Molecular Recognition at an Organic−Aqueous Interface: Heterocalixarenes as Anion Binding Agents in Liquid Polymeric Membrane Ion-Selective Electrodes

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Abstract: Poly(vinyl chloride) (PVC)-derived ion-selective electrodes (ISEs) have been prepared from a neutral anion binding receptor, *meso*-octamethylcalix[4]pyrrole (**1**). Analogous systems were also prepared from the novel pyridine-containing analogues of **1**, namely dichlorocalix[2]pyrrole[2]pyridine (**2**) and tetrachlorocalix[4]pyridine (**3**). At lower pH values (i.e., 3.5 and 5.5), ISEs derived from **1** display strong anionic (negative slope) responses toward Br^-, Cl^-, and $H_2PO_4^-$ and, to a much lesser extent, F^-. By contrast, at high pH (i.e., pH 9.0) ISEs derived from **1** not only display cationic (positive slope) responses toward chloride and bromide anions but also selectivities (i.e., $Br^- < Cl^- < OH^- \approx F^- < HPO_4^{2-}$) that are non-Hofmeister in nature. This is considered consistent with the PVC-supported receptor **1** behaving as a direct anion binding agent at low pH but acting, at least in part, as an hydroxide-complexing receptor at higher pH. For the ISEs based on **2** and **3**, no special non-Hofmeister selectivity is observed at pH 9.0. However, at lower pH values both increased anionic responses and improved selectivities for hydrophilic anions (e.g., F^- and $H_2PO_4^-$) are observed. These observations are rationalized in terms of protonation effects involving the pyridine-containing receptors from which these ISEs are derived. For all the receptors discussed in this paper, the addition of tridodecylmethylammonium chloride (TDDMA), a known lipophilic additive, serves to increase the magnitude of the ISE response but only at the price of greatly reduced anion selectivity.

Introduction

Calix[4]pyrrole (**1**), dichlorocalix[2]pyrrole[2]pyridine (**2**), and tetrachlorocalix[4]pyridine (**3**) (Figure 1) constitute a matched set of macrocyclic analogues that, under conditions where the pyridine subunits remain unprotonated, should act as relatively strong, intermediate, and weak anion binding agents, respectively.[1] Recent solution-phase studies, carried out in dichloromethane-d_2, have served to confirm that calix[4]pyrrole **1**, although a neutral entity, does indeed act as an effective anion receptor, showing selectivities for $F^- > Cl^- > H_2PO_4^-$.[2] On the basis of solid-state structural studies and low-temperature ^{19}F NMR spectroscopic analyses, this recognition behavior is currently rationalized in terms of an ability to stabilize nonisotropic pyrrole NH-anion hydrogen bonds.[3] Since systems **2** and **3**, in their neutral forms, should be far less effective hydrogen bond donors than **1**, appropriate intercomparisons among the matched set of heterocalixarene analogues defined by **1**−**3** could provide important further support for this critical mechanistic proposal. Toward this end, we have prepared poly(vinyl chloride) (PVC)-derived ion selective electrodes (ISEs) containing receptors **1**−**3** and wish to report here that the calixpyrrole-based system **1** shows strong, non-Hofmeister anion-selective responses under conditions where the dichlorocalix[2]pyrrole[2]pyridine and tetrachlorocalix[4]pyridine-based systems do not.

Carrier-based ISEs constitute an established set of analytical tools that in optimal cases can provide a convenient means of detecting selectively one or more analytes within a complex mixture. In point of fact, it is primarily the stability constant of the ion−carrier complex that dictates the operational selectivity of a given sensor.[4] From a more mechanistic perspective, the potentiometric response of membrane-based ISEs containing a specific ligand can be used to provide information about the mode of analyte binding as well as, at least potentially, molecular insights into the details of the relevant substrate−receptor interactions. Not surprisingly, therefore, the construction of ISEs is particularly interesting from the perspective of the supramolecular chemist; such systems could provide a convenient method for characterizing, under interfacial organic−aqueous conditions, the substrate binding characteristics of receptors that might not otherwise be amenable to study in the presence of water due to, e.g., poor aqueous solubility and/or overly weak binding affinities. ISEs are also of obvious interest because they can help translate the chemistry of new substrate binding systems into tools that can be used to recognize selectively various targeted species in the presence of potentially interfering analytes. In the specific case of anion recognition,

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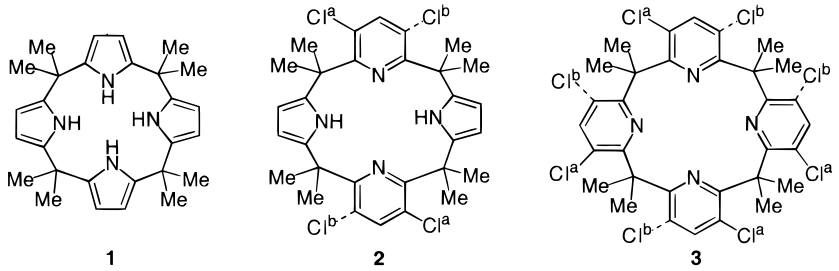

Figure 1. Structures of investigated receptors **1**−**3**. Receptors **2** and **3** were obtained and studied as a mixture of isomers. Thus, in these structures each of the individual pyridine subunits bears a single chlorine substituents at either the 3 or 5 positions (Cl^a or Cl^b), but not both.

this approach has been explored extensively by Umezawa, Meyerhoff, Simon, Reinhoudt, and others using a range of receptors including protonated sapphyrins[5] and protonated polyamines[5] as well as a variety of Lewis acidic systems such as metalloporphyrins[6,7,9−12] uranylsalenophenes,[8] metallocenes,[13] other organometallic derivatives,[14,15] and fluorinated compounds.[16] Not yet studied as potential sensory elements, however, are neutral, nonaromatic anion-binding agents such as calix[4]pyrrole **1** and its analogues. ISEs based on these newer materials are the subject of this paper.

Experimental Section

Reagents. High molecular weight poly(vinyl chloride) (PVC), 2-nitrophenyl octyl ether (*o*-NPOE), tridodecylmethylammonium chloride (TDDMA), and tetrahydrofuran (THF; stored over 3 Å molecular sieves) were purchased from Fluka Chemika A.G. (Germany). The sodium salts of fluoride, chloride, bromide, and di- and hydrophosphates were purchased from Lachema s.p. (Brno, Czech Republic). All reagents were of the highest grade commercially available and used without further purification. Distilled water was used to prepare standard solutions.

Syntheses of *meso*-octamethylcalix[4]pyrrole (**1**), dichlorocalix[2]-pyrrole[2]pyridine (**2**), and tetrachlorocalix[4]pyridine (**3**) have been reported previously.[1,2]

Membranes and Cell Assembly. PVC-membranes based on **1**−**3** were made by adding the appropriate receptor to a mixture of PVC and plasiticizer (*o*-NPOE) both in the presence and absence of an ancillary lipophilic additive, tridodecylmethylammonium chloride (TDDMA). The resultant mixtures, made up as per Table 1, were then taken up in THF (ca. 0.7 mL per 100 mg of resultant mixture), poured into a metallic tube, and allowed to dry for 24 h. A circle (diameter, 12 mm; thickness, 0.15 mm) was cut out from the resulting polymeric disk. Membranes obtained in this way were then fixed on a polymeric mounting ring (inner diameter: 8 mm) and mounted on a liquid membrane-type ISE body obtained from Crytur, Monokrystaly s.p. (Turnov, Czech Republic). Control electrodes, containing just TDDMA, were also prepared using an analogous approach. The cell assembly for potentiometric measurements was as follows:

$$Hg/Hg_2Cl_2,\ KCl\ (satd)|3\ M\ KCl|test\ solution|$$
$$modified\ PVC\ membrane|0.01\ M\ KCl|Ag/AgCl$$

EMF Measurements. Potentiometric measurements were made using a digital voltammeter, model M1T330, obtained from Metra Blansko s.p. (Czech Republic). The reference electrode was a Hg/Hg_2Cl_2, KCl (satd) electrode obtained from Crytur, Monokrystaly s.p. (Turnov, Czech Republic). The pH was monitored using glass electrode Type 01-29 B (Labio Prague, Czech Republic) on a pH-Meter type OP-205/1 (Budapest, Hungary). Before each set of measurements, the electrodes were soaked in water and adjusted to the relevant experimental pH by means of added NaOH or H_2SO_4, in the absence of analyte (for at least 5−10 min and sometimes overnight). All potentiometric measurements were carried out at ambient temperature.

Analyte solutions were prepared by diluting stock solutions with water adjusted to the experimentally desired pH by means of added NaOH or H_2SO_4. Calibration curves were constructed by plotting the observed potential vs the logarithm of the concentration of the substrate present in the analyte solution. Key parameters, namely sensitivity (S, mV/decade) and linear working range (M), were then deduced and

Table 1. Composition of Membranes Based on Receptors **1**−**3** and TDDMA

		composition, wt %			
membrane	active component	active component	cationic additive	plasticizer	PVC
■	**1**−**3**	1.0		66.0	33.0
●	**1**−**3**	1.0	0.2	65.9	32.9
control experiment	TDDMA	0.2		66.5	33.3

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Table 2. Potentiometric Sensitivity toward Anions of PVC-Membranes Based on **1**−**3** as a Function of pH and Lipophilic Additive,TDDMA[a]

		pH = 3.5		pH = 5.5		pH = 9.0	
		■	●	■	●	■	●
anion	active component	S, mV/decade (linear range, M)	S, mV/decade (linear range, M)	S, mV/decade (linear range, M)	S, mV/decade (linear range, M)	S, mV/decade (linear range, M)	S, mV/decade (linear range, M)
F^-	**1**	−4 (10^{-3}−10^{-1})	−34 (10^{-3}−10^{-1})	−7 (10^{-3}−10^{-1})	−28 (10^{-2}−10^{-1})	−4 (10^{-4}−10^{-1})	−3 (10^{-4}−10^{-1})
	2	−28 (10^{-2}−10^{-1})	−47 (10^{-3}−10^{-1})	−8 (10^{-3}−10^{-1})	−25 (10^{-3}−10^{-1})	+10 (10^{-3}−10^{-1})	+30 (10^{-2}−10^{-1})
	3	−31 (10^{-3}−10^{-1})	−42 (10^{-3}−10^{-1})	−16 (10^{-2}−10^{-1})	−27 (10^{-4}−10^{-1})	+7 (10^{-4}−10^{-1})	−6 (10^{-4}−10^{-1})
	TDDMA		−86 (10^{-2}−10^{-1})		−25 (10^{-2}−10^{-1})		−10 (10^{-2}−10^{-1})
Cl^-	**1**	−20 (10^{-4}−10^{-1})	−26 (10^{-4}−10^{-1})	−5 (10^{-3}−10^{-1})	−22 (10^{-4}−10^{-1})	+15 (10^{-3}−10^{-1})	−4 (10^{-4}−10^{-1})
	2	−4 (10^{-4}−10^{-1})	−3 (10^{-4}−10^{-1})	+8 (10^{-4}−10^{-1})	−25 (10^{-4}−10^{-1})	+15 (10^{-2}−10^{-1})	0 (10^{-4}−10^{-2})
	3	−13 (10^{-3}−10^{-1})	−36 (10^{-4}−10^{-1})	−6 (10^{-3}−10^{-1})	−44 (10^{-4}−10^{-1})	0 (10^{-4}−10^{-1})	−26 (10^{-3}−10^{-1})
	TDDMA		−46 (10^{-3}−10^{-1})		−37 (10^{-4}−10^{-1})		−21 (10^{-3}−10^{-1})
Br^-	**1**	−25 (10^{-4}−10^{-1})	−38 (10^{-}−10^{-1})	−20 (10^{-4}−10^{-1})	−40 (10^{-3}−10^{-1})	+19 (10^{-2}−10^{-1})	0 (10^{-4}−10^{-1})
	2	−10 (10^{-3}−10^{-1})	−47 (10^{-4}−10^{-1})	+2 (10^{-4}−10^{-1})	−42 (10^{-3}−10^{-1})	−13 (10^{-2}−10^{-1})	+1 (10^{-2}−10^{-1})
	3	−18 (10^{-3}−10^{-1})	−43 (10^{-4}−10^{-1})	−12 (10^{-3}−10^{-1})	−43 (10^{-4}−10^{-1})	−4 (10^{-2}−10^{-1})	−17 (10^{-3}−10^{-1})
$H_2PO_4^-$/ HPO_4^{2-}	**1**	−16 (10^{-2}−10^{-1})	−12 (10^{-3}−10^{-1})	0 (10^{-4}−10^{-1})	−9 (10^{-3}−10^{-1})	0 (10^{-4}−10^{-1})	−2 (10^{-2}−10^{-1})
	2	−14 (10^{-3}−10^{-1})	−35 (10^{-2}−10^{-1})	+13 (10^{-3}−10^{-1})	−14 (10^{-3}−10^{-1})	+19 (10^{-3}−10^{-1})	−14 (10^{-2}−10^{-1})
	3	−18 (10^{-3}−10^{-1})	−32 (10^{-2}−10^{-1})	+16 (10^{-3}−10^{-1})	−28 (10^{-3}−10^{-1})	0 (10^{-4}−10^{-1})	−15 (10^{-3}−10^{-1})
	TDDMA		−21 (10^{-2}−10^{-1})		−30 (10^{-2}−10^{-1})		−13 (10^{-2}−10^{-1})

[a] Columns ■ and ● refer to experiments carried out in the absence and presence of TDDMA, respectively, whereas those denoted as just TDDMA (rows) refer to control experiments involving PVC-supported ISEs containing TDDMA as the sole anion recognition species. See text for details.

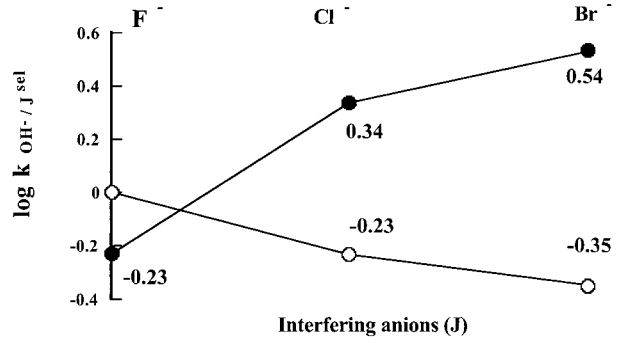

Figure 2. Response selectivities for PVC-membranes based on receptors **1** (open circles) and **2** (closed circles) for OH^- relative to halides (i.e., log $k_{OH^-/J}^{sel}$, where $J = F^-$, Cl^-, and Br^-) at pH 9.0. In these experiments, the selectivity factors (log $k_{I/J}^{sel}$) were determined using the matched potential method[17] as described in the text.

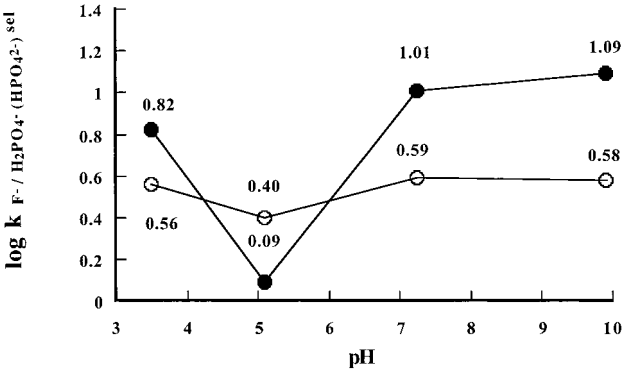

Figure 3. Response selectivities and pH effects for PVC-membranes based on receptors **1** (open circles) and **2** (closed circles) for $H_2PO_4^-$ vs HPO_4^{2-} relative to F^- (i.e., log $k_{F^-/H_2PO_4^-(HPO_4^{2-})}^{sel}$). In these experiments, the selectivity factors (log $k_{I/J}^{sel}$) were determined using the matched potential method[17] as described in the text.

collected in Table 2 (cf. Results and Discussion). In certain instances, especially those wherein a non-Nernstian response was observed, the selectivity factor ($k_{I/J}^{sel}$) was measured using the matched potential method;[17] these results are displayed in Figures 2 and 3.

Results and Discussion

Receptors **1**−**3**, being rather understudied heterocalixarene derivatives, could constitute a homologous series of molecular receptors that might prove useful in the design and assembly of novel electrochemical-based sensors, electrodes, and other supramolecular devices. To test this possibility in a realistic fashion, we elected, for the reasons outlined in the Introduction, to study these materials as potential sensory elements in standard liquid membrane ion-selective electrodes (ISEs). Here, our fundamental goal was to investigate the effects of pH on the magnitude of the ISE response and its contribution, if any, to the potentiometric discrimination that ISEs containing receptors **1**−**3** might display toward the following anions: F^-, Cl^-, Br^-, and ($H_2PO_4^-$/HPO_4^{2-}). A priori, it was expected that, in the case of receptors **1**−**3**, respectively, the selectivity observed toward a given anion would be governed by: (i) what were for the most part specific (i.e., anisotropic) hydrogen-bonding interactions, (ii) a combination of both hydrogen-bonding interactions and generalized Coulombic effects that might be difficult to deconvolute, and (iii) almost purely Coulombic effects.

Given the above, it was expected that the following equilibria, of fundamental molecular recognition interest, would prove critical in terms of mediating the production of a putative potentiometric response:

$$B^+_s + A^-_s + L_m \leftrightarrow B^+_m + L\,A^-_m \quad (1)$$

$$H^+_s + L_m \leftrightarrow LH^+_m;\ A^-_s + LH^+_m \leftrightarrow LH^+\,A^-_m \quad (2)$$

$$H^+_s \leftrightarrow H^+_m \quad (3)$$

$$A^-_s \leftrightarrow A^-_m \quad (4)$$

$$B^+_s \leftrightarrow B^+_m \quad (5)$$

Here, L and LH^+ refer to the free and protonated forms, respectively, of a given receptor (i.e., **1**, and **2**, or **3**); B^+ and H^+ represent cationic species such as sodium cation and protons, respectively; A^- represents the anionic analyte species under consideration; and subscripts s and m refer to species either present in the bathing solution or contained in the membrane, respectively.

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As can be seen from an inspection of Table 2, ISEs made up from calix[4]pyrrole **1** display both anionic (negative slope) and cationic (positive slopes for Cl^- and Br^-) responses at pH 3.5−5.5 and 9.0, respectively. The anionic response observed at lower pH was as expected, since, under these conditions, **1** should act as a straightforward anion-binding receptor. By contrast the weak cationic response seen at pH 9.0 was not. It is currently rationalized in terms of **1** showing a high selectivity for OH^- and a rather low affinity for Cl^- or Br^-. The ensuing strong interactions between the PVC-supported calix[4]pyrrole and hydroxide anion could lead to the formation of what is effectively a negatively charged complex within membrane phase. This negatively charged complex, in turn, would attract various cations into the polymer membrane with the resulting partitioning leading to the observation of a positive potentiometric response as is indeed seen by experiment (i.e., Donnan failure).[4]

The above proposal, which would also translate into a modest potentiometric anion response, is consistent with potentiometric selectivity studies carried out at pH 9.0 using OH^- as the primary anion. The resulting log $k_{OH^-/J}^{sel}$ values, where $J = F^-$, Cl^-, and Br^-, are plotted in Figure 2 and serve to demonstrate that ISEs derived from **1** deviate from the so-called Hofmeister selectivity series at pH 9.0. In particular, a selectivity order of $Br^- < Cl^- < OH^- \approx F^- < HPO_4^{2-}$ is observed, whereas one of $HPO_4^{2-} \approx OH^- \approx F^- < Cl^- < Br^-$ would be predicted if pure Hofmeister behavior were observed.[18]

With F^- as the analyte, no special cation-exchange mechanism needs to be invoked at pH 9.0. On the other hand, little sensitivity toward this anion was noted over any portion of the 3.5 < pH < 9.0 range studied (the so-called *S* values for F^- range from between −4 and −7 mV/decade in the absence of added TDDMA; cf. Table 2). Such behavior, which is not generally seen in the case of ISEs based on stronger cation-derived anion receptors (cf. control systems based on TDDMA only in Table 2), is thought to reflect the high hydration energy of fluoride anion and kinetic limitations that derive therefrom.[19] In particular, because of its very high free energy of hydration, the process of fluoride anion complexation within the PVC phase would be extremely slow if the transition state associated with anion recognition involved nonsolvated ions.

Not inconsistent with the low sensitivity observed toward F^- is the finding that TDDMA-free ISEs based on **1** are more selective for $H_2PO_4^-/HPO_4^{2-}$ than F^- over a wide range of pH (cf. Table 2 and Figure 3) even though the converse is true in homogeneous dichloromethane solution (for **1**, the relevant K_a values are 17 170 and 97 M^{-1} for F^- and $H_2PO_4^-$, respectively[2]). Apparently, the near-equal experimental and Gibbs hydration enthalpies for these two anions −510 and −522, −465 and −465, for F^- and $H_2PO_4^-$, respectively serves to mask any differences in organic phase binding affinity.[20]

In ISEs derived from receptor **2**, it is expected that both the pyrrolic groups and the pyridine nitrogen atoms will govern the selectivity of the system. For instance, at high pH where the pyridine nitrogens are not expected to be protonated and where internal NH···N (pyrrolic NH···pyridine) hydrogen bonds might pertain, ISEs based on **2** lose functionality. Indeed, the selectivity pattern for such systems at pH 9.0 is fully reversed compared to that for ISEs derived from **1** ($F^- < OH^- < Cl^- < Br^-$; Figure 2) and becomes just what one would expect based on a consideration of the Hofmeister series. This result, which is underscored by the data in Table 2, leads us to conclude that under these more basic conditions the sensing characteristics of ISEs based on **2** are in large measure defined by the substrate lipophilicity rather than some intrinsic property of the receptor. Positive (cationic) deviations are also seen at this pH.

At pH 5.5, it is expected that some fraction of the pyridine centers present in **2** will be protonated (pK_a for pyridinium cation = 5.19[21]). Such protonation processes will serve not only to generate positive sites within the macrocyclic core that can interact with anionic substrates but also to "liberate" the pyrrole NH donor functionality from internal NH···N (pyrrolic NH··· pyridine) hydrogen bonds. Thus, an overall improvement in the anion-binding efficiency is expected at this pH. In point of fact, the sensitivity toward F^- (−8 mV/decade) observed for a PVC-membrane ISE based on **2** at this pH is similar to the one observed for ISEs based on **1** at pH 3.5. On the other hand, a rather weak potentiometric response toward chloride, phosphate, and bromide anions is seen for ISEs based on **2** at this pH, with similar observations being made in the case of ISEs based on **3**.

At pH 3.5, the potentiometric response of ISEs based on **2** is greatly increased, as is that of ISEs based on **3**. In both cases, a high level of pyridine protonation and the ready availability of both pyrrole- and pyridine-based NH hydrogen bond donor functionality is expected to improve anion binding. Indeed, both systems show response sensitivities toward fluoride and phosphate anions that are enhanced relative to those seen for ISEs based on **1** (Table 2). With the exception of Cl^- in the case of **2**, this is also true for the halide anions, bromide and chloride. This is consistent with the normal, neutral NH···anion hydrogen-bonding motif of the calixpyrroles being augmented by electrostatic interactions involving the protonated pyridine centers.

The above results can be rationalized in terms of the response function of PVC membranes based on **2** being defined by two underlying and competing mechanisms, namely receptor-derived anion recognition and anion-exchange processes involving the protonated form of the receptor. In fact, ISEs based on **2** are effective carriers for cations (H^+, Na^+) as well as for anions. Indeed, the response of ISEs based on **2**, as well as those based on **3**, may be considered as being that of a pH-sensitive membrane whose basic properties are modulated by an interference-like sensitivity toward anions. For such systems, the extent of anion interference will be a function of (i) the basicity constant (K_b) of the ligand, (ii) the nature and quantity of any ancillary anions present in the sample solution, and (iii) the concentration of the primary cation in the sample, in this case H^+.[22] Thus, at low pH values the membrane-supported ISE based on **2** shows a strong anion response in the presence of F^- (−28 mV/decade), $H_2PO_4^-$ (−14 mV/decade), and a slight, interference-like effect in the presence of either Cl^- (−4 mV/decade) or Br^- (−10 mV/decade). At pH 5.5, the anion interference disappears ($H_2PO_4^-$/ HPO_4^{2-}, Cl^-, Br^-) or becomes increasingly less apparent as is true for F^- (−8 mV/decade) with similar trends being observed for the ISEs based on **3**. At pH 9.0, by contrast, ISE membranes containing receptor **2** display a positive deviation, an effect ascribed to cation interference. While this cation interference clearly serves to modulate the anion binding behavior of ISEs based on receptor **2**, in marked contradistinction to what is true for analoguous systems containing calixpyrrole **1**, the anion selectivities observed at very high pH appear in this instance to reflect not

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only the lipophilicity of a given anion but also its ability to complex with the embedded receptor. On the basis of previous solution-phase studies, this latter critical feature is known to correlate quite well with size.[1−3] Thus, the selectivity factor (log $k_{I/J}^{sel}$) observed at pH 9.0 for ISEs based on **2**, namely $F^- < OH^- < Cl^- < Br^- < HPO_4^{2-}$ (cf., Figures 2 and 3), is considered consistent with the idea that both anion lipophilicity and size play competing influential roles. On a more global level, the very fact that the response order for F^-, OH^-, and HPO_4^{2-} is reversed compared to what would be predicted based on a consideration of the Hofmeister series ($HPO_4^{2-} < OH^- < F^-$) serves to establish unequivocally that the response selectivities for ISEs containing **2** are influenced, at least to a considerable degree, by the intrinsic anion-binding properties of the embedded receptor.

One further feature of the ISEs based on **2** that is worth highlighting is that the pH-dependent nature of the binding phenomena makes the fluoride-to-phosphate selectivities of these electrodes quite different from those derived from **1**. Indeed, while these latter systems show pH-independent behavior, ISEs based on **2** display selectivity factors (log $k_{F^-/H_2PO_4^-(HPO_4^{2-})}^{sel}$) that are constant between pH 10 and 7.25, dip down to a minimum at pH 5.1, and then are increased at pH 3.5. Thus, it appears that the special protonation characteristics of mixed calixpyrrole-calixpyridine receptors such as **2** can be potentially exploited to generate ISE systems that are fine-tuned in terms of their anion selectivities simply by choosing appropriately the conditions of the experiment.

To understand better the mechanistic origins of the above results, the potentiometric characteristics of PVC-membranes based on **1**−**3** with added TDDMA were surveyed. It was observed that the cationic responses seen in many cases disappeared upon the addition TDDMA (Table 2). These results support the idea that the observed positive response is the result of cation exchange within the membrane phase. Other, more generalized background effects are also seen upon the addition of TDDMA. For instance, the pH-dependence of the potentiometric response for ligands **2** and **3** is, in large measure, seen to disappear. Likewise, the higher relative sensitivity toward F^- seen for ISEs based on **2**, as compared to **1**, is found to be diminished in the presence of TDDMA. In fact, in a more generalized sense, the anion selectivity patterns observed for all three receptors **1**−**3** is found to be reduced in the presence of TDDMA. However, the absolute response of the ISEs containing TDDMA toward various anions is seen to be increased relative to that of the original receptor-only derived systems. This is consistent with the TDDMA-containg ISEs acting as cation-exchange mediators and interacting with anions via straight electrostatic interactions (i.e., Coulombic attractions).

Conclusions

In summary, the potentiometric selectivity for membrane ISEs (PVC-membranes) based on dichlorocalix[2]pyrrole[2]pyridine (**2**) and tetrachlorocalix[4]pyridine (**3**) toward a range of investigated anions, namely F^-, Cl^-, Br^-, $H_2PO_4^-/HPO_4^{2-}$, was found to be pH dependent. In the specific case of the hybrid system **2**, the potentiometric selectivity reflects the presence of both pyridinium-derived Coulombic attractions and "pure" calixpyrrole-like pyrrole NH···anion hydrogen-bond donation interactions, as is particularly apparent in analyzing the ISE response toward hydrophilic anions such as fluoride and phosphate. Also potentially important in the case of this receptor are proton-induced receptor deformations and adjustments to the binding cavity size, effects that could help rationalize the lower selectivities seen for the larger halides Cl^- and Br^-. Such protonation effects are not believed to be operative in the case of the ISEs based on **1**. Here, pure pyrrole NH···anionic substrate hydrogen-bonding interactions are thought to mediate anion recognition. As a consequence, the potentiometric selectivity of ISEs based on **1** is for the most part pH independent. However, some small changes in potentiometric response for Cl^- and Br^- are observed that most likely reflect the greater lipophilicity of these anions.

On a more forward-looking level, the present results lead us to suggest that the calixpyrroles and their derivatives could have an important role to play in the generation of PVC-based ISEs. The fact that anti-Hofmeister anion recognition behavior is seen for receptors **1** and **2** under experimental conditions whose defining attributes include a well-defined aqueous sample/membrane interface leads us to propose further that, using these systems or close analogues, key insights into the mode and mechanism of binding could be obtained for a range of other anionic analytes, including ones such as nucleotides, salycilates, and barbituates, that are of obvious biological importance.

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