2H) 7.19-7.39 (bm, 2H, [Core] *Ar*-CONHCC<u>H</u>CO, 2H, [Polymer] *Ar o*-C<u>H</u>) 6.72-6.90 (bm, 2H, [Core] *Ar*-CONHCCHCHC<u>H</u>CO) 2.25 (bs, 3H, [Polymer] C<u>H</u>$_3$)) ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C 168.8, 163.8, 162.8, 151.2, 139.1, 130.9, 130.7, 129.7, 121.3, 120.9, 117.5, 114.0, 21.0 FTIR (cm^{-1})

2009-2158 (aromatic C-H) 1741 (ester C=O stretch) 1369, 1286, 757 GPC-M_n = 4009 M_w = 12973 PD = 3.2, NMR-M_n = 4670.

Polymerisation of 3, 5-diacetoxybenzoic acid with N, N'- Bis-(3-acetoxy-phenyl)-isophthalamide core using a 1:20 ratio (3)

The general procedure was followed where 3, 5-Diacetoxy benzoic acid (2.18 g, 9.15 mmol), 4- N, N'-Bis-(3-acetoxy-phenyl)-isophthalamide (0.25 g, 0.72 mmol) and diphenyl ether (3.01 g, 17.68 mmol) were reacted together, yielding the polymer (white solid powder). Yield 1.42 g, 65% (my mass)^{1}HNMR ($CDCl_3$, 400 MHz) δ_H 8.50-8.71 (bm, 2H, [Core] N<u>H</u>) 8.22-8.43 (bm, 1H, [Core] *Ar*-OCCC<u>H</u>CCO) 8.09-8.19 (bm, 2H, [Core] *Ar*-COCC<u>H</u>) 7.75-8.11 (bm, 1H [Core] *Ar*-COCCHC<u>H</u>CHCCO, 2H [Polymer] *Ar p*-C<u>H</u>) 7.19-7.62 (bm, 4H, [Core] *Ar*-CONHCC<u>H</u>CHCHCO, *Ar* -CONHCC<u>H</u>CO2H, [Core] *Ar*-CONHCC<u>H</u>CO, 2H, [Polymer] *Ar o*-C<u>H</u>) 6.72-6.89 (bm, 2H, [Core] *Ar*-CONHCCHC<u>H</u>CHCO) 2.31 (bs, 3H, [Polymer] C<u>H</u>$_3$) ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C 168.8, 162.8, 151.2, 130.9, 130.7, 129.7, 123.2, 121.3, 120.9, 118.9, 21.0 FTIR (cm^{-1}) 2972, 2931, 2505 (aromatic C-H stretch), 1742 (ester C=O stretch), 1442, 1277, 754 GPC M_n = 10343 M_w = 42137 PD = 4.07 NMR-M_n = 12,299

Titrations

^{1}H NMR titrations were carried out using a standard NMR titration technique. Samples of host solution were prepared with a known concentration in $CHCl_3$ (1-10mM). Guest solutions were prepared in $CDCl_3$ with concentrations ranging from 0.1-1.0 M. Each titration began with 0.7 mL of the host species in an NMR tube. The anionic guest was added in aliquots (10-25 µL) to the host. The fitting software used took account of dilution. NMR scans (32) were run following each addition and the position of the NH chemical shift (ppm) was monitored. Solutions were made up fresh and used immediately after preparation. Anionic guests were added as tetrabutylammonium salts. Topspin 2.6 software was used to process the NMR spectra generated. Changes in chemical shift were fitted to a 1:1 binding isotherm in Microsoft Excel program. A representative series of spectra is shown below in figure 1.

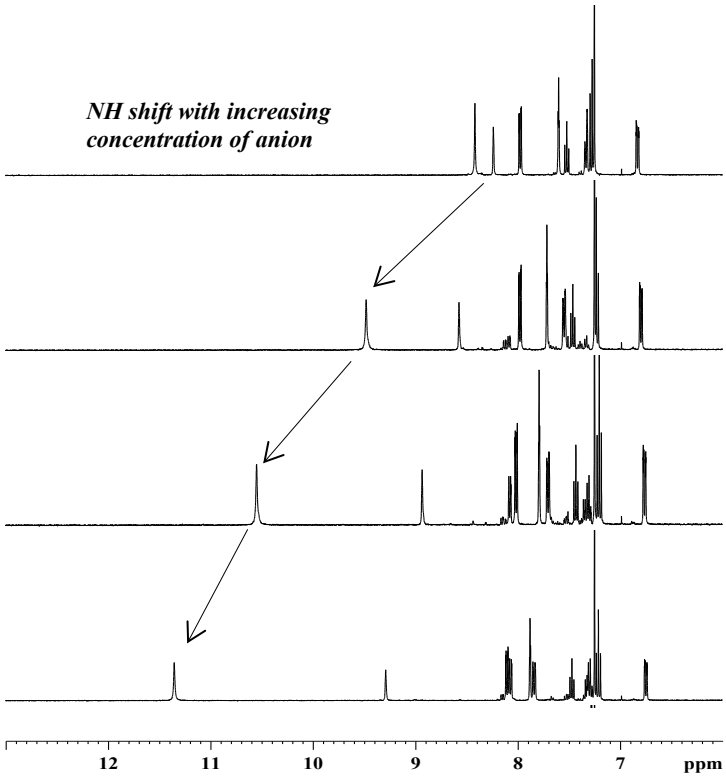


Figure 1; *Representative series of ^{1}H NMR spectra depicting the change in resonances when anion was titrated with host. Arrows indicate the change in NH resonance as the anion is added (increased anion concentration top to bottom - tetrabutylammonium bromide and host **1**).*

Representative Titration Data for Hosts and Anions

^{1}HNMR Titration data to the core unit 1

Tetrabutylammonium fluoride/isophthalamide corc 1

[H] mmol	[G] mmol	δ NH
1	0	0
0.986	0.141	0.85
0.972	0.278	1.7
0.959	0.411	2.59
0.946	0.541	3.12
0.933	0.667	3.39
0.921	0.789	3.54
0.909	0.909	3.64
0.897	1.026	3.71
0.886	1.139	3.76

Tetrabutylammonium chloride/isophthalamide corc 1

[H] mmol	[G] mmol	δ NH
1	0	0
0.972	0.278	0.83
0.946	0.541	1.81
0.933	0.667	2.17
0.921	0.789	2.42
0.909	0.909	2.57
0.897	1.026	2.66
0.886	1.139	2.72
0.875	1.25	2.75

Tetrabutylammonium bromide/isophthalamide corc 1

[H] mmol	[G] mmol	δ NH
5.00	0.000	0
4.794	1.027	0.58
4.605	1.973	1.11
4.430	2.848	1.58
4.268	3.658	1.94
4.191	4.041	2.07
4.117	4.411	2.16
4.0462	4.768	2.24
3.977	5.113	2.29
3.846	5.769	2.36
3.783	6.081	2.38
3.608	6.958	2.43
3.500	7.500	2.45
3.333	8.333	2.47
3.181	9.090	2.49

Tetrabutylammonium iodide/isophthalamide corc 1

[H] mmol	[G] mmol	δ NH
5.000	0	0
4.794	1.027	0.37
4.605	1.973	0.7
4.430	2.848	0.96
4.268	3.658	1.17
4.191	4.041	1.26
4.117	4.411	1.33
3.977	5.113	1.46
3.910	5.446	1.51
3.846	5.769	1.56
3.783	6.081	1.6
3.608	6.958	1.69
3.500	7.500	1.74
3.333	8.333	1.81
3.043	9.78	1.91
2.800	11.000	1.94

^{1}HNMR Titration data to the HBP 2

Tetrabutylammonium fluoride/HBP 2

[H] mmol	[G] mmol	δ NH
5	0	0
4.93	0.704	1.1
4.861	1.389	1.73
4.795	2.055	2.26
4.73	2.703	2.55
4.667	3.333	2.73
4.605	3.947	2.89
4.545	4.545	3.01
4.487	5.128	3.1
4.43	5.696	3.17
4.375	6.25	3.21

Tetrabutylammonium chloride/HBP 2

[H] mmol	[G] mmol	δ NH
5.00	0.00	0
4.929	0.704	1.04
4.861	1.388	1.84
4.794	2.054	2.18
4.729	2.702	2.36
4.666	3.333	2.45
4.605	3.947	2.51
4.545	4.545	2.54
4.487	5.128	2.56
4.430	5.696	2.58
4.375	6.250	2.59

Tetrabutylammonium bromide/HBP 2

[H] mmol	[G] mmol	δ NH
5.00	0.00	0
4.929	0.704	0.89
4.8611	1.388	1.48
4.794	2.054	1.78
4.729	2.700	1.94
4.666	3.333	2.02
4.605	3.942	2.08
4.545	4.545	2.13
4.487	5.128	2.15
4.430	5.696	2.18
4.375	6.250	2.19
4.242	7.575	2.22
4.117	8.823	2.24

Tetrabutylammonium iodide/HBP 2

[H] mmol	[G] mmol	δ NH

5.00	0.00	0
4.895	1.048	0.58
4.795	2.054	0.91
4.697	3.020	1.12

[H] mmol	[G] mmol	δ NH
5	0	0
4.861	1.389	1.06
4.73	2.703	1.73
4.667	3.333	2.01
4.605	3.947	2.23
4.545	4.545	2.38
4.487	5.128	2.52
4.43	5.696	2.6
4.375	6.25	2.66
4.321	6.79	2.72
4.242	7.576	2.8
4.167	8.333	2.85
4.07	9.302	2.93
3.977	10.227	3.01
3.889	11.111	3.05

^{1}HNMR Titration data to the HBP 3

Tetrabutylammonium fluoride/ HBP 3

[H] mmol	[G] mmol	δ NH
5.00	0.00	0
4.929	0.704	0.77
4.861	1.388	1.38
4.794	2.054	1.8
4.729	2.702	2.03
4.666	3.333	2.19
4.605	3.947	2.31
4.545	4.545	2.39
4.487	5.128	2.44

4.430	5.696	2.48

Tetrabutylammonium chloride/HBP 3

Tetrabutylammonium bromide/HBP 3

[H] mmol	[G] mmol	δ NH
5.00	0.00	0
4.895	1.048	0.88
4.794	2.054	1.38
4.697	3.020	1.68
4.605	3.947	1.86
4.516	4.838	1.97
4.430	5.696	2.03
4.347	6.521	2.08
4.268	7.317	2.11
4.191	8.083	2.15

4.117	8.823	2.17
4.00	10.00	2.19

Tetrabutylammonium iodide/HBP 3

[H] mmol	[G] mmol	δ NH
5.00	0.00	0
4.794	1.027	0.35
4.605	1.973	0.68
4.430	2.848	1.00
4.268	3.658	1.19
4.117	4.411	1.32
4.046	4.768	1.37
3.977	5.113	1.42
3.910	5.446	1.46
3.846	5.769	1.50
3.783	6.081	1.53
3.723	6.382	1.56
3.608	6.958	1.61
3.500	7.500	1.65
3.333	8.333	1.71