

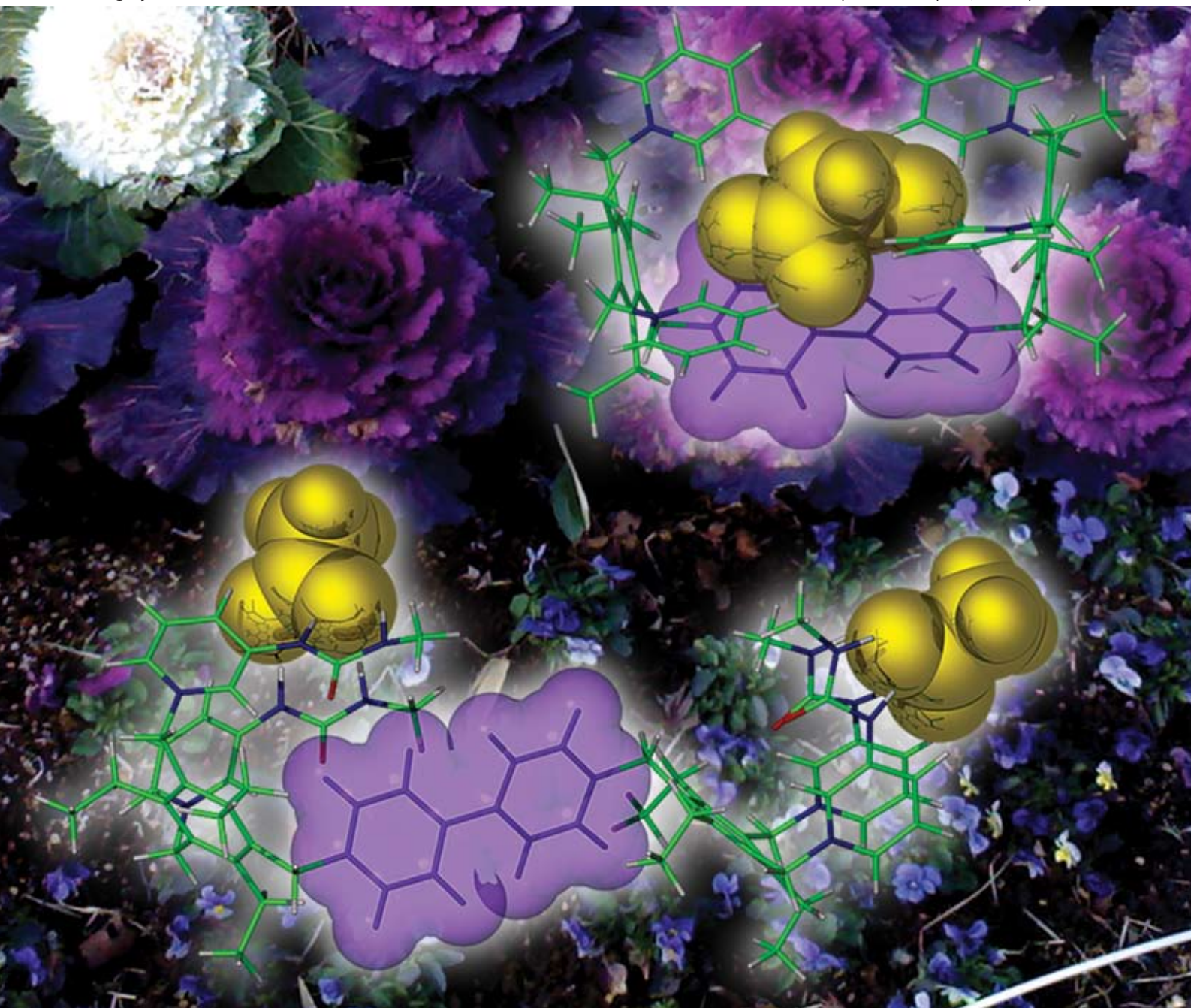
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Intramolecular binding site competition as a means of tuning the response of a colourimetric anion sensor†‡

Sara Jane Dickson,^a Emma V. B. Wallace,^a Adam N. Swinburne,^a Martin J. Paterson,^b Gareth O. Lloyd,^a Andrew Beeby,^a Warwick J. Belcher^c and Jonathan W. Steed^{*a}

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Two new viologen-based anion hosts, **2** and **3**, are reported, incorporating two tripodal binding domains. Binding of carboxylate anions, particularly acetate, malonate and succinate by pyridinium derivative **2** results in an intense purple colouration. DFT calculations on representative system **2**-malonate reveal that this absorption arises from charge-transfer from the anion to the bipyridinium unit. Anion binding by **3** does not initially result in a colour change because anions are bound at the periphery of the receptor; however, addition of more than two equivalents of acetate or more than one equivalent of dicarboxylate turn the colourimetric response on.

The low-lying reduction potential of 4,4'-bipyridinium derivatives ('viologens') has made them extremely useful as reporter groups in supramolecular systems and sensing ensembles,^{1–4} with the binding of various electron donors giving rise to a purple colouration, assigned to the radical cation arising from single electron reduction of the viologen chromophore.⁵ The redox potential of viologens and their ability to form coloured charge-transfer complexes is very dependent on the nature of the substituents on the pyridyl nitrogen atoms and on the counter anion.⁵ Commonly in anion binding and sensing systems, inter-anion selective binding and/or discrimination^{6,7} is achieved by including a number of binding sites able to interact simultaneously with a single anion, producing a well-defined anion binding cavity or cleft. A good example of such cooperative receptors are those based on the 2,4,6-trisubstituted-1,3,5-triethylbenzene core.^{8–21} This scaffold affords a degree of pre-organisation arising from the steric preference for alternation about the central, hexa-substituted ring.¹¹ In previous work, we have shown that pyridinium derivatives of this core make effective anion binding hosts, interacting with anions *via* CH \cdots X[–] hydrogen bonds.^{13–16,22} While it is possible to make a tripodal 4,4'-bipyridine-derived receptor, functionalized at one end of the bipyridine units, that is able to bind ATP in aqueous solu-

tion,²² no viologen derivatives have been synthesized. We now report the anion binding and sensing ability of a series of potentially di- or multitopic receptors based on a bis(triethylbenzyl)-viologen core, in which it is possible to set up internal competition and thus tune interactions with the viologen chromophore.

The key starting material, **1**, as its bromide salt is readily prepared in excellent yield by the reaction of 4,4'-bipyridyl with excess 1,3,5-tri(bromomethyl)-2,4,6-triethylbenzene.¹⁰ A further reaction with either pyridine or 1-pyridin-3-yl-3-*para*-tolyl-urea^{13,23,24} gives the tetrapodal receptors **2** and **3**, respectively, again as bromide salts. Metathesis with NH₄PF₆ yields the hexafluorophosphate salts.

The anion binding abilities of receptors **2** and **3** were probed by ¹H NMR spectroscopic and UV-vis spectrophotometric titrations in acetonitrile solution. The NMR spectroscopic data revealed that both compounds bind halides strongly, consistent with previous observations on related hosts.¹³ The NMR titration data shows that the hosts bind to two chloride anions with log *K*₁₁ = 3.95 and log *K*₁₂ = 3.21 for **2**, and log *K*₁₁ = 3.55 and log *K*₁₂ = 3.39 for **3**. The affinity for bromide is similar, with log *K*₁₁ = 3.75 and log *K*₁₂ = 3.69 for **3**. Interestingly, the addition of carboxylate anions (acetate, malonate and succinate) to both new hosts results in the rapid formation of an intense purple colouration. The solutions remain colourless in the presence of a wide variety of other anions (halides, nitrate and perchlorate) (Fig. 1). While the colour change is immediately evident for **2** upon addition of even sub-stoichiometric amounts of both acetate and the dicarboxylates, the purple colouration does not become significant for urea host **3** until in excess of one equivalent of the dicarboxylates or in excess of two equivalents of acetate are added. This purple colour is strongly suggestive of the formation of a charge-transfer complex of these anions with the viologen core, a phenomenon that has been noted in modest degree for viologens with biologically-relevant phosphates, but is surprising given the high oxidation potentials of the anions.²⁵ As a control, the reaction of carboxylate anions was also attempted with starting material **1**, which would be expected to be less readily reduced because of the lack of additional pyridinium functionalities. Consistent with expectation, this experiment did not result in any colour change.

In the cases of both hosts **2** and **3**, the purple colour gradually fades to red and ultimately orange on standing in aerated solution. Viologen radical cations are known to react

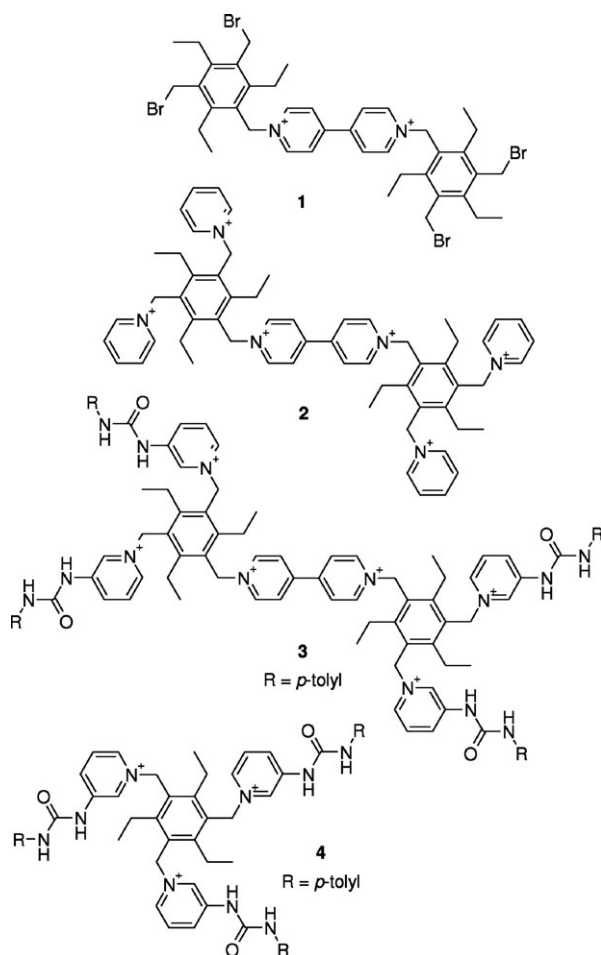
^a Department of Chemistry, Durham University, South Road, Durham, UK DH1 3LE. E-mail: jon.steed@durham.ac.uk

^b School of Engineering and Physical Sciences, Heriott-Watt University, Edinburgh, UK EH14 4AS

^c University of Newcastle, School of Mathematical & Physical Science, Callaghan, NSW 2308, Australia

† Dedicated to Professor Jerry Atwood on the occasion of his 65th birthday.

‡ Electronic supplementary information (ESI) available: Experimental data and selected NMR spectra. See DOI: 10.1039/b800094h



readily with molecular oxygen, hence anion complexation was studied in de-gassed solutions. De-gassing resulted in a persistent purple colour in the presence of carboxylates that took much longer to fade. The anion-induced colour changes were studied by UV-vis spectrophotometric titration both in the

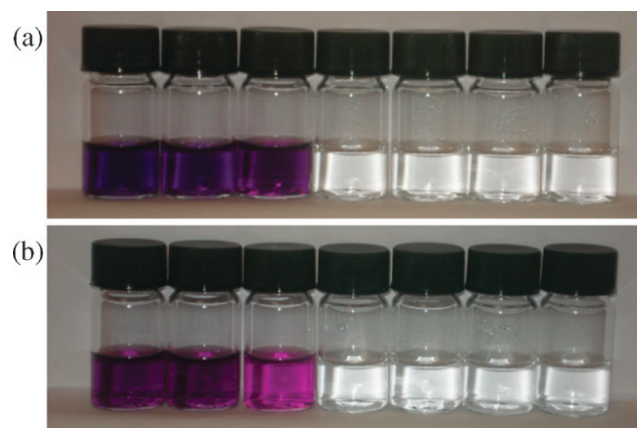


Fig. 1 De-gassed 1×10^{-4} M solutions of hosts **2** and **3** in the presence of NBu_4^+ salts of the following anions (from left to right): succinate, malonate, acetate, chloride, bromide, nitrate and perrhenate. (a) Host **2** with one equivalent of anion. (b) Host **3** with four equivalents of anion.

presence and absence of oxygen. Representative UV-vis spectra for complex **3** are shown in Fig. 2 and additional spectra are given in the ESI.†

The de-gassed data (Fig. 2(b)) show a smooth growth of a band at 543 nm, with a shoulder to lower wavelength. The intensity of this band increases suddenly upon the addition of more than two equivalents of acetate. Receptor **2** exhibits an analogous band and shoulder at 542 nm. This band immediately reaches close to its maximum intensity upon addition of one equivalent of acetate. We interpret these results in terms of competitive anion binding by the urea and pyridinium groups in **3**. Anion binding to the urea groups is remote from the viologen centre and hence results in little charge-transfer. Once the two pairs of urea anion binding sites are saturated, then binding of the third equivalent of acetate or second equivalent of dicarboxylate occurs near to the viologen chromophore, resulting in a visible charge-transfer response. In contrast, in the case of **2**, there are no competing urea anion binding sites, and the first equivalent of added acetate is bound near to the viologen chromophore, giving an immediate colour change.

As a further control, an analogous titration was carried out on a tripodal 1-pyridin-3-yl-3-*para*-tolyl-urea derived host, **4**, previously reported by us¹³ containing three ureidopyridinium groups, but no bipyridinium moiety. While the titration clearly shows significant interaction (Fig. 3), no colour changes were observed in the visible region, suggesting that alternative processes, such as deprotonation of the urea groups in the analogous **3**, are not involved in the colour change process.

At present, the cause of the orange colouration, with an absorption centred on 488 nm, observed in the presence of

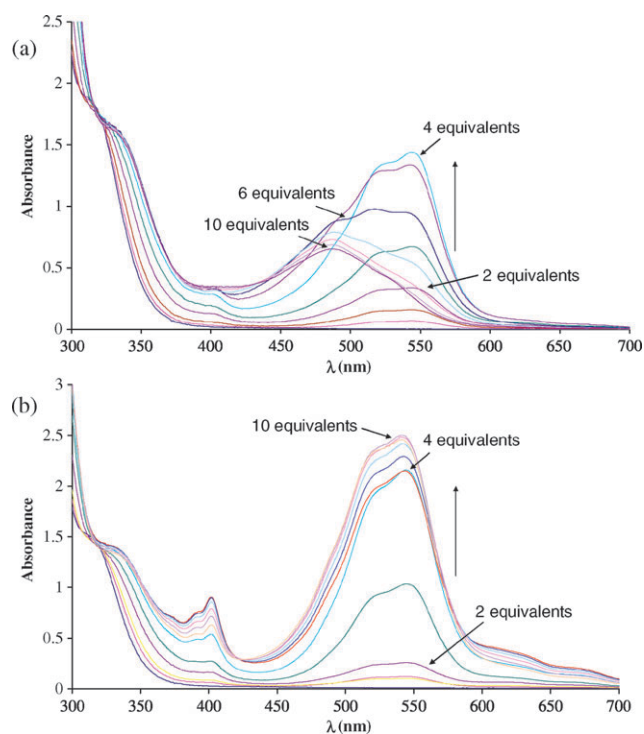


Fig. 2 UV-vis spectra of **3** upon titration with tetrabutylammonium acetate (a) in the presence of oxygen and (b) in de-gassed solution.

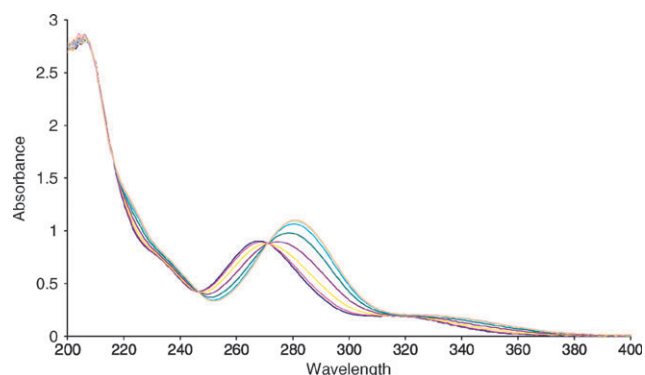


Fig. 3 UV-vis spectra of **4** upon titration with tetrabutylammonium acetate. No changes are observed above 400 nm.

oxygen, is unclear (Fig. 2(a)). However, ^1H NMR spectra recorded in an acetate titration with **2** in the presence of oxygen rapidly show the loss of the resonance assigned to the methylene group attached to the bipyridinium moiety, suggesting chemical decomposition, probably brought about by displacement by hydroxide arising from dioxygen reduction. Evidence for this possibility comes from examination of the ^1H NMR spectra of **3** upon titration with acetate under aerobic conditions. No decomposition is evident until more than two equivalents of acetate are added, and the purple colour of the charge-transfer complex is produced, implying that the decomposition is linked to the formation of the viologen radical cation. While, as a result of this additional process, it was not possible to determine the dicarboxylate binding constants by NMR methods; the NMR data provide excellent qualitative information about carboxylate binding mode. Thus, upon addition of up to two equivalents of acetate to **3**, very little chemical shift change is observed for the pyridinium resonances, whereas the two urea NH signals broaden considerably and shift from 8.26 and 8.95 ppm to 10.95 and 12.80 ppm, respectively (at 2.5 equivalents (Fig. 4)). In contrast, for **2**, the pyridinium CH resonances exhibit a considerable chemical shift change upon the addition of carboxylates. This evidence strongly suggests that binding of the first two equivalents of acetate in **3** is at the urea moieties, remote from the bipyridinium core, consistent with the UV-vis data. The binding mode was further probed crystallographically and by DFT calculation.

We undertook an X-ray crystal structure determination of the hexafluorophosphate salt of pyridinium host **2**.§ The compound crystallises with one independent hexacation, six

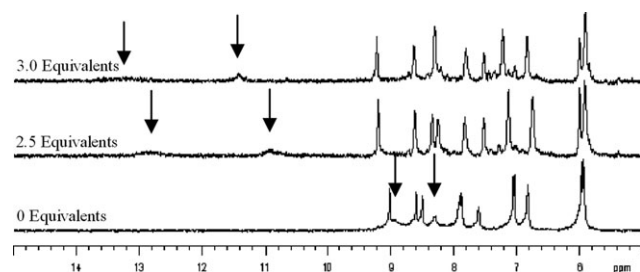


Fig. 4 ^1H NMR spectra of **3** upon titration with $\text{NBu}_4^+\text{MeCO}_2^-$. Urea NH resonances are indicated by arrows.

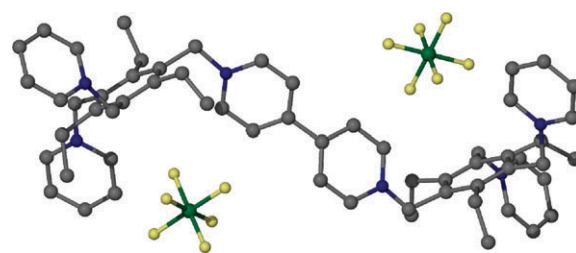


Fig. 5 X-Ray molecular structure of the cation in **2** showing two of the hexafluorophosphate anions located in close proximity to the viologen core.

PF_6^- anions and an isolated pocket of disordered acetonitrile solvent. The triethylbenzene units adopt a *transoid* conformation across the central bipyridinium unit, and in each tripodal sub-unit, one pyridinium substituent is co-aligned with the bipyridinium group, while the other points in the opposite direction. The molecular structure of the cation is shown in Fig. 5. Fig. 5 also shows the location of the two PF_6^- counter ions that are closest to the centres of the triethylbenzene tripodal units. In solution, our previous work on related tripodal hosts suggests that these cavity or cleft sites are the initial anion binding sites.¹⁶ In the present case, both intracavity anions are in close proximity to the bipyridinium core, supporting the suggestion that anion binding in **2** results in the immediate formation of a charge-transfer complex, in which the anion is located close to the viologen.

In order to gain further insights into the anion binding modes and the origin of the colour changes, we undertook DFT calculations²⁶ on the representative systems **2**-malonate and **3**-(acetate)₂, the former of which displays the purple colouration, whereas the latter requires further acetate addition to change colour (*i.e.* the colour change becomes significant once in excess of two equivalents of acetate have been added). Geometry optimization was performed using the hybrid B3LYP density functional, with the following basis: 4-31G on the viologen system, 6-31+G* on the anion (malonate or acetate), and a set of diffuse s and p functions augmenting the basis on the proximal hydrogen atoms to the anions. The calculated geometry of **2**-malonate is shown in Fig. 6(a), which reveals the ability of the host to enfold the anion, binding *via* charge-assisted pyridinium $\text{CH}\cdots\text{O}$ interactions. The anion is situated close to the bipyridinium core in a suitable geometry to give charge-transfer interactions. The electronic absorption characteristics of **2**-malonate were investigated using time-dependent linear response density functional theory based on the B3LYP functional and the 6-31G* basis on all atoms. The calculations revealed a dominant single particle-hole configuration state at 2.25 eV (550 nm, in good agreement with the observed visible absorption) (Fig. 7). The transition thus arises from the promotion of an electron in a localised π orbital on the malonate anion to the π^* orbital on the bipyridinium moiety. The transition has a large oscillator strength ($f = 0.005$) and so would be expected to give rise to an intense vibronic band, consistent with observation. The calculated structure of **3**-(acetate)₂ is shown in Fig. 6(b). The acetate anions interact with the strongly hydrogen bonding urea groups, as observed for analogous host **4**¹³ and consistent

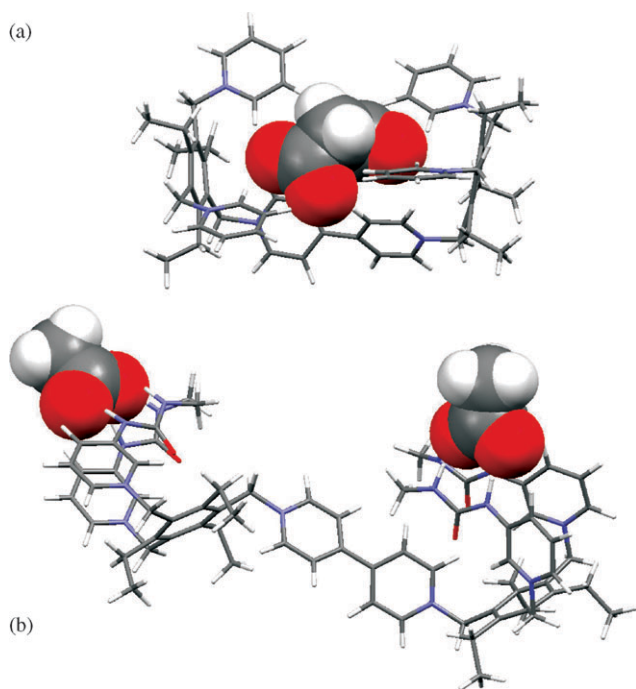


Fig. 6 DFT-calculated structures for (a) 2-malonate and (b) 3-(acetate)₂. Anions shown in space-filling mode.

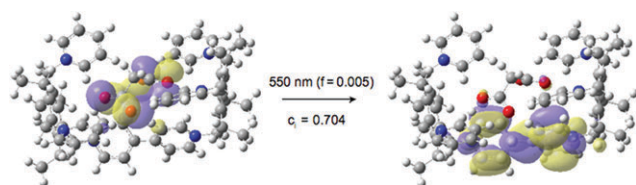


Fig. 7 DFT-calculated electronic absorption in 2-malonate at 550 nm showing charge-transfer from the anion to the bipyridinium moiety.

with the NMR spectroscopic data shown in Fig. 4, and are remote from the viologen core. Calculations of the electronic absorption characteristics of this system indicate that there is no comparable transition in the 550 nm region of the electronic absorption spectrum.

In conclusion, we have reported a polytopic receptor design, in which carboxylate binding brings about a visual colour change at relatively low concentrations. The amount of anion needed to trigger a colourimetric response depends in a step-fashion on the identity of the peripheral binding groups. This ability to tune the amount of acetate needed to cause a response by internal binding site competition, coupled to the distinct carboxylate selectivity, could prove highly useful in anion sensing applications.

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§ Crystal data for **2**: C₆₂H₇₃F₃₆N₇P₆, *M* = 1786.10, colourless plate, 0.42 × 0.26 × 0.14 mm³, monoclinic, space group *P*2₁/*c* (no. 14), *a* =

27.132(5), *b* = 9.4203(16), *c* = 30.586(5) Å, β = 103.680(6)°, *V* = 7596(2) Å³, *Z* = 4, *D*_c = 1.562 g cm⁻³, *F*₀₀₀ = 3632, Smart 6 K, Mo-K_α radiation, λ = 0.71073 Å, *T* = 120(2) K, 2θ_{max} = 50.0°, 43 497 reflections collected, 13 381 unique (*R*_{int} = 0.1288). Final GoF = 0.976, *R*1 = 0.1144, *wR*2 = 0.2870, *R* indices based on 5393 reflections with *I* > 2σ(*I*) (refinement on *F*²), 1056 parameters, 54 restraints. Lp and absorption corrections applied, μ = 0.274 mm⁻¹. CCDC 675534. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b800094h

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