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Anion sensors based on β,β′-disubstituted porphyrin derivatives

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Abstract—The synthesis of a disulfonamide appended porphyrin receptor (**1**) for anionic guests is presented. The distinct attribute of the receptor, compared to other porphyrin based receptors, centers on the attachment of the anion binding site to the porphyrin chromophore's β-positions through a polycyclic conjugated linkage. UV–vis and ^{1}H NMR spectroscopy has been utilized to detect the binding of a variety of anions such as the halides, dihydrogen phosphate, hydrogen sulfate, and acetate. From these spectroscopic investigations, the strength of anion binding has been determined.

There is current interest in the design of sensors for anionic and zwitterionic species. Considering their rich spectroscopic and electrochemical properties, porphyrin derivatives are ideally suited for sensor design.[1] Porphyrin based receptors for anions have been constructed through the derivatization of the porphyrin *meso*-positions with appropriately positioned binding substituents that create a binding pocket for anionic species.[2] Functionalization of porphyrins at the β-position has also yielded several novel structures and synthetic receptors;[3] although this strategy has rarely been utilized for anion receptor design.[4] A current trend in anion sensor design has been to append the host with a chromophore or fluorophore either covalently[5] or non-covalently;[6] this strategy has yielded impressive optical and fluorescent anion sensors. We report here an approach to the use of the porphyrin chromophore for anion sensing purposes through the synthesis and evaluation of a β,β′-disulfonamidequinoxaline appended porphyrin derivative (**1**, Fig. 1). The novelty of the receptor arises from the attachment of the anion recognition element to the porphyrin chromophore through a rigid conjugated spacer.

The free-base receptor **1** was synthesized by the condensation of the *ortho*-diamine functionalized disulfonamide **2** with tetraphenylporphyrin-2,3-dione (**3**) in deoxygenated toluene at 90°C (Scheme 1). Receptor **1** was obtained in 72% yield as a purple solid after purification by silica-gel column chromatography. Compound **2** was available in quantitative yield from the known dinitrodisulfonamide precursor[7] by hydrogenation with Pd/C in ethanol. Tetraphenylporphyrin-2,3-dione (**3**) is a known compound[8] that is highly versatile in the synthesis of porphyrin arrays. We also report here a simple two-step synthesis of **3** (Scheme 1) using a protocol that we established for the synthesis of tetraphenylporphyrin-2,3,12,13-tetraone[9] from 2,3,

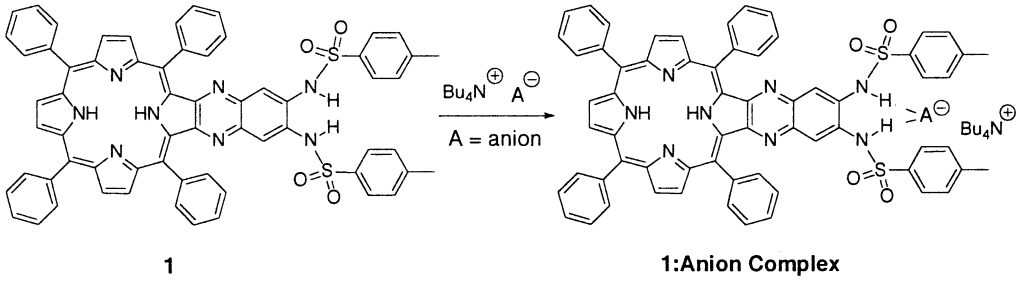

Figure 1. Receptor **1** and its anion complex.

Keywords: porphyrin; anion recognition; sensor; host–guest chemistry.

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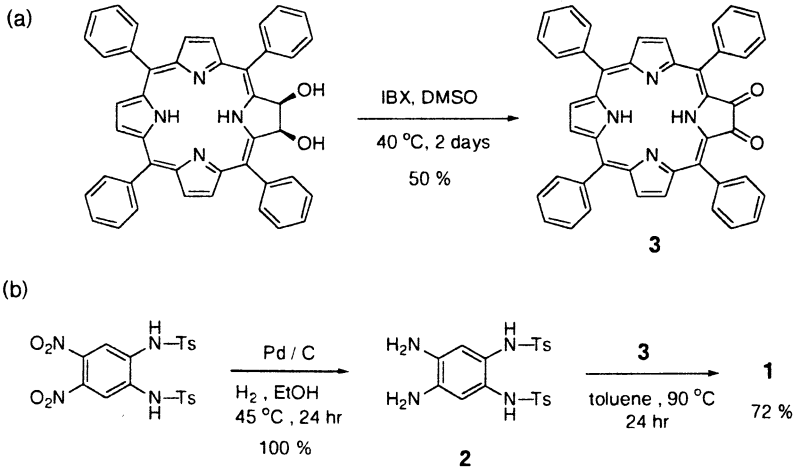
12,13-tetrahydroxy tetraphenylporphyrin. We obtained the porphyrin-α-dione **3** in 50% yield (25% overall from tetraphenylporphyrin, not optimized) by oxidation of the diol precursor[10] using IBX in DMSO.[11]

The association of **1** with anion guests (as their tetrabutylammonium salts) in dichloromethane was studied using UV–vis spectroscopy. Anion binding was detected by the perturbation of the porphyrin Soret and Q-bands. The Soret band of **1** at 422 nm was red shifted 12–16 nm upon the addition of the anions and isosbestic points were observed in the spectra in each titration. Fig. 2 illustrates the UV–vis spectra obtained from the addition of a CH_2Cl_2 solution of tetrabutylammonium fluoride to receptor **1** in CH_2Cl_2. Similar spectra were observed for the titration of **1** with each anion. Association constants of the receptor:anion complex were calculated using non-linear least squares fit[12] of the binding curves (Fig. 2 inset for example) to a 1:1 or 1:2 binding model[13] and are reported in Table 1. For Cl^-, HSO_4^-, Br^-, and I^-, non-linear regression analysis of the binding curves cleanly fit a 1:1 binding model. The binding curves for F^-, $H_2PO_4^-$ and $CH_3CO_2^-$ were fit to both a 1:1 and a 1:2 binding



Scheme 1. (a) The synthesis of tetraphenylporphyrin-2,3-dione. (b) The synthesis of receptor **1**.

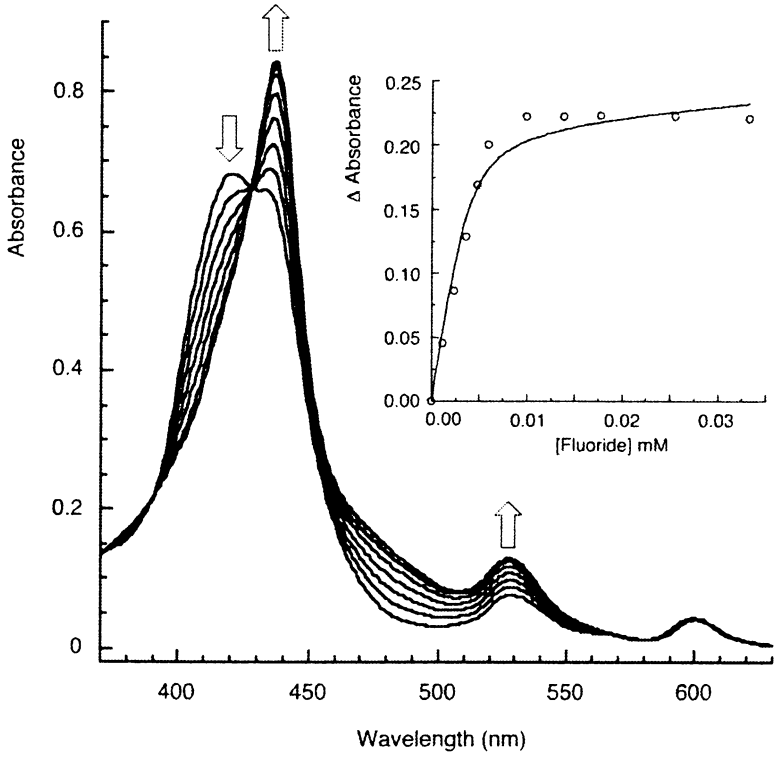


Figure 2. The UV–vis titration spectra of receptor **1** with tetrabutylammonium fluoride (CH_2Cl_2, 295 K). The λ_{max} of **1** at 422 nm shifted to 438 nm upon complexation. The inset represents the change in absorbance of **1** at 438 nm with varying molar equivalents of fluoride. [**1**] = 3.8×10^{-6} M, [Bu_4NF] = 1.1×10^{-6} M–3.4×10^{-5} M.

Table 1. Association constants (M^{-1}) of anions with porphyrin receptor **1**[a]

Anion	K_{11} (M^{-1})	K_{12} (M^{-1})
Fluoride	255000	1700
Dihydrogenphosphate	70000	600
Acetate	30000	260
Chloride	4400	–
Hydrogensulfate	1900	–
Bromide	960	–
Iodide	470	–

[a] Determined by UV–vis in CH_2Cl_2 at 295 K. [**1**] = 3.8×10^{-6} M, anion guest concentration range: 1.1×10^{-6} M–2.4×10^{-2} M. Error for $CH_3CO_2^-$, Cl^-, HSO_4^-, Br^- and I^-<10%. Error for F^- and $H_2PO_4^-$ = 30%. Data was obtained from three independent experiments. Anions used in this study were in the form of their tetrabutylammonium salts, which were dried at 70°C under high vacuum for 24 h prior to use.

model. Although the curve fits for these three anions are modest at best, the 1:2 binding model offered a small improvement in the analysis, which suggests a second anion weakly binds. The selectivity trend observed ($F^->H_2PO_4^->CH_3CO_2^->Cl^->HSO_4^->Br^->I^-$) for the anion recognition properties of receptor **1** follows the expected trend considering that the disulfonamide arrangement does not match the shape of any particular anion nor does it provide a discrete cavity within which binding can take place. The selectivity trend essentially parallels the basicity of the anions. The main binding interaction consists of hydrogen bond interactions between the acidic sulfonamide N–H hydrogens and the anion. The sulfonamide moiety has been utilized in other host systems for the recognition of anionic species;[14] the binding constants observed in this study are approximately the same as those observed in the disulfonamide receptor reported by Crabtree (benzene-1,3-disulfonic acid bis-phenylamide) where the anions were reported to bind in a cooperative manner with both sulfonamide N–H's. Receptor **1** binds fluoride more strongly than the disulfonamide receptor reported by Crabtree, which may reflect a better fit of fluoride within the cavity of **1**. Receptor **1** is selective for fluoride ($K_{11} = 2.55\times10^5$), which is significant considering the interest in developing sensors that target this biologically relevant anion.

The recognition properties of **1** were also investigated using ^{1}H NMR spectroscopy for fluoride and chloride binding (Fig. 3). Upfield proton shifts were observed in the β-pyrrole signals, one of the tosyl aryl doublets (the other tosyl aryl doublet is not resolved), the pyrazino aryl proton signal and the tosyl methyl signal (Fig. 3). These results are consistent with an increase in electron density in the receptor due to **1** acting as a Lewis acid in its interaction with the anionic guest. We were not able to follow the sulfonamide N–H signal due to broadening of this signal. The *meso*-phenyl hydrogen signals were essentially unchanged during the titration. Considering the small chemical shift changes observed (0.1–0.2 ppm), we were not able to accurately determine binding constants from the NMR data. The NMR data does, however, indicate the **1** is more selective for fluoride than chloride, which supports the UV–vis results. As Fig. 3 shows, the titration of **1** with tetrabutylammonium fluoride is essentially complete upon the addition of 3–4 equivalents of fluoride unlike that of chloride addition.

In summary, we have synthesized a new type of porphyrin-based receptor for anion sensing purposes that is derived from β-substitution of a porphyrin scaffold rather than the more common approach of *meso* functionalization. In this particular case, the porphyrin serves as the chromophore for anion binding detection. We are currently tailoring these types of receptors to be specific for the anion of choice. We are also working to elaborate these types of molecules at the *meso* position and examining the incorporation of a metal center for the creation of ditopic and tritopic receptors. We will report on these efforts in due course.

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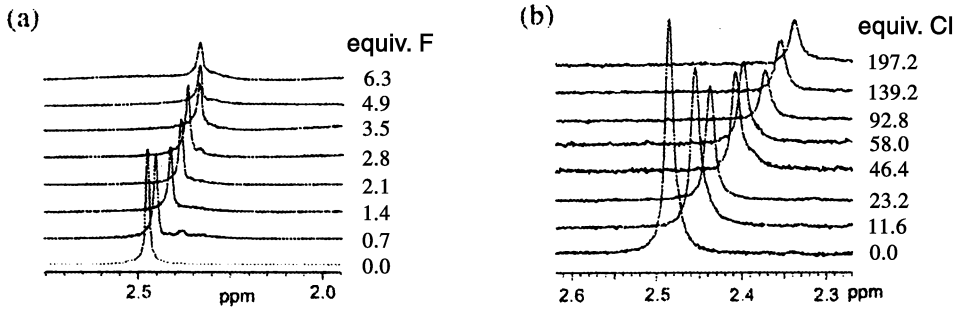

Figure 3. Partial ^{1}H NMR spectrum for the titration study of **1** with (a) tetrabutylammonium fluoride and (b) tetrabutylammonium chloride in CD_2Cl_2. The spectra show the shift of the tosyl methyl hydrogens. [**1**] = 3.6×10^{-3} M.

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