

A low pH sensor from an esterified pillar[5]arene

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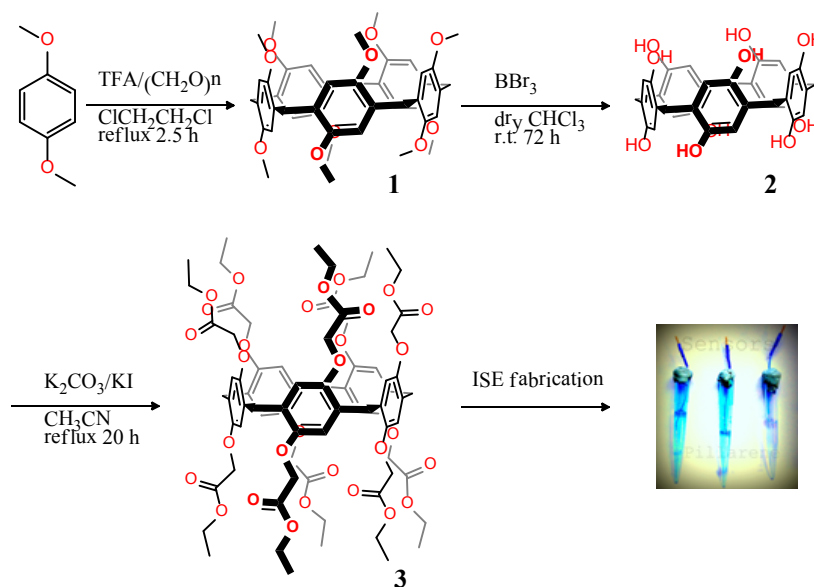
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Materials and Methods

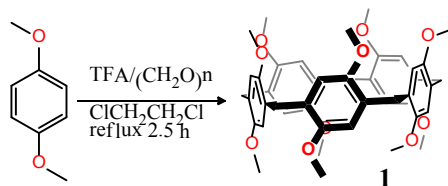
All the chemicals, solvents and reagents were purchased commercially and used without further purification. Compounds were synthesised according to the literature with amendments as described. All compounds were characterised by NMR and mass spectrometry to confirm their identities through comparison with literature values. Dye experiments were performed by using an agarose gel membrane incorporating phenolphthalein. NMR data were collected by a Bruker Avance DMX-360 spectrometer with tetramethylsilane (TMS) as the internal reference. Chemical shifts are reported in parts per million (ppm) downfield from TMS (0 ppm) as the internal standard. Multiplicities in the ^1H NMR spectra are reported as (s) singlet, (d) doublet and (t) triplet. Electrospray ionization mass spectra were recorded with a Bruker microTOF spectrometer. Ion selective electrodes were manufactured according to the published procedure.^{S1} Electrolytes were prepared in the range of pH 0.5 to 7. Electrochemical data were collected with an Ag/AgCl reference electrode using CH instruments software.

Synthetic route



Scheme S1: Synthesis of pillar[5]arene derivatives

Synthesis of 1,4-dimethoxypillar[5]arene (**1**)^{S2}



Dimethoxypillar[5]arene (**1**) was prepared by the reaction of 1,4-dimethoxybenzene (13.82 g, 0.1 mol) and freshly ground paraformaldehyde (3.00 g, 0.1 mol) in 1,2-dichloroethane (950 ml). After stirring at room temperature for 10 min. trifluoroacetic acid (50 ml) was added and the resulting mixture refluxed for 2.5 h at 90°C. During reflux, the colour of the reaction was observed to change from pale yellow to light green then dark green. After cooling, the reaction mixture was added into methanol (1000 ml). The resulting yellow-green precipitate was collected by filtration and dissolved in CHCl₃, initially 150 ml with further solvent added as necessary, before acetone was added (up to a 1:1 volume ratio) to give a yellowish white precipitate. The crude product was recrystallized from CHCl₃ and washed with acetone to give a white crystalline product in 70% yield (10.5 g). ¹H NMR (360 MHz, CDCl₃) δ: 6.77 (s, 10H), 3.77 (s, 10H), 3.66 (s, 30H); mass spec. (*m/z*): 773 (M + Na⁺).

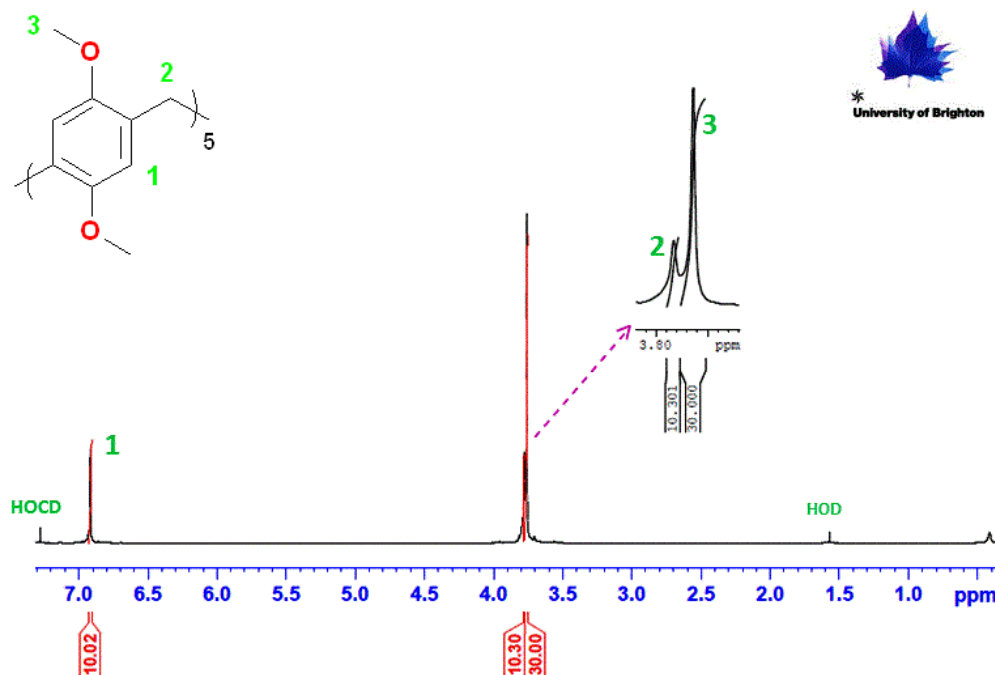


Figure S1. ¹H NMR of **1**

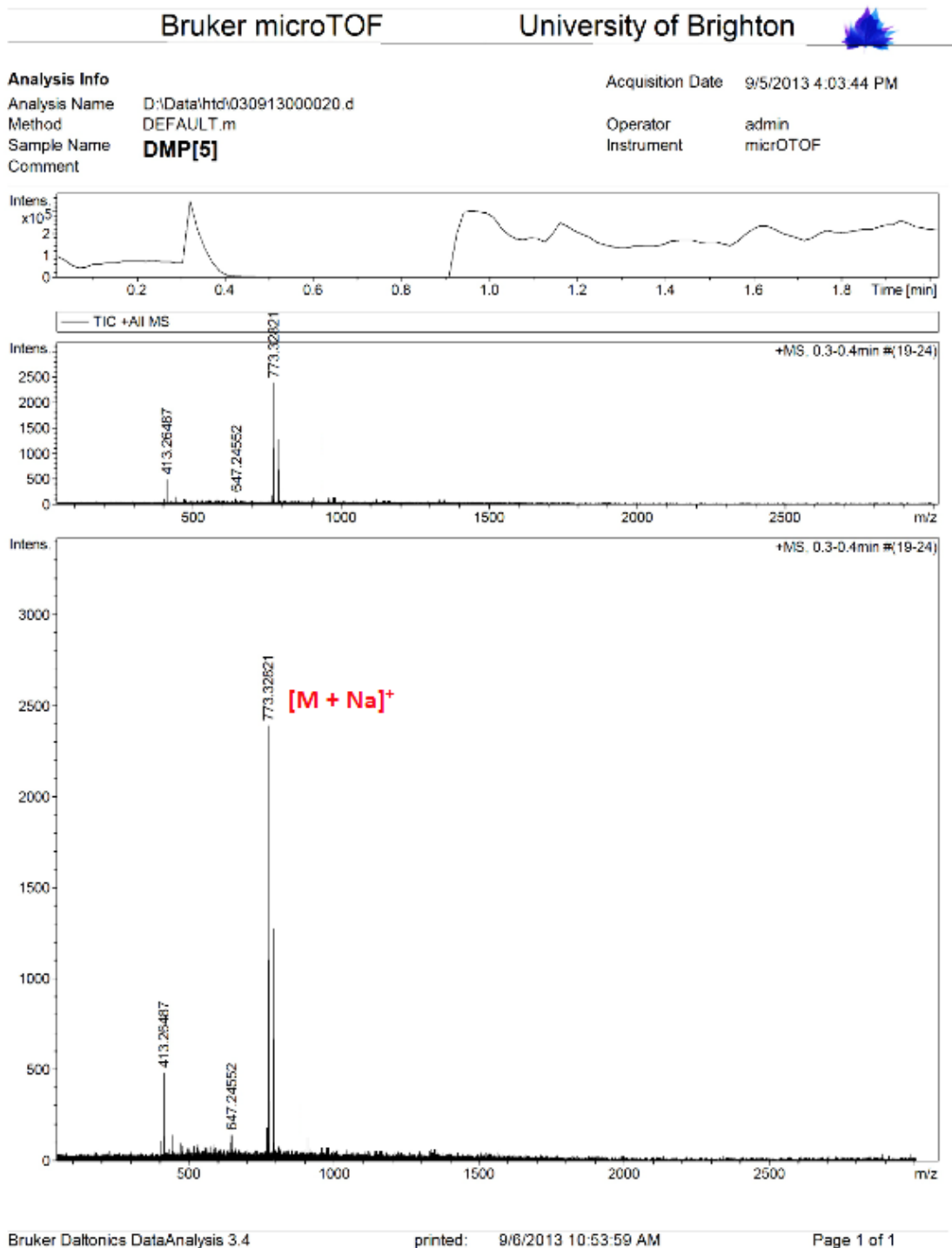
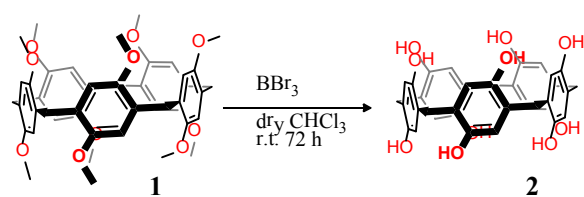
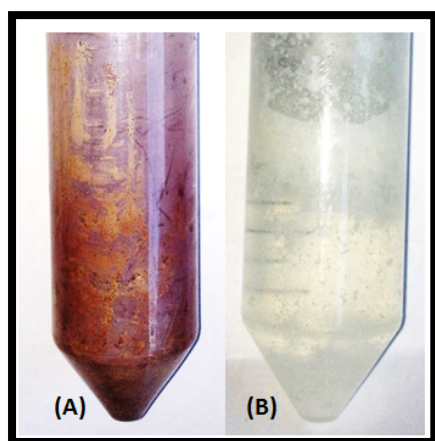


Figure S2. Electrospray ionization mass spectrum of **1**

Synthesis of pillar[5]arene (**2**)^{S3}



Compound **1** (1.5 g, 2 mmol) was stirred in anhydrous CHCl_3 (150 ml) for 10 min. BBr_3 (5.6 ml, 15.6 g, 62 mmol) was then added slowly and the resulting mixture stirred at r.t. for a further 72 h. Water (100ml) was then added and the reaction mixture stirred for 24 h at r.t. The resulting white precipitate was filtered and washed with water to give **2** as a white powder in 91% yield. $^1\text{H NMR}$ (360 MHz, CD_3COCD_3) δ : 6.64 (s, 10H), 3.66 (s, 10H), 7.99 (s, 10H); mass spec. (m/z): 610 (M^+).



Note: Pillar[5]arene (**2**) was synthesised as a white powder but upon standing the colour changes to brown colour due to oxidation. The simple expedient of storing under deionised water immediately after isolation renders the compound stable for several days.

Figure S3. Pillar[5]arene (**2**) stored in the absence (**A**) and presence (**B**) of water.

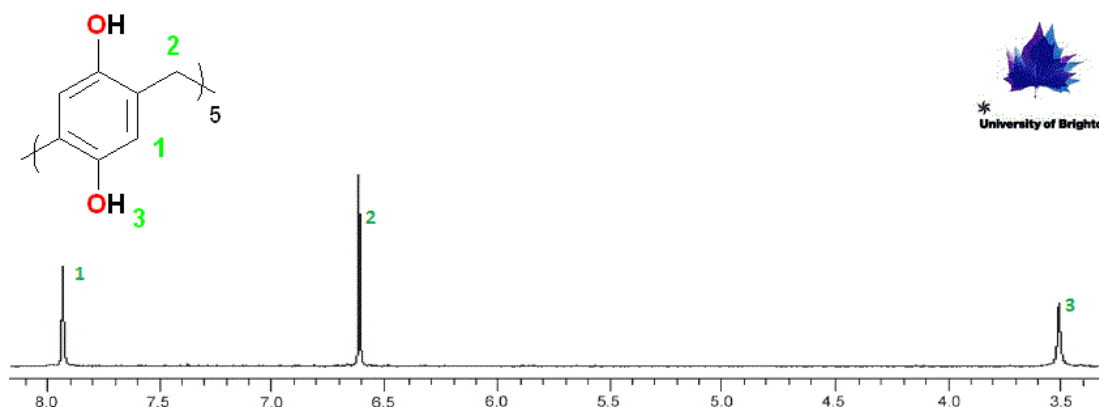


Figure S4. $^1\text{H NMR}$ of **2**

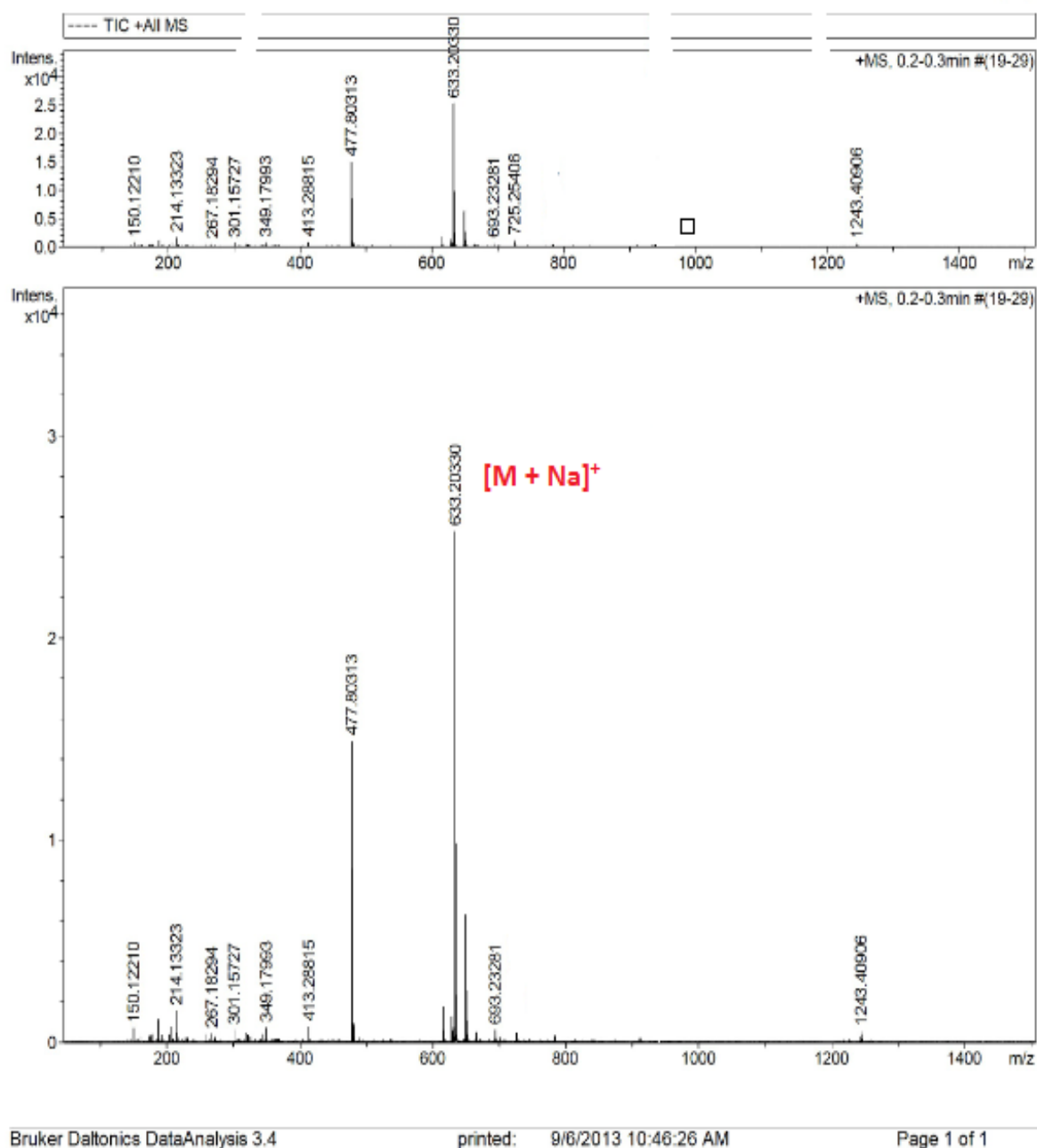
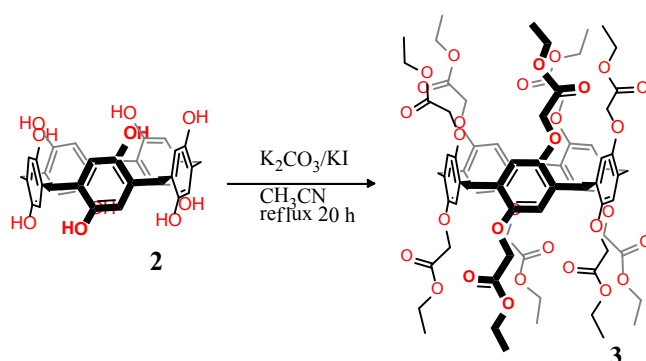


Figure S5. Electrospray ionization mass spectrum of **2**.

Synthesis of pillar[5]arene ethyl ester (**3**)^{S4, S5}



Pillar[5]arene (**2**) (1.5 g, 2.4 mmol) was dissolved in CH_3CN (70 ml). K_2CO_3 (3.6 g, 26 mmol) was added and the mixture stirred for 45 min. at r.t. KI (35 mg) and excess ethyl bromoacetate (5.0 ml, 7.5 g, 45 mmol) were added to the reaction mixture which was then refluxed for 20 h under nitrogen. After cooling the reaction mixture it was filtered and washed with chloroform (20 ml). Solvent was removed from the pale yellow organic layer under reduced pressure. The resulting pale yellow oily solid was subjected to the column chromatography (silica gel 60-70 size; CH_2Cl_2 :acetone, 100:0 → 90:10). The second fraction to elute (R_f : 0.6) was collected and recrystallised from acetone to give **3** as a white crystalline product in 82% yield. 1H NMR (360 MHz, $CDCl_3$) δ : 7.04 (s, 10H), 4.56 (q, 20H), 4.09 (m, 20H), 3.86 (s, 10H), 0.99 (t, 30H). ^{13}C NMR ($CDCl_3$, 360 MHz) δ : 169.3 (carbonyl), 148.96, 128.69, 114.45 (aromatic), 65.7 (*O*-methylene), 60.85 (*O*-ethylene) 29.21 (methylene bridge), 13.81 (terminal methyl); mass spec. (m/z) 1493 ($M + Na^+$); m.p.: 197.2 °C (lit. 196.7 °C).

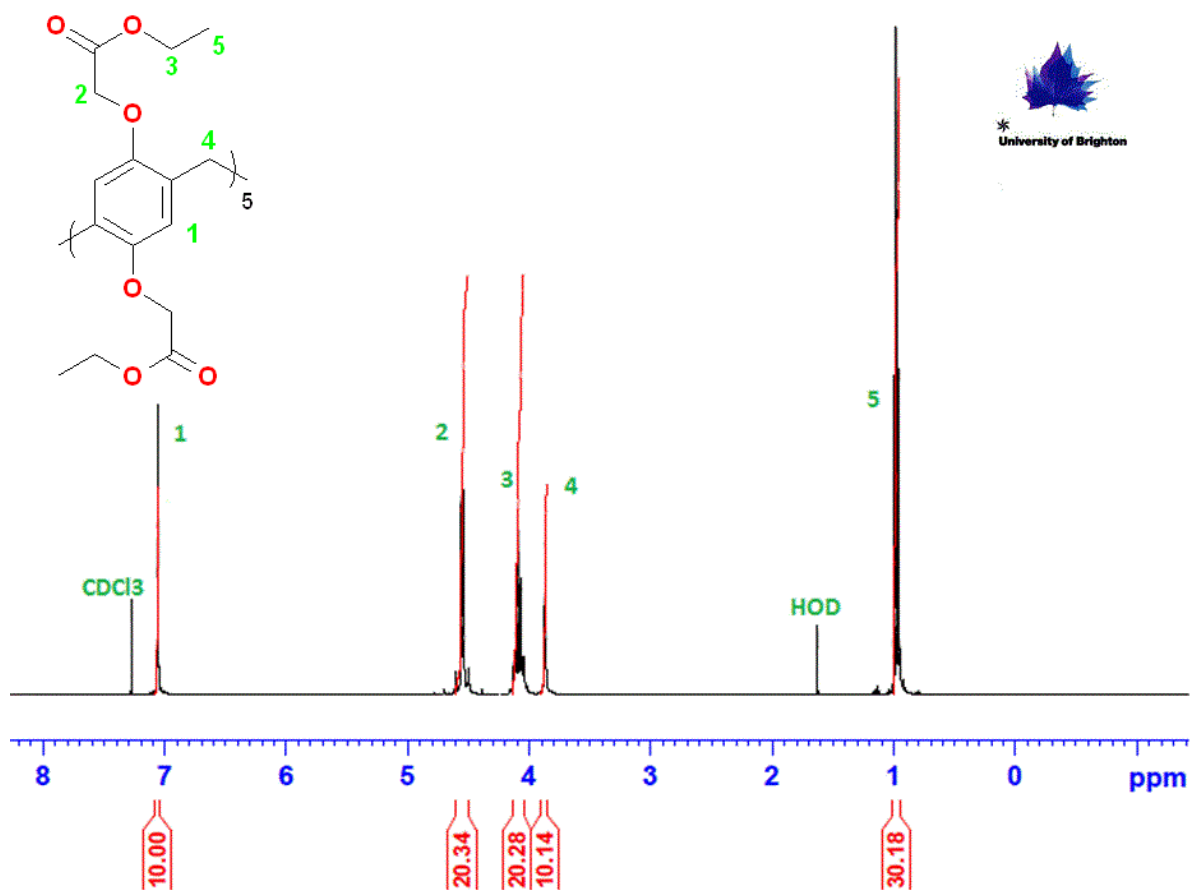


Figure S6. ^1H NMR of **3**

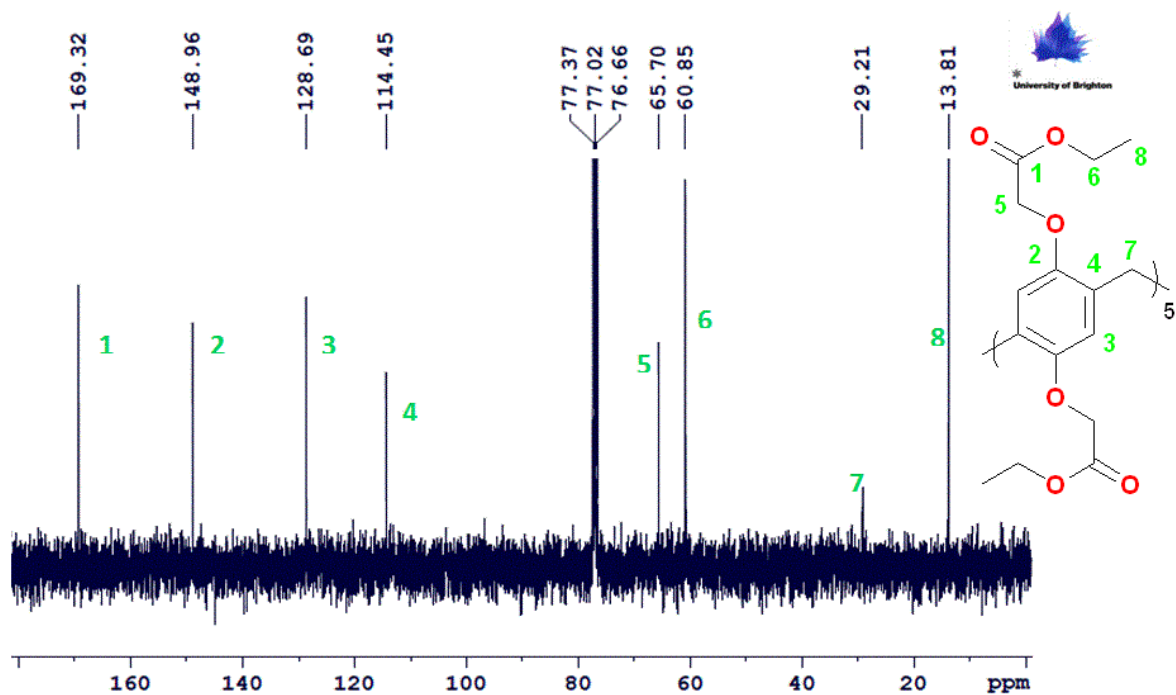


Figure S7. ^{13}C NMR of **3**

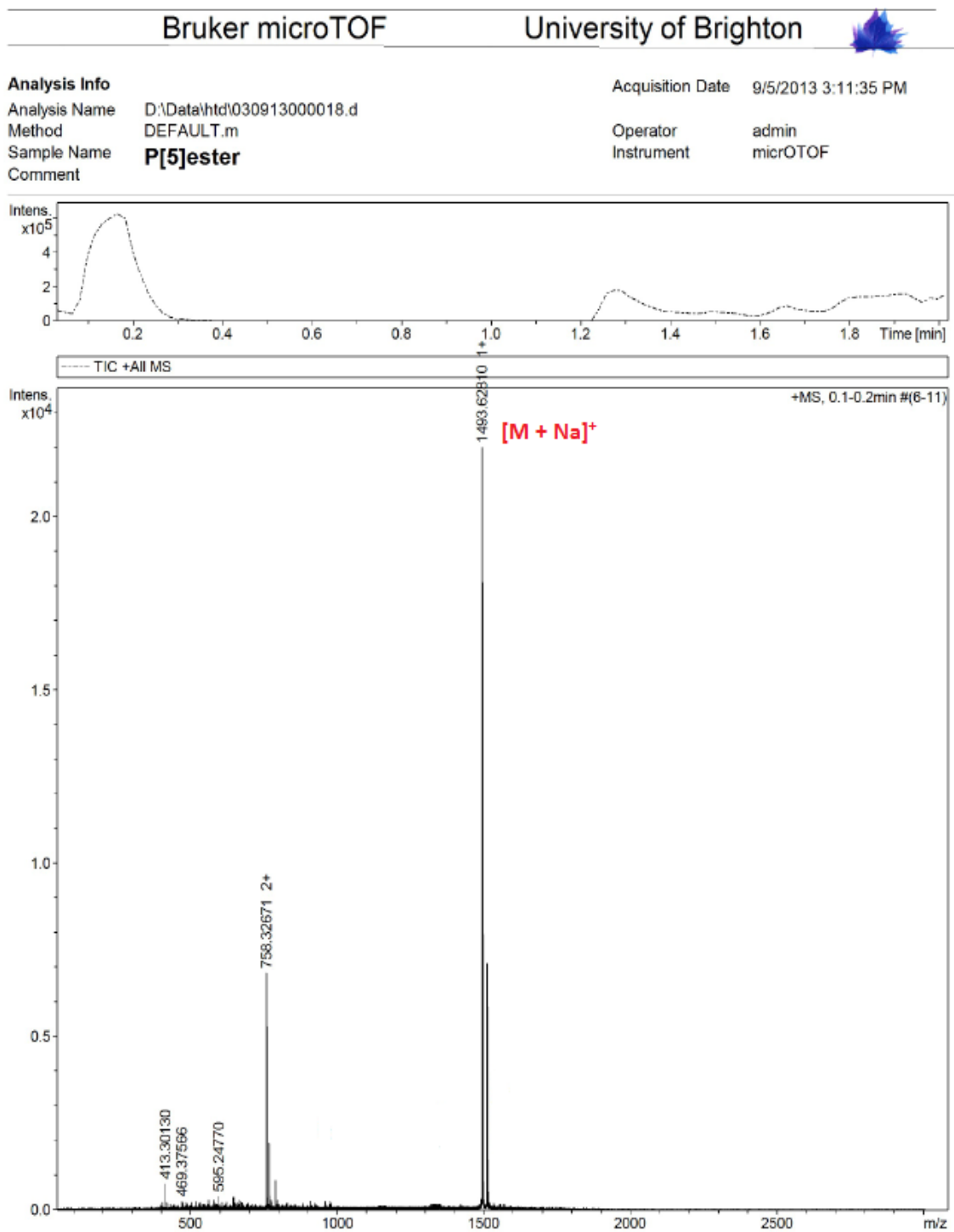


Figure S8. Electrospray ionization mass spectrum of **3**

Effect of **3** on the rate of pH change

Agarose gels containing phenolphthalein responded significantly faster to the addition of 0.1 M HCl.

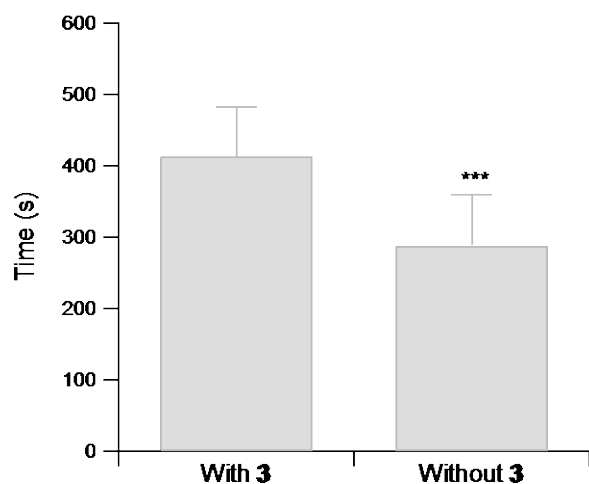


Figure S9: Time taken for the phenolphthalein indicator to turn clear in the absence and presence of **3**. Data shown as mean ± S.D, n=14-16, ***p<0.001.

Preparation of ion selective electrode membranes^{S5}



Figure S9. Ion selective electrodes incorporating **3** (Ag/AgCl wire and internal solution 0.1 M KCl)

Compound **3** (5 mg) was dissolved in THF (2.5 ml) to give a 2.0 mg/ml solution (**A**). Potassium tetrakis(4-chlorophenyl)borate (2.0 mg) was dissolved in THF (20 ml) to give a 0.1 mg/ml solution (**B**). PVC (66 mg) and, using a 200 μ l micropipette, bis(2-ethylhexyl)sebacate (164 μ l, 150 mg) (**C**) were taken separately in round bottom flasks with SubaSeals (or glass beakers with plastic lids that could be pierced with a needle) to avoid evaporation. THF (1 ml) was added to **C** followed by **B** (1 ml) and finally **A** (1 ml). The mixture was covered with parafilm and stirred for 2 h before

being left to evaporate in a fume hood until it had set as a transparent plastic membrane (usually overnight). THF (1ml) was added using a glass syringe to re-dissolve the dried membrane and the mixture stirred with a glass pipette until the polymer membrane completely dissolved (approximately 3-5 minutes). Using a new glass pipette, a drop of the membrane solution was transferred onto a clean glass slide to give a thin layer of the solution. One end of the micropipette tip electrode was dipped onto the drop quickly to form a thin membrane. The exterior of the electrode body was wiped with tissue to remove any residual membrane solution. The electrode body was kept upright with the membrane side facing down. Cast membranes were left to dry overnight at room temperature.

Justification for the choice of electrode modifier

The poor solubility of **1** in most solvents militates against its use in polymer-based sensors due to the uneven distribution of the compound that would result. The instability of **2** under normal atmospheric conditions (see ESI, Fig. S3) renders it unsuitable for this purpose too. Crucially, neither **1** nor **2** have been shown to form water-filled channels. Consequently, compound **3**, with superior solubility and the ability to bind guest water molecules, has been the only pillar[5]arene investigated so far.

Assembling the ion-selective electrode

Chloridised (Ag/AgCl) wires were rinsed with deionized water and then with 0.1M KCl. The wire was inserted inside the electrode body and placed 5 mm from the membrane. The electrode body was threaded with connection wire inside Portex tubing (ensuring enough overlap between the silver and connection wire). The epoxy resin and hardener were mixed in a 1:1 ratio. A small amount of the glue was applied at the tubing interface and the wire was positioned as close to the membrane as possible. Excess glue was wiped off and the assembly left to dry with the membrane side down to avoid inducing air bubbles. ISEs were stored in 0.1M KCl solution at 4°C when not in use.

Electrochemical analysis

Ion selective electrodes containing **3** were tested against range of 0.1M KCl solutions from pH 0.5 to 4.0 in steps of 0.5 pH units with Ag/AgCl as the reference electrode.

pH	Sensor response (V)						
	ISE 1	ISE 2	ISE 3	ISE 4	ISE 5	Mean	St. Dev.
1	128.9	126.1	118	126	130	125.80	4.70
1.5	116	109.7	105	110	120	112.14	5.88
2	107.4	101.1	96.7	98	111	102.84	6.15
2.5	99.4	94.1	91.8	92.3	103	96.12	4.88
3	94	90.7	87.7	91	101	92.88	5.06
3.5	87	88.1	87.5	86	99	89.52	5.36
4	84	85	84.8	83	97	86.76	5.78

Table S1. Data for individual ISEs

Note that if data from the best three ISEs are used the mean error drops from 5.40 to 2.05. Importantly, the errors at pH 3.5 and 4.0, where the potential difference is small, drop from ± 5.36 and ± 5.78 to ± 0.86 and ± 0.82 , respectively; the differences in the data points then become statistically significant.

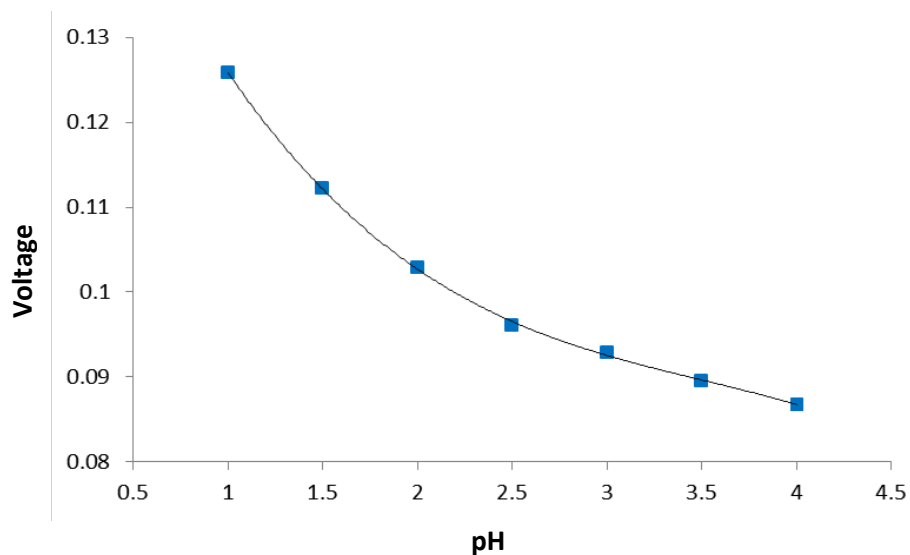


Figure S10. pH dependence fitted to a third order function ($y = -0.0014 x^3 + 0.0151 x^2 - 0.0584 x + 0.1706$; $R^2 = 0.9997$)

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