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COMMUNICATION

Open aryl triazole receptors: planar sheets, spheres and anion binding†‡

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The morphology of the aggregates formed from the self-assembly of aryl triazole amphiphiles is disrupted upon the binding of a bromide anion due to the conformational changes experienced by these receptors.

Biology, medicine, catalysis, or environmental sciences are disciplines in which anions play a pivotal role.[1,2] The anionic nature of many substrates engaged in natural processes prompts research directly related to these charged species like fundamental non-covalent binding studies,[3] anion-assisted asymmetric catalysis[4] or design of new receptors.[5] Most of the neutral hosts reported for anion recognition—calixpyrroles,[6] ureas[7] or polypyrroles[8]—utilize strong N–H groups to bind the anionic guest. However, receptors involving weaker neutral C–H groups are yet scarce. 1,4-Substituted 1,2,3-triazole-based macrocycles[9] and foldamers[10] elegantly exemplify the utilization of slightly polarized C–H hydrogen bonding systems to bind halide anions.[11] Many of these anion receptors are endowed with hydrophilic chains that lend them an amphiphilic character. These amphiphiles are able to self-assemble into supramolecular structures whose shape, size and function can be modulated by external factors.[12,13]

Herein, we take advantage of the conformational changes observed in triazole-based foldamers[10] upon halogen anion complexation to disrupt the morphology of the supramolecular structures formed by the self-assembly of aryl triazole amphiphiles **1** and **2** (Fig. 1). The chemical structure of the lateral aryl moiety attached to the 1,2,3-triazole conditions the morphology of the self-assembled aggregates, and flat lamellae are observed for **1** whilst compound **2** forms spheres. The bromide complexation induces conformational changes in the aryl triazole receptors breaking these supramolecular structures.

Target aryl triazole oligomers **1** and **2** have been readily prepared by utilizing a Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of azides and alkynes[14] starting from 3,5-dibromophenol and [1,1′-biphenyl]-4-amine or 1-naphthalen-amine in only five synthetic steps with 25 and 89% yields, respectively

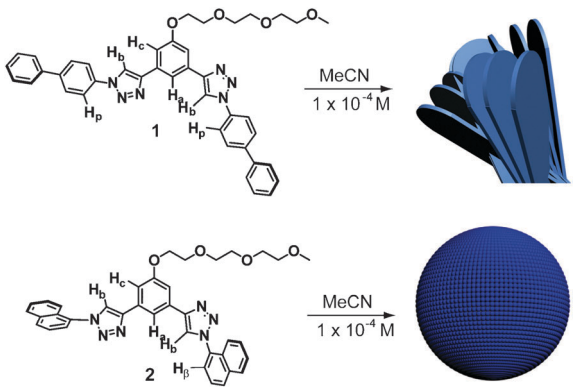

Fig. 1 Chemical structures of the aryl triazole receptors **1** and **2** and schematic illustration of the supramolecular structures formed by their self-assembly in polar acetonitrile.

(Scheme S1, ESI†). The chemical structures of compounds **1** and **2** have been confirmed by NMR and FTIR spectroscopy and MALDI-TOF spectrometry (see ESI†).

Single crystals suitable for X-ray diffraction were obtained by slow evaporation of solution of **1** in acetonitrile.§ The internal dipole of the molecules is stabilized by a zig-zag *"anti"* conformation of the 1,2,3-triazole moieties, these heteroaromatic rings being coplanar to the central alkoxybenzene (Fig. 2a and Table S1, ESI†).[10c] The planar geometry of **1** enhances the cofacial π–π stacking with lateral offset (Fig. 2b). Additional intermolecular interactions between the lateral biphenyl-triazole units with the triethylene glycol (TEG) chains pointing outwards are also responsible for the compact packing (Fig. 2c).

The self-assembly of triazoles **1** and **2** in solution and onto surfaces has been investigated by concentration-dependent ^{1}H NMR experiments of **1** in $CDCl_3$ and by scanning electron microscopy (SEM) imaging. The former studies feature slight upfield shifts for all the aromatic resonances upon increasing concentration which suggests the π–π stacking of the aromatic moieties (Fig. S1, ESI†).[15] Fitting the variation of the chemical shift corresponding to H_a (see Fig. 1 for numbering) with increasing concentration to the isodesmic or equal-*K* model sheds a low binding constant (K_a) of ~8 M^{-1}.[9a,16] The scarce solubility of these receptors in polar acetonitrile impeded the calculation of the binding constant in these conditions. However, a clear indication of the π-stacking of the reported aryl triazoles **1** and **2** in polar CD_3CN can be extracted from NOE experiments (Fig. S2 and S3, ESI†). The irradiation of the proton corresponding to the 1,2,3-triazole ring (H_b in Fig. 1) in a

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† Electronic supplementary information (ESI) available: Fig. S1–S11 and experimental section. CCDC 804817. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0cc05685e

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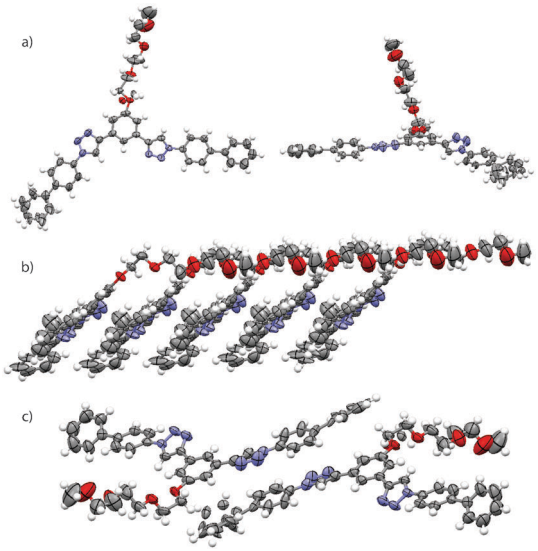

Fig. 2 X-Ray crystal structure of **1**: (a) top (left) and side (right) views; (b) cofacial π–π stacking with lateral offset; (c) intermolecular interactions between lateral biphenyl-triazole units (CCDC: 804817).†

concentrated solution of **1** in $CDCl_3$ (114 mM) results in a clear NOE effect with the two protons of the central alkoxybenzene moiety (H_a and H_c) and one of the *para* hydrogens of the biphenyl unit. These findings are diagnostic of the zig-zag *"anti"* conformation of the 1,2,3-triazoles determined by X-ray diffraction (Fig. S2, top, ESI†). However, if H_b is irradiated in a more diluted sample (1 mM) in $CDCl_3$, the NOE effects are only visible for H_c and for the protons in the biphenyl unit, the interaction with H_a being very weak (Fig. S2, middle, ESI†). At this concentration, compound **1** is molecularly dissolved and the arm with H_b pointing toward H_a could be slightly rotated thus cancelling the NOE effect between these two protons. The aggregation of receptor **1** in CD_3CN is clearly observed in the NOE experiment utilizing a 1 mM solution. In this experiment, irradiating H_b results again in a NOE effect with H_a, H_c and the biphenyl moiety (Fig. S2, bottom, ESI†). A similar behaviour has been observed in the NOE experiments of receptor **2**. Once again, for a concentrated solution of **2** in $CDCl_3$ (100 mM) or diluted solution (1 mM) in CD_3CN, NOE effects are observed between protons H_b and H_a, H_c and the naphthalene moiety, diagnostic of the aggregation (Fig. S3, ESI†).

The supramolecular organization of receptor **1** into flat lamellae has been visualized by SEM. SEM images of a solution of this receptor in acetonitrile (1×10^{-4} M) on a glass substrate exhibit stratified bidimensional lamellae that form leaf-like structures (Fig. 3a and Fig. S4, ESI†).

The lack of planarity of the different aromatic fragments in compound **2** impedes its self-assembly into flat lamellae, and big spheres with diameters of ~1.8 μm are observed by SEM imaging upon deposition of **2** (1×10^{-4} M, acetonitrile) onto a glass substrate (Fig. 3b and Fig. S5, ESI†). Although the mechanism followed by compound **2** to self-associate into spheres is unclear, we postulate that the formation of dimers by CH–π H-bonds involving the lateral naphthalene units could be a key step.[17] The π–π stacking of the resulting dimers finally would yield the spherical objects (Fig. S6, ESI†).

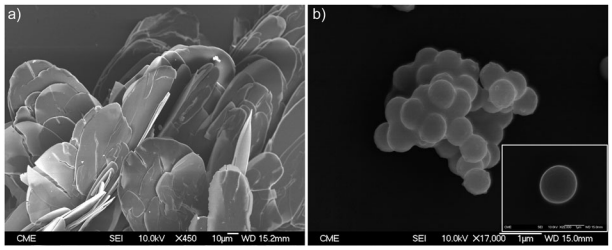

Fig. 3 SEM images (298 K, 1×10^{-4} M in acetonitrile, glass substrate) of flat lamellae formed from **1** (a) and spheres formed from **2** (b). The scale bar in the inset of (b) is 1 μm.

The ability of receptors **1** and **2** to bind anions has preliminary been tested by the complexation of bromide and studied by ^{1}H NMR titration experiments (Fig. S7 and S8, ESI†). To eliminate the self-aggregation observed for aryl-triazoles **1** and **2**, all the titration experiments have been performed at 1 mM in $CDCl_3$. The addition of tetrabutylammonium bromide (TBABr) to **1** deshields the resonances of the protons corresponding to the 1,2,3-triazoles and the central aromatic ring (H_a and H_b) and also the proton *para* of the lateral biphenyl units, the resonance of proton H_c being unaffected. These variations imply that five C–H···Br^- H-bonds participate in the formation of the complex. The changes in the chemical shift of H_a and H_b upon addition of TBABr fit well with a 1 : 1 binding isotherm [18] affording binding constants (K_a) of ~15 M^{-1} (Fig. S7, ESI†). These values for K_a are smaller to that previously reported for referable 1,2,3-triazole receptors and can be justified by considering the lack of preorganization.[9,10c]

The spectral changes observed in the titration studies clearly suggest the conformational switch of one of the aryl-triazole fragments to render a "*syn*" conformation with protons H_a, H_b, and H_p pointing to the inner cavity of the molecule and H-bonded with the bromide anion (Fig. 4). The conformational changes experienced by **1** upon bromide binding are fairly detected by NOE experiments. Whilst in free **1**, the irradiation of the resonance corresponding to H_b ($\delta \approx 8.35$) affects H_c and H_p, and H_a is only slightly affected, the addition of TBABr changes the conformation of the receptor and a clear connectivity of H_b with H_a is observed (Fig. 4).

The titration of 1,2,3-triazole **2** with increasing amount of TBABr shows negligible changes in the chemical shift of any of the protons forming the inner cavity of the receptor (H_a, H_b, and H_β) (Fig. S8, ESI†) and would imply that compound **2** is not able to complex the bromide anion. The calculated geometry of **2** considering a zig-zag "*anti*" conformation for the 1,2,3-triazole rings demonstrates that the naphthyl units would be out of the plane formed by the two 1,2,3-triazoles and the central alkoxybenzene unit (Fig. S9, ESI†). Taking into account this geometry, only three weak C–H···Br^- H-bonds, involving H_a and H_b, would participate in the complexation of the bromide anion being insufficient to form stable complexes. However, the complexation of the bromide anion by receptor **2** has been detected by NOE experiments. The irradiation of the triazole proton H_b of **2** in $CDCl_3$ (1 mM) demonstrates the spatial connectivity of H_b and H_c (at $\delta \approx 7.63$) and the lack of interaction with the central proton of the alkoxybenzene (H_a) (Fig. S10, top, ESI†). The addition of TBABr changes the NOE spectrum

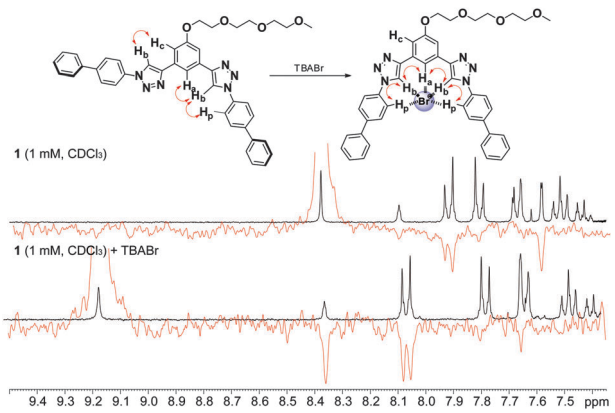

Fig. 4 Partial ^{1}H NMR spectra (300 MHz, 298 K) (black) and NOE experiments (red) of aryl triazole **1** in $CDCl_3$ at 1 mM without (top) and with TBABr (bottom). In the upper part of the spectra, the NOE contacts are represented by curved arrows.

and the interaction between protons H_b and H_a is clearly visible. This experiment also demonstrates the connectivity of H_b with H_β (Fig. S10, bottom, ESI†) which indicates the slight planarization of the whole molecule to generate an inner cavity in which five C–H H-bonds complex the bromide anion (Fig. S9, ESI†).

The anion binding, even if weak, and the subsequent conformational modifications experienced by receptors **1** and **2** trigger the change in the morphology of the supramolecular structures formed upon aggregation of the resulting complexes. The *syn* conformation adopted by the 1,2,3-triazole moieties of both **1** and **2** upon bromide complexation in order to maximize the number of H-bonds between the neutral C–H groups and the bromide anion and the presence of the tetrabutyl counterion impede the formation of organized supramolecular structures.

In summary, we report on the synthesis, self-assembly and bromide anion binding of two different amphiphilic aryl triazole receptors. The geometry of compound **1**—decorated with lateral biphenyl moieties—is highly planar with a *syn* conformation of the 1,2,3-triazole rings as demonstrated by the X-ray data and self-assembles into flat lamellae. In contrast, compound **2** possesses lateral naphthalene units responsible for a more distorted geometry that finally results in the formation of spherical objects upon self-assembly. The addition of a bromide anion to these two receptors induces the formation of slightly polarized C–H hydrogen bonds between the aromatic moieties and the anion. The formation of this H-bonding array implies a U-like conformation of the receptors. The conformational changes produced by the complexation of bromide disrupt the apparition of organized supramolecular structures.

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Notes and references

§ Crystal data for **1**: $C_{41}H_{38}N_6O_4$, M = 678.77, monoclinic, a = 33.436(4) Å, b = 5.8453(6) Å, c = 17.8776(19) Å, α = 90.00°, β = 96.269(2)°, γ = 90.00°, V = 3473.2(6) Å^3, T = 293(2) K, space group $P2(1)/c$, Z = 4, 25 183 reflections measured, 6101 independent reflections (R_{int} = 0.1344). The final R_1 values were 0.0906 ($I > 2\sigma(I)$). The final w$R(F^2)$ values were 0.2322 ($I > 2\sigma(I)$). The final R_1 values were 0.2415 (all data). The final w$R(F^2)$ values were 0.3279 (all data).

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