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Neutral bis(benzimidazole) Λ-shaped anion receptor

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ABSTRACT

A neutral receptor, integrating a series of –N(H) and –C(H) donor groups organized in a Λ-shape motif was designed and prepared. This compound can form stable 1:1 complexes in acetonitrile solution with halides (F^-, Cl^-, Br^-, and I^-) and nitrate (NO_3^-) anions. The main binding site in the receptor is on the cleft and recognition occurs through a series of co-operative hydrogen bonding interactions including intramolecular hydrogen bonds which stabilizes the co-planar conformation of the host–guest complex. For halides, complex stability is determined by anion basicity, but for anions having other geometries, size and shape complementarity play a major role.

Introduction

The detection and removal of certain anions, such as fluoride and nitrate, are issues of relevance in public health and environmental quality. For this purpose, it is important to properly design and synthesize versatile receptors. In synthetic anion receptor chemistry, the molecular design of the host must take into consideration: (i) basicity of the anionic guests, (ii) nature of the non-covalent interactions involved, (iii) solvent, and (iv) host–guest geometric complementarity.[1] According to their electrostatic charge, two different kinds of anion receptors have been developed: cationic and neutral. For the latter, the most common motifs incorporated are: ureas,[2] thioureas,[3] amides,[4] squaramides,[5] pyrroles,[6] indoles,[7]and lately, –C(H) hydrogen bond donors.[8]

Particularly, imidazole- and benzimidazole-based receptors interact with anions predominantly through $-N(H)\cdots X^-$ hydrogen bonding. Baitalik[9] and Ye[10] reported that ruthenium(II) complexes of 4,5-bis(benzimidazol-2-yl)imidazole and 2,2′-biimidazole form hydrogen bonded adducts with a variety of anions in acetonitrile with association constants ranging from 10^4 to 10^6 M^{-1}; especially, the interaction with fluoride and acetate develops intense colors, naked eye visible, due to a stepwise deprotonation of the –N(H) fragments. On the other hand, Gale and co-workers[11] have shown that tautomeric switching in benzimidazole-based receptors in DMSO-aqueous solution can modulate their affinity for certain anionic guests via hydrogen bond interactions, making them selective for a specific anion; however, for the monoatomic anionic guests only weak binding is observed.

As part of our ongoing research on the self-assembly of supramolecular complexes based on benzimidazolium derivatives,[12] we have designed and synthesized a neutral 1,3-bis(benzimidazole)benzene anion receptor, **BBB**. The 1,3-substitution pattern would provide two strong –N(H) hydrogen bonds donors and an aryl –C(H) bond, in a Λ-shaped arrangement, allowing the interaction of this receptor with diverse anions, as it has previously been observed for similar-shaped complexes.[4c,13]

The expected most-stable molecular arrangement of **BBB** would be a non-planar structure, with the central aromatic ring on a different plane respect to the benzimidazole rings. In the presence of anions, a co-planar conformation is anticipated containing three hydrogen bond donors converging into a cleft and two intramolecular hydrogen bonds assisting the complexation (Scheme 1). This host–guest geometrical arrangement, which can establish the maximum number of non-covalent interactions and displays a suitable complementary, is likely to be the most stable.

In this Letter we report the synthesis and characterization of a neutral bis(benzimidazole)benzene receptor with –N(H) and –C(H) donor motifs and its association in acetonitrile with diverse anions such as halides, nitrate, and perchlorate.

Results and discussion

Compound 1,3-bis(1*H*-benzo[*d*]imidazol-2-yl)benzene, **BBB**, was synthesized by a condensation reaction between isophthalic acid and two equivalents of 1,2-diaminobenzene under high temperature and acidic conditions (Scheme 2). This compound was isolated in a 57% yield and is slightly soluble in acetonitrile and soluble in dimethylsulfoxide; it was fully characterized by ^{1}H and ^{13}C NMR spectroscopy as well as HR-MS (ESI-TOF).

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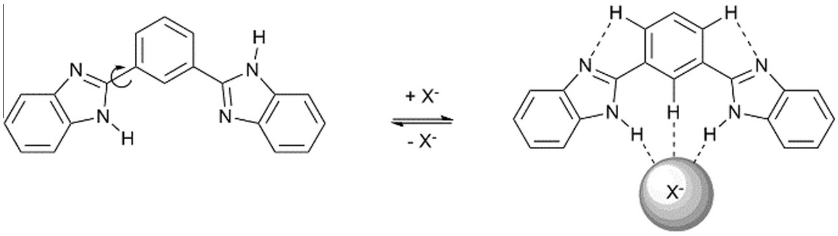
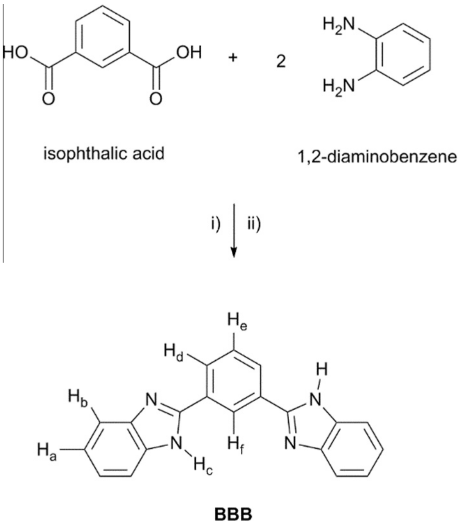


Scheme 1. Binding motif for a hypothetical anion (X^-) in the cleft of a neutral receptor **BBB**.



Scheme 2. Synthetic procedure for the preparation of receptor **BBB** and labeling scheme. Reagents and conditions: (i) polyphosphoric acid, 190 °C, 24 h; (ii) NaOH (aq), pH = 7.

The ^1H NMR spectrum of compound **BBB** in DMSO-d_6 showed the expected resonances for the proposed molecular structure: (i) a single high frequency signal (13.1 ppm) attributed to the protons –N(H) of the imidazole rings, (ii) an AB_2C pattern for the aromatic protons of the 1,3-disubstituted benzene, and (iii) an AA′BB′ pattern for the aromatic protons of the benzimidazole rings. In addition, the ^{13}C NMR spectrum displayed the expected eleven signals in the aromatic region. The identity of all signals was confirmed by NMR 2D experiments (see Supplementary data). Experimental high-resolution mass spectra (ESI-TOF) showed a peak at $m/z = 311.1294$, which corresponds to the expected molecular ion, displaying an isotopic pattern consistent with the proposed formula and with a relative error in the molecular weight of 1 ppm (see Supplementary data).

The neutral **BBB** bis(benzimidazole)benzene compound should act as an anion receptor by combining two strong –N(H) donor groups with a weaker aryl –C(H) donor motif. The orientation of the three hydrogen bonds in a convergent form should optimize the interactions with specific anions. The selected anions have diverse shapes and basicity, and include (i) halides, with a spherical shape, (ii) trigonal planar nitrate, and (iii) perchlorate as a tetrahedral oxoanion.

We performed a series of ^1H NMR titrations in acetonitrile between neutral receptor **BBB** with tetrabutylammonium (TBA) salts of several halides (F^-, Cl^-, Br^-, and I^-). Experimental results of the interaction with fluoride will be discussed in the following section due to its particular behavior. The consecutive addition of a concentrated acetonitrile solution, 0.1 M, of TBA halide salts to a 2×10^{-3} M solution of neutral receptor **BBB** in acetonitrile-d_3 led to gradual changes in the chemical shifts and widths of the receptor proton resonances (Fig. 1).

Upon saturation of the corresponding halide (Cl^-, Br^-, and I^-), protons H_f and H_d of receptor as well as the –N(H_c) protons, are shifted toward higher frequencies, characteristic of hydrogen bonding interactions: [**BBB**·Cl^-] (ppm) H_f $\Delta\delta = +0.95$, H_d $\Delta\delta = +0.16$; [**BBB**·Br^-] (ppm): H_f $\Delta\delta = +0.83$, H_d $\Delta\delta = +0.17$; [**BBB**·I^-] (ppm): H_f $\Delta\delta = +0.40$, H_d $\Delta\delta = +0.16$. As a representative example, Figure 2 shows a stacked plot of the titration of **BBB** with TBABr.

There is a direct correlation between the maximum chemical shift of proton H_f and the halide basicity; it is known that halides show a similar trend in their basicity in acetonitrile with respect to their values in aqueous solutions.[14] This behavior is indicative of a direct interaction between this proton and the anion. Furthermore, proton H_d preserves the same chemical shift regardless of the halide used in the titration experiments; this result is probably due to an intramolecular hydrogen bond between proton H_d and the lone pair of the benzimidazole nitrogen atoms. This particular interaction would be a consequence of a co-planar arrangement of the aromatic rings in the receptor, induced by the presence of the anion inside the cleft.

In order to support the proposed host–guest geometrical arrangement, a series of DFT calculations were performed using the Spartan ’08 software package[15] (see Supplementary data). Equilibrium geometries for neutral receptor **BBB** and the 1:1 complex with chloride [**BBB**·Cl^-] are shown in Figure 3. Geometrical optimization analysis for **BBB** renders a semi-planar molecular arrangement with both benzimidazole rings in an *anti*-conformation (the four dihedral angles concerning the central aromatic rings and the two benzimidazole substituents span from 4° to 6°), whereas for complex [**BBB**·Cl^-] the anion occupies the cleft formed by two –N(H) (3.26 Å; 178.6°) and one aryl –C(H) (3.49 Å; 178.6°) hydrogen bonds; with the rings in a co-planar conformation

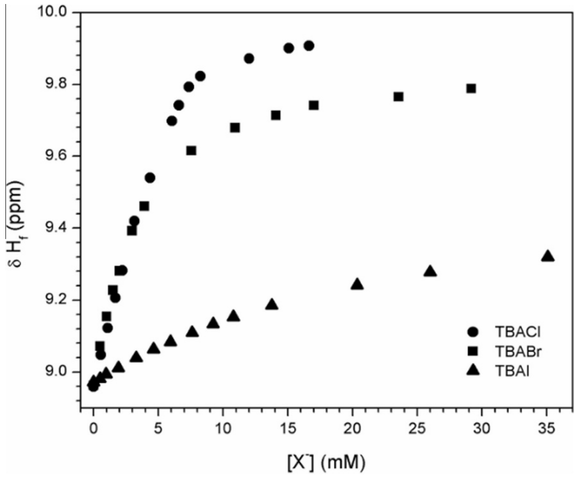


Figure 1. Change in chemical shift of proton H_f for the ^1H NMR titration of neutral compound BBB (2×10^{-3} M) with the stepwise addition of tetrabutylammonium salts (0.1 M) of chloride (●), bromide (■) and iodide (▲) in an acetonitrile-d_3 solution.