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"Wurster-Type" Ureas as Redox-Active Receptors for Anions

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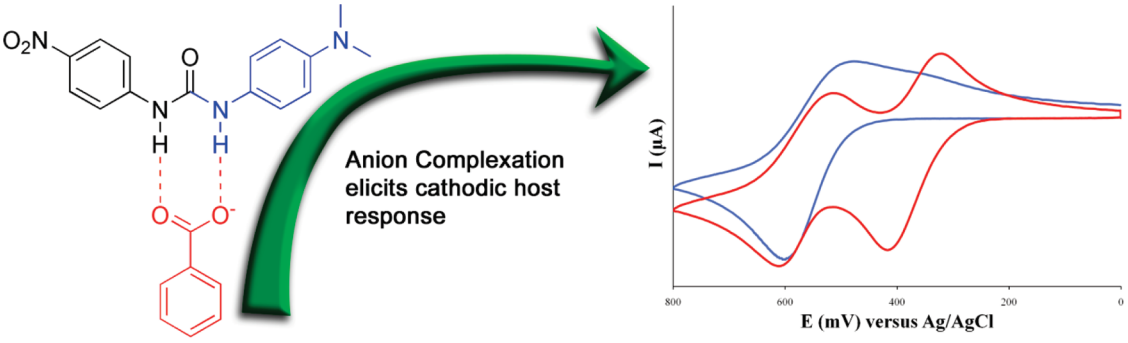

Four redox-active receptors, **1**−**4**, based on the incorporation of *p*-phenylenediamine(s) within a urea framework, were synthesized, and the affinities of two for a series of anions were quantified through UV−vis and NMR spectroscopic studies. The structure of **1** was confirmed by X-ray crystallography. For the oxoanions studied, complex stabilities approached 10^6 M^{-1} in acetonitrile and decreased with the decreasing basicity of the anion ($CH_3COO^- > C_6H_5COO^- > H_2PO_4^- > NO_2^- > NO_3^-$). The presence of the urea functionality caused an increase in the oxidation potential of the *p*-phenylenediamine subunit compared to that of free *p*-phenylenediamine. Electrochemical studies of the anion complexes revealed two-wave behavior with the appearance of a second oxidation wave cathodic to that in the free receptors and characteristic of the bound anion. Ab initio DFT studies of a representative acetate complex revealed the consequences of host oxidation state on complex structure.

Introduction

Forty years after Park and Simmons first selectively bound halides,[1] anion recognition is a focus of supramolecular chemists around the world.[2] Modern interest is largely driven by the significance of anions in biological systems; the area of transmembrane anion transport in particular has received much recent attention.[3] Anionic pollutants, such as phosphate from agricultural fertilizers,[4] and industrial pollutants such as pertechnetate[5] reinforce interest in the application of anion receptors as sensors.

Electroneutral anion receptors for use in organic media are frequently designed around hydrogen bond donor functionalities such as ureas[6] and amides.[7] In the last 10−15 years

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the quest for increased affinity and selectivity has led to the development of elaborate organic frameworks possessing well-defined binding cavities of multiple chelating hydrogen bond donor moieties.[8] Sessler and co-workers' classic calix-4-pyrrole framework led to the recent publication of novel receptors strapped with chromogenic dipyrrolylquinoxalines that exhibit selectivity for fluoride, dihydrogen phosphate, and acetate anions.[9] Other elaborate frameworks have yielded receptors that also show remarkably high selectivities.[10]

Hayashita and co-workers,[11] as well as Fabbrizzi and co-workers,[12] have recently shown that "trivial" anion receptors based on phenylurea have much to offer our understanding of anion recognition; both groups have shown that this motif is capable of strong binding ($\sim 10^6$ M^{-1}) in polar solvents such as acetonitrile and that affinity increases in the same order as the anion basicity. Further, Gale and co-workers studied the anion binding properties of 1,3-diphenylurea itself and demonstrated that despite the absence of electron-withdrawing functionalities, this simple receptor is capable of effectively binding anions in DMSO, a competitive polar solvent.[4] Gunnlaugsson and co-workers recently employed an amide-functionalized variant of the same diarylurea motif in a receptor capable of binding two anions in a cooperative "allosteric" fashion.[13]

There is considerable interest in the design of receptors that are further functionalized to record or signal a binding event. The basic template of these responsive receptors consists of a recognition site coupled to a subunit that undergoes a measurable change in one or more physical properties, such as color, fluorescence, or shifts in redox potential upon binding.[14,15] In particular, redox-active anion and cation receptors based on ferrocene[16] and tetrathiafulvalene[17] have received much attention. Redox-active cation receptors that employ a functional equivalent of Wurster's reagent, *N*,*N*′-tetramethyl-*p*-phenylenediamine (*p*-TMPD), as a signaling subunit, are also well-studied, but those for anions are unknown.[18] Here we report the synthesis, characterization, anion affinities and electrochemistry of Wurster-type ureas, new anion receptors that incorporate *p*-phenylenediamine within the urea framework.

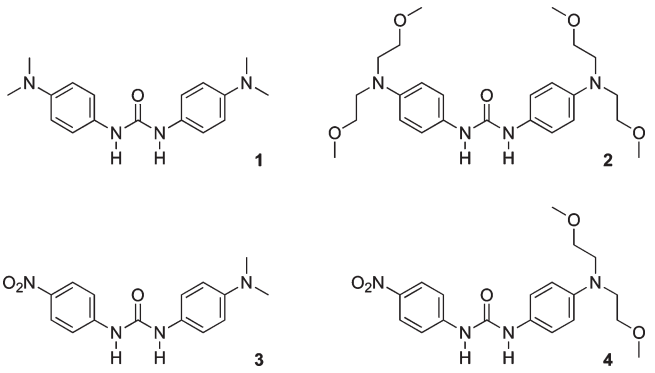

FIGURE 1. Receptors studied in this work.

We studied **1**−**4** (Figure 1), simple *N*,*N*′-diphenylurea derivatives functionalized to mimic the electrochemical properties of *p*-TMPD. Incorporating the hydrogen bond donor(s) in the redox center facilitates possible anion-dependent electrochemical changes, and the optical properties of the chromogenic centers may change on interaction with anions. Symmetric receptor **1** was first synthesized in 1941 by Gerchuk for the treatment of blood parasites,[19] and more recently, Nangia and co-workers synthesized receptor **3** for the study of hydrogen-bond-directed homomolecular crystal formation.[20] Neither **1** nor **3** has been studied in the context of anion recognition. Receptors **2** and **4** are acetonitrile-soluble analogues of **1** and **3**, respectively.

Results and Discussion

Receptor Design and Synthesis. As has been previously shown for cationic receptors, replacement of a donor atom functionality with a redox-active phenylenediamine unit adds redox activity (in some cases, reversible) without compromising the ability of the host to form complexes.[18] For example, it was shown that replacement of a single O atom in 18-crown-6 with an *N*,*N*-dimethylamino-*p*-phenylenediamino

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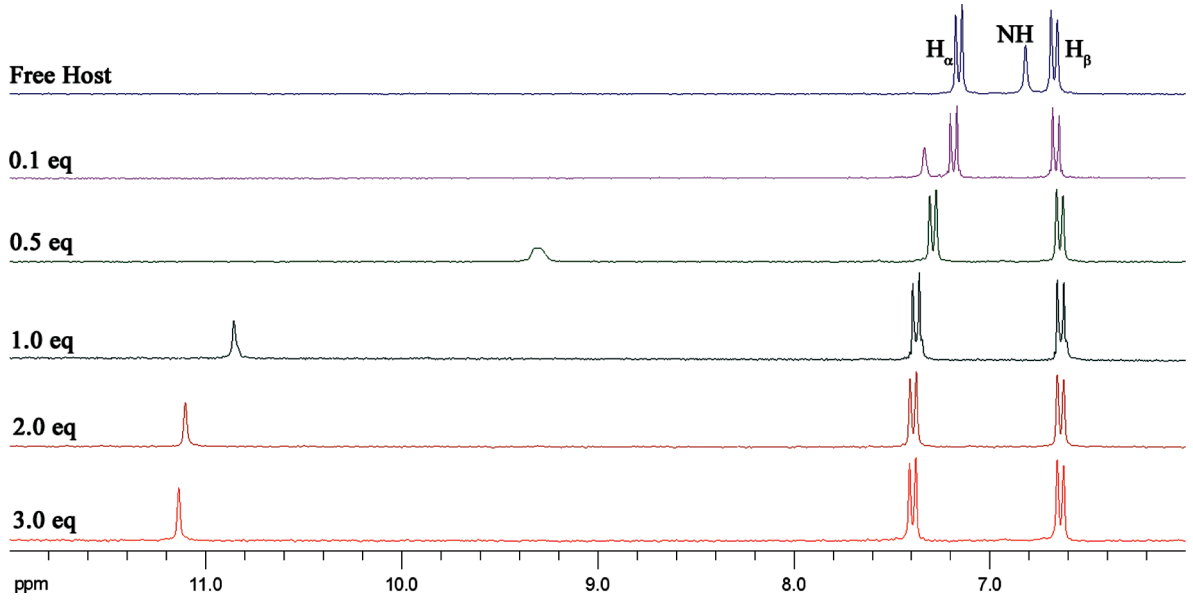
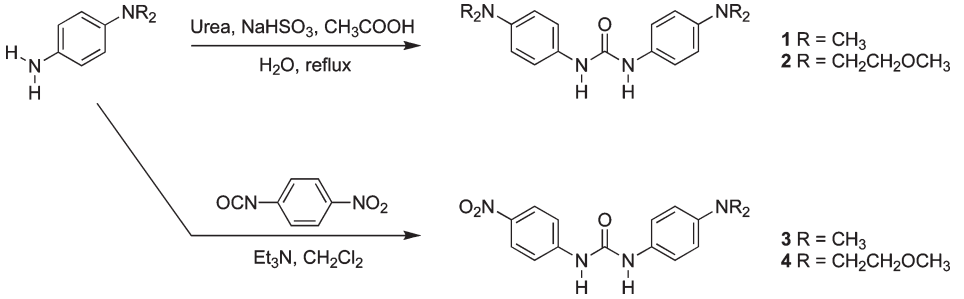


FIGURE 2. Illustrative ^{1}H NMR titration of a 5×10^{-3} M solution of **2** in CD_3CN with $[Bu_4N]CH_3COO$.

SCHEME 1. Preparation of 1−4



group gave a Wurster's crown ether that not only was selective for the potassium ion, like 18-crown-6, but was electrochemically responsive to cations. In this study, we have extended this approach for the first time to anion binding receptors. The chosen receptor target was the hydrogen bond donor urea because of its well-chronicled ability to form complexes with anions and the strategic location of N atoms that can be used to fuse the anion binding urea core to a phenylenediamine redox center. Thus, by replacing the amino groups of urea with surrogate phenylenediamino groups, we anticipated having comparable anion binding ability with the additional function of redox activity. As shown in Figure 1, the receptors prepared for this study contain either one or two phenylenediamine units within a urea framework. The urea N−H groups are available for hydrogen bonding while also serving as a component in the redox-active phenylenediamine subunit.

Receptor **1** is a symmetrical system containing two equivalent electrochemical centers connected through the *para* position by a urea group. Receptor **3** is an asymmetrical system containing a single electrochemical center and the electron-withdrawing *p*-nitrophenyl functionality, which increases the acidity of the urea NH groups. In both cases, the distal amino group of the phenylenediamine moieties is methylated to improve the electrochemical behavior of the redox center. Indeed, Wurster's reagent, *p*-TMPD, is characterized by having two reversible one-electron oxidations. Due to the limited solubility of **1** and **3** in most common solvents, we also prepared analogous compounds **2** and **4**, which are identical in structure with **1** and **3**, respectively, save for the replacement of the methyl groups with alkyl ether functionalities. These latter hosts did in fact have better solubility, and both **1** and **3** were used in all solution studies.

Receptors **1** and **2** were synthesized in single steps from suitable phenylenediamine precursors and urea via the method used by Yan et al. to prepare phenylurea precursors for dyes (Scheme 1).[21] Receptors **3** and **4** were synthesized by reaction of the same phenylenediamine precursors used in preparing **1** and **2** with 4-nitrophenylisocyanate according to the method of Nangia and co-workers, who had previously prepared **3**.[20a]

Measurements of Association Constants. Two analytical methods were used for the calculation of association constants: NMR spectroscopy and UV−vis spectroscopy. Exploratory NMR titration studies of receptor **4** with acetate and benzoate showed titration profiles almost linear with the addition of guest, indicating association constants beyond the sensitivity of this method (i.e., K greater than 10^5 M^{-1}). Literature studies for related

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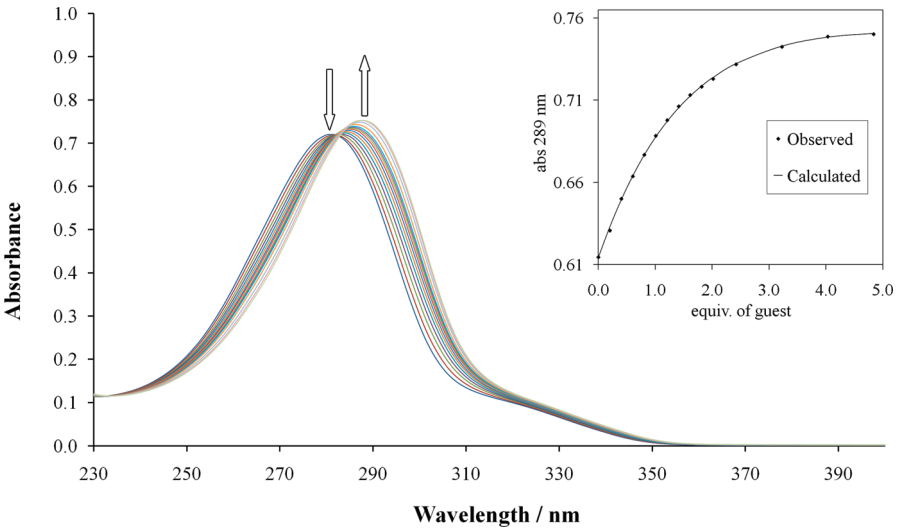

FIGURE 3. Family of UV−vis spectra taken in the course of the titration of a 1.75×10^{-5} M solution of **2** in CH_3CN with a standard solution of $[Bu_4N]CH_3COO$. Inset shows the titration profile from which the association constant was determined, log $K = 4.4$ M^{-1}.

compounds exhibiting association constants of similar magnitude were carried out using UV−vis spectroscopy.[11,12] This method was then used to determine association constants above 10^3 M^{-1}. In most of the combinations of receptor and guest, association constants below this level could not be determined accurately via UV−vis spectroscopy because the required parameter, [concentration of complex]/[maximum possible concentration of complex], could not be raised sufficiently to calculate a reliable equilibrium constant and yet still permit the accurate measurement of absorbances within the sensitivity range of the spectrophotometer. Consequently, association constants below 10^3 M^{-1} were determined via ^{1}H NMR spectroscopy. To ensure that the two methods were measuring like binding phenomena, the association constant of receptor **4** with NO_2^- was determined via both analytical methods and both values were in close agreement: log $K = 3.3 \pm 0.1$ via UV−vis spectroscopy; log $K = 3.5 \pm 0.1$ via ^{1}H NMR spectroscopy.

The interaction of receptor **2** with acetate as the tetrabutylammonium salt was investigated by ^{1}H NMR spectroscopy. A 5×10^{-3} M CD_3CN solution of **2** was titrated with acetate, which was added stepwise up to 3 equiv. Figure 2 illustrates the spectral shifts of the aromatic protons of the phenyl rings, H_α (closest to the urea moiety) and H_β, and the symmetric urea NH protons, on the addition of acetate. Three effects are observed from the hydrogen bond formation between the urea and the anion, two of which are described by Boiocchi et al. for the related compound 1,3-bis(4-nitrophenyl)-urea:[12] (i) There is a deshielding effect on the urea NH groups caused by the proximity of the anion, resulting in a progressive downshield shift of the NH protons. Although this movement continues a further 0.3 ppm after the addition of 1 equiv of acetate, it is largely complete at this point of the titration, having traveled 4 ppm. (ii) The increase in electron density in the phenyl rings with through-bond propagation causes the aromatic C−H protons to be more shielded. This is observed as a small upfield shift in C−H_β (< 0.1 ppm) which ceases after the addition of 1 equiv of acetate. (iii) The polarization of the C−H_α bonds by an electrostatic through-space effect resulting in a deshielding and subsequent 0.2 ppm downfield shift of the C−H_α protons that is nearly complete at the addition of 1 equiv and ceases by the addition of 2 equiv of acetate. This effect is expected to be short-range and is therefore less significant or not observed for C−H_β.

The NMR spectra indicate the formation of a discrete H-bond complex. Simple urea derivatives in the literature typically conform to a 1:1 (host:guest) binding model with anions, and Figure 2 shows that little change in chemical shifts occurs after the addition of 1 equiv of the acetate anion to **2**.[11,12]

UV−vis titration studies were carried out to determine the association constants of **2** and **4** with a series of anions (CH_3COO^-, $C_6H_5COO^-$, $H_2PO_4^-$, Cl^-, NO_2^-, and NO_3^- as their tetrabutylammonium salts). Receptor **2** shows a λ_{max} at 281 nm. Receptor **4** shows a similar λ_{max} at 271 nm and another at 332 nm. These absorbances are assigned as intramolecular charge transfer (CT) absorption bands.[22] The presence of two CT absorption bands for receptor **4** can be ascribed to the asymmetry of the system. Increasing the anion concentration produced a bathochromic shift in these CT absorption bands for both receptors. Under the concentration parameters used for the more strongly bound anions, addition of NO_2^- and NO_3^- did not elicit a measurable change in the CT absorption band of receptor **2**, and NO_3^- did not elicit a measurable change in either of the CT absorption bands of receptor **4**. ^{1}H NMR spectroscopy was used to determine these three association constants.

Figures 3 and 4 are examples of separate UV−vis titrations of receptors **2** and **4**, respectively, with acetate. The arrows denote the wavelengths of decreasing and increasing absorbance. Both figures show clear isosbestic points: 283 nm for **2** and 357 nm for **4**. These results demonstrate that complex formation of receptor with acetate is taking place via hydrogen bonding to stabilize the electronic excitation state of the chromophore.[22] Analogous behavior was observed for $C_6H_5COO^-$, $H_2PO_4^-$, and Cl^- with receptor

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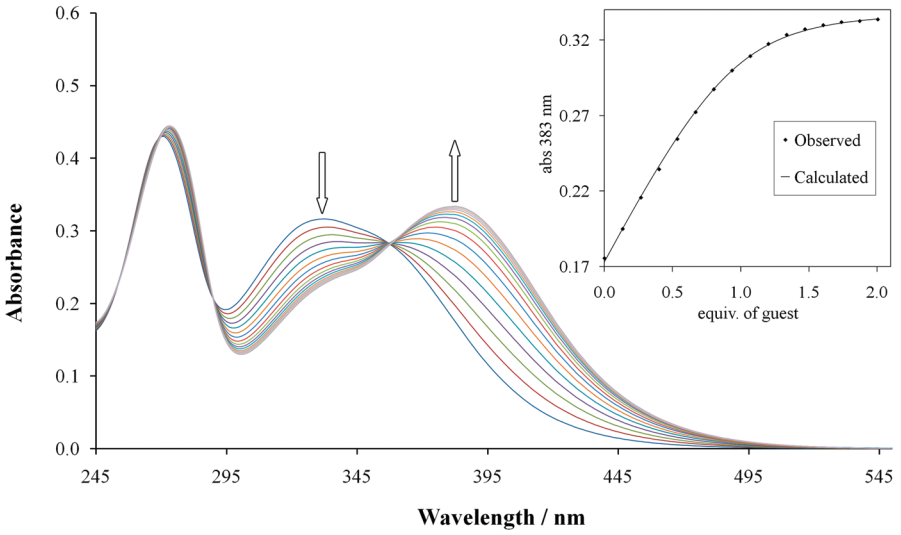

FIGURE 4. Family of UV−vis spectra taken in the course of the titration of a 2.00×10^{-5} M solution of **4** in CH_3CN with a standard solution of $[Bu_4N]CH_3COO$. Inset shows the titration profile from which the association constant was determined, log $K = 5.7$ M^{-1}.

2 and for $C_6H_5COO^-$, $H_2PO_4^-$, Cl^-, and NO_2^- with receptor **4**. Table 1 shows that the changes in absorption spectra are clearly anion-dependent. Nonlinear regression analyses were carried out, and good curve fitting was achieved by using at least 15 titers for each experiment and through the tuning of the experimental concentrations of guest. For the oxoanions studied with these receptors, the magnitudes of the complexation-induced bathochromic shifts in the CT λ_{max} bands follow the order of oxoanion basicity, and the degree of change reflects the stabilities of the complexes. Complex formation also results in enhanced molar absorptivity, but with no obvious trend that can be related to binding strength.

The values for the association constants obtained via ^1H NMR for NO_2^- and NO_3^- with **4** and NO_3^- with **2** continue the trend of binding strength and oxoanion basicity observed via UV−vis spectroscopy. Receptor **4** exhibits association constants considerably higher than those of **2** for the same oxoanion substrates (a factor of 10 or greater for all anions other than NO_3^-). Of note are the receptors' affinities for chloride; chloride is the lone spherical anion in this series, and despite the apparent difference in hydrogen bond acidity of the urea NH protons of the two receptors, receptor **2** has a log K of 3.2 for chloride and receptor **4** has a log K of 3.6, only 2.5 times higher in binding strength. This result may indicate that the complementarity of the bidentate oxoanions for the urea moiety allows the increased hydrogen bond donor acidity of **4** to have a greater impact on strength of association. The selectivity exhibited by **2** appears smaller than that exhibited by the stronger receptor **4**, consistent with the Affinity-Selectivity Principle, which states that as affinities rise, the spread of binding constants also increases so that selectivities for the more strongly bound guest tend to increase.[10c]

Cyclic Voltammetry. The electrochemical properties of receptors **2** and **4** and their complexes were investigated using cyclic voltammetry. Free receptor **2** undergoes two oxidations (107 and 241 mV relative to Fc/Fc^+) that, by analogy to the well-studied electrochemistry of Wurster's reagent (*p*-TMPD), are ascribed to the one-electron oxidation of each phenylenediamine subunit. The fusion of the urea subunit to the phenylenediamine cores in **2** causes a >300 mV increase in the oxidation potential of the phenylenediamine moiety versus *p*-TMPD with a concomitant decrease in reversible character, though coupled reductions are clearly present. Because the identical redox centers in **2** oxidize at different potentials, they must be in communication with one another through the urea bridge. Oxidation of one causes an anodic shift in the oxidation of the other. Absence of communication would result in the redox centers oxidizing at the same potential with only a single oxidation wave appearing in the voltammogram for **2**, a phenomenon not observed. Free receptor **4**, containing only one phenylenediamine unit, undergoes a single one-electron oxidation at 180 mV relative to Fc/Fc^+. The higher oxidation potential of **4** versus **2** results from the electron-withdrawing effect of the nitrophenyl group, which like the communication between the two redox centers in **2** is felt through the urea linkage.

TABLE 1. Association Constants, UV−vis Data, and Voltammetric Data for Receptors 2 and 4 in Acetonitrile at 298 K

host	guest[a]	log K[b]	λ_{max}(nm)	ε (M^{-1} cm^{-1})	ΔE_{ox} (V)[c]	BEF[d]
2	none		281	41 210		
2	CH_3COO^-	4.4 (1)	289	48 538	−0.173	844
2	$C_6H_5COO^-$	4.1 (1)	288	46 992	−0.162	550
2	$H_2PO_4^-$	3.5 (2)	285	38 818	[e]	
2	Cl^-	3.2 (1)	285	44 320	−0.034	[f]
2	NO_2^-	2.4 (1)[g]			−0.135	192
2	NO_3^-	1.7 (1)[g]			[h]	
4	none		332	15 803		
4	CH_3COO^-	5.7 (1)	383	17 965	−0.246	14489
4	$C_6H_5COO^-$	5.4 (1)	382	17 667	−0.184	1295
4	$H_2PO_4^-$	4.5 (2)	382	19 122	[e]	
4	Cl^-	3.6 (1)	369	17 100	−0.016	[f]
4	NO_2^-	3.5 (1)	370	20 542	−0.137	208
4	NO_3^-	2.2 (1)[g]			[h]	

[a] Bu_4N^+ salts. [b] Value in parentheses is the uncertainty of the last figure. [c] Change in oxidation potential of the host upon addition of 0.5 eq of anion. [d] Binding Enhancement Factor (BEF): $K_{ox}/K = \exp[-nF(E_c - E_f)/RT]$.[23,24] [e] First oxidation potential of complex was unresolved by CV. [f] Two wave behavior not observed. [g] Determined by ^1H NMR titration. [h] First oxidation potential of host appears unchanged upon addition of guest.

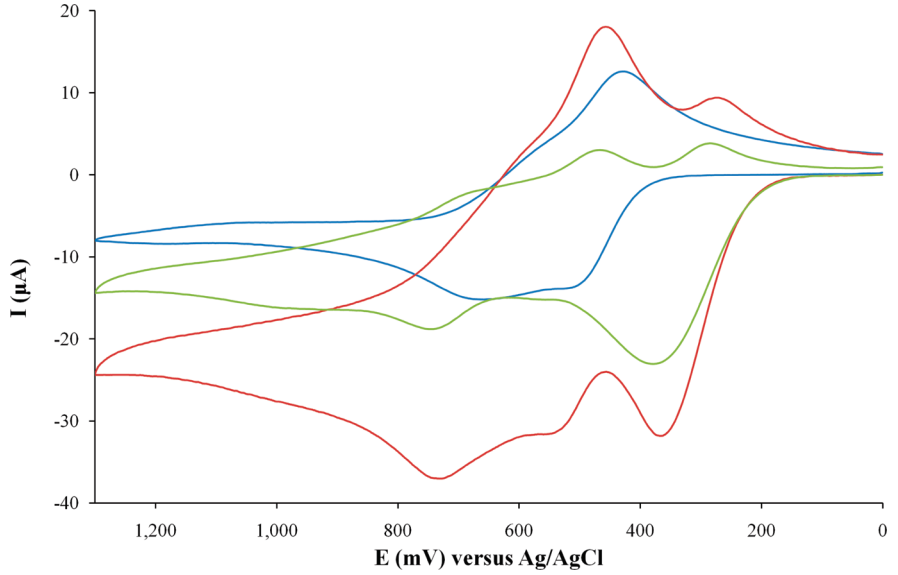

FIGURE 5. Cyclic voltammograms (0.1 M $[Bu_4N]ClO_4$, CH_3CN, 100 mV/s) of **2** (blue line), **2** + 0.5 equiv of $[Bu_4N]C_6H_5COO$ (red line), and **2** + 1.0 equiv of $[Bu_4N]C_6H_5COO$ (green line).

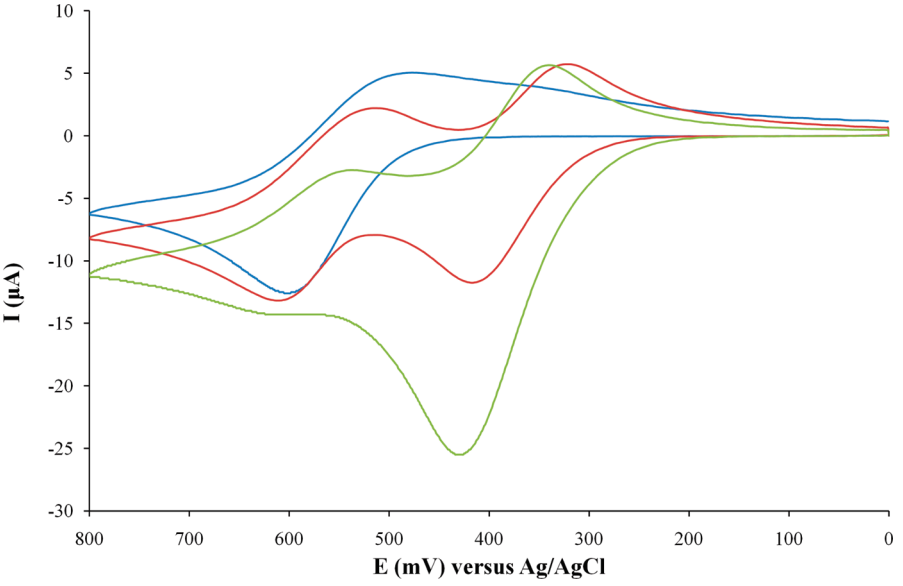

FIGURE 6. Cyclic voltammograms (0.1 M $[Bu_4N]ClO_4$, CH_3CN, 100 mV/s) of **4** (blue line), **4** + 0.5 equiv of $[Bu_4N]C_6H_5COO$ (red line), and **4** + 1.0 equif of $[Bu_4N]C_6H_5COO$ (green line).

Unlike *p*-TMPD, which undergoes two distinct one-electron oxidations to generate, successively, a delocalized radical cation and a quinoid-like dication, no oxidation beyond removal of a single electron per phenylenediamine unit was observed for either **2** or **4** at potentials approaching the solvent limit (approximately 1300 mV vs Fc/Fc^+).

Addition of cations to Wurster's crown ethers has been shown to cause anodic shifts in the oxidation potentials of the hosts with the magnitudes of the shifts related to complex stabilities. By comparison, anion binding should facilitate oxidation of Wurster-type hosts and therefore result in *cathodic* responses in the oxidation potentials of the host molecules. As summarized in Table 1 and shown in Figures 5 and 6, addition of anions to receptors **2** and **4** does indeed lower the oxidation potentials of the hosts. For both receptors, the addition of substoichiometric quantities of CH_3COO^-, $C_6H_5COO^-$, and NO_2^- revealed binary (or "two-wave") behavior as has been described for cation receptors.[23,24] Thus, addition of 0.5 equiv of these anions to either **2** or **4** results in the appearance of two distinct oxidation waves for free and bound host (see Figures 5 and 6), signifying relatively slow exchange of guest. For complexes that display binary behavior, a binding enhancement factor (BEF) can be calculated directly from the voltammetric data to provide a measure of the increase in complex stability

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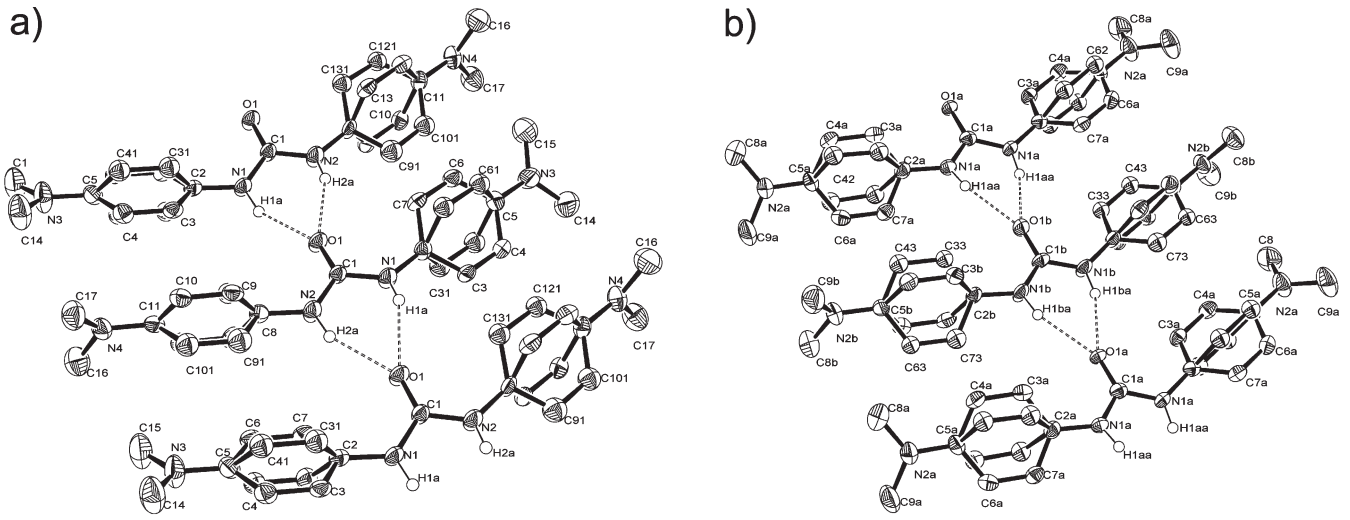

FIGURE 7. X-ray structure of **1** showing the solid-state interactions between neighboring molecules. Three unique geometries of **1** are present in two distinct H-bonded chains shown as a and b. Displacement ellipsoids are scaled to the 50% probability level. The phenyl rings are disordered as shown. Only H atoms involved in intermolecular hydrogen bonds are drawn. Dashed lines indicate the hydrogen bond interactions.

upon oxidation of the host in the form of the ratio K_{ox}/K (where K_{ox} is the formation constant of the anion complex with the host oxidized and K is the formation constant of the same complex with neutral host). The binding enhancement factors are shown in Table 1.[23,24] There is a clear correlation between stability constant of the neutral host complex and the corresponding binding enhancement factor with $\mathbf{4}\cdot CH_3COO^-$, the most stable complex studied, displaying a BEF on the order of 10^4.

The electrochemical behaviors of receptors **2** and **4** in the presence of the remaining ions (Cl^-, NO_3^-, and $H_2PO_4^-$) are distinct from the other anions. With each host, addition of substoichiometric amounts of chloride (<1 equiv) gives a voltammogram with a single oxidation wave attributable to complex formation that decreases in potential as more chloride is added. This wave corresponds to a weighted average of the oxidation potentials of the free host and complex and, in contrast with the binary behavior exhibited by the previous oxoanions studied (CH_3COO^-, $C_6H_5COO^-$, and NO_2^-), reflects relatively rapid exchange of the chloride ion.[24,25] Similar "one-wave" behavior was observed for the alkali metal complexes of Wurster's crown ethers.[18b] In the presence of up to 5 molar equiv of NO_3^- there was no measurable oxidation wave cathodically shifted versus that of free host for either **2** or **4**. This supports the stability constant data that showed NO_3^- complexes to be the least stable of the anions studied. In the voltammograms of **2** and **4** with $H_2PO_4^-$, the oxidation potential of the complex was unresolved with the only notable change seen as broadening of the host oxidation and reduction waves.

To gain insight into the observed oxidation waves at higher potentials in the voltammograms of chloride and nitrite complexes of **2** and **4**, we studied solutions of the tetrabutylammonium salts of each anion in the absence of host by cyclic voltammetry. For example, voltammograms of **2** and **4** in the presence of 0.5 equiv of TBACl include an oxidation wave at 379 mV relative to Fc/Fc^+. This wave broadens and shifts to greater potentials upon addition of more TBACl, reaching a maximum of approximately 700 mV. The voltammogram of TBACl in the absence of host confirms that this oxidation is due to the chloride anion. Others have also reported on the oxidation of TBACl in CH_3CN.[26] In the case of receptor **2**, the second oxidation wave of the host is obscured by this chloride oxidation. Likewise, other oxidation processes in addition to those assigned to **2** and **4** were present in the voltammograms of the nitrite complexes. These are attributed to the oxidation of the nitrite anion because two oxidation waves at 209 and 629 mV relative to Fc/Fc^+ were observed in the voltammogram of $TBANO_2$ in the absence of host. The remaining anions did not oxidize in the window of study (0 to 1300 mV vs Ag/AgCl).

TABLE 2. Hydrogen Bond Data for 1[a]

donor	acceptor	N−H···O (Å)	H···O (Å)	N−H···O (deg)
N1−H1a	O1	3.025	2.145	151.4
N2−H2a	O1	3.060	2.180	155.1
N1a−H1aa	O1b	3.010	2.129	151.7
N1b−H1ba	O1a	3.058	2.178	156.3

[a]Atom labels are shown in Figure 7.

X-ray Crystallography. Functionalized ureas are of considerable interest as building blocks that form persistent hydrogen-bonded chains in the design of novel materials with targeted structures.[20] For example, crystallographic properties of **3** have previously been described by Nangia and co-workers in their studies of H-bond-induced urea tape structures for crystal engineering applications.[20a] Molecules of **3** form extended chains in the solid state through hydrogen bonding interactions between the carbonyl O atom of one molecule and the neighboring N−H functionalities of the urea subunit of a second molecule. A second hydrogen bonding interaction between C−H moieties of

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(26) (a) Kádár, M.; Takáts, Z.; Karancsi, T.; Farsang, G. *Electroanalysis* **1999**, *11*, 809–813. (b) Kolthoff, I. M.; Coetzee, J. F. *J. Am. Chem. Soc.* **1957**, *79*, 1852–1858. (c) Sereno, L.; Macagno, V. A.; Giordano, M. C. *Electrochim. Acta* **1972**, *17*, 561–575.

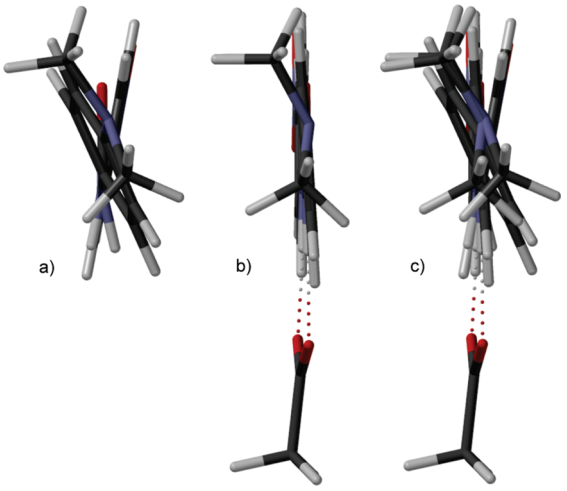

FIGURE 8. DMol3 DFT calculated structures of (a) neutral receptor **3** and (b) **3**·CH_3COO^-; (c) overlay of neutral receptor **3** and **3**·CH_3COO^-.

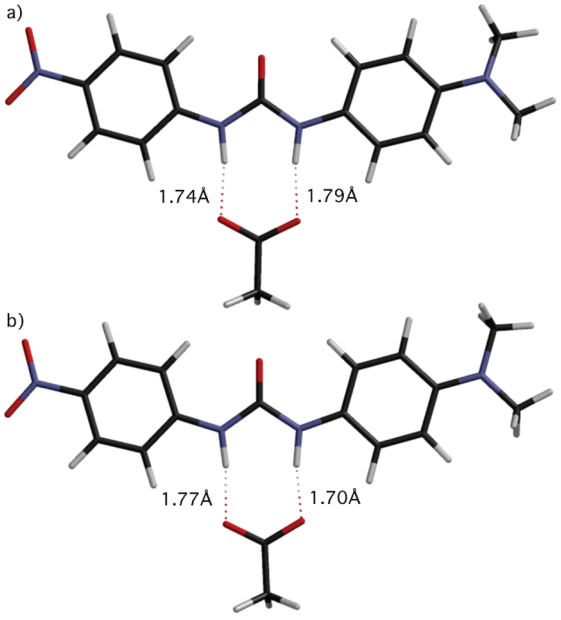

FIGURE 9. Comparison of DMol3 DFT calculated structures of (a) the acetate complex of neutral receptor **3** and (b) the acetate complex of singly oxidized receptor **3**.

the terminal methyl groups and the O atoms of the nitro groups on molecules in adjacent chains results in an overall "urea tape" α network, a 2-D layer of hydrogen-bonded molecules of **3**. In the course of our work, we also crystallized **3**, though by slow evaporation of an acetone/methanol solution. An X-ray analysis showed the same crystallographic parameters and resultant structure as reported by Nangia and co-workers.

To gain insight into the hydrogen bonding interactions in **1** (and, by inference, **2**), a crystal of **1** suitable for X-ray analysis was obtained by slow evaporation of an acetonitrile solution. Molecules of **1**, like **3**, form extended 1-D chains held together by hydrogen bonding between the urea N−H groups and neighboring carbonyl O atoms. Subunits of the two distinct chains present in the structure are shown in Figure 7 with selected distances and angles for the hydrogen bonding listed in Table 2. There are three crystallographically unique molecules per asymmetric unit. All three have disordered phenyl rings. The site occupancies for the disordered molecules have been refined independently, but the extent of the disorder came to the same value for all three molecules. One of the unique molecules is the repeat unit in one chain (Figure 7a) with each successive molecule rotated 180° with respect to its neighbor. The other two crystallographically unique molecules alternate to comprise the second chain (Figure 7b). The H-bond donor−acceptor distances (3.010−3.060 Å) firmly place these H-bonds into Jeffrey's "moderate, mostly electrostatic" category (2.5−3.2 Å).[27] It should also be noted that, unlike what is observed in the crystal of **3**, there are no interchain hydrogen bonds in the structure of **1**.

Computational Studies. Wurster's crown ethers and their alkali metal complexes have been studied previously via ab initio methods.[28] For the present work, a series of ab initio DFT studies of neutral receptor **3** as both free host and complexed with acetate were carried out to represent the anion complexation for this class of receptors. The singly oxidized host was also studied. The calculated structure of uncomplexed **3** shows that the free host is clearly nonplanar (Figure 8a). Acetate complexation causes a move toward greater planarity (Figure 8b). This change is likely due to the greater complementarity of a planar bidentate guest anion to a host offering near-parallel H-bonds and the increased conjugate character of the complexed host conferred by binding acetate. The complexed singly oxidized host is slightly less planar than the complexed neutral host; the dihedral angle involving the dimethylamino group is 4.1° in the complex (it is 0.5° in the oxidized free host), whereas the nitroaniline group has a dihedral angle of 0.3° (versus 0.6° in the oxidized free host).

The calculated structure for the neutral host **3** complexed with acetate reveals a distinct asymmetry in N···H···O distances: 2.79 Å (1.74 Å NH···O) on the nitrophenyl side of the urea and 2.83 Å (1.79 Å NH···O) on the redox active dimethylaminophenyl side (Figure 9a), a difference of 0.05 Å. The calculated structure of the singly oxidized host **3** with acetate (Figure 9b) shows a difference in the acetate positioning in the complex. While the H-bonding is asymmetric in (a), it is interesting that the long−short ordering changes upon oxidation. The shortest H-bond distance corresponds to the oxidized host and is on the NH on the redox-active dimethylaminophenyl side of the urea (2.75 Å N···H···O; 1.70 Å NH···O). It is also apparent that there is H-bond shortening upon oxidation of the host, and this is a logical result of the electron density decrease on the host molecule. Oxidation of the host also results in coplanarity of the dimethylamino group and shortening of the N−C(aryl) bond of the urea (neutral 1.43 Å; oxidized 1.39 Å). As seen in the X-ray structure of **1**, the donor−acceptor distances for the H-bonds in the calculated structure of **3** fit the "moderate, mostly electrostatic" category described by Jeffrey.[27]

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(28) Sargent, A. L.; Mosley, B. J.; Sibert, J. W. *J. Phys. Chem. A* **2006**, *110*, 3826–3837.

Conclusion

We have presented the first full anion recognition study of urea-containing receptors based on Wurster's reagent, *p*-TMPD. The electrochemically active phenylenediamine subunits retain redox activity despite functionalization with an electron-withdrawing urea group. Both receptors **2** and **4** demonstrate electronic communication through the urea carbonyl with the symmetric, two redox center-containing compound **2** showing a distinct oxidation for each phenylenediamine moiety. In the asymmetric receptor **4**, the electron-withdrawing effect of the nitro group is felt through the urea carbonyl, as evidenced by the higher oxidation potential of the phenylenediamine unit versus that in **2**. Both **2** and **4** form stable complexes with anions that were monitored by cathodic shifts in the oxidation potentials of the hosts. The sequences of log *K* values of **2** and **4** follow the basicities of the oxoanions[12] with greater binding enhancement upon host oxidation occurring for the complexes with the larger *K* values. Modeling studies on the asymmetric receptor **3** reveal that complexation with acetate induces a hydrogen bond on the nitro side that is shorter than that on the dimethylaminophenyl side (1.74 vs 1.79 Å). Upon oxidation of the host, the complex is changed such that the hydrogen bond from the electron-deficient, oxidized aminophenyl side becomes the shorter of the two, 1.70 Å, and that of the nitro lengthens to 1.77 Å.

Experimental Section

Determination of Association Constants by Titration. Tetrabutylammonium salts were obtained in their anhydrous forms. All solutions were prepared using anhydrous CH_3CN (or anhydrous CD_3CN for NMR studies). Hygroscopic salts were maintained in their dry state by storing under dry argon in a glovebox. Salts were weighed under argon and not exposed to air prior to solution preparation.

Via ^{1}H NMR Spectroscopy. The following is a typical example of the procedure used. A solution of 1,3-bis{4-[bis(2-methoxy-ethyl)-amino]-phenyl}-urea **4** (5.0 mM) in CD_3CN was prepared, and a known volume (600 μL) was added to a standard NMR tube. The ^{1}H NMR spectrum was then collected for this sample at 298 K. Aliquots of a solution of tetrabutylammonium acetate (70.0 mM) in CD_3CN were then added to the NMR tube. After each addition, the contents of the tube were mixed well, and a spectrum collected. Fifteen additions were made: additions 1−12 were 5 μL; additions 13, 14, and 15 were 10, 15 and 30 μL, respectively. Spectra were analyzed and peak measurements were taken. Numbers were analyzed and curves were fitted using the HypNMR 2006 software package to derive a value for *K*, the equilibrium constant of association.[29]

Via UV−vis Spectrophotometry. The following is a typical example of the procedure used. To a 1 cm path length quartz cuvette was added 2.5 mL of anhydrous CH_3CN, and the cuvette was stoppered. The cuvette was allowed to equilibrate at 298 K for 10 min. A blank UV−vis spectrum was then measured. The cuvette was unstoppered, the solvent was removed, and the cuvette was dried. A known volume (2.5 mL) of a solution of 1,3-bis{4-[bis(2-methoxy-ethyl)-amino]-phenyl}-urea **4** (0.035 mM) in CH_3CN was added to the cuvette, and the cuvette was stoppered. The cuvette was allowed to equilibrate at 298 K for 10 min, and then a UV−vis spectrum representative of the free host was measured. Aliquots of a solution of tetrabutylammonium acetate (3.5 mM) in CH_3CN were then added to the cuvette. After each addition, the contents of the tube were mixed well using a miniature stirring bar, and a spectrum was collected at 298 K. Fifteen additions of 5 μL were made. Spectra were analyzed, and curves were fitted with the HYPERQUAD software package.[30]

Electrochemistry. Cyclic voltammetry was performed using a conventional three-electrode configuration consisting of a platinum disk working electrode, platinum wire auxiliary electrode, and Ag/AgCl reference electrode. Anhydrous CH_3CN was used in the preparation of all solutions. Electrochemical grade tetrabutylammonium perchlorate, $[Bu_4N]ClO_4$, was used as the supporting electrolyte. (*WARNING: perchlorate salts are potentially explosive. They should be handled in small quantities and with caution.*) Typically, a known volume (5 mL) of a receptor solution (2 mM) in 0.1 M $[Bu_4N]ClO_4$ supporting electrolyte was placed in a single-compartment electrochemical cell and purged with nitrogen gas while stirring for 10 min. Stirring was stopped and a nitrogen atmosphere was maintained above the solution while the experiment was in progress, and all electrodes were cleaned after each run. Coordination studies were performed by the addition of 0.5 molar equiv of a tetrabutylammonium salt, followed by another 0.5 molar equiv (thus bringing the overall salt concentration to 1 molar equiv), and finally by the addition of a further 4 molar equiv of salt. Tetrabutylammonium salts of the monovalent anions acetate, benzoate, dihydrogenphosphate, chloride, nitrite, and nitrate were employed for this work. Free host potentials are cited versus the ferrocene/ferrocenium (Fc/Fc^+) couple at room temperature at a scan rate of 100 mV s^{-1}.

X-ray Crystallography. X-ray experimental data for **1**, $C_{17}H_{22}N_4O$. Crystals grew as colorless needles by slow evaporation from DMSO. The data crystal was a needle that had the approximate dimensions $0.37\times0.07\times0.04$ mm^3. The data were collected on a diffractometer using a graphite monochromator with Mo Kα radiation ($\lambda = 0.71073$ Å). A total of 223X frames of data were collected using ω-scans with a scan range of 1.8° and a counting time of 263 s per frame. The data were collected at 153 K. Details of crystal data are listed in Table 3. Data reduction was performed using DENZO-SMN.[31] The structure was solved by direct methods using SIR97[32] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[33] The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2×Ueq of the attached atom (1.5×Ueq for methyl hydrogen atoms). The function $\Sigma w(|F_o|^2 - |F_c|^2)^2$ was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.0701*P)^2 + (9.7055*P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.228, with $R(F)$ equal to 0.0767 and a goodness of fit, S, = 1.10. Definitions used for calculating $R(F)$, $R_w(F^2)$, and the goodness of fit, S, are given below Table 3. The data were checked for secondary extinction effects, but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[34] Figures were generated using ORTEP-3 for Windows.[35]

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(35) Ortep-3 for Windows: Farrugia, L. J. *J. Appl. Crystallogr.* **1997**, *30*, 565.

TABLE 3. Crystal Data for receptor 1

formula	$C_{17}H_{22}N_4O$
M	289.39
color	colorless
dimension (mm)	0.37 × 0.07 × 0.04
crystal system	monoclinic
space group	$C2/c$
a [Å]	36.9809(13)
b [Å]	9.4549(7)
c [Å]	21.9873(11)
α [deg]	90
β [deg]	126.232(2)
γ [deg]	90
V [Å^3]	6201.3(6)
Z	16
ρ_{calcd} [g cm^{-3}]	1.278
μ Mo Kα [mm^{-1}]	0.083
scan type	ω-scans
θ range [deg]	1.85−25.00
measured reflns	10237
unique reflns	5468
R_{int}	0.0658
R1, wR2 (strong data)[a]	0.0767, 0.1818
R1, wR2 (all data)[a]	0.1842, 0.2281
GOF[b]	1.126
refined parameters	479
max/min residuals [e Å^{-3}]	0.604/−0.304

[a] $R1 = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|\}$ for reflections with $F_o > 4(\Sigma(F_o))$, $wR2 = \{\Sigma w(|F_o|^2 - |F_c|^2)^2/\Sigma w(|F_o|)^4\}^{1/2}$ where w is the weight given each reflection. [b] $[\Sigma w(|F_o|^2 - |F_c|^2)^2/(n-p)]^{1/2}$, where n is the number of reflections and p is the number of refined parameters.

Computational Methods. All DMol3 DFT calculations[36a,b] employed the Becke−Tsuneda−Hirao gradient-corrected functional[36c,d] with double numerical plus polarization basis sets, a 20 bohr cutoff, and a fine integration grid and ran to the default convergence criteria of 10^{-6} Hartrees for the SCF and 10^{-3} hartrees/bohr for the gradient in geometry optimizations.

Details of Synthetic Procedures. All reactions were carried out under dry argon unless stated otherwise. Solvents were purchased commercially as HPLC or ACS grade. All other commercially available reagents were used as purchased.

1,3-Bis(4-dimethylaminophenyl)urea 1. Compound **1** was prepared using the method for preparing derivatized ureas of Yan et al.[21] A mixture of urea (0.47 g, 7.8 mmol), *N*,*N*-dimethyl-*p*-phenylenediamine (1.8 g, 13 mmol, 1.7 equiv), $NaHSO_3$ (0.24 g, 2.3 mmol, 0.30 equiv), CH_3COOH (0.27 mL, 4.7 mmol, 0.60 equiv), and H_2O (50 mL) was stirred at reflux for 48 h. The reaction mixture was cooled to room temperature, and the product was filtered. The residue was washed with hot water to remove residual urea and unreacted amine to yield **1** as an off-white solid (2.0 g, 85% yield): mp 259 °C; ^{1}H NMR (270.17 MHz, $CDCl_3$, TMS) δ 2.82 (6H, s, C*H*$_3$), 6.68 (4H, d, Ar-*H*, J = 9.2 Hz), 7.23 (4H, d, Ar-*H*, J = 8.9 Hz), 8.13 (2H, s, N*H*); ^{13}C NMR (67.93 MHz, DMSO-d_6) δ 41.7, 114.0, 120.4, 131.0, 146.9, 154.0, 164.2. MS(CI) m/z 299 (M^+); HRMS(CI) m/z 299.1873 (M^+) (calcd for $C_{17}H_{22}N_4O$, m/z 299.1872).

1,3-Bis{4-[bis-(2-methoxyethyl)amino]phenyl}urea 2. Compound **2** was prepared from **6** and urea using an identical method to that for **1**. Yield: 63%; mp 134 °C; ^{1}H NMR (270.17 MHz, $CDCl_3$, TMS) δ 3.35 (12H, s, C*H*$_3$), 3.53 (16H, m, C*H*$_2$), 6.43 (2H, s, N*H*), 6.68 (4H, d, J = 8.4 Hz, Ar−*H*), 7.15 (4H, d, J = 8.9 Hz, Ar-*H*); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 51.4, 59.1, 70.1, 112.8, 124.9, 126.9, 145.9, 155.5. MS(CI) m/z 475 (M^+); HRMS(CI) m/z 475.2921 (M^+) (calcd for $C_{25}H_{38}N_4O_5$, m/z 475.2920).

1-(4-Dimethylaminophenyl)-3-(4-nitrophenyl)urea 3. This compound was previously prepared by Reddy et al. and synthesized via the same procedure for the present work.[20]

1-{4-Bis(2-methoxyethyl)amino]phenyl}-3-(4-nitrophenyl)urea 4. To a round-bottom flask (100 mL) were added **6** (0.59 g, 2.6 mmol), dichloromethane (20 mL), and triethylamine (0.73 mL, 5.3 mmol, 2.0 equiv). To this stirring mixture was added dropwise a solution of 4-nitrophenylisocyanate (0.48 g, 2.9 mmol, 1.1 equiv) in dichloromethane (20 mL). The reaction was allowed to stir for 16 h under argon. The reaction mixture was placed directly on a column (Al_2O_3) and eluted with 2% methanol:dichloromethane. The product-containing fractions were combined, and the solvent was removed under reduced pressure. The residue was dissolved in hot methanol and filtered, and the filtrate was allowed to cool to room temperature and then placed in a refrigerator at 5 °C for 16 h, after which time orange crystals were observed. The crystals were removed by filtration, washed with diethyl ether, and then dried under vacuum for 24 h to give pure **4** as an orange crystalline solid (0.72 g, 70% yield): mp 158 °C; ^{1}H NMR (270.17 MHz, $CDCl_3$, TMS) δ 3.37 (6H, s, C*H*$_3$), 3.57 (8H, m, C*H*$_2$), 6.40 (s, NH), 6.74 (2H, d, Ar-*H*, J = 8.9 Hz), 6.96 (s, NH), 7.13 (2H, d, Ar-*H*, J = 8.9 Hz), 7.52 (2H, d, Ar-*H*, J = 9.2 Hz), 8.14 (2H, d, Ar-*H*, J = 9.2 Hz); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 51.0, 59.1, 70.1, 112.5, 118.1, 125.1, 127.3, 142.5, 144.9, 153.7. MS(CI) m/z 389 (M^+); HRMS-(CI) m/z 389.1825 (M^+) (calcd for $C_{19}H_{24}N_4O_5$, m/z 389.1825).

***N*,*N*-Bis(2-methoxyethyl)-4-nitrophenylamine 5.** Bis(2-methoxyethyl)amine (1.50 g, 11.3 mmol), 1-fluoro-4-nitrobenzene (4.77 g, 33.8 mmol, 2.99 equiv), and sodium carbonate (5.97 g, 56.3 mmol, 4.98 equiv) in DMF (30 mL) were stirred under argon at 90 °C for 24 h. The solvent was removed by distillation at reduced pressure. The residue was dissolved with a mixture of water (50 mL) and dichloromethane (50 mL). The phases were allowed to separate and the water phase was discarded. The organic phase was dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The resulting yellow oil was purified via column chromatography (silica gel eluted with 1% methanol:chloroform) to yield **2** as a yellow oil (2.61 g, 94%): ^{1}H NMR (270.17 MHz, $CDCl_3$, TMS) δ 3.36 (6H, s, C*H*$_3$), 3.59 (4H, t, C*H*$_2$, J = 5.7 Hz), 3.68 (4H, t, C*H*$_2$, J = 5.7 Hz), 6.68 (2H, d, Ar-*H*, J = 9.6 Hz), 8.09 (2H, d, Ar-*H*, J = 9.1 Hz); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 51.3, 59.2, 69.9, 110.6, 126.3, 137.1, 153.0. MS(CI) m/z 255 (M^+).

***N*,*N*-Bis(2-methoxyethyl)benzene-1,4-diamine 6.** A mixture of **5** (2.00 g, 7.87 mmol) and 10% Pd/C (0.335 g, 0.315 mmol, 0.0400 equiv) in ethyl acetate (60 mL) was stirred under an atmosphere of H_2 at room temperature for 48 h. The solid catalyst was removed via filtration and washed with dichloromethane (20 mL). The solvent mixture was removed from the filtrate under reduced pressure to yield **3** as a brown oil (1.64 g, 95%): ^{1}H NMR (270.17 MHz, $CDCl_3$, TMS) δ 3.33 (6H, s, C*H*$_3$), 3.46 (8H, m, C*H*$_2$), 6.63 (4H, m, Ar-*H*); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 52.1, 59.0, 70.5, 115.3, 116.9, 137.7, 141.7. MS(CI) m/z 225 (M^+).

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Supporting Information Available: Materials and methods; ^{1}H and ^{13}C NMR spectra for all compounds; table of Cartesian coordinates and DFT/BOP/DNP energies of optimized molecular structures; X-ray crystallographic data for **1** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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