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A pyrrole-based triazolium-phane with NH and cationic CH donor groups as a receptor for tetrahedral oxyanions that functions in polar media†

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The pyrrole-based triazolium-phane $\mathbf{1}^{4+}\cdot 4BF_4^-$ has been prepared *via* the tetraalkylation of a macrocycle originally prepared *via* click chemistry. It displays a high selectivity for tetrahedral oxyanions relative to various test monoanions and trigonal planar anions in mixed polar organic–aqueous media. This selectivity is solvent dependent and is less pronounced in acetonitrile. Theoretical calculations were carried out in with the chloride anion in an effort to understand the influence of solvent on the intrinsic hydrogen bonding ability of the donor groups (pyrrole N–H, benzene C–H and triazolium C–H). The host–guest interactions between receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ and representative tetrahedral oxyanions were further analysed by ^{1}H NMR spectroscopy, and the findings proved consistent with the differences in the intrinsic strength of the various H-bond donor groups inferred from the electronic structure calculations carried out in methanol, namely that $(CH)^+$–anion interactions are less important in an energetic sense than neutral CH–anion interactions in polar media. Single crystal X-ray diffraction analyses of the mixed salts $\mathbf{1}^{4+}\cdot HP_2O_7^{3-}\cdot BF_4^-$ and $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$ confirmed that receptor $\mathbf{1}^{4+}$ can bind the pyrophosphate and phosphate anions in the solid state.

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Introduction

One goal of supramolecular chemistry[1] is to create synthetic receptors that have both high affinity and high selectivity for biologically and environmentally important anionic species.[2] Anions are ubiquitous in the natural world and critical to the maintenance of life as we know it.[3] Pyrophosphate, for instance, is a by-product of ATP hydrolysis under cellular conditions.[4] It is involved in DNA polymerase-catalysed DNA replication[5] and the detection pyrophosphate could thus provide for real-time DNA sequencing.[6] Its analogue, inorganic phosphate, has physiological relevance in biological energy storage and signal transduction, in addition to being a structural component in teeth and bones.[7] Sulphate, because of its low solubility (typically *ca.* 1%) in borosilicate glass, has been identified as problematic in the vitrification of radioactive waste.[8] Not surprisingly, therefore, considerable effort has been devoted to the design and synthesis of receptors capable of recognizing and detecting these tetrahedral oxyanions.[2] Systems incorporating neutral or cationic NH hydrogen bond donor groups (*e.g.*, pyrrole, urea, amide, ammonium, and guanidinium),[9] as well as neutral or cationic CH hydrogen bond donor motifs (*e.g.*, phenyl, triazole, triazolium, and imidazolium),[10,11] have been particularly effective in this regard. It is noteworthy that positively charged imidazolium derivatives can interact with anions through $(C–H)^+\cdots X^-$ type ionic hydrogen bonds, which are generally stronger than the corresponding hydrogen-bonding interactions stabilized by neutral pyrrole and urea moieties.[10f] Recently, 1,2,3-triazolium motifs with cationic CH hydrogen bond donor groups have garnered attention for their potential use in transition metal-based catalysis[12] and organocatalysis.[13] However, they have yet to be exploited extensively in anion recognition chemistry.[10b,14] Moreover, the use of the triazolium motif in conjunction with other anion recognition subunits remains all but unexplored. Here, we report a new synthetic anion receptor, $\mathbf{1}^{4+}$, that combines both pyrrole and triazolium anion recognition motifs within one macrocyclic framework. It exhibits high selectivity and affinity for tetrahedral oxyanions *via* an anion exchange process and functions effectively in mixed organic–aqueous media. Based on a combination of theoretical, solution phase, and single crystal X-ray diffraction analyses, we propose that oxyanion recognition is stabilized *via* a combination of C–H··· and N–H···anion hydrogen bonding and electrostatic interactions, both in solution and in the solid

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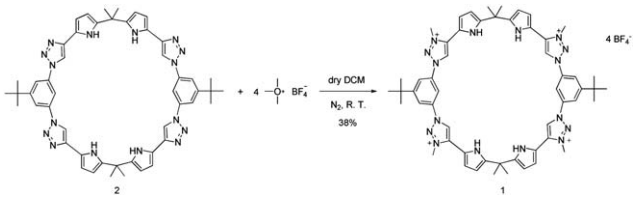
† Electronic supplementary information (ESI) available: Full experimental details and X-ray experimental section. CCDC nos. 849576, 849577, and 849578 for $\mathbf{1}^{4+}\cdot 4BF_4^-\cdot CH_3OH\cdot 3H_2O$, $\mathbf{1}^{4+}\cdot HP_2O_7^{3-}\cdot BF_4^-$, and $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$, respectively. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3sc22144j



Scheme 1 Synthesis of the tetracationic triazolium macrocycle $\mathbf{1}^{4+}$.

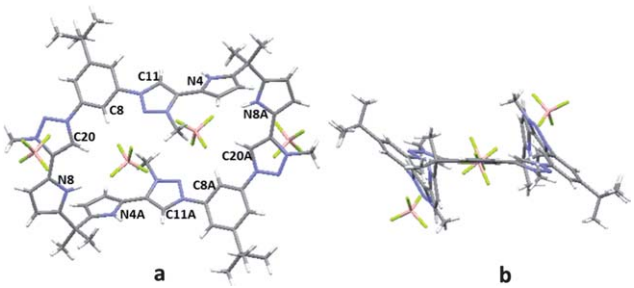


Fig. 1 (a) Top and (b) side views of the single crystal X-ray structure of $\mathbf{1}^{4+}\cdot 4BF_4^-\cdot CH_3OH\cdot 3H_2O$.† All solvent molecules have been omitted for clarity.

state. We also conclude that in highly polar media, such as methanol, phenyl CH–anion interactions play a greater stabilizing role in anion binding than do triazolium $(CH)^+\cdots$anion interactions. This seemingly counterintuitive result reflects the disparate solvent dependence of the underlying hydrogen bonding and electrostatic interactions associated with the individual recognition motifs. It also serves to underscore the benefits of creating and testing receptor systems that allow a variety of potential binding motifs to be assessed under carefully controlled conditions.

The paucity of attention devoted to 1,2,3-triazolium-based $(CH)^+$–anion interactions stands in marked contrast to what is true for neutral triazoles. Triazoles, first pioneered for anion recognition by Flood and Li, have emerged recently as important new anion binding motifs.[10d] One reason triazole systems are attractive is because they can be accessed *via* so-called "click" chemistry, specifically the copper(I)-catalyzed azide alkyne 1,3-dipolar cycloaddition (CuAAC) reaction.[15,16] They can also be readily incorporated into a variety of cyclic and acyclic structures. One further appeal of triazoles is that, at least in principle, they can be converted to the corresponding triazolium salts by simple alkylation.[10b] With this consideration in mind we sought to prepare the tetracationic macrocycle $\mathbf{1}^{4+}$ by subjecting the corresponding triazole system **2** to methylation (Scheme 1). As detailed below, this strategy proved easy to implement and gave rise to an anion receptor $\mathbf{1}^{4+}$, a macrocyclic system that contains four triazolium subunits. A notable feature of this new receptor is that it contains three different types of putative hydrogen bond donor groups (benzene CH, triazolium CH, and pyrrole NH). Thus, a key rationale for preparing receptor $\mathbf{1}^{4+}$ was that it would allow an assessment of the relative importance of the different subunit-anion interactions it might support.

Results and discussion

The synthesis of calix[2]1,3-bis(pyrro-2-yl)(1,4)-1,2,3-triazolophane **2** (Scheme 1) was accomplished in three steps as recently reported.[10a] Briefly, the key fragment 1,3-bis(pyrro-2-yl)(1,4)-1,2,3-triazolo-benzene was prepared under standard click conditions,[15] followed by removal of the *t*-BOC protecting group;[17] it was then cyclized with acetone to form macrocycle **2**.[18] This was followed by a methylation reaction using Meerwein's salt to give the tetracationic triazolium macrocycle tetrafluoroborate salt $\mathbf{1}^{4+}\cdot 4BF_4^-$ (**1** = calix[2]1,3-bis(pyrro-2-yl)(1,4)-3-methyl-5H-1,2,3-triazolium-phane tetrafluoroborate) in 38% yield.[10b] Colourless single crystals of $\mathbf{1}^{4+}\cdot 4BF_4^-$ were obtained *via* vapour diffusion (diethyl ether into a methanol solution of the salt). Salt $\mathbf{1}^{4+}\cdot 4BF_4^-$ was characterized on the basis of its spectroscopic properties (*cf.* ESI†) and *via* single crystal X-ray diffraction analysis.

A single crystal X-ray diffraction analysis of $\mathbf{1}^{4+}\cdot 4BF_4^-$ revealed a nearly planar macrocyclic structure (Fig. 1).† Two of the BF_4^- counter anions were found to be located within the inner cavity of the tetracationic cyclophane built up from the constituent phenyl, pyrrole, and triazolium subunits. The two other counter anions were found to lie outside the cage; they are not involved in any apparent interactions with the macrocycle, at least in the solid state. The macrocycle $\mathbf{1}^{4+}\cdot 4BF_4^-$ is centrosymmetric. The pyrrole groups (N4, N4A) and the triazolium motifs (C11, C11A) are twisted out of the plane. The hydrogen atoms on the pyrrole NH (N8, N8A), triazolium CH (C20, C20A) and the endocyclic hydrogen atoms of the N^1-linked phenyl units (C8, C8A) are pointing into the center of the ring. Based on the geometric parameters (N– and C–F distances of $\leq$3 Å) these endocyclic hydrogen atoms are involved in NH$\cdots$F, CH$\cdots$F hydrogen bond interactions with one of the BF_4^- anions bound within the macrocyclic ring.

The anion binding properties of $\mathbf{1}^{4+}\cdot 4BF_4^-$ in solution were analysed initially using UV-Vis spectroscopy. Standard titrations, associated curve fittings,[19] and Job plots provided support for the proposal that hydrogen pyrophosphate, hydrogen sulphate and dihydrogen phosphate anions (all studied as their corresponding tetrabutylammonium (TBA) salts) are bound to $\mathbf{1}^{4+}\cdot 4BF_4^-$ strongly in acetone–H_2O solution (2 : 3; pH = 7.2; HEPES buffer) at 300 K ($HP_2O_7^{3-}$: $K_a = (2.49 \pm 0.15) \times 10^5\ M^{-1}$; HSO_4^-: $K_a = (3.92 \pm 0.36) \times 10^5\ M^{-1}$; $H_2PO_4^-$: $K_a = (3.53 \pm 0.14) \times 10^4\ M^{-1}$) and with 1 : 1 binding stoichiometries (Table 1). To avoid interference from potential aggregation effects, the effective association constants (K_a) were determined at $[\mathbf{1}^{4+}\cdot 4BF_4^-] \leq 50\ \mu M$ and were found to be independent of initial receptor concentration under these conditions. The binding isotherms used to determine the K_a values were generated by recording the changes in the UV-Vis absorption spectrum as a function of hydrogen sulphate, hydrogen pyrophosphate and dihydrogen phosphate concentration (shown for $\mathbf{1}^{4+}\cdot 4BF_4^-$ in Fig. 2a–c, respectively). Based on Job-plot analyses, which proved consistent with a 1 : 1 binding stoichiometry in the case of these test anions (Fig. 2d–f, respectively), the data were fit to a 1 : 1 binding isotherm. Analogous studies were carried out in methanol and acetonitrile. The calculated K_a

Table 1 Binding affinities of different anions to receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ in three different solvent systems[a]

	CH_3CN[b]		CH_3OH[b]		Acetone–H_2O (2 : 3)[b] (pH = 7.2 in HEPES buffer)	
Guest	Stoichiometry (host : guest)	K_a (M^{-1})	Stoichiometry (host : guest)	K_a (M^{-1})	Stoichiometry (host : guest)	K_a (M^{-1})
HSO_4^-	1 : 1	$K_a = (9.88 \pm 1.18) \times 10^6$	1 : 1	$K_a = (1.60 \pm 0.22) \times 10^7$	1 : 1	$K_a = (3.92 \pm 0.36) \times 10^5$
$HP_2O_7^{3-}$	1 : 1	$K_a = (9.89 \pm 1.06) \times 10^5$	1 : 1	$K_a = (1.17 \pm 0.1) \times 10^7$	1 : 1	$K_a = (2.49 \pm 0.15) \times 10^5$
$H_2PO_4^-$	1 : 2	$K_{a1} = (6.44 \pm 0.16) \times 10^3$ $K_{a2} = (1.03 \pm 0.04) \times 10^5$	1 : 1	$K_a = (1.73 \pm 0.15) \times 10^6$	1 : 1	$K_a = (3.53 \pm 0.14) \times 10^4$
CH_3COO^-	1 : 1	$K_a = (2.25 \pm 0.14) \times 10^6$	1 : 1	$K_a = (1.79 \pm 0.01) \times 10^3$	n.d.[c]	n.d.
NO_3^-	1 : 1	$K_a = (5.99 \pm 0.61) \times 10^5$	1 : 1	$K_a = (7.90 \pm 0.50) \times 10^3$	n.d.	n.d.
Cl^-	1 : 1	$K_a = (4.48 \pm 0.53) \times 10^6$	1 : 1	$K_a = (2.93 \pm 0.05) \times 10^3$	n.d.	n.d.
Br^-	1 : 1	$K_a = (2.46 \pm 0.25) \times 10^6$	1 : 1	$K_a = (4.90 \pm 0.34) \times 10^3$	n.d.	n.d.

[a] Determined by UV-Vis titrations carried out at 300 K using the tetrabutylammonium (TBA) salts of the indicated anions. [b] For studies in CH_3CN and CH_3OH, $[\mathbf{1}^{4+}\cdot 4BF_4^-] = 1.00 \times 10^{-5}$ M; for studies in acetone–H_2O (2 : 3; pH = 7.2; HEPES buffer), $[\mathbf{1}^{4+}\cdot 4BF_4^-] = 5.00 \times 10^{-5}$ M. [c] n.d. = not determined; affinity too modest to be measured accurately.

values and binding stoichiometries (as inferred from Job plots) for all three solvent systems are summarized in Table 1.

Strictly speaking the K_a values in Table 1 are displacement constants and reflect possible initial interactions between the BF_4^- counter anions and receptor $\mathbf{1}^{4+}$. However, in practice the interactions between the BF_4^- counter anions and the receptor are expected to be modest. Further, they will be identical for all anions considered in this study. Therefore, we believe that the K_a values tabulated in Table 1, which represent lower bounds, can be used for the purpose of inter-analyte comparisons.

From an inspection of Table 1, the effect of solvent on the anion binding behaviour of receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ can be inferred. While in acetonitrile a general lack of anion selectivity is seen (the binding constants for various test anions range between 10^5 and 10^6 M^{-1}), in methanol, considerable selectivity for tetrahedral oxyanions is seen relative to other typical anionic

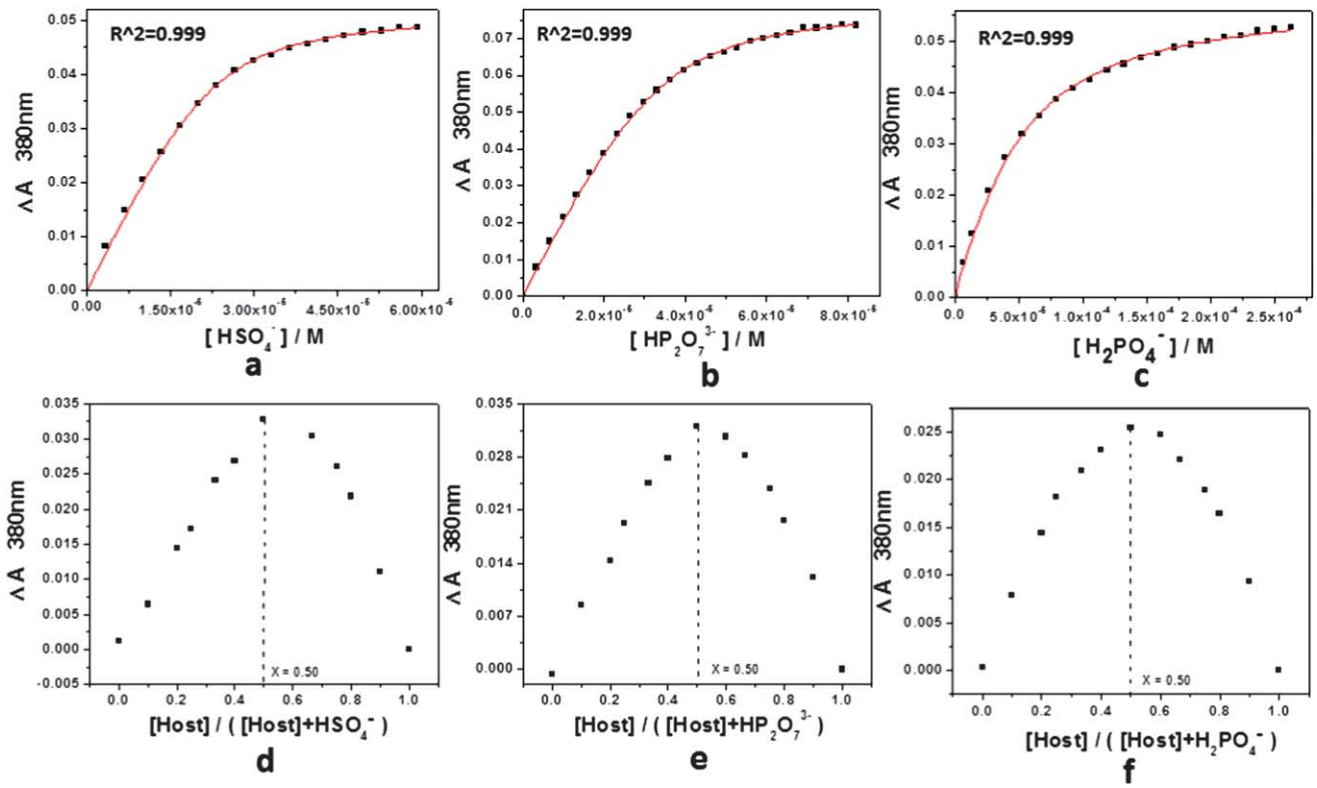


Fig. 2 Variations in absorbance (■) at 380 nm of a solution of receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ (5.00×10^{-5} M) in acetone–H_2O (2 : 3; pH = 7.2; HEPES buffer) as a function of tetrabutylammonium (TBA) anion salt concentration. (a) $TBAHSO_4$ (0–6.0×10^{-5} M), (b) $(TBA)_3HP_2O_7$ (0–8.0×10^{-5} M), and (c) $TBAH_2PO_4$ (0–2.5×10^{-4} M) (c) at 300 K. Job plots corresponding to the interaction between (d) $\mathbf{1}^{4+}\cdot 4BF_4^-$ and $TBAHSO_4$, (e) $(TBA)_3HP_2O_7$, and (f) $TBAH_2PO_4$ in acetone–H_2O (2 : 3; pH = 7.2; HEPES buffer) at 300 K; [host] + [guest] = 5.00×10^{-5} M. In all cases, a maximum value at 0.5 is observed; this is consistent with a 1 : 1 (host : guest) binding stoichiometry.

analytes (*e.g.*, acetate, nitrate, chloride and bromide; all studied as the corresponding TBA salts). This selectivity is maintained and even enhanced in acetone–H_2O (2 : 3; pH = 7.2; HEPES buffer). In fact, under these latter, mixed aqueous solvent conditions, receptor $\mathbf{1}^{4+}$ (as its tetrakis BF_4^- salt) binds the tetrahedral oxyanions hydrogen sulphate, hydrogen pyrophosphate and dihydrogen phosphate anions with affinities of 10^4 to 10^5 M^{-1}. However, it displays no appreciable affinity for any of the other test anions (*i.e.*, chloride, bromide, nitrate, and acetate).

The combination of high affinity and selectivity for tetrahedral oxyanions in mixed aqueous medium is noteworthy. While systems that bind tetrahedral oxyanions in organic media based on hydrogen-bonding interaction are well known, there are few that operate in the presence of large quantities of water. In prior work, Kubik and coworkers demonstrated that synthetic cyclopeptides containing alternating aromatic and L-proline residues could bind inorganic anions, such as halides and sulphate, efficiently in 80% H_2O–CH_3OH, although little appreciable selectivity for the sulphate anion was observed.[20] In separate work, Delgado and coworkers demonstrated that protonated hexaamine-cage receptors could efficiently interact with tetrahedral oxyanions in 50% H_2O–CH_3OH at low pH.[21] In earlier work, Lehn and coworkers reported that guanidinium-containing macrocycles could be used for the recognition of phosphate in water.[22] However, these latter receptors formed less stable anion complexes than the corresponding protonated ammonium-based receptors. There thus remains a need for new receptors that are selective for tetrahedral oxyanions and which function in mixed aqueous media at neutral pH.

To understand the solvent dependence noted above and to allow a comparison of the intrinsic hydrogen bonding ability of the donor groups present in receptor $\mathbf{1}^{4+}$, ΔG values for the formation of the representative complexes between the Cl^- anion and the simple donors shown in Fig. 3 were computed in the gas phase under vacuum conditions (*cf.* ESI† for Cartesian coordinates and absolute energies).[23] Similar calculations were carried out in several pure solvents (*e.g.*, $CHCl_3$, acetone, CH_3CN, CH_3OH, and H_2O).[24]

In prior studies, comparison of hydrogen bonding interactions between C–H and N–H donor groups with different anion shapes (chloride, nitrate, perchlorate) established that similar binding energy trends are observed for this group of monovalent anions.[10e,25] Therefore, we have used the chloride as a representative anion, primarily because the system is small and

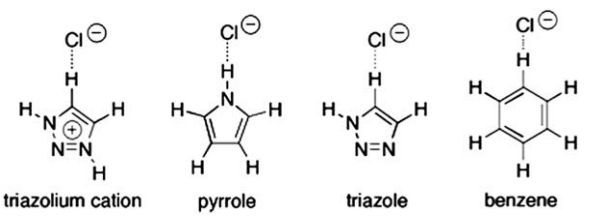


Fig. 3 Representations of the possible hydrogen bonding interactions that can be stabilized by the subunits present in receptor $\mathbf{1}^{4+}$. The energetics of these interactions are considered in Table 2.

Table 2 Influence of solvent on calculated ΔG values (kcal mol^{-1}) for the formation of hydrogen-bonded complexes between Cl^- and representative C–H hydrogen bond donors (Fig. 3)

	Solvent					
Donor	Vacuum	$CHCl_3$	Acetone	CH_3CN	CH_3OH	H_2O
Triazolium C–H	−89.2	−4.0	11.5	14.0	19.5	20.7
Pyrrole N–H	−15.6	−3.0	−1.9	−1.3	3.9	4.1
Triazole C–H	−12.4	2.5	4.8	5.4	8.7	8.6
Benzene C–H	−2.4	5.7	6.1	6.4	8.9	8.6

the number of possible minima is limited. The results, summarized in Table 2, reveal that although the formation of the triazolium complex is by far the most favourable in vacuum, the binding affinity (as measured by ΔG) decreases dramatically for the corresponding process in $CHCl_3$. This interaction becomes even less favourable in the case of more polar solvents.

In the case of higher dielectric constant solvents, *i.e.*, $\varepsilon > 20$ (acetone, CH_3CN, CH_3OH, and H_2O), the calculated ΔG values lead to the inference that the driving force for hydrogen bond formation decreases in the following order: pyrrole > triazole > benzene > triazolium cation. The driving force for forming complexes between the Cl^- anion and three putative hydrogen bonding donors present in the macrocycle $\mathbf{1}^{4+}\cdot 4BF_4^-$ (pyrrole N–H, benzene C–H and triazolium C–H) all decrease on passing from acetonitrile to methanol (Table 2).

This conclusion is fully consistent with the results of the UV-Vis experimental studies discussed above: in the case of both theory and experiment, the binding constants for interactions with monoanions were found to become smaller as the polarity of the medium increased (*e.g.*, on moving from acetonitrile to methanol).[26] However, for tetrahedral oxyanions, the binding constants proved to be both inherently high and rather independent of solvent polarity. This could reflect the greater size and complexity of these latter ions, features that would tend to augment the importance of specific hydrogen bonding interactions relative to competitive anion solvation.

Independent of rationale, it is important to underscore that the theoretical analyses lead to the seemingly counterintuitive conclusion that in methanol the benzene CH–anion hydrogen bond interactions are more important for anion binding than the corresponding triazolium CH–anion interactions. Experimental support for this conclusion was obtained from detailed ^1H NMR analyses as detailed below.

The host–guest interactions between receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ and representative tetrahedral oxyanions were further analysed by ^1H NMR spectroscopy. Proton NMR titrations were carried out in deuterated methanol using the respective TBA salts. Unfortunately, solubility considerations precluded analogous titrations being carried out in either CD_3CN or 60% D_2O/40% acetone-d_6. The titrations were performed as follows: a solution of receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ (4 mM, CD_3OD) was titrated with up to 10 equiv. of the TBA anion salt of choice. A representative titration is shown in Fig. 4 for $(TBA)_3HP_2O_7$. It is worth noting that the pyrrole NH protons were generally not visible under the conditions of these titrations, presumably as the result of fast

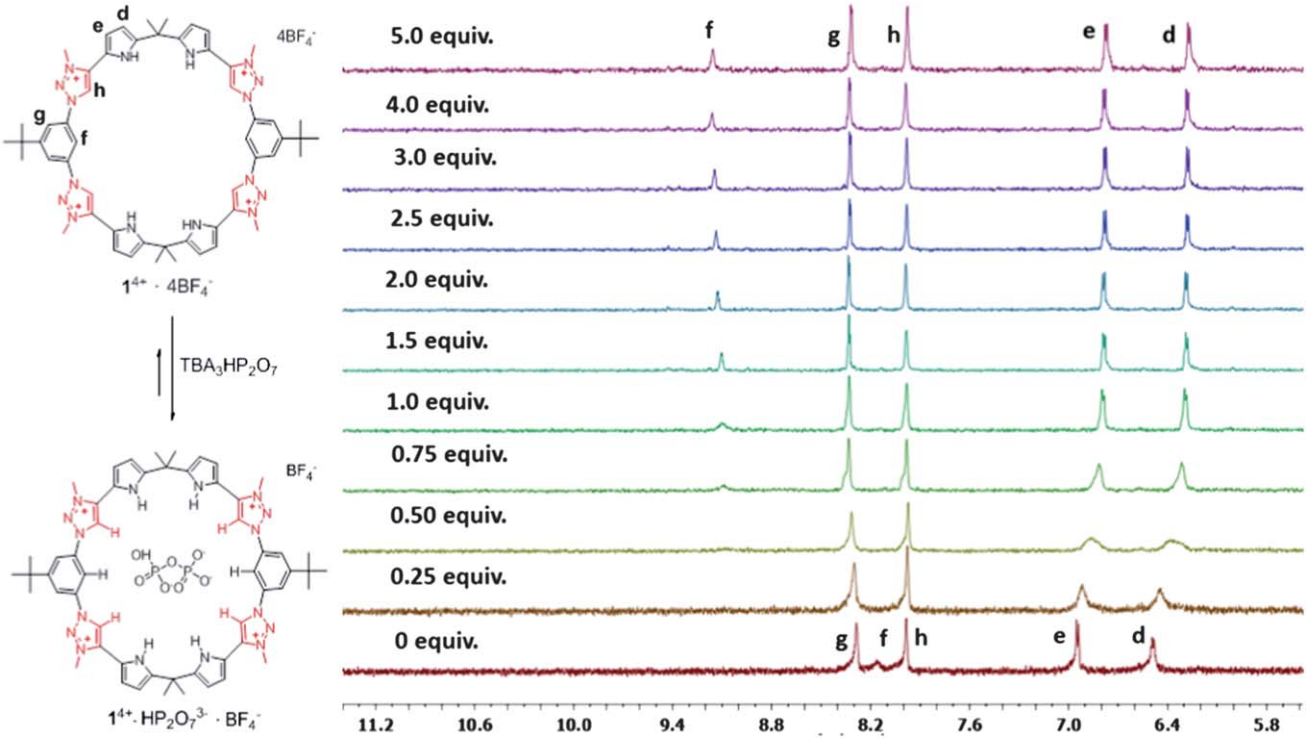


Fig. 4 ^{1}H NMR spectra (aromatic region) of receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ (4 mM) recorded in the presence of increasing concentrations of $(TBA)_3HP_2O_7$ (CD_3OD, 300 K).

exchange with the CD_3OD solvent. As a general rule, and as can be seen by inspection of Fig. 4, little shift in the signals for the triazolium CH protons was typically seen. In contrast, the resonances corresponding to the endocyclic hydrogen atoms of the N^1-linked phenyl unit were observed to shift downfield by 1.01 ppm, 0.48 ppm, and 0.45 ppm upon the addition of 5 equiv. of $(TBA)_3HP_2O_7$, $TBAH_2PO_4$ and $TBAHSO_4$, respectively (*cf.* ESI†). Such differing shift behaviour is consistent with the differences in the intrinsic strength of the various H-bond donor groups inferred from the electronic structure calculations carried out in methanol using the chloride anion. The calculated ΔG values of the interaction of chloride with benzene C–H and triazolium C–H complexes are 8.9 and 19.5 kcal mol^{-1} in methanol (Table 2). This combination of theory and experiment provides support for the conclusion that the anion interactions stabilized by a benzene C–H hydrogen bond is stronger than that stabilized by a triazolium C–H hydrogen bond in methanol. However, it is to be noted that this analysis and inference does not account for the effect, if any, of anion-induced conformational changes on the benzene C–H and triazolium C–H chemical shift values.

Proton NMR titrations were also carried out in deuterated methanol using receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$ and both monoanionic and trigonal planar anionic salts, such as TBAOAc, $TBANO_3$, TBACl, and TBABr (*cf.* ESI†). The hydrogen signals for the endocyclic hydrogen atoms of the N^1-linked phenyl unit shifted slightly during the associated NMR titrations. On the other hand, little observable shift was seen for the triazolium CH signal. Such findings are consistent with the relative contribution of these two CH donor motifs as inferred from the theoretical analyses (*vide supra*). Moreover, they provide support for the conclusions drawn from the UV-Vis titration experiments, namely that in methanol receptor $\mathbf{1}^{4+}\cdot 4BF_4^-$interacts with tetrahedral oxyanions much more strongly than it does with other simple anions.

Further support for the proposal that receptor $\mathbf{1}^{4+}$ is able to interact with the pyrophosphate and phosphate anions came from single crystal X-ray diffractions analyses. For instance, crystallization of mixture consisting of the starting salt $\mathbf{1}^{4+}\cdot 4BF_4^-$ and $(TBA)_3HP_2O_7$ in methanol *via* the slow diffusion of diethyl ether afforded crystals of $\mathbf{1}^{4+}\cdot HP_2O_7^{3-}\cdot BF_4^-$. The resulting structure confirmed that in this mixed salt the receptor–pyrophosphate anion ratio was 1 : 1 (Fig. 5). It also revealed that the macrocycle adopts a folded conformation, forming a clip-like slot into which the pyrophosphate anion inserts. The BF_4^- anion resides outside of the cavity. All the pyrrole NH, triazolium CH and endocyclic benzene CH protons point into the centre of the ring and are involved in hydrogen bonding interactions with the bound pyrophosphate guest, as inferred from bond distances (pyrrole NH···O approx. 1.9 Å, triazolium CH···O approx. 2.0 Å, benzene CH···O approx. 3.4 Å). The resulting conformation thus stands in contrast to what is seen in the case of the free host, $\mathbf{1}^{4+}\cdot 4BF_4^-$.

The addition of tetrabutylammonium dihydrogen phosphate ($TBAH_2PO_4$) to a methanolic solution of $\mathbf{1}^{4+}\cdot 4BF_4^-$ and subjecting it to crystallization *via* diffusion of diethyl ether resulted in the isolation of single crystals of a complex with a formal stoichiometry $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$. The resulting structure is shown in Fig. 6. It includes two complex salts; these consists of $\mathbf{1}^{4+}\cdot 2H_2PO_4^-\cdot 2BF_4^-$ and $\mathbf{1}^{4+}\cdot 4BF_4^-$, respectively (Fig. 6a). The

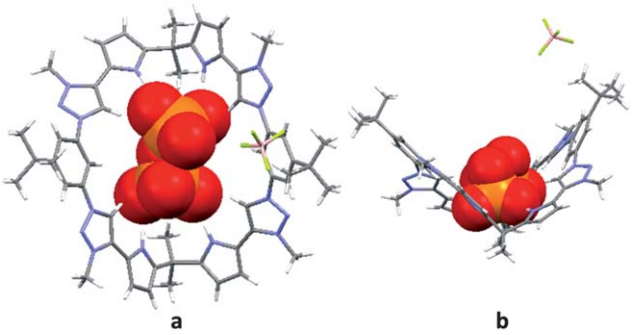


Fig. 5 (a) Top and (b) side views of a single-crystal X-ray diffraction structure of $\mathbf{1}^{4+}\cdot HP_2O_7^{3-}\cdot BF_4^-$ in which the pyrophosphate anion is in a space filling representation and the tetrafluoroborate anion resides outside of the ring.†

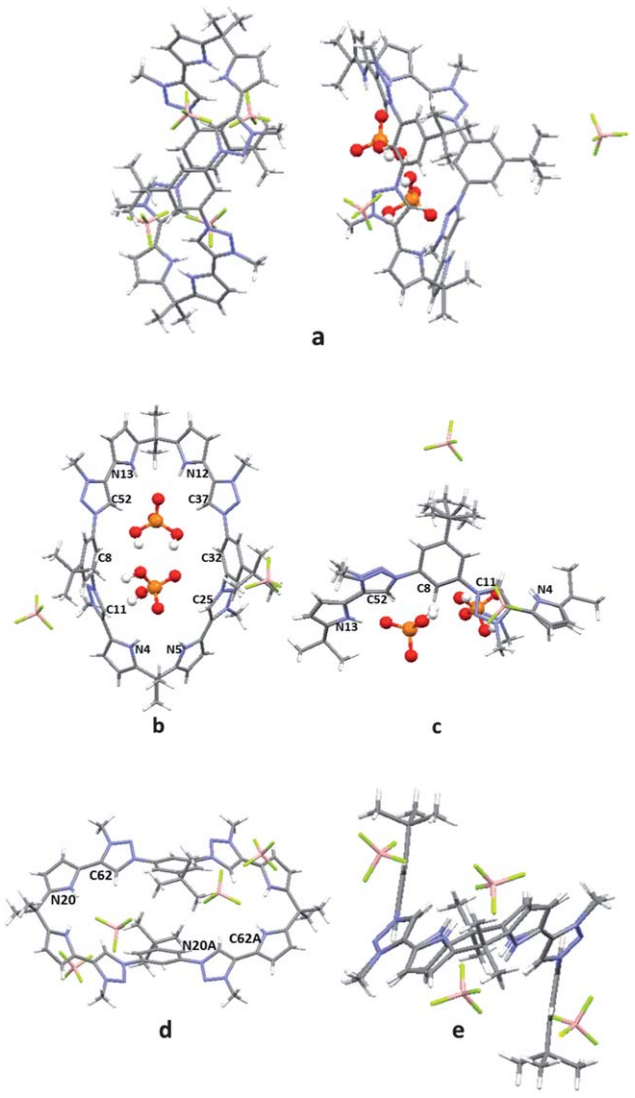


Fig. 6 (a) View of the single-crystal X-ray diffraction structure of the complex salt mixture with formal stoichiometry $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$.† This structure consists of two salt systems. The first consists of $\mathbf{1}^{4+}\cdot 2H_2PO_4^-\cdot 2BF_4^-$, whereas the other corresponds to the starting receptor salt, $\mathbf{1}^{4+}\cdot 4BF_4^-$. (b) Top and (c) side views of the salt $\mathbf{1}^{4+}\cdot 2H_2PO_4^-\cdot 2BF_4^-$ contained within the overall complex salt structure, $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$. Note the two phosphate anions located in the centre of the ring. (d) Top and (e) side views of the salt $\mathbf{1}^{4+}\cdot 4BF_4^-$ contained within the overall complex salt structure, $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$.

structure of $\mathbf{1}^{4+}\cdot 2H_2PO_4^-\cdot 2BF_4^-$ displays the same folded conformation as observed in the case of $\mathbf{1}^{4+}\cdot HP_2O_7^{3-}\cdot BF_4^-$, with two phosphate anions located in the centre of the ring (Fig. 6b and c). However, in contrast to this latter structure, in $\mathbf{1}^{4+}\cdot 2H_2PO_4^-\cdot 2BF_4^-$ the pyrrole NH (N4, N5) and triazolium CH (C11, C25) protons point away from the centre of the ring. Apparent N–H···O and C–H···O hydrogen bonds are seen between the macrocycle and phosphate anions (the pyrrole NH···O distance is approx. 2.1 Å; the triazolium CH···O distance is approx. 2.8 Å; the endocyclic benzene CH···O distance is approx. 2.6 Å).

The other salt ($\mathbf{1}^{4+}\cdot 4BF_4^-$) present in the mixed complex (Fig. 6d and e) is characterized by a planar conformation similar to that seen in the structure of $\mathbf{1}^{4+}\cdot 4BF_4^-$ obtained from single crystals grown in the absence of dihydrogen phosphate (*cf.* Fig. 1). However, in the case of the salt present in the mixed complex, the pyrrole groups, triazolium motifs and benzene rings are all twisted out of the mean macrocyclic plane. As a result, the associated NH, triazolium CH and endocyclic benzene CH protons point away from the centre of the ring. Two BF_4^- anions are found to be located closely above and below the plane of the ring, presumably as the result of hydrogen bond interactions with the pyrrole NH (N20, N20A) and triazolium CH (C62, C62A) protons. The relevant pyrrole NH···F and triazolium CH···F distances are *ca.* 2.1 Å and 2.7 Å, respectively. Another pair of BF_4^- ions is located outside of the ring.

Conclusion

In summary, the pyrrole-based triazolium-phane $\mathbf{1}^{4+}\cdot 4BF_4^-$ has been prepared *via* the tetraalkylation of a macrocycle originally prepared *via* click chemistry. It displays a high selectivity for tetrahedral oxyanions relative to various test monoanions and trigonal planar anions in mixed polar organic–aqueous solvent media. This selectivity is solvent dependent and is less pronounced in acetonitrile. Single crystal X-ray diffraction analyses of the mixed salts $\mathbf{1}^{4+}\cdot HP_2O_7^{3-}\cdot BF_4^-$ and $3\mathbf{1}^{4+}\cdot 4H_2PO_4^-\cdot 8BF_4^-$ support for the notion that receptor $\mathbf{1}^{4+}$ can bind the pyrophosphate and phosphate anions in the solid state. Detailed solution phase studies, carried out in polar media, provide support for this conclusion.

The present results serve to underscore the benefits of combining various hydrogen bond donor motifs within a single receptor to achieve the recognition of particular anionic substrates. The fact that the motifs in question are contained within a relatively flexible macrocyclic framework in the case of $\mathbf{1}^{4+}$ allowed for a direct comparison of the relative importance of NH–, CH–, and $(CH)^+$–anion interactions. The associated results, both experimental and theoretical, provided support for the seemingly counterintuitive conclusion that triazolium $(CH)^+$–anion interactions are less important in an energetic sense than neutral aromatic CH–anion interactions, at least in methanol. These findings have important implications for future receptor design, particularly systems designed to recognize anions in highly polar organic media or aqueous environments.

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