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Surprisingly Selective Sulfate Extraction by a Simple Monofunctional Di(imino)guanidinium Micelle-Forming Anion Receptor

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We report a novel di(imino)guanidinium anion extractant with unparalleled selectivity for sulfate in a liquid-liquid separation system. In addition to a 4.4 order-of-magnitude enhancement in affinity compared to a standard benchmark, our alkylated di(imino)guanidinium receptor is economically synthesized and features good compatibility with application-relevant aliphatic solvents. Small-angle X-ray scattering results reveal the formation of reverse-micelles, which together with the significant organic-phase water content challenge traditional notions of selectivity in extraction of superhydrophilic anions.

Superhydrophilic anions such as sulfate are notoriously difficult to separate from aqueous solutions.[1] This is attributed to their high free energies of hydration (−1080 kJ mol^{-1} for sulfate),[2] which make their removal from aqueous solutions very unfavorable in comparison to less hydrophilic anions (e.g., −381 kJ mol^{-1} for chloride). Targeted separation of superhydrophilic anions from aqueous solutions is necessary for a range of important applications, including processing radioactive wastes,[1a] oil production,[3a] desalination,[3b] resource recovery,[3c] and carbon capture.[3d] Crystallization has been among the oldest and most effective techniques, historically using inorganic cations such as Ba^{2+} to exploit strong lattice energies. Organic systems incorporating molecular-recognition principles have allowed deliberate control of selectivity in anion binding[4–5] as broadly reflected in a variety of separations.[1,5] For crystallization of oxoanions, we have achieved success by, for example, organizing urea hydrogen-bond donor groups to coordinatively saturate the 12 theoretical coordination sites of sulfate to selectively outcompete the strong hydration.[6] An alternative, recently explored approach to anion recognition is to bind hydrated anions, either within hydrophobic cavities of hosts in aqueous solutions[7a] or with hydrogen-bonding ligands in the crystalline state.[7b] Along the latter line, we recently demonstrated that sulfate can be crystallized as a partially hydrated ion using bispyridylguanidinium or bisiminoguanidinium ligands,[8] circumventing the energy cost of complete dehydration yet yielding very high selectivity. This inspired us to introduce the synthetically accessible iminoguanidinium functionality into liquid-liquid extractants by rendering them lipophilic through substitution with hydrophobic groups. Contrasting with crystallization, liquid-liquid extraction of superhydrophilic anions like sulfate entails unique challenges. Namely, the selectivity of anion extraction into oil generally follows the persistent Hofmeister series, favoring extraction of less hydrophilic anions,[1] and hydrophilic anions tend to retain their hydration shells in oil, leading to uncontrolled aggregation and phase transitions. While it was anticipated that adapting the iminoguanidinium group for extraction would be a stepping stone to synthesis of more elaborate multifunctional lipophilic receptors, we discovered and report here the astonishing selectivity of the starting point, a simple monofunctional iminoguanidinium extractant for sulfate over competing chloride, to our knowledge the most selective sulfate extractant yet reported.

Our prototype di(imino)guanidinium reagent (DIG, Scheme 1) in its chloride form, bearing lipophilic functionalities on either side of the core hydrogen-bond donor group, features a readily approachable synthesis and unusually high solubility in aliphatic oils. The synthesis (see SI) was effected in three-steps with a high overall yield of 68.8%, a marked improvement compared with that for hydrophilic guanidinium receptors (typically <10–15%).[9] The DIG-Cl salt is freely soluble in Isopar L, a branched isoparaffinic hydrocarbon solvent widely used in industrial solvent extraction. As shown below, working concentrations of at least 0.5 M are accessible without addition of polar modifiers. By contrast, the benchmark tri(C_{8-10})alkylmethyl quaternary ammonium chloride extractant Aliquat 336 (A336), used in hydrometallurgical solvent extraction,[10] can only be dissolved to 0.006 M in Isopar L without modifier.

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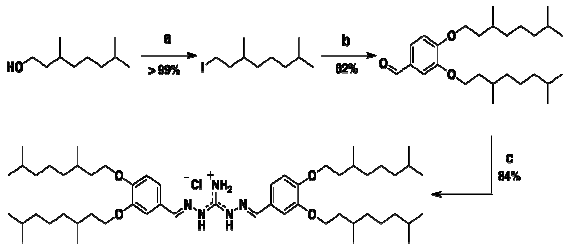

Scheme 1. Synthetic route giving DIG-Cl. The reagents for each step of the synthesis of DIG-Cl are as follows: a. imidazole, iodine, triphenylphosphine; b. 3,4-dihydroxybenzaldehyde, potassium carbonate; c. 1,3-diaminoguanidinium chloride.

As shown in Figure 1, DIG at 1–30 mM in 1,2-dichloroethane (DCE) far outperforms A336 in selective extraction of sulfate in competition with 100-fold excess chloride. Using $^{35}SO_4^{2-}$ tracer, distribution ratios ($D(SO_4^{2-})$ = $[SO_4^{2-}]_{org}/[SO_4^{2-}]_{aq}$, where the subscripts refer to the phase analyzed) for DIG reach 1470 at 30 mM, while A336 reaches only 0.052, 28,000 times less. In Isopar L, *D* reaches 5300. Insolubility of A336 prevented any measure of sulfate extraction by A336 in Isopar L (see SI). Using the separation factor, defined as the ratio of *D* values for two different ions (*SF* = $D(SO_4^{2-})/D(Cl^-)$), as the metric for selectivity, DIG achieves a maximum *SF* of 4300 in comparison with a maximum of 0.02 for A336. To put *SF* = 4300 in perspective, SF values > 1 for sulfate vs. chloride even for elaborately designed receptors are rare.[1a] The low values for A336 show that, as expected, A336 with no hydrogen-bond donor ability is not effective for liquid-liquid separation of sulfate from chloride. We therefore infer a remarkably selective hydrogen-bonding interaction between DIG and the sulfate anion.

The gradients in the plots of log(*D*) versus log[R] in Figure 1 suggest a complicated and changing extraction stoichiometry that likely involves extensive aggregation. Sulfate anion exchange by the chloride form of cationic receptors such as DIG is most simply represented by

$$2[R^+Cl^-]_{org} + SO_4^{2-}{}_{(aq)} \rightleftharpoons [R_2^+SO_4^{2-}]_{org} + 2Cl^-{}_{(aq)} \qquad (1)$$

However, complex mechanisms are more frequently encountered where molecular aggregates are involved with various aggregation numbers *x* and *y* according to (2) for the case of low sulfate loading:

$$\frac{y}{x}[R_x^+Cl_x^-]_{org} + SO_4^{2-}{}_{(aq)} \rightleftharpoons \left[R_y^+Cl_{(y-2)}^-SO_4^{2-}\right]_{org} + 2Cl^-{}_{(aq)} \quad (2)$$

A gradient of 2 is consistent with the mechanism outlined in (1), and one expects such behavior for low concentrations of extractant or use of polar diluents. If aggregates are involved as shown in equilibrium (2), then the gradient will be *y*/*x*. With caution not to over-analyze the sparse data, it may be noted that the extraction experiments using DIG-Cl in 1,2-DCE show initial gradients that are roughly 2 (i.e., 2.0 for 1,2-DCE and 1.9 for Isopar L), suggesting the simple equilibrium (1). However, depending on the diluent, the curves exhibit a nonlinear dependence overall, consistent with aggregation occurring with changing stoichiometry as the DIG concentration increases. The apparent decrease in slope to 0.3 at high concentration in Isopar L suggests that the reactant aggregates become larger than the product aggregates. Alternatively, we can question whether the extraction is correctly represented as purely anion exchange. Current efforts are directed at elucidating the mass-action behavior.

DIG-Cl in Isopar L was found to be highly hydrated. To investigate the role of water in the formation of stable receptor-anion complexes in the oil phase, the uptake of water by DIG-Cl in oil was measured by Karl Fischer titrations (see SI). The water content of Isopar L solutions of DIG-Cl in equilibrium with pure water increased linearly with DIG-Cl concentration in the range 0.005–0.5 M with a slope of 2.519 ± 0.002. Water is thus involved in the solvation of the DIG-chloride in the solvent phase.

Consistent with the presence of appreciable concentrations of water in oil and concentration dependence in the extraction data (Figure 1), X-ray scattering shows that reverse micelles may be present. Reverse micelles form in amphiphile-oil-water mixtures to minimize exposure of the hydrophilic core to the hydrophobic solvent. They are manifested as nanoscale clusters made up from water, ions, and amphiphile 'head-groups' (see SI). To investigate the structure of the proposed reverse micelles, small-angle X-ray scattering (SAXS) measurements were performed with varying concentration of DIG in Isopar L. SAXS works on the principle that X-rays interact with fluctuations in electron density within a material

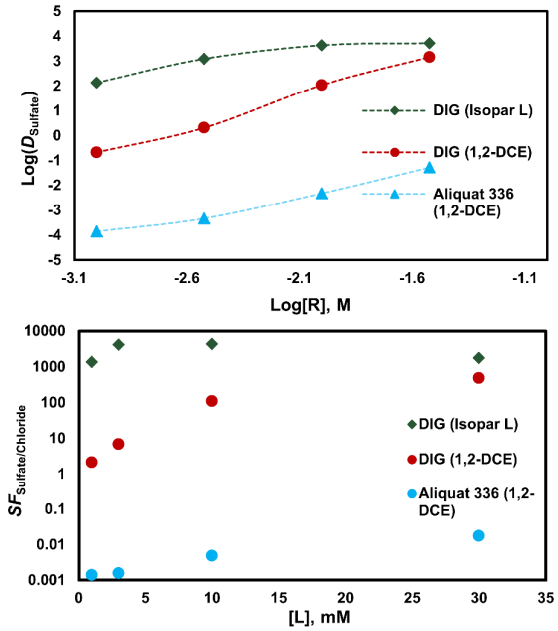

Figure 1. TOP: Log(*D*) for sulfate plotted against log[R], where [R] is the concentration of extractant. Aqueous phase was 0.1 mM Na_2SO_4 and 10 mM NaCl. Equal phase volumes were mixed at 25.0 ± 0.2 °C. Data for (Aliquat 336) A336 in Isopar L are not shown because of its low solubility. BOTTOM: Comparison of separation factors (*SF*) for sulfate over chloride for various concentrations of DIG and A336.

and are scattered, yielding information on nanoscale morphology. For reverse micelles, the electron-dense cores scatter X-rays against the surrounding aliphatic medium (see SI). Figure 2(a) shows the SAXS data after subtracting the incoherent scattering from the background Isopar L solvent. The form of the scattering data is typical for 'particle scattering',[11] which is consistent with reverse micellar aggregates. With increasing extractant concentration, a broad correlation peak emerges at q = 1.5 nm^{-1}, which is typical for concentrated colloidal systems that do not flocculate (i.e., particles that repel).[11] This suggests that DIG-Cl forms nanoscale colloidal structures in Isopar L that remain particle-like in nature across a large concentration range, without flocculation or growth into interconnected mesophases.

To derive real-space information from the scattering data, the generalized indirect Fourier transform (GIFT) method was applied using the Percus-Yevick hard-sphere structure factor model to account for the interactions at concentrated conditions (this method is described in numerous publications and is summarized in the SI).[12] The GIFT analysis generates pair distance distribution functions (PDDFs, Figure 2b) from the scattering data that correspond to the average morphology of the scattering particles. Across the concentration range, the PDDFs are all bell-shaped functions that are consistent with spherical particles.[14] The volume fraction of these particles (assumed to be inverted micelles), their average radius and aggregation number of DIG-Cl per scattering particle (calculated from the GIFT analysis; see SI) is presented in Figure 2(c-e). This shows that increasing DIG-Cl concentration drives the formation of colloidal particles that increase moderately in volume fraction, size, and aggregation number. An increase in aggregation number of DIG-Cl species is consistent with a decrease in the slope of the extraction data in Figure 1. The metrics presented in Figure 2(c-e) are comparable to the large reverse micelles encountered in water-in-oil microemulsions stabilized by surfactants,[12] suggesting that DIG-Cl behaves like a surfactant in the liquid-liquid system. These large reverse micelles are remarkably stable to flocculation and mesophase formation across the concentration range, especially considering the water-saturating conditions.

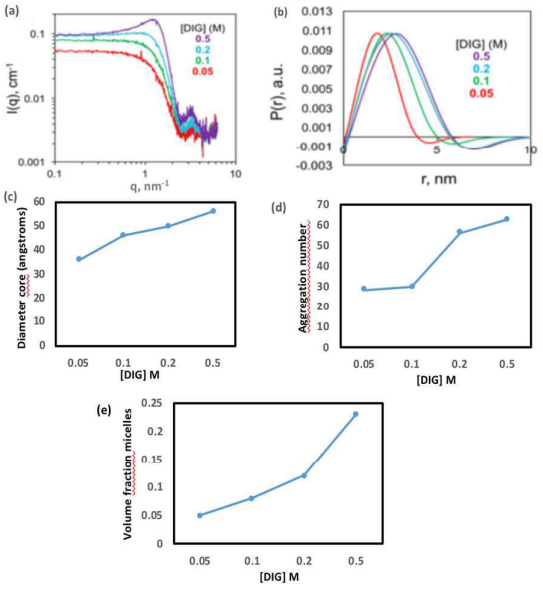

Figure 2. (a) SAXS and (b) PDDF for varying DIG-chloride concentration in Isopar L after equilibration with water. (c) diamete of micelles. (d) variation of micelle volume fraction. (e) DIG aggregation number with concentration.

Our DIG receptor is remarkable in both the unparalleled high selectivity for sulfate over chloride as well as the unique ability to solubilize the superhydrophilic ion pairs in the aliphatic hydrocarbon solvent. Our previous crystallization studies suggest that the ability of iminoguanidinium groups to separate sulfate originates from the binding of the partially hydrated anion.[8] This previous work, as well as the high water concentration in the oil that coincides with the formation of reverse micelles, leads us to speculate that sulfate-water clusters are also extracted by our DIG-Cl receptor in the liquid-liquid system. Experiments are currently in progress to examine the aggregation behaviour of the DIG system in the presence of sulfate. Sulfate is known to require 12 H-bond donors to satisfy its coordination sphere,[6] and these cannot come from the aliphatic Isopar L solvent (unlike 1,2-DCE). The X-ray structural analysis of the sulfate salt of a smaller analog of DIG (the four branched aliphatic chains were replaced by Me groups) with single crystals grown from water/DMSO, revealed the aggregation of four DIG receptors around sulfate, with the guanidinium groups coordinating the anion via six NH···O hydrogen bonds (Figure 3). The sulfate is additionally coordinated by a water molecule via an OH···O hydrogen bond, and by a DMSO molecule via 2 CH···O hydrogen bonds. Thus, for steric reasons, the sulfate anion cannot accommodate six guanidinium groups to achieve coordination saturation even with the smaller DIG analogue, and it reaches out to solvent molecules to increase its coordination number. With the larger lipophilic DIG analog used in the extraction experiments, we expect that even fewer DIG molecules can be packed around the anion, which requires a larger number of solvating water molecules to complete the sulfate coordination. Therefore, it is logical to assume that the significant quantities of water in the oil, likely in

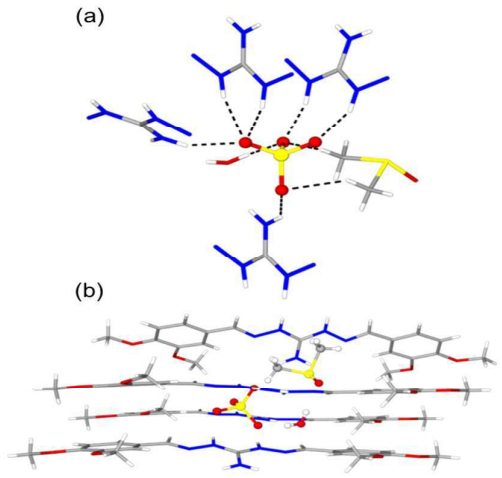

Figure 3. X-ray crystal structure of $(DIG)_2SO_4(H_2O)(DMSO)$ in which DIG has been truncated to methyl groups. (a) Sulfate hydrogen bonding by 4 guanidinium groups, one water and one DMSO solvent molecules, with a total anion-coordination number of 9. (b) Packing of 4 DIG receptors around the partly solvated sulfate anion.

reverse micelles, are involved in solvating the extracted superhydrophilic anion. The remarkable propensity to form spherical colloid-like aggregates that resist flocculation across a wide concentration range allows this reagent to be deployed at high concentrations, as needed for many process applications.

In summary, we report a new anion receptor that gives unparalleled selectivity for sulfate over chloride in a liquid-liquid extraction system. The remarkable selectivity and stable phase properties may originate from the extraction of partially hydrated anions into reverse micelles. In addition to a 4.4 orders-of-magnitude increase in sulfate vs. chloride selectivity (relative to an industrial benchmark), our receptor is simple, easily synthesized, and is uniquely compatible with application-relevant solvents. This is the first selective and process-compatible extractant for sulfate, finally enabling effective liquid-liquid separation processes for superhydrophilic anions.

Acknowledgments

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Conflicts of interest

The authors declare no competing financial interest.

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