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Synthesis of Urea Picket Porphyrins and Their Use in the Elucidation of the Role Buried Solvent Plays in the Selectivity and Stoichiometry of Anion Binding Receptors

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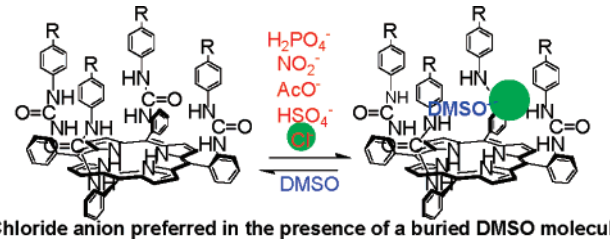

Chloride anion preferred in the presence of a buried DMSO molecule.

The synthesis of α,α-5,10-diurea and α,α,α-5,10,15-triurea picket porphyrins are detailed in this report. In previous reports, these porphyrins, along with α,α,α,α-5,10,15,20-tetraurea picket porphyrin, were used to demonstrate the important role one buried solvent molecule plays in the selectivity and stoichiometry of binding inorganic anions. Building on prior work, this report discusses the results of acetate anion binding studies between tetra- and diurea picket porphyrins (the latter does not contain a buried solvent molecule in the anion−receptor complex), compares differences in thermodynamic data obtained from van't Hoff plots of a porphyrin anion receptor able to utilize buried solvent in its binding motif with one that does not, and compares the crystal structure of a tetraurea porphyrin **1**−chloride anion complex that contains buried solvent with new X-ray crystal structures of tetraurea porphyrin **1**−dichloride or bisdihydrogenphosphate anion complexes that contain no buried solvent. Data from our previous work, and the work described herein, demonstrates that one buried solvent molecule provides stability to the receptor−anion complex that is similar in energy to a moderately strong hydrogen bond.

Introduction

By and large, it is accepted by the biological community that buried water plays an important role in biopolymer stability.[1−13] Additionally, it has been suggested that buried water may play a role in biopolymer−ligand binding interactions, such as in the selective binding of a drug to its biological target.[14,15] There is speculation in this acceptance, for a quantitative experimental

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description of water molecules in a biopolymer interface is a formidable task. Spectroscopic studies in solution often have difficulty distinguishing bulk from buried water, or the lifetime of a buried water molecule may not allow for spectroscopic experiments. This experimental limitation has led to several computational studies of biopolymers using crystal structures combined with computational models in an attempt to describe water at the ligand−biopolymer interface.[14,15a] Of course, a resolution of 2.0 Å or less is needed for crystallographic structures to permit reliable discrimination of water molecules, and this limits the use of protein crystal structures to just those few that are of high enough resolution.[15] In point of fact, much of the belief in the importance of buried water's role in biopolymer structure and function is based on in silico studies. Interestingly, while there are several recent examples of X-ray crystal structures of anion−receptor complexes that contain a buried water that is bound to both receptor and anion,[16] the buried water in these complexes is described as only structural, filling in space where there is a mismatched receptor−anion pocket.

Unfortunately, there is a paucity of experimental thermodynamic data based on straightforward model studies that is available with regard to the effect buried water (or buried solvent in general) has on the selectivity and affinity of receptors for ligand binding. Consequently, there are few hard and fast rules that explain how local environments and shape within receptors determine which functional groups will be associated with a strongly preferred water site as opposed to one barely distinguishable from bulk solvent.[14] Our group's interest in the design of recognition elements for hydrated anionic phospholipids in vivo has led us into an ongoing study examining the effects on anion complexation when a ubiquitous solvent or water molecule is incorporated into an anion−receptor binding motif. Our initial studies, detailed in a recent report, vividly demonstrate the effect of a buried organic solvent molecule that was incorporated within urea picket porphyrin anion receptors.[17] Essentially, the receptor-bound DMSO molecule became an additional anion recognition unit within the receptor pocket (Figure 1). We have termed this type of receptor−solvent−ligand structure an "ordered solvent shell" about the anion. Specifically in the case of the porphyrin receptors, *one* buried solvent molecule acted as a determinant for the affinity, selectivity, and stoichiometry of anion binding in a receptor that utilized neutral hydrogen bonding as recognition units. Data from our previous work, and the work described herein, demonstrates that the buried solvent molecule provides stability to the receptor−anion complex that

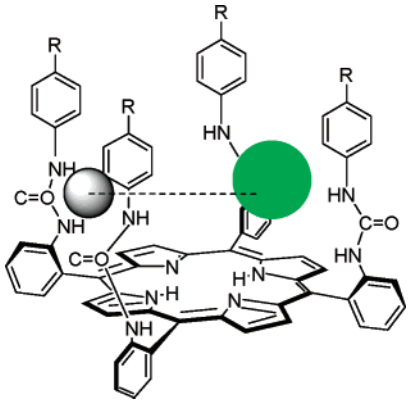
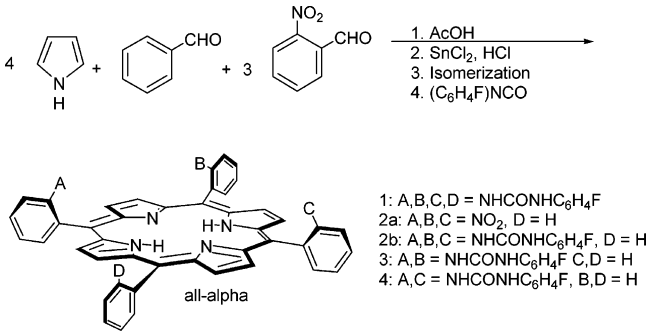


FIGURE 1. Schematic of porphyrin **1** complexed to chloride anion and bound DMSO molecule. Green ball represents bound chloride anion, smaller gray ball represents bound DMSO molecule whose partially positive-charged sulfur is in van der Waals contact with the anion.

SCHEME 1. Adler Synthesis of Picket Porphyrins



is similar in energy to a moderately strong hydrogen bond. Indeed, more stability is added to our receptor−ligand complex by the one buried solvent molecule than the extra stability afforded to several reported receptors that bind ion pairs.[18]

In this article, we provide the details for the synthesis of the di- and triurea picket porphyrin receptors utilized in the above report. We present corroborating evidence on the important role buried solvent plays in inorganic anion binding with a comparison of acetate anion binding studies between tetra- and diurea picket porphyrins (the latter does not contain a buried solvent molecule in the anion−receptor complex) and a comparison of thermodynamic data obtained from van't Hoff plots of tetra- and diurea picket porphyrins. Finally, we compare the crystal structure of a porphyrin−anion complex that contains buried solvent with two new X-ray crystal structures of porphyrin−dianion complexes that contain no buried solvent.

Results and Discussion

Porphyrin Receptor Synthesis. The structure of the picket urea porphyrins and their synthetic schemes are shown in Schemes 1−3. The triurea picket porphyrin **2b** was prepared in the same manner as that for our reported tetraurea picket porphyrins[19] (Scheme 1). Thus, the Adler[20] method was used to prepare the trinitro porphyrin **2a**. The nitro groups were reduced to amines followed by the addition of the 4-fluorophenylisocyanate to furnish the triurea picket porphyrin **2b**. Overall

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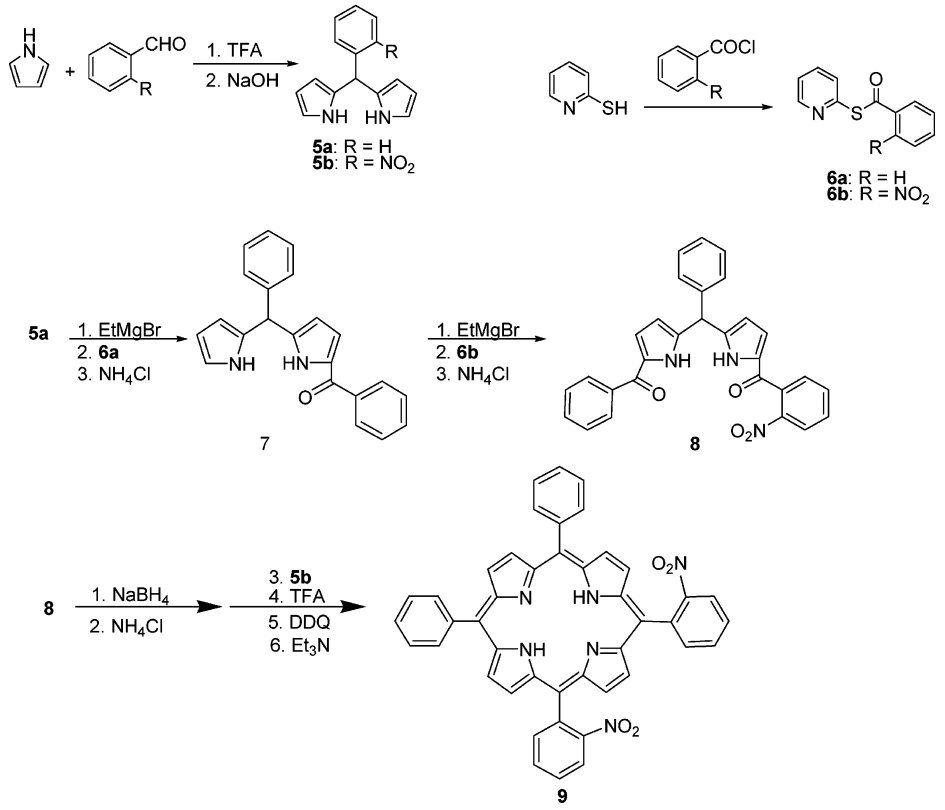
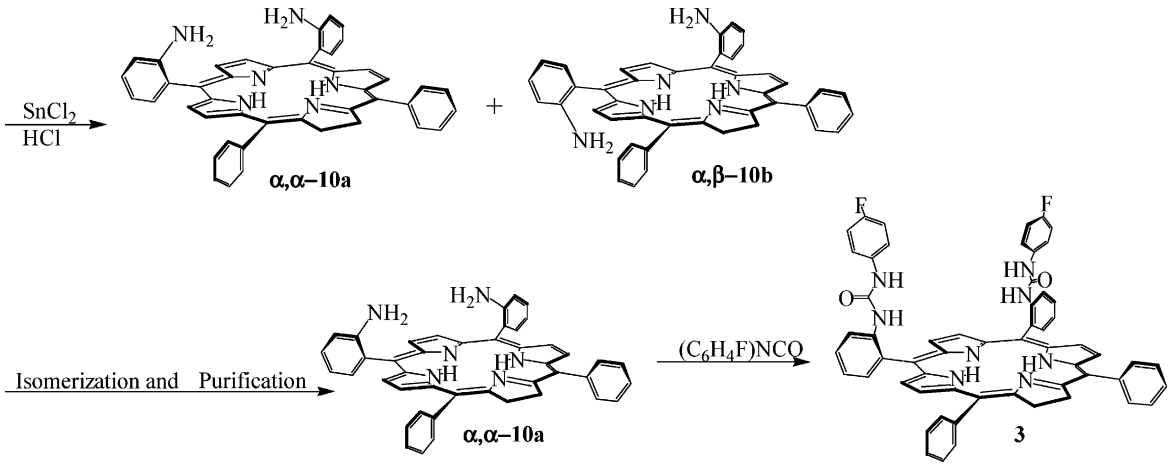
SCHEME 2. Asymmetric Synthesis of Porphyrin Macrocycle



SCHEME 3. Synthesis of Diurea Picket Porphyrin 3



yields of the triurea picket porphyrin usually ranged between 2 and 3% after extensive purification at the aminoporphyrin stage to remove di- and tetraaminoporphyrin byproducts and isomerization of the triamino atropisomers to furnish the all-α isomer.

The same approach to prepare the 5,10-diurea picket porphyrin **3** proved problematic because of the difficulty in separation of the two atropisomers of 5,10-diurea picket porphyrins **3** from the two atropisomers of 5,15-diurea picket porphyrins **4**. To avoid the formation of the trans-isomer **4** and the need for extensive purification protocols, porphyrin **3** was prepared in a step-by-step method to directly furnish the asymmetric macrocyclic ring[21] (Schemes 2 and 3).

The condensation reaction between pyrrole and benzaldehyde or 2-nitrobenzaldehyde furnished dipyrromethanes **5a** or **5b**, respectively (Scheme 2). Reaction of dipyrromethane **5a** with ethyl magnesium bromide to form the dipyrromethane anion was followed by the addition of thioester **6a** to furnish monoacylated **7** in 72% yield. In the same manner, reaction of dipyrromethane **7** with ethyl magnesium bromide followed by thioester **6b** furnished diacylated **8** in 30% yield. The latter reaction was very sensitive to the equivalents of the Grignard reagent used. More than 2.5 equiv of Grignard to dipyrromethane led to lower yields because of the destruction of the

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TABLE 1. Association Constants[a] (M^{-1}) for Porphyrins 1 and 3 in DMSO (Errors Range from 5 to 15%)

	Cl^-	$H_2PO_4^-$	AcO^-
1	$>10^5$	1.4×10^3	1.4×10^2
3	2.7×10^2	1.5×10^4	7.7×10^4

[a] Each *K* was determined from an average of three titrations and an average of several different proton shifts.

product (we postulated that the magnesium would coordinate to the nitro groups and would allow the anionic ethyl group to be placed where it could readily react with the carbonyl functional group). Less than 2.5 equiv of Grignard to dipyrromethane led to lower yields of **8** presumably because of less formation of the acylated dipyrromethane anion (more starting material was recovered).

Diacyl **8** was reduced to the diol with excess $NaBH_4$ and without purification was reacted with dipyrromethane **5b** in TFA. The porphyrinogen formed in the 2 + 2 condensation was oxidized with DDQ to furnish the 5,10-bis(2-nitrophenyl)-porphyrin **9** typically in 18−24% yields. The nitro groups were reduced to amines using $SnCl_2$ in HCl followed by isomerization of the atropisomer mixture of **10a** and **10b** producing a majority of the all-α **10a** (Scheme 3). 4-Fluorophenylisocyanate was then reacted with the purified all-α atropisomer to furnish the 5,10-diurea picket porphyrin **3** in 20−25% yield over the three steps. Purification of the diurea porphyrin formed in the last step proved problematic because of similar running impurities when utilizing silica gel or alumina gel chromatography (impurities in enough quantity that made it impossible to recrystallize the crude reaction material), and this led to lower purified yields.

Additional Thermodynamic Data that Corroborate the Ordered Solvent Shell Model. (i) Comparison of Acetate Anion Binding in Tetra- and Diurea Picket Porphyrin Receptors. Association constants were determined for porphyrin **3** by following its titrations with tetrabutylammonium acetate salt in DMSO-d_6 using ^1H NMR.[22] The stoichiometry of binding is 1:1,[23] and binding constants for **3**, along with those of tetraurea picket porphyrin **1** for comparison, are shown in Table 1. These new experimental results further corroborate our "ordered solvent shell" model, in which buried solvent dictates the receptor's selectivity for chloride anion. In this model, the tetraurea receptor's binding motif includes a buried DMSO molecule that complexes to a urea picket and is positioned in the receptor pocket so as to stabilize the spherical chloride anion bound between two adjacent urea pickets; hence the term ordered solvent shell. Effectively, the solvent acts as an extension of the binding unit within the receptor pocket, affording a stabilizing charge−dipole interaction with the anion.

To bind a larger dihydrogenphosphate or acetate anion would require the removal of the DMSO molecule from the receptor's pocket, with resultant loss of solvation stability. We have previously reported that the stabilization afforded by the DMSO ordered solvent shell about the anion results in a chloride/phosphate binding ratio for porphyrin **1** >200:1, and we now show that the chloride/acetate anion binding ratio for **1** is 1000:1 (as is the binding ratio for **1**: bisulfate or nitrate anions[19]). The

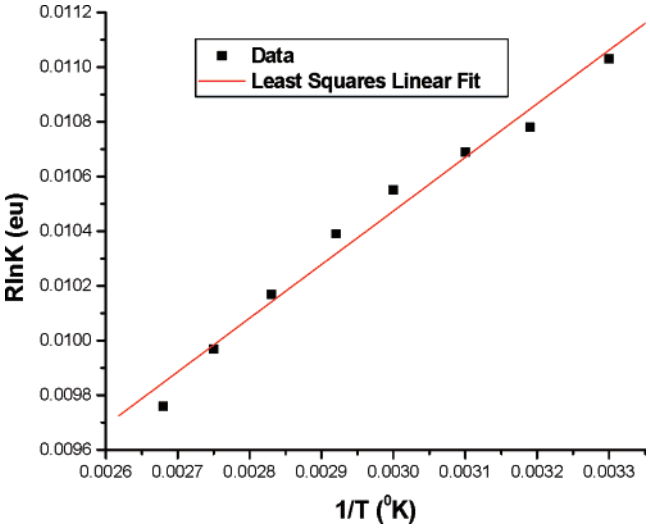

FIGURE 2. Van't Hoff plot of porphyrin **3** complexed with chloride anion.

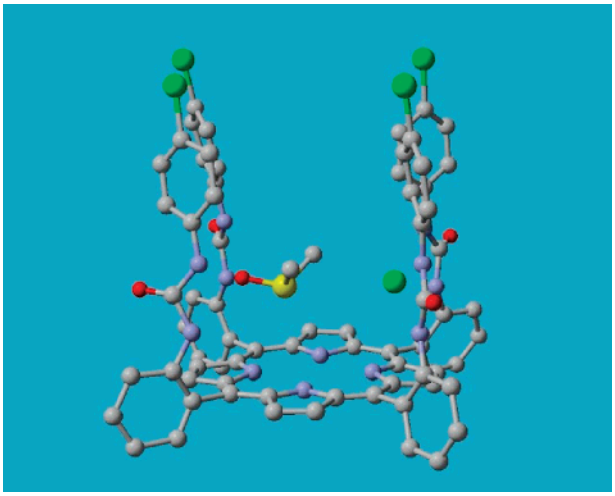

FIGURE 3. X-ray crystal structure of porphyrin **1** complexed with chloride anion and bound DMSO molecule, grown in DMSO (hydrogens not shown for clarity).[19] The structure shows the ion−dipole interaction between the partially charged sulfur and anion.

TABLE 2. Δ*H* and Δ*S* for Porphyrins **1** and **3** Determined from Van't Hoff Plots

	1	3
Δ*H*	−14.8 kcal/mol	−1.96 kcal/mol
Δ*S*	−32.7 eu	4.6 eu

diurea picket porphyrin **3** contains no extra urea picket to bind a DMSO solvent molecule when binding an anion and thus no buried solvent to mediate stabilization of the chloride anion. Its chloride/dihydrogenphosphate anion binding ratio is 1:55,[17] and for chloride/acetate anion the binding ratio is 1:120 for porphyrin **3**. *This is a 3 order of magnitude shift in anion binding ratio for chloride and dihydrogenphosphate anions, and 5 order of magnitude shift in anion binding ratio for chloride and acetate anions, between the two porphyrin receptors*. This shift in binding ratios occurs even though the anion binding units (two urea groups) are identical. The difference in the two receptors' anion affinities translates into 2−4 kcal/mol stability furnished

(22) Binding constants were determined by nonlinear regression analysis using EQNMR for Windows: Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311−312.

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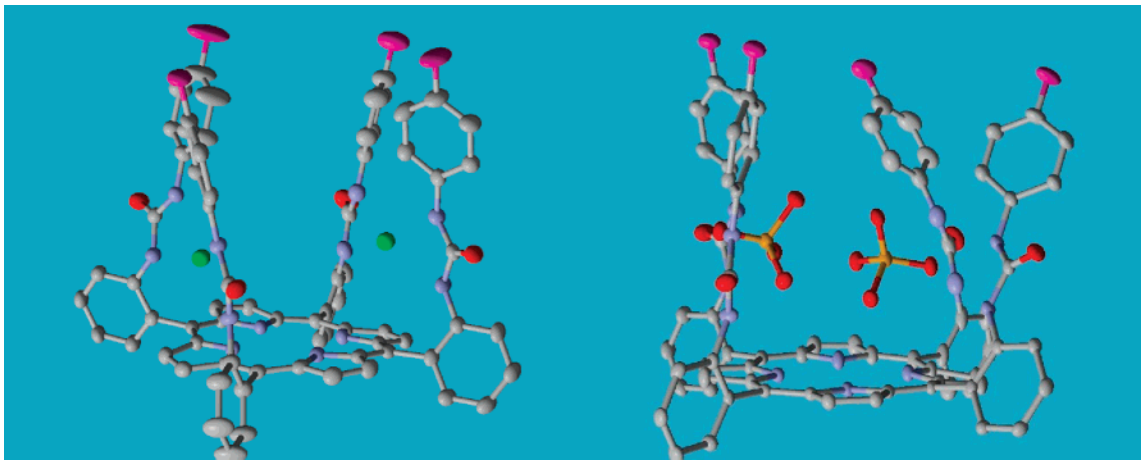

FIGURE 4. Left: X-ray crystal structure of porphyrin **1** complexed with two chloride anions grown in CH_2Cl_2 (hydrogens and counterions not shown for clarity). Right: X-ray crystal structure of porphyrin **1** complexed with two dihydrogenphosphate anions grown in CH_2Cl_2 (hydrogens and counterions not shown for clarity). The two phosphate anions are positioned in the receptor pocket to allow hydrogen bonding with each other.

to a diurea−chloride anion binding motif *by the one buried solvent molecule*.

Our receptor−anion complexes clearly demonstrate that just one buried solvent molecule in the receptor's binding pocket can make a remarkable difference in a receptor's anion binding affinity, selectivity, and even the stoichiometry of anion binding (vide infra). This is further corroborated by experimental results that show when porphyrin **1** is placed within a polymer matrix (sans solvent) that is wrapped around an electrode, the electrode becomes an ISE that is more sensitive to acetate anion than chloride anion.[24]

(ii) Comparison of ΔH and ΔS of Binding for Porphyrins 1 and 3. The enthalpy and entropy of anion binding for porphyrin receptors **1** and **3** were determined from van't Hoff plots[25] (Figure 2 and Table 2), and the differences in the thermodynamic properties of the two porphyrin−halide complexes are clearly evident. The large negative entropy associated with the porphyrin **1**−bromide anion complex shows that the complex is highly ordered, not surprisingly since buried solvent is part of the binding motif.[26] It also shows there is a compensatory high negative enthalpy associated with this complex due to the stabilizing nature of the ordered solvent shell afforded by the buried solvent.[19] On the other hand, the entropy and enthalpy associated with the porphyrin **3**−chloride anion complex were decidedly smaller,[26] more so than what would be expected based solely on the change in k_{on} and k_{off} due to statistical factors associated with the receptor's different number of potential binding sites. The ΔS of halide anion binding for porphyrin **3**, unlike that for porphyrin **1**, is slightly positive. Perhaps this is due in part to the differences in desolvation between the two binding events, but the anion−receptor complex is certainly more loosely constructed than in the receptor−anion complex with a buried solvent. The anion's enthalpy of desolvation may be more positive in the absence of buried solvent than in its presence, which could lead to a comparative decrease in the k_{on} of anion binding.[19] Any solvent shell that may be associated with the anion−porphyrin **3** complex would not be as "ordered", presumably which would lead to a comparative increase in the k_{off} of anion binding. The binding constant would be diminished in either case, as is observed for the halide−porphyrin **3** complex.

X-ray Crystal Structures of Anion−Receptor Complexes sans Buried Solvent. Our previously reported crystal structure (Figure 3) of the chloride anion−porphyrin **1** complex grown in DMSO shows a DMSO molecule bound to the receptor pocket and positioned to interact in a stabilizing fashion with the halide.[19] New crystal structures of chloride anion−receptor **1** and phosphate anion−receptor **1** complexes grown in CH_2Cl_2 show no buried solvent (Figure 4). Additionally, the crystal structures now show that the anion−receptor complex contains two anions instead of just one, which agrees with the stoichiometry of anion binding with porphyrin **1** determined from Job plots in a CD_2Cl_2 solution.[17] Absent a buried DMSO molecule, the receptor's pocket can entertain two anions. The presence, or lack thereof, of one buried solvent molecule dictates the stoichiometry of anion binding in receptor **1**.

It is interesting to note the structure of the bisdihydrogenphosphate anion−porphyrin **1** complex. Each phosphate anion is bound between two urea groups by only one of its oxygens, not two, as was expected from modeling studies. This allows the two phosphate anions to be positioned in the receptor pocket in such a manner as to enable hydrogen bonding with each other. In this case, absent a buried solvent molecule, each phosphate anion acts as an extension of the receptor pocket to stabilize the other.

Conclusions

The convergent binding of anion and receptor-bound DMSO solvent molecule in a tetraurea picket porphyrin receptor can lead to 2−4 kcal/mol stability in binding of chloride anion over that of a dihydrogenphosphate or acetate anion in DMSO. This is in stark contrast to the binding of these three anions to a diurea picket porphyrin, a receptor unable to bind solvent while also binding an anion. These results clearly demonstrate that buried solvent, when acting as an ordered solvent shell, greatly influences the affinity, selectivity, and even stoichiometry of

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(26) In the case of porphyrin **1**, chloride anion could not be used for it bound too tightly to enable an accurate determination by ^{1}H NMR. In the case of porphyrin **3**, chloride anion binding constants could be accurately determined from ^{1}H NMR, whereas bromide anion's binding constants were too weak for accurate determinations at higher temperatures.

anion binding. Because of its potential importance to the understanding of biological systems in general, and drug design in particular, we are currently doing research to determine how well this ordered solvent sphere translates to water-bound anion receptors.

Experimental Section

NMR Titrations. NMR titrations of tetrabutylammonium acetate and porphyrin **3** were done as previously reported.[19] Variable temperature experiments for van't Hoff analysis were run with a 300 MHz ^{1}HNMR. Stock solutions of porphyrin **3** (0.01169 M) and tetrabutylammonium salts of chloride (0.1225M) were carefully measured with a microgram scale and mixed in a volumetric flask (2 mL). Samples were made with DMSO-d_6, and all spectra were referenced to DMSO-d_6 (2.50 ppm). The NMR samples were prepared by mixing porphyrin **3** with the tetrabutylammonium salt at 1:6 equivalence ratios. The temperature of the sample was varied from 30 to 100 °C, and a spectrum was recorded at each 10 °C increment. ΔH and ΔS of binding were determined as previously reported.[19,25]

5,10-Bis-(2-nitrophenyl)-15,20-diphenylporphyrin (9). (a) Step I: Reduction of Diacyldipyrromethane 8. Diacyldipyrromethane **8** (1 equiv, 1.0 mmol, 0.48 g) was dissolved in a solution of THF/methanol (40 mL THF/4 mL methanol), and $NaBH_4$ (20 equiv, 20 mmol, 0.76 g) was added to the solution in 0.25-g portions. After 40 min, the reaction solution was poured into the solution of CH_2Cl_2 (110 mL) and NH_4Cl (55 mL). While the solution was being poured, the mixture was vigorously stirred with a glass rod to prevent the solution from bumping because of the exothermic quench. The organic phase was washed with water two times and dried over Na_2SO_4. The organic solvent was removed under reduced pressure to furnish the crude diol as an amorphous pale yellow solid.

(b) Step II: 2 + 2 Synthesis of Porphyrin Macrocycle. A solution of dry CH_3CN (400 mL) and freshly purified 2-nitrodipyrromethane **5b** (1 equiv, 1 mmol, 0.27 g) was added to the flask containing the crude diol. The solution was stirred vigorously for 5 min to allow the formation of a homogeneous mixture. Then TFA (0.92 mL, 12 mmol) was added dropwise rapidly, and after 3.5 min, DDQ (3 equiv, 3 mmol, 0.68 g) was added to the reaction mixture to oxidize the intermediate porphyrinogen macrocycle. TEA (1.7 mL, 12 mmol) was added after 1 h, and the crude reaction was passed through an alumina gel column (eluted with CH_2Cl_2) until no color remained in the eluent. The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography (eluted with CH_2Cl_2). The solvent from the collected porphyrin solution was removed under reduced pressure, and the product was recrystallized from ethanol, yielding a purple solid as a mixture of atropisomers (0.15 g, 0.2 mmol, 21% yield over steps I and II). ^{1}H NMR (DMSO, 400 MHz): δ −2.86 (br s, 2H), 7.80−7.88 (m, 6H), 8.14−8.20 (m, 6H), 8.28 (t, 2H, J = 7.7 Hz), 8.34−8.36 (m, 1H), 8.49 (q, 1H, J = 4.4 Hz), 8.55 (q, 1H, J = 4.9 Hz), 8.57−8.59 (m, 2H), 8.73 (br d, 4H, J = 5.5 Hz), 8.82−8.84 (m, 4H); ^{13}C NMR (DMSO, 100 MHz): δ 114.4, 114.4, 120.8, 124, 124.1, 126.8, 128.0, 130.4, 131.8, 134, 134.6, 134.7, 136.5, 136.5, 140.8, 151.2, 151.2, 151.4, 151.4; ESMS: *m*/*z* (relative intensity): 705.4 (100, M + 1).

5,10-Bis-(2-aminophenyl)-15,20-diphenylporphyrin (10). Dinitroporphyrin **9** (1 equiv, 0.71 mmol, 0.5 g) was dissolved in hydrochloric acid (30 mL) and stirred at room temperature under nitrogen. After the porphyrin had dissolved, an excess amount of $SnCl_2 \cdot H_2O$ (1.2 g) was added, and the reaction mixture was stirred for 2 h. Then over a 15 min period, the mixture was brought to 65−70 °C and held for 25 min at that temperature. The reaction mixture was cooled to room temperature and was cautiously quenched with concentrated NH_4OH to avoid excess heat evolution by the neutralization reaction. Once the reaction mixture gained a red color and turned basic beyond pH 8, as indicated by pH paper, CH_2Cl_2 (50 mL) was added, and the solution was stirred overnight. The organic layer was separated from the aqueous layer, and any salts in the organic layer were filtered using a Celite pad. The filtered organic solution was dried over sodium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (eluted with 1% isopropylamine in CH_2Cl_2) to furnish the mixture of atropisomers α,α-diaminoporphyrin **10a** and α,β-diaminoporphyrin **10b** (0.32 g, 0.5 mmol, 70% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ −2.72 (br s, 2H), 3.52 (br s, 4H), 7.08 (d, 2H, J = 4.1 Hz), 7.15 (t, 2H, J = 7.4 Hz), 7.58 (t, 2H, J = 7.8 Hz), 7.72−7.77 (m, 6H), 7.86 (d, 2H, J = 4.4 Hz), 8.19 (t, 4H, J = 3.9 Hz), 8.87 (q, 8H, J = 11.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 115.2, 115.2, 115.4, 115.4, 117.5, 120.5, 126.7, 120.5, 126.7, 127, 127.8, 129.6, 134.8, 142, 146.8; ESMS: *m*/*z* (relative intensity): 645.5 (100, M + 1).

α,α-5,10-Bis-(2-(4-fluorophenyl)phenylurea)-15,20-diphenylporphyrin (3). (a) Step I: Isomerization of Atropisomer Mixture of 10a and 10b. A 500-mL three-neck flask was set up with the following: an overhead stirrer, a condenser fitted with septum and needle to release pressure, and a septum fitted with cannulation needle to deliver nitrogen saturated with benzene from a separate flask that contained benzene and a gas dispersion tube. Silica gel (72 g) was mixed with benzene (160 mL) in the three-neck round-bottom flask and stirred for 2 h at 74 °C. A mixture of α,α- and α,β-diaminoporphyrin **10** (0.31 mol, 2 g) was added to the silica gel slurry, which was stirred for 24 h at the same temperature. The apparatus was checked periodically to adjust nitrogen flow, benzene level, and the temperature. Once the slurry cooled, the porphyrin was removed from the silica using acetone. The solvent was removed under reduced pressure at room temperature to preserve the α,α configuration. The α,α-aminoporphyrin **10a** was separated from the α,β-aminoporphyrin **10b** using silica gel chromatography (eluting with CH_2Cl_2/IPA, 99/1) to furnish the α,α-aminoporphyrin **10a** (1.6 g, 0.25 mmol, 81% yield) as dark purple crystals.

(b) Step II: Formation of Urea Picket Porphyrin. The α,α-aminoporphyrin **10a** (1 equiv, 0.51 mmol, 0.33 g) was dried in a vacuum desiccator over P_2O_5 for 48 h. Porphyrin **10a** was carefully transferred to a dried 100-mL round-bottom flask from the desiccator inside a nitrogen bag. While in the bag, a dried addition funnel closed with rubber septum was attached to the flask. Once the apparatus was taken out of the bag and fixed with a nitrogen line, dry $CHCl_3$ (26 mL) was added to dissolve the porphyrin. A solution of dry $CHCl_3$ (9 mL) and 4-fluorophenylisocyanate (4 equiv, 2.1 mmol, 0.23 mL) was syringed into the addition funnel, and the isocyanate solution was added dropwise to the stirring porphyrin solution. The reaction was quenched after 25 h by adding water, and the aqueous layer was extracted with $CHCl_3$. The solvent was removed under reduced pressure, and the crude reaction mixture was purified by silica gel chromatography (eluting with a stepwise gradient of solvents: 99/1 mixture of CH_2Cl_2/ethyl acetate was used until the elution of a UV absorbing band, upon which time the solvent was changed to a 95/5 mixture of CH_2Cl_2/ethyl acetate). Porphyrin **3** was collected and recrystallized from a mixture of ether and petroleum ether to furnish 0.15 g (0.16 mmol, 32% yield) and 0.18 g (0.19 mmol, 38% yield), respectively, over two reactions of the above scale. Mp: 232−234 °C; UV/visible (CH_2Cl_2): λ nm (ϵ, $cm^{-1}\,M^{-1}$, $\times 10^3$) 644 (2.53), 589 (5.06), 550 (5.50), 515 (15.9), 419 (271.2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ −2.72 (br s, 2H), 6.77 (t, 4H, J = 4.5 Hz), 6.91 (q, 4H, J = 6 Hz), 7.41 (t, 2H, J = 7.4 Hz), 7.48 (s, 2H), 7.77−7.88 (m, 10H), 8.12−8.22 (m, 6H), 8.43 (d, 2H, J = 4.4 Hz), 8.76−8.85 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 114.8, 115.1, 119.3, 120.3, 121.6, 127, 128.2, 129.2, 131.3, 134, 134.3, 135.2, 135.4, 139.1, 141, 152.5, 155.4, 158.5; ESMS: *m*/*z* (relative intensity): 919.5 (100, M + 1); Anal. Calcd for $C_{58}H_{40}F_2N_8O_2$: C, 75.80; H, 4.39; N, 12.19. Found: C, 75.58; H, 4.28; N, 11.95.

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Supporting Information Available: Copies of ^{1}H NMR spectra of compounds **6b**, **8**, porphyrins **9**, **10**, and **2b**, and ^{1}H NMR and ES-MS spectra of porphyrin **3**, ^{1}H NMR titration isotherms of porphyrins **1** and **3** with tetrabutlyammonium acetate in DMSO, synthesis and characterization of compounds **5a**, **5b**, **6a**, **6b**, **7**, **8**, and porphyrin **2b**, and CIFs for the dichloride anion−porphyrin **1** complex and for the bisdihydrogenphosphate anion−porphyrin **1** complex, and space-filled crystal structure of dihydrogenphosphate anion−porphyrin **1** complex showing hydrogen bonding between bound phosphate anions. This material is available free of charge via the Internet at http://pubs.acs.org.

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