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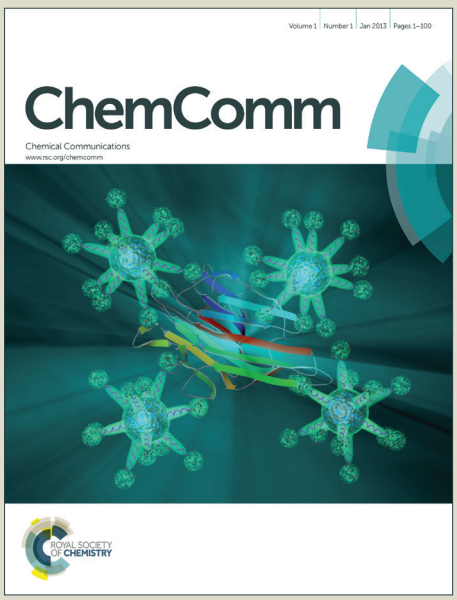

ROYAL SOCIETY OF CHEMISTRY

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Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Discovery of anion-π interactions in the recognition mechanism of inorganic anions by 1,2,3-triazolium rings†

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

A bis(triazolium)-based receptor designed for anion recognition is presented. NMR spectroscopic data indicate that one triazolium ring is acting as a hydrogen bond donor, whereas the second triazolium ring behaves as an anion-π receptor. The simultaneous presence of two noncovalent interactions allows to achieve a highly selective binding of the hydrogenpyrophosphate anion.

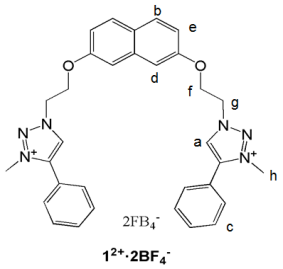
Among the most promising binding strategies to target anions that have recently attracted much attention in the literature are hydrogen bonding involving C-H donor units and anion-π interactions.[1] 1,2,3-Triazoles have rapidly gained recognition as excellent hydrogen donors for selective anion binding, a flexible triazolophane,[2] a triazole-based cyclic peptide,[3] and a preorganized and rigid triazole-based macrocyclic,[4] showing self-assembly as well as the anion binding properties of foldamers,[5,6] all demonstrate 1,2,3-triazoles participating in noncovalent interactions. Interestingly, 1,2,3-triazole-linked dendrimers also showed the ability of binding oxo anions through the 1,2,3-triazole ring localized inside the dendrimer.[7] It has been reported[8] that there are two sources that contribute to the triazole unexpected anion binding affinity. First, the electronegativities of the three nitrogen atoms combine to polarize the C−H bond. Second, the electron lone pairs on the nitrogen atoms act to establish and orient along the C−H bond a large 5 D dipole, with its positive end directed almost in line with the C^5−H bond. These combined effects make them interesting candidates for amide bond surrogates.[9-12]

Since the C(5)-H···A^- binding ability is strongly enhanced by converting the triazole unit into a triazolium cation, the latter is expected to be a still more efficient anion captor.[13,14] The chelating ability of the triazolium ligands for dianions can be easily tuned by transforming them into tridentate structures or by creating multivalent macrocycles.[15] It has been demonstrated that this kind of receptors strongly complexes oxoanions, whereas the nonmethylated analogue show a very weak interactions under similar conditions.[16,17] In this context, a number of more complex supramolecular structures containing triazolium cations and tetratriazolium cages, which exhibit strong anion binding affinities, in all cases involving hydrogen bonds, towards fluorides, chlorides and some oxoanions have been reported.[18]

Typically, anion-π interactions are termed as favourable non-covalent contacts between an electron deficient (π-acidic) aromatic system and an anion.[19] This interaction is proposed to arise from a negatively charged species having a Coulombic attraction to an area of low electron density in an electron-deficient aromatic ring. Despite the numerous solid state examples, theoretical treatments, significant interest in the fundamental nature and its potential application, surprisingly few solution phase examples recognize the anion-π interaction.[20]

Here, we describe a receptor capable of anion binding by combination of hydrogen bonding and anion-π interaction. We are interested in pursuing this goal to create receptors in which selectivity arises not from size and shape matching with a particular anionic guest, but rather from the combined intrinsic anion preference of two distinct noncovalent interactions.[21-23] In an attempt to probe the efficacy of the anion-π interaction towards hydrogen bonding interactions to bind anions in solution, the receptor molecule **1** was prepared. Designed receptor **1** focused on two triazolium cations which could be able to act as recognition motifs utilizing either hydrogen bonds or their electron-deficient aromatic rings.

The novel bidentate triazolium receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ was prepared from 2,7-bis(2-azidoethoxy)naphthalene, available in 86% yield from sodium azide and 2,7-bis(2-hydroxyethoxy)naphthalene bis(methanesulfonate)ester,[24] by a copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC)[25] with 1-ethynylbenzene. Methylation of both triazole rings with trimethyloxonium tetrafluoroborate afforded the triazolium receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ in 40% yield (see ESI).



$\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$

Scheme 1. Receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$

The anion binding properties of the bis-triazolium receptors $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ was evaluated by ^{1}H-, ^{31}P and ^{13}C-NMR experiments toward several anions ($HP_2O_7^{3-}$, $H_2PO_4^-$, SO_4^{2-}, HSO_4^-, NO_3^-, F^-, Cl^-, Br^-, I^-, AcO^-, ClO_4^-, PF_6^- and $C_6H_5CO_2^-$) as tetrabutylammonium salts in the mixture

CD_3CN/CD_3OD (9:1, v/v)

The ^{1}H-NMR spectrum of the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$, exhibits four sets of signals, the first of them is due to the O-CH_2-CH_2-triazolium which appear as a two different triplets at δ = 5.03 and δ = 4.57 ppm, respectively and the singlet of the N-CH_3 protons at δ = 4.17 ppm. The second characteristic set of signals correspond to the naphthalene protons, which appeared at δ = 7.02, 7.20 and 7.71 ppm, respectively. The phenyl protons appear as a multiplets around δ = 7.6 ppm and finally the –C*H* proton of the triazolium ring appears as a clear and sharp singlet at δ = 8.65 ppm.

Stepwise addition of the above-mentioned set of anions to a solution of the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ showed that only the addition of $HP_2O_7^{3-}$ anions induced remarkable perturbation in the ^{1}H-NMR spectrum. Thus, the addition of increasing amounts of $HP_2O_7^{3-}$ anions to a solution of $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ in CD_3CN/CD_3OD (9:1, v/v) induced the splitting of the triazolium H_a protons in two different signals, one of them was significantly downfield shifted by $\Delta\delta$ = 0.71 ppm, whereas the other signal was upfield shifted by $\Delta\delta$ = 0.12 ppm (Fig. 1a). The outer naphthalene protons H_b and H_e were upfield shifted by $\Delta\delta$ = –0.06, $\Delta\delta$ = –0.07 ppm, whereas the inner naphthalene H_d protons were downfield shifted by $\Delta\delta$ = 0.13 ppm (Fig. 1b). Finally the triplets corresponding to the O-CH_2-CH_2-triazolium moved practically in the same magnitude $\Delta\delta$ = 0.19 while the N-CH_3 signal was almost unaffected by the presence of the $HP_2O_7^{3-}$ anions (Fig. 1c).

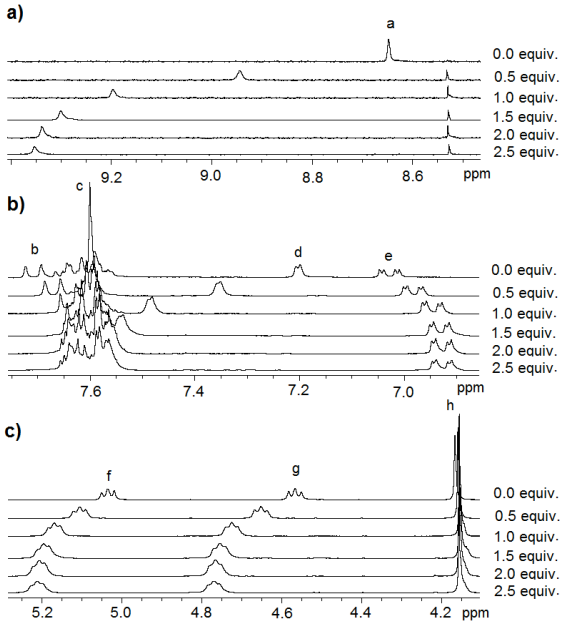


Figure 1: ^{1}H NMR spectral changes observed in $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ in CD_3CN/CD_3OD (9:1, v/v) during the addition of up to 2.5 equivalents of $HP_2O_7^{3-}$ ions.

The chemical shift of the triazolium protons H_a was monitored during addition of the $HP_2O_7^{3-}$ anion to the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ Job plot analysis of the titration data revealed a 1:1 receptor to anion binding stoichiometry (see ESI). The calculated association constant for $HP_2O_7^{3-}$ ions was found to be 3000 ± 350 M^{-1} and was obtained by fitting the titration data to a 1:1 host-guest binding model using the WinEQNMR program.[26]

The addition of 1 equiv. of $HP_2O_7^{3-}$ ions to the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ promotes significant changes in the ^{13}C NMR spectrum. The most affected carbon atom was the N-*C*H_3 which was upfield shifted by $\Delta\delta$ = –1.9 ppm, and the C-4 and C-5 carbon atoms of the triazolium ring were also upfield shifted in identical magnitude, although in less extension $\Delta\delta$ = –0.4 ppm. Whereas the methylene O-*C*H_2 ($\Delta\delta$ = +0.5 ppm), and the naphthalene carbon atoms C-1, C-8 ($\Delta\delta$ = +0.6 ppm), and the quaternary carbon atoms C-1a ($\Delta\delta$ = +0.4 ppm) and C-5a ($\Delta\delta$ = +0.4 ppm) were downfield shifted (see ESI). The remaining carbon atoms practically were unaffected by the presence of $HP_2O_7^{3-}$ anions.

^{31}P spectral changes were also studied after addition of 1 equiv. of the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ to a solution of $HP_2O_7^{3-}$ anions in CD_3CN/CD_3OD (9:1, v/v). Prototropy makes both P atoms (P_α and P_β) isochrones; they appear as a broad singlet (intermediate proton transfer rate) at –6.13 ppm. By addition of 1 equiv of the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ in the same solvent, the signal moves upfield (and becomes narrow, faster proton transfer) to –7.28 ppm ($\Delta\delta$ = –1.15 ppm). Upfield effects of about –3.0 ppm were reported for hydrogenpyrophosphate trianion with other receptors.[27]

We have calculated at the B97D/6-31+G(d) level, including the solvent effect (CH_3CN) by means of the PCM method, the geometries and energies of the neutral receptor $\mathbf{1}^{2+}$, and those of its complexes with four anions: Br^-, SO_4^{2-}, $H_2PO_4^-$ and $HP_2O_7^{3-}$. For the receptor $\mathbf{1}^{2+}\cdot\mathbf{2BF_4}^-$ we have obtained three geometries, two minima and one structure of imposed C_2 symmetry with a small negative frequency (4 cm^{-1}). To these three geometries correspond the following relative energies: a) 0.0, b) 2.1 and c) 22.3 kJ mol^{-1} (see ESI).

Then, we calculated the complexes; in two cases (sulphate, hydrogenpyrophosphate) we obtained two minima but in the cases of the bromide and dihydrogenphosphate anions only one minimum was found.

Case of the bromide. The Br^- anion interacts in one side with the H atom of the triazolium CH (hydrogen bond, HB) and on the other side with the system of the triazolium ring (anion···π bond). We will name this structure an H/π one. This seems to indicate that both kind of interaction are of similar strength. Obviously, the positive charge on the triazolium ring make the C–H more acidic and, at the same time, favours its interaction with the bromide. With regard to the minimum of lowest energy and the Br^- anion, the complex corresponds to a stabilization energy of –89.7 kJ mol^{-1}. (see ESI)

Case of the sulphate. Note the HB interaction between two naphthalene CHs and one of the O atoms of one side of the phosphate anion. The corresponding stabilization energies are a) –68.5 kJ mol^{-1} and b) –64.7 kJ mol^{-1}. Thus the H/π is more stable than the π/π one. (see ESI)

Case of the hydrogenphosphate. The structure corresponds to an H/π interaction and to a related energy of –57.3 kJ mol^{-1}. Besides two naphthalene CHs pointing towards an O atom, the OH group points toward the naphthalene ring in an almost O–H···π interaction. (see ESI)

Case of the hydrogenpyrophosphate. In this case, two

minima were located; they are represented in Fig. 2.

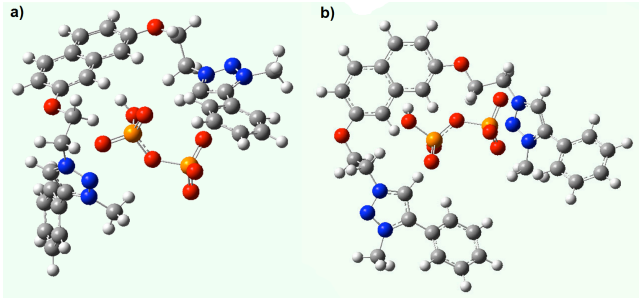


Figure 2: Structure of the $\mathbf{1}^{2+}\cdot\mathbf{HP_2O_7}^{3-}$ minima. a) Left, only one half of the anion is involved in the interactions; b) right, the whole anion is involved in the interactions.

Both structures are of the H/π class, but very different in the participation of the hydrogenpyrophosphate anion: only one half or the whole molecule. However, the interaction energies are very similar: a) –97.5 and b) –95.9 kJ mol^{-1}. (Table 1)

Table 1. Interaction energies in kJ mol^{-1}.

Anion	Minimum H/π	Minimum π/π
Br^-	–89.7	----
SO_4^{2-}	–68.5	–64.7
$H_2PO_4^{2-}$	–57.3	----
$HP_2O_7^{3-}$	–97.7/–95.9	----

According to these data, the strongest interaction (the best recognition) take place with $HP_2O_7^{3-}$; the difference between both kinds of interactions (Fig 2) is very small (1.6 kJ mol^{-1}) and beyond discussion. In all cases, the H/π interaction is either the only one or the stronger with regard to the π/π one.

In conclusion, the bis(triazolium) receptor **1** has proved to be a powerful benchmark for exploring the potential of a positive interaction between an unprecedented anion-π- and hydrogen-bonding-based molecular recognition in solution. The crucial importance of this new kind of interaction between two triazolium cations is highlighted by the fact that receptor **1** behaves as a highly selective molecular sensor for hydrogenpyrophosphate in solution. The main contribution of theoretical calculations has been: i) to provide a model for the unexpected asymmetric H/π interaction: ii) to range the interaction energies for the anions in the order $HP_2O_7^{3-} > Br^- > SO_4^{2-} > H_2PO_4^-$.

This work was supported by European Commission FP7-PEOPLE-2012-CIG and MICINN-Spain and FEDER, projects CTQ2011-27175, and CTQ2012-13129-C02-02) and the Comunidad Autónoma de Madrid (Project MADRISOLAR2, ref. S2009/PPQ-1533).

Notes and references

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† Electronic Supplementary Information (ESI) available: Synthesis. ^{1}H-^{13}C- and ^{31}P NMR Spectra, Anion Binding Studies, Geometry and energy of the systems calculated See DOI: 10.1039/b000000x

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