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Fluorinated calixpyrroles: anion-binding extractants that reduce the Hofmeister bias

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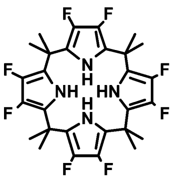
β-Octafluoro-*meso*-octamethylcalix[4]pyrrole (1) and β-decafluoro-*meso*-decamethylcalix[5]pyrrole (2) were found to extract caesium salts of smaller anions (bromide and chloride for 1 and nitrate for 2) as effectively as that of iodide into nitrobenzene (NB) thereby overcoming the Hofmeister bias normally observed for processes of this type.

β-Fluorinated calix[4]pyrrole **1** and calix[5]pyrrole **2**, strong, neutral anion-binding agents, were found to transport small anions effectively while overcoming the classical solvation-based Hofmeister anion bias selectivity. These two receptors showed an ability to extract smaller anions (Br^- and Cl^- for **1** and NO_3^- and F^- for **2**) as effectively as iodide into nitrobenzene (NB). The present results also provide a rare case of liquid–liquid extraction of inorganic salts effected using an anion receptor in the absence of a cation co-extractant.



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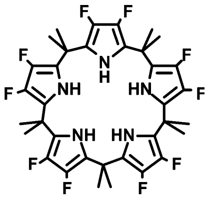

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Recently, considerable effort has been devoted to the problem of developing new, efficient anion receptors.[1,2] This interest reflects the ubiquity of anions in biology, as well as their importance in applications such as sensing, transport, and separations. Among the systems being developed, neutral anion-binding systems are of particular interest, in part because they could be exploited in liquid–liquid distribution systems designed to effect the separation of a selected anion or ion pair. In this regard, the anion host can be viewed as a counterpart to the cation extractants that have traditionally been used to transport inorganic salts into an organic phase.[3]

For small charge-dense anions, efficient extractions are often difficult to achieve,[3] due to the highly positive Gibbs energy of anion partitioning.[4] This solvation-based selectivity bias in favor of large, charge-diffuse anions constitutes the Hofmeister effect,[5] a phenomenon that is ubiquitous in liquid–liquid and related distribution systems.[6] Hence, an important scientific challenge, with implications for separations and sensing applications, is to overcome this natural tendency in order to gain control over selectivity.

The use of anion receptors to offset the normal Hofmeister anion selectivity in liquid–liquid systems is, in fact, known. In the area of membrane electrodes[2d] and membrane transport,[7] considerable success has been achieved using receptors containing Lewis acid sites.[1,2] By contrast, receptors possessing only hydrogen-bond donor (HBD) groups have been less successful, with but a few reports of evidence for non-Hofmeister extractive behavior.[8] Nonetheless, studies employing HBD anion extractants used alone[8b,9] or in "dual-host" combinations of independently functioning cation and anion extractants[10] have served to demonstrate that HBD anion receptors can be used to weaken or attenuate the Hofmeister effect. It has also been noted[6] that non-Hofmeister selectivity should be attainable in principle through hydrogen-bond donation at least as strong as that of the source phase, water.

One set of anion receptors that could provide the needed HBD strength are the polyfluorinated calix[*n*]pyrroles **1** and **2**. These are relatively new members[11] of a venerable class of macrocycles, the so-called calix[*n*]pyrroles, that have attracted attention recently because they act as simple-to-make anion-binding agents.[12] Replacement of the β-pyrrolic protons by electron-withdrawing fluorine atoms considerably increases the affinity of calix[4]pyrroles for anions.[11b,13] It also permits the isolation of several higher-order calix[*n*]pyrroles, including the β-decafluoro-*meso*-decamethylcalix[5]pyrrole **2**. The high anion affinities displayed by **1** and **2**[11,13] led us to explore whether they could be used to effect anion-selective separations in a liquid–liquid distribution system involving a series of caesium salts of widely varying anion size.

For our experimental purposes, a model system for study was sought in which complexation is simple and competing effects such as ion-pairing and strong anion solvation are minimized. Nitrobenzene (NB) thus seemed the ideal water-immiscible diluent, as it has a high dielectric constant (ε = 34.8) and low HBD strength; coincidentally, NB is closely related to the mobile phases used in membrane electrodes.[2d] By analogy to cation-recognition systems,[3] the simple equilibrium behavior given below (where R is the anion receptor) was therefore expected to be approached as a working hypothesis in the case of relatively extractable caesium cations:

$$\mathrm{Cs^+\,(aq) + X^-\,(aq) \rightleftharpoons Cs^+\,(org) + X^-\,(org)} \tag{1}$$

$$\mathrm{Cs^+\,(aq) + X^-\,(aq) + R\,(org) \rightleftharpoons Cs^+\,(org) + R{\cdot}X^-\,(org)} \tag{2}$$

Based on previous ^{1}H-NMR spectroscopic studies of **1** and **2**,[11] formation of a simple 1 : 1 anion–calixpyrrole complex in the organic phase was considered likely. To the extent this assumption and those inherent in eqns. (1) and (2) hold, the heterogeneous anion extraction selectivity should be governed by two factors, namely 1) anion partitioning between the two immiscible phases and 2) formation of the anionic receptor–anion complex in the organic phase.

Fig. 1 compares the distribution ratio ($D_{\mathrm{Cs}} = [\mathrm{Cs}]_{\mathrm{org}}/[\mathrm{Cs}]_{\mathrm{aq}}$) for various caesium salts CsX (X = ClO_4^-, I^-, NO_3^-, Br^-, Cl^-, or F^-) from water into NB with or without receptors **1** or **2** at 10 mM. In these experiments, D_{Cs} was measured as a

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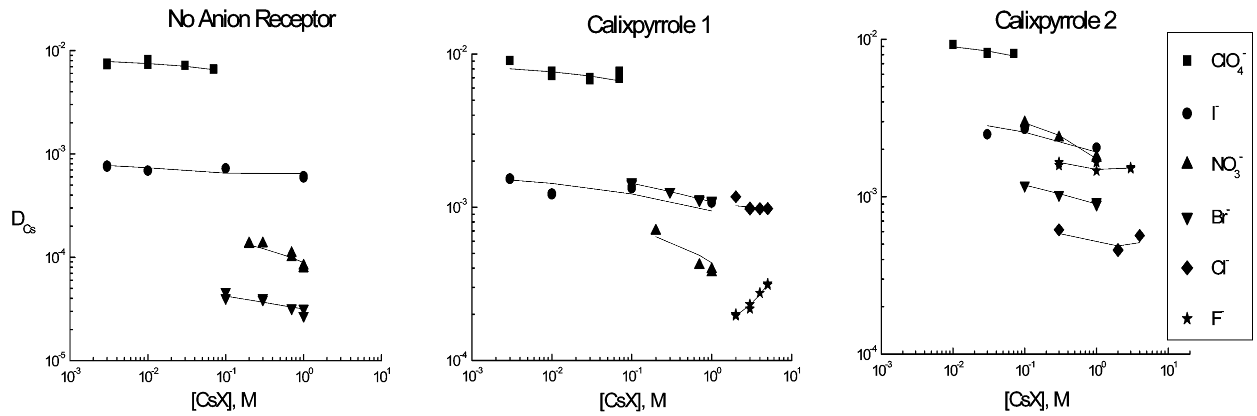

Fig. 1 Extraction of caesium salts from water into neat nitrobenzene (NB) (left) or 10 mM solutions of **1** (middle) or **2** (right) in NB. Aqueous phase: CsX + 0.1 mM HX ($X^- = ClO_4^-$, I^-, NO_3^-, Br^-, Cl^-, or F^-). Equal volumes of organic and aqueous phases were gently agitated for 2 h at 25 °C. Experimental uncertainty in the caesium distribution ratios D_{Cs} is ±5%.

function of the aqueous salt concentration using ^{137}Cs tracer techniques described earlier.[14] In the absence of **1** or **2**, the expected Hofmeister bias is apparent in the observed extraction order $ClO_4^- > I^- > NO_3^- > Br^-$, corresponding to the decrease in anion radius. The extraction of CsCl and CsF into the organic phase was undetectable ($D_{Cs} < 10^{-5}$). By contrast, **1** or **2** strongly enhances the extraction of the salts of small anions, with a marked departure from Hofmeister bias. Extraction of $CsClO_4$ is not enhanced significantly, and that of CsI only weakly. Interestingly, **1** and **2** displayed somewhat different anion selectivities. Receptor **1** exhibited little discrimination among Cl^-, Br^-, and I^-, anions that were extracted more effectively than NO_3^- and F^-. Receptor **2** exhibited a preference for NO_3^- and F^- comparable with that observed for the more lipophilic anion I^-, while the Hofmeister order was preserved for other halogen anions $I^- > Br^- > Cl^-$.

The non-monotonic dependence of D_{Cs} on anion radius caused by the fluorinated calixpyrroles is rationalized in terms of the preferential binding of Cl^- and Br^- by **1** and NO_3^- and F^- anions by **2**. This observation is consistent with previously observed homogeneous selectivity of **1** toward Cl^-, at least relative to Br^- and NO_3^-. Nonetheless, it is remarkable that **1** and **2** put the ion-pair extraction of the highly hydrophilic anions Cl^- and F^-, respectively, nearly on par with that seen for normally much more extractable I^-. This leads us to predict that β-fluorinated calixpyrroles could have an important role to play in effecting the separation of hydrophilic anions in, for example, radioactive-waste remediation.

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