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Enhanced liquid–liquid anion exchange using macrocyclic anion receptors: effect of receptor structure on sulphate–nitrate exchange selectivity

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When certain macrocyclic anion receptors are added to a chloroform solution of the nitrate form of a lipophilic quaternary ammonium salt (methyltri-$C_{8,10}$-ammonium nitrate, Aliquat 336N), the extraction of sulphate from an aqueous sodium nitrate solution via exchange with the organic-phase nitrate is significantly enhanced. Eight macrocycles were surveyed, including two derivatives of a tetraamide macrocycle, five derivatives of calix[4]pyrrole and β-decafluorocalix[5]pyrrole. Under the hypothesis that the enhancement originates from sulphate binding by the anion receptors in the chloroform phase, it was possible to obtain reasonable fits to the sulphate distribution survey data based on the formation of 1:1 and 2:1 receptor:sulphate complexes in the chloroform phase. Apparent 1:1 sulphate-binding constants obtained from the model in this system fell in the range $\log K_{bind} = 2.1–4.8$. Comparison of the results for the various anion receptors included in this study reveals that sulphate binding is sensitive to the nature of the substituents on the parent macrocycle scaffolds in a way that does not follow straightforwardly from simple chemical expectations, such as electron-withdrawing effects on hydrogen-bond donor strength.

Keywords: liquid–liquid anion exchange; anion binding; macrocycle; calixpyrrole; equilibrium model; extraction

1. Introduction

With the development of the coordination chemistry of anions (*1*), the utility of anion receptors continues to expand into various applications (*2–7*). These uses include, for example, sensing, ion-selective electrodes, drug development, catalysis, electron-transfer modelling, template synthesis and separations. Such applications all have in common the critical anion-binding process that in large part provides the needed selectivity and driving force. Although selective binding is commonly equated with 'recognition', Lehn long ago pointed out that recognition also requires an associated function that in essence 'reads out' the chemical information created in the binding process (*8*). The function coupled to the binding event typically provides for a useful change in the chemical or physical properties of the system, for example redox potentials, emission lifetimes, spectral signatures, diffusivity, reactivity, etc. Therein arises a fundamental chemical question regarding the extent to which the intended function alters the binding process and vice versa. In this report, we show how neutral anion receptors may be employed in a relatively novel application (*9*, *10*) to impart selectivity in the functional process of liquid–liquid anion exchange. In essence, anion binding occurring in a water-immiscible organic phase contacted with an aqueous electrolyte solution effects a redistribution of the anions between the two phases. In experimentally observing anion recognition in terms of the altered anion extractability in such systems, we are therefore endeavouring in the 'big picture' to understand how the overall selectivity obtained can be related to the inherent selectivities of the underlying binding and ion-partitioning processes and to the mutual influence of these processes.

An abundance of neutral anion receptors has appeared in the past three decades, representing a potentially useful pool of molecules that can be exploited for extraction chemistry (*1–3*). In order to function in extraction, the receptors must be lipophilic, and for those that are not, it is assumed that suitable derivatives possessing sufficiently bulky hydrocarbon groups can usually be synthesised. Despite their well-known ability to bind anions selectively in homogeneous solution, however, neutral anion receptors by themselves have not proven so far to be particularly useful in effecting anion separations via liquid–liquid extraction. Part of the problem, which we have discussed

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previously (*9*, *11*, *12*), lies in the inability of most anion receptors to overcome the solvation-based Hofmeister bias. This selectivity trend has its origins in the fact that the thermodynamics of partitioning anions from water into an organic medium exhibits a strong bias that favours charge-diffuse ions (*11–14*). This bias persists in most solvent systems (*15*) and can even still dominate in the presence of anion receptors (*16*, *17*). The challenge of gaining control of anion selectivity in liquid–liquid extraction can in principle (*10–12*) be met with anion receptors bearing a sufficient number of strong hydrogen-bond donors rigidly positioned in space so as to be complementary for a targeted anion. A few examples attesting to the validity of this expectation have been reported (*18–21*).

Related to the Hofmeister bias, an additional aspect of the problem is that anion receptors typically lack the binding strength needed to effect extraction of an ion pair, except when the cation is very weakly hydrated. Reminiscent of the analogous case encountered in the pioneering work on crown ethers as cation extractants (*22*, *23*), strong ion-pair extraction by a lipophilic anion receptor requires that the binding of the target anion in the organic phase be not only strong enough to overcome the hydration of the targeted ion, but also strong enough to drive the extraction of its countercation into the organic phase. Consulting tabulated standard Gibbs energies of ion partitioning (ΔG_p°) (*15*), one may quickly see that partitioning of inorganic salts in the absence of any receptor is highly unfavourable. For a typical salt, such as KBr, partitioning of the separate ions into nitrobenzene, for example, is at best feeble, with an overall ΔG_p° of the order of 50 kJ/mol. These energetics, in turn, mean that an unusually high anion-binding constant of the order of $10^9\,M^{-1}$ in the organic phase is required to effect appreciable ion-pair extraction. The Cs^+ ion is the most weakly hydrated cation of the stable alkali metals (*15*), and we were able to obtain measurable extraction of caesium salts of univalent anions using powerful fluorinated calixpyrroles, for example; however, even in this case, extraction was weak (*20*).

Three approaches to a more favourable anion extraction by a neutral anion receptor appear attractive from an operational perspective. The first of these is the so-called dual-host approach, wherein separate receptors are added to effect the independent binding of both the cation and the anion, respectively (*24*, *25*). Another approach is the use of an ion-pair receptor, in which the same host is used to bind both a cation and an anion, thereby forming a neutral complex (*26*). The third approach, which represents the topic of this paper, is to employ synergised ion exchange, in which a neutral anion receptor is combined with a lipophilic anion exchanger. In general, synergistic ion-exchange extraction systems have been known since the 1950s. However, at that time, the processes in question involved only cation extraction by lipophilic acids combined with simple neutral ligands, which were added as synergists to provide for additional coordination (*27*). The onset of macrocyclic chemistry, specifically marked by the first report of crown ethers as cation host molecules (*22*), led to the use of neutral macrocycles as synergists for the extraction of univalent and divalent metal cations by cation exchange (*28*). Remarkably, analogous synergistic systems for liquid–liquid anion exchange had not been reported until recently (*9*, *10*).

Liquid–liquid anion exchange is a venerable industrial separation technique (*29*) whose usefulness has hitherto been made possible owing to a characteristic selectivity (*13*) referred to as the Hofmeister bias (*10*). Consequently, liquid–liquid anion exchange has been responsible for a significant portion of the total worldwide hydrometallurgical processing of certain metals capable of forming complex anions, such as uranium, molybdenum, vanadium and gold for over a half century (*29–31*). Such separations are predominantly accomplished by rather simple lipophilic amines in which the means to influence selectivity lie primarily in changing the steric nature of hydrocarbon substituents on the amine nitrogen (*29*, *30*). Even so, the gross selectivity obtained still follows the Hofmeister bias, namely a preference for charge-diffuse, weakly hydrated anions. We propose that synergised anion exchange may open the door to new uses of liquid–liquid anion exchange by introducing new selectivity patterns that depart from the Hofmeister bias and that can be controlled by design.

Given what therefore amounts to the challenge of extracting a highly hydrated, poorly extractable anion in competition with an easily extractable one, we have chosen to work initially with a prototype system that involves the use of neutral anion receptors as anion-exchange synergists applied to the problem of extracting trace sulphate from a sodium nitrate solution. This choice of problems reflects a desire to test whether the judicious choice of a receptor can overcome or perturb the Hofmeister bias (which greatly favours nitrate) and, in so doing, test further the third of the extraction strategies alluded to above. In addition, we recognised that sulphate separation is itself of considerable interest in the context of improving the vitrification of nuclear waste (*9*, *32*, *33*). Thus, its removal from nitrate-rich mixtures typical of such wastes has a potential utility that serves to underscore the need for purely fundamental enquiry.

The specific anion receptors chosen for study include tetraamide macrocycles and calixpyrroles. To date, both classes have shown promise in being able to produce significant enhancements in the anion exchange of sulphate (*9*, *10*). This presumed utility in the area of anion extraction is supported by a considerable body of predicative work, including both analytical and structural analyses. For instance, macrocyclic polyamides have

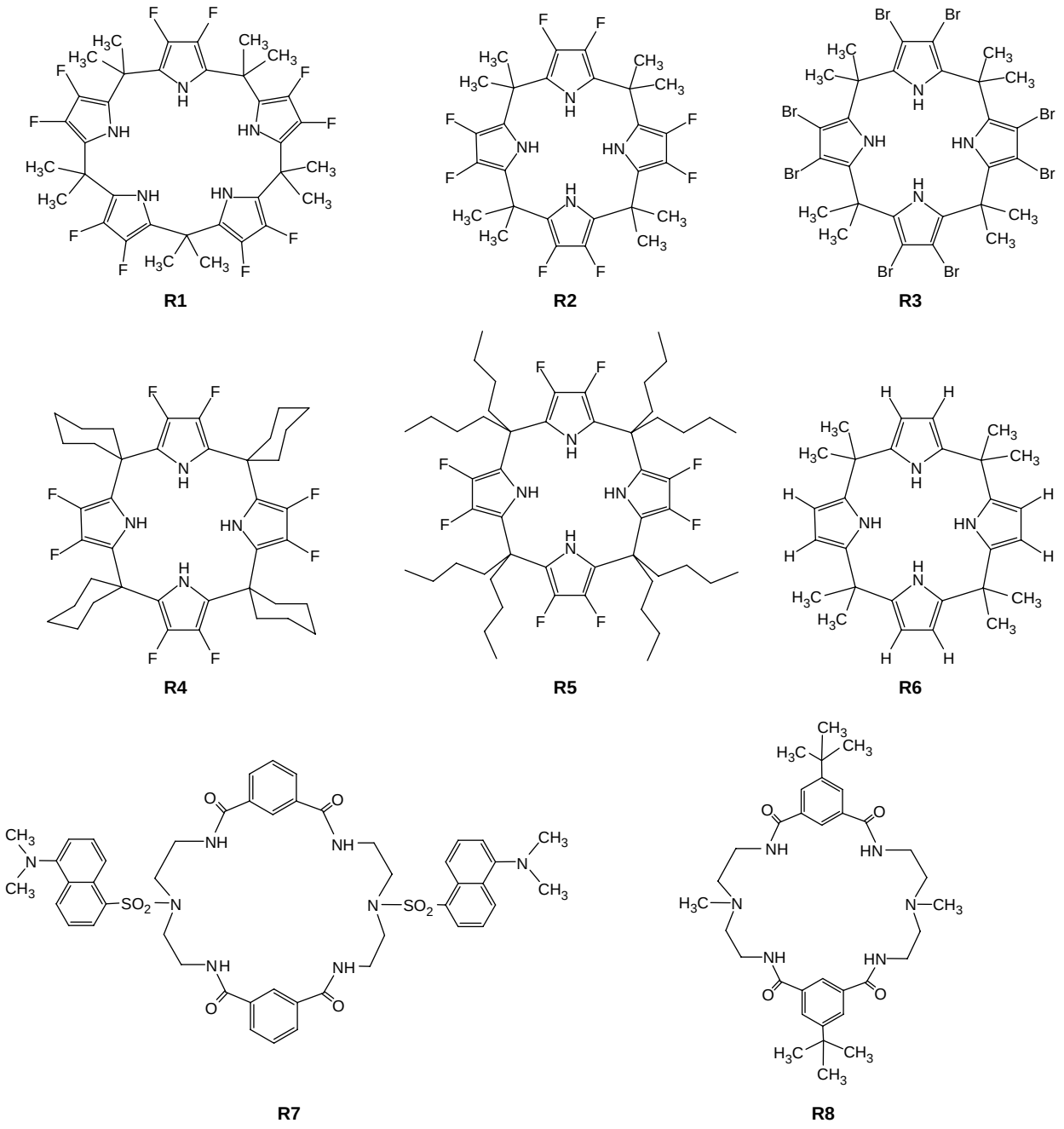


Figure 1. Anion receptors used in this study.

demonstrated the ability to incorporate sulphate to varying degrees within a defined cavity (*34*, *35*), including one tetraamide example in which the sulphate anion is encapsulated by eight hydrogen bonds (H-bonds) within a sandwich structure (*36*). Likewise, since their rediscovery in the context of anion binding (*37*), calixpyrroles have proven to be robust and easy-to-synthesise frameworks capable of strong binding of anions and even ion pairs (*38*, *39*). Both families of macrocycles can be formulated with a variety of substituents. These changes in structure convey different steric and electronic effects that have yet to be completely understood. The present comparative survey was undertaken in part with a view to addressing this latter need. In particular, the broad goal of this line of investigation was to examine a series of closely related receptor systems and to determine the effect of structural modifications on the anion and ion-pair extraction efficiency.

The compounds examined in the present paper, displayed in Figure 1, provide a 'matched set' of macrocycle

structural frameworks and substituent effects. The two tetraamide macrocycles **R7** and **R8** had been surveyed earlier and found to be active in enhancing sulphate extraction (*9*, *10*). These macrocycles, in particular, provide an indication of the effect of substitution at the amine nitrogen atoms. The *t*-butyl substituents on the phenyl groups in **R8**, assumed to have at best a minor effect on anion binding, provide needed lipophilicity, as the more water-soluble analogue lacking these bulky substituents was inactive in sulphate extraction enhancement (*10*). The fluorinated calixpyrroles **R1** (*40*) and **R2** (*41*) were strongly active in the same experiments. The parent calix[4]pyrrole **R6** also has the distinction of acting as an ion-pair receptor under certain conditions, making it and its analogues (which have yet to be studied as ion-pair receptors) of some additional interest (*42–44*). In general, the electron-withdrawing effect of halogenation of the beta-pyrrolic positions on H-bond donor strength is expected to increase the anion-binding affinity, and the anticipated enhancements in *K* were clearly evident in the binding of several anions by the fluorinated calixpyrroles **R1** and **R2** (*45*). The case for the perbrominated calix[4]pyrrole **R3** (*46*) is not so clear. Whereas initial results for binding of fluoride, chloride and dihydrogen phosphate by **R3** showed somewhat higher affinity than exhibited by **R6** (*46*), a subsequent study under somewhat different conditions showed decreased chloride and acetate-binding affinity for **R3** as compared with **R6** (*47*). A decrease in the binding affinity (relative to **R6**) seen upon bromination may reflect the countermanding effect of steric interactions involving the bulky bromine atoms. These putative steric interactions could serve to inhibit anion binding directly or have an adverse effect on the macrocycle conformation by, for example, destabilizing the cone conformation that is more conducive to anion binding (*41*). The fluorinated calix[4]-pyrrole derivatives **R4** and **R5** are new compounds. Their extended alkylation at the *meso* positions would be expected to lend additional lipophilicity to the structures, but also might induce steric and conformational effects whose influence on the binding and extraction we considered difficult to gauge in the absence of experiment.

The systems chosen for study were analysed as extractants using the anion exchanger methyltri-$C_{8,10}$-ammonium nitrate. Commercially available under the name Aliquat® 336N, this reagent is a methylated tertiary amine whose alkyl groups consist of a random mixture of primarily *n*-octyl and *n*-decyl groups. It was chosen as the anion exchanger for the present work because it provides good anion-exchange capacity and is endowed with favourable solubility properties relative to symmetrical tetraalkyl quaternary ammonium or phosphonium alternatives. Chloroform was chosen as the water-immiscible diluent, mainly because of the limited solubilities of the receptors in other standard diluents. Chloroform has the added benefit of suppressing molecular aggregation of polar solutes, which here includes the receptors and quaternary ammonium salts (*48*), thereby simplifying the analysis of binding behaviour.

As an aid to the survey of anion receptors reported herein, we have specifically endeavoured to develop and test a mass-action equilibrium model of synergised anion exchange that relates the observed behaviour to selective anion binding. This desire was prompted by the need for a model that would allow us to interpret quantitatively the enhancement in sulphate extraction that had been seen in the context of our preliminary studies involving the use of neutral tetraamide macrocycles or calixpyrroles in conjunction with Aliquat 336N (*9*, *10*). Here, our working hypothesis is that the enhancement in extraction efficiency seen using these receptors stems from preferential sulphate binding. To the extent such an assumption is correct, then appropriately derived mass-action relationships based on binding equilibria should be able to reproduce the mathematical form of the observed distribution behaviour. To be effective, such a putative model will also have to include at least one anion-exchange equilibrium. However, if well constructed and well correlated with experiment, a model-based analysis should make it possible to separate the binding and exchange equilibria for individual inspection. Thus, it should be possible to use the enhancement of liquid–liquid anion exchange to estimate in a quantitative fashion (either relative or absolute) the underlying anion-binding constants.

A simple experiment was devised to test the respective abilities of the selected receptors (Figure 1) to enhance the anion exchange of sulphate. In the experiment, the receptor concentration in chloroform was varied in the presence of a constant 10 mM concentration of the quaternary ammonium nitrate exchanger (i.e. Aliquat 336N). In those cases where the receptor in question functions as a stronger receptor for sulphate vs. nitrate, a greater distribution of sulphate to the organic phase (from a starting aqueous phase consisting of 10 mM aqueous sodium nitrate containing 0.1 mM sodium sulphate) is expected as the receptor concentration increases. While it is recognised that much more extensive experiments would need to be conducted in order to explore the effect of each compositional variable on the extraction process, the present simple approach appealed to us because of the large amount of information that could be obtained from the limited quantities of the receptors available, all of which are products of synthesis (see Section 2). Specifically, as detailed below, it allowed us to test an initial equilibrium model and to account adequately for the observed extraction enhancement. Furthermore, apparent 1:1 and 2:1 receptor–sulphate binding constants in chloroform could be obtained. This, in turn, allowed the relative sulphate binding strengths of the various receptors to be determined and assessed.

2. Experimental section

2.1 General

Non-aqueous titrations employed a Metrohm Potentiograph E536 automatic titrator fitted with an Orion 8103 ROSS™ combination electrode. Water-content determinations were made using a Metrohm Karl Fischer Coulometer. Liquid scintillation counting was accomplished using a Packard Tri-Carb 2500TR Model B2500P3 Liquid Scintillation Analyzer. Liquid–liquid contacting was performed using a Glas-Col laboratory rotator, and samples were phase-separated at 2060*g* in a Beckman Coulter refrigerated centrifuge maintained at 25 ± 1°C.

2.2 Materials

2.2.1 Reagent chemicals

NMR solvents were purchased from Aldrich Chemical Company (Milwaukee, MI, USA) or Cambridge Isotopes, Inc. (Andover, MA, USA). The salts sodium nitrate and sodium sulphate (EM Science, Gibbstown, NJ, USA) were of reagent grade and used as received. The aqueous solutions were prepared using distilled water deionised to 18 MΩ cm. Chloroform (Aldrich Chemical Co.) of 99.9% purity was washed two times with distilled, deionised water followed by centrifugation for several minutes in order to remove the ethanol stabiliser for extraction experiments. This washing was done immediately prior to use.

2.2.2 Radiotracer

The radiotracer $^{35}SO_4^{2-}$ was obtained from Isotope Products Laboratory (Burbank, CA, USA) as Na_2SO_4 in water (no added carrier). It was added to the aqueous phase (10 mM $NaNO_3$, 0.1 mM Na_2SO_4) at an activity level of 0.45–1.0 μCi/ml.

2.2.3 Aliquat 336 purification

Aliquat 336, a methyltrialkylammonium chloride (Aldrich Chemical Co., CAS No. 63393-96-4) possessing *n*-octyl and *n*-decyl alkyl groups in an approximately 2:1 ratio, is a commonly used quaternary ammonium extractant. (The reader should note that Aliquat 336 corresponds to the chloride form and Aliquat 336N corresponds to the nitrate form, both commercially available.) As obtained from Aldrich Chemical Co., this room-temperature ionic liquid contains ~10% impurities, including Alamine 336 (the trialkyl amine before methylation), sodium chloride and water (*49*). Purification of Aliquat 336 was accomplished by dissolving the extractant in absolute ethanol (Aaper Alcohol and Chemical Co., Shelbyville, KY, USA), and then contacting the resulting solution with Dowex 50W-X2-100 (Aldrich Chemical Co., CAS No. 12612-37-2) in a beaker for 48 h. The loaded resin was washed with fresh ethanol on a column and eluted with 1 N HCl in ethanol. After removal of the ethanol by rotary evaporation, the remaining material was dissolved in hexanes (J.T. Baker) and then washed five times with equal volumes of 0.01 N NaOH (Fisher Scientific, Pittsburgh, PA, USA) in 0.5 M NaCl (Aldrich Chemical Co.) until the pH of the wash became basic. This was followed by three washes with 0.5 N NaCl. The hexane layer was evaporated to near dryness, and the resulting viscous liquid was redissolved in cyclohexane (Eastman Kodak, Rochester, NY, USA). Thin-layer chromatography revealed that the ion-exchange procedure had removed an unidentified impurity. The cyclohexane solution was extracted with an equal volume of 1:1 water–acetonitrile (EM Science) to remove Alamine 336 (titration showed that it is not removed by the ion exchange). After discarding the cyclohexane layer, the water and acetonitrile were removed by rotary evaporation, and the purified Aliquat 336 (37% yield) was dried under high vacuum overnight. The product was characterised in $CDCl_3$ using NMR spectroscopy (Bruker Avance 400 wide-bore NMR spectrometer). This analysis revealed the absence of impurity peaks that had been observed in the as-received material. Non-aqueous titration in 3:1 1,2-dichloroethane–glacial acetic acid (J.T. Baker) with trifluoromethane sulphonic acid in glacial acetic acid showed an amine content of 0.5 w/w % (vs. 1.9% in the as-received material); titration in 9:1 acetic anhydride–glacial acetic acid gave a neutral equivalent of 434 g/equivalent (*50*). This neutral equivalent corresponds to an average chain length for the long-chain alkyl groups of 8.6 carbons. The water content was determined to be 1.27% by Karl Fischer coulometric titration.

The purified Aliquat 336 was then converted to the nitrate form via metathesis by contacting several times with 1.5 M $NaNO_3$, as confirmed using a 5% solution of $AgNO_3$ (visually checking for AgCl precipitation). The formula weight of the Aliquat 336N, 437 g/mol, was obtained by non-aqueous titration (see above) (*50*). Stock solutions of 10 mM Aliquat 336N were prepared in freshly washed chloroform and receptors added at the appropriate concentration. Working solutions were prepared and used immediately.

2.3 Synthesis of calixpyrroles

The following receptors were synthesised according to literature procedures: β-decafluoro-*meso*-decamethylcalix[4]pyrrole (**R1**) (*40*), β-octafluoro-*meso*-octamethylcalix[4]pyrrole (**R2**) (*41*), β-octabromo-*meso*-octamethylcalix[4]pyrrole (**R3**) (*46*), and octamethylcalix[4]pyrrole (**R6**) (*37*).

2.3.1 General

Proton and carbon NMR spectra were recorded on either a Varian 400 MHz spectrometer or a Bruker 300 MHz

spectrometer as indicated. Chemical shifts are reported as δ in ppm using the residual solvent signal as an internal standard. Low-resolution CI mass and high-resolution CI mass spectra were obtained from the University of Texas at Austin Mass Spectrometry Laboratory.

2.3.2 β-Octafluoro-meso-tetraspirocyclohexylcalix[4] pyrrole (receptor **R4**)

To a round bottom flask, methanol (50 ml), 3,4-difluoropyrrole (1.03 g, 10.0 mmol) and cyclohexanone (0.98 g, 1.04 ml, 10.0 mmol) were added. After dissolution, methanesulphonic acid (0.96 g, 650 μl, 10.0 mmol) was slowly added and the solution was heated at reflux with stirring for 24 h. The reaction was allowed to cool to room temperature and was then added to a 500 ml separatory funnel along with dichloromethane (100 ml) and aqueous $NaHCO_3$ (100 ml, saturated). The organic layer was washed with water (2 × 100 ml), dried over Na_2SO_4 and filtered. The bulk of the solvent was then removed by rotary evaporation. The resulting crude reaction mixture was then purified by flash chromatography over silica gel using hexanes:ethyl acetate (9:1) as the eluent. This resulted in isolation of **R4** as the bis-ethyl acetate adduct (1.64 g, 1.80 mmol, 72%), which formed a white solid. After drying under reduced pressure at 50°C for 24 h, the compound was characterised. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C) δ: 6.34 (br s, 4H), 2.11 (br s, 16H), 1.50 (br s, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 135.6 (d, $J = 246.9$ Hz), 113.0, 40.9, 34.5, 25.3, 22.9; HR-MS (CI+): Calcd for $C_{40}H_{45}N_4F_8$ 733.3516, Found 733.3513. Crystal data for **R4** CCDC 748083 $C_{40}H_{44}F_8N_4$, $M_r = 732.79$, $T = 153(2)$ K, tetragonal, space group = I-4, $a = 10.6558(4)$, $b = 10.6558(4)$, $c = 15.5399(6)$ Å, $\beta = 90°$, $V = 1764.49(12)$ Å^3, $\rho_{calc} = 1.379$ mg/m^3, $\mu = 0.111$ mm^{-1}, $Z = 2$, reflections collected: 7850, independent reflections: 1043 ($R_{int} = 0.0228$), final R indices [$I > 2\sigma I$]: $R_1 = 0.0334$, $wR_2 = 0.0805$, R indices (all data): $R_1 = 0.0398$, $wR_2 = 0.0836$. Crystal data for **R4**–TBAF–0.5 hexane CCDC 748084 $C_{59}H_{87}F_9N_5$, $M_r = 1037.34$, $T = 153(2)$ K, triclinic, space group = P-1, $a = 12.6427(2)$, $b = 13.8935(2)$, $c = 18.2770(4)$ Å, $\beta = 90.131(1)°$, $V = 2777.60(8)$ Å^3, $\rho_{calc} = 1.240$ mg/m^3, $\mu = 0.093$ mm^{-1}, $Z = 2$, reflections collected: 19,877, independent reflections: 12,474 ($R_{int} = 0.0256$), final R indices [$I > 2\sigma I$]: $R_1 = 0.0604$, $wR_2 = 0.1349$, R indices (all data): $R_1 = 0.1026$, $wR_2 = 0.1465$.

2.3.3 β-Octafluoro-meso-octa(n-butyl)calix[4]pyrrole (receptor **R5**)

Using the general method used to prepare **R4** above, methanol (5 ml), 3,4-difluoropyrrole (0.103 g, 1.00 mmol), 5-nonanone (0.142 g, 173 μl, 1.00 mmol) and methanesulphonic acid (0.096 g, 65 μl, 1.00 mmol) were reacted to give, after chromatography, **R5** (0.184 g, 0.202 mmol, 81%) as a white solid. Spectral data: ^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ: 6.10 (br s, 4H), 1.90 (unresolved m, 16H), 1.24 (m, $J = 7.20$ Hz, 16H), 1.00 (unresolved m, 16H), 0.84 (t, $J = 7.20$ Hz, 24H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ: 137.2 (d, $J = 240.3$ Hz), 113.5, 44.9, 36.8, 26.5, 22.9, 14.0; HR-MS (CI+): Calcd for $C_{52}H_{76}N_4F_8$ 908.5942, Found: 908.5926.

2.4 Synthesis of tetraamide macrocycles

The approach to the preparation of tetraamide macrocycles is based upon preparation of a suitably derivatised diethylenetriamine and then subsequent reaction with isophthaloyl dichloride (*36*). *N′*-Methyl-2,2′-diaminodiethylamine was purchased from TCI America, while other chemicals and reagents for preparation of compounds **R7** and **R8** were purchased from Sigma-Aldrich and were used as received.

2.4.1 N′-Dansyl-2,2′-bis(phthalimidylethyl)amine (intermediate **3**)

Bis(phthalimidylethyl)amine **2** (2.0 g, 5.5 mmol), prepared according to a previous method (*51*), was added to dansyl chloride (1.48 g, 5.5 mmol) and K_2CO_3 (0.5 g) in CH_3CN (100 ml), and the suspension was refluxed for 24 h. The reaction mixture was filtered, and the solution was concentrated under reduced pressure. The viscous yellow residue was dissolved in $CHCl_3$ (50 ml), washed with 1 N HCl (50 ml) and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure gave a yellow solid, **3** (3.1 g, 5.2 mmol, 95%). ^{1}H NMR (500 MHz, $CDCl_3$ TMS) δ: 8.24 (1H, d, Ds-*H*), 8.14 (d, 1H, Ds-*H*), 7.62 (d, 1H, Ds-*H*), 7.63 (m, 8H, Phth-*H*), 7.41 (t, 1H, Ds-*H*), 7.24 (b, 1H, Ds-*H*), 6.74 (d, 1H, Ds-*H*), 3.93 (t, 4H, CH_2), 3.87 (t, 4H, CH_2), 2.74 (s, 6H, CH_3).

2.4.2 N′-Dansyl-2,2′-diaminodiethylamine (intermediate **4**)

N′-Dansyl-2,2′-bis(phthalimidylethyl)amine **3** (2.63 g, 4.41 mmol) and hydrazine monohydrate (0.47 g, 9.7 mmol) in CH_3OH (100 ml) were heated at reflux for 4 h. The reaction mixture was then stirred for additional 12 h at room temperature. The solvent was removed under reduced pressure to leave a yellow residue, which was suspended in H_2O (100 ml) and conc. HCl (5 ml). The mixture was kept at 60°C under stirring for 30 min., and the solution was collected by filtration. The filtrate was washed by $CHCl_3$, after which Na_2CO_3 was added to the aqueous phase to adjust the pH to around 10. The aqueous solution was extracted with $CHCl_3$ (3 × 50 ml). The combined organic layers were dried over $MgSO_4$

and evaporated under reduced pressure to yield a light yellow oil, **4** (0.78 g, 2.3 mmol, 53%). FAB-MS *m/z*: 337.1 [LH^+]. ^{1}H NMR (500 MHz, $CDCl_3$ TMS) δ: 8.55 (1H, d, Ds-*H*), 8.29 (d, 1H, Ds-*H*), 8.21 (d, 1H, Ds-*H*), 7.53 (m, 2H, Ds-*H*), 7.17 (d, 1H, Ds-*H*), 3.34 (t, 4H, CH_2), 2.82 (s, 6H, CH_3), 2.82 (t, 4H, CH_2), 2.74 (s, 6H, CH_3).

2.4.3 *N,N-Bis-dansyl-m-xylyl-tetraamide (receptor **R7**)*

A solution of *N′*-dansyl-2,2′-diaminodiethylamine **4** (0.94 g, 2.80 mmol) and triethyl amine (0.62 g, 6.14 mmol) in CH_2Cl_2 (500 ml) and a solution of isophthaloyl dichloride (0.57 g, 2.80 mmol) in CH_2Cl_2 (500 ml) were simultaneously added to stirring CH_2Cl_2 (500 ml) and allowed to react for 4 h under an N_2 atmosphere at 0°C. The reaction mixture was stirred at room temperature for 24 h. The solution was concentrated under reduced pressure, and the residue was redissolved in CH_2Cl_2 (100 ml). The organic phase was washed with H_2O (2 × 50 ml), dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (Al_2O_3, 2% methanol in CH_2Cl_2) to yield a yellow solid, **R7** (1.12 g, 1.20 mmol, 65%). Analytical data: Anal. Calcd for $C_{48}H_{52}N_8O_8S_2{\cdot}H_2O$: C, 60.61; H, 5.72; N, 11.78. Found: C, 60.20; H, 5.47; N, 11.15. FAB-MS *m/z*: 933.3 [LH^+]. ^{1}H NMR (500 MHz, DMSO-d_6, TMS) δ: 8.93 (b, 4H, N*H*), 8.20–7.12 (m, 20H, Ar-*H*), 3.59 (b, 4H, CH_2), 3.41 (b, 4H, CH_2), 2.82 (b, 12H, CH_3). Although, we consider the elemental analysis acceptable for present purposes when the compound is formulated as a monohydrate, better agreement is obtained by assumption of incomplete removal of trace volatiles (H_2O, CH_3OH and CH_2Cl_2), none of which are considered an issue for the distribution survey studies at the low levels involved.

2.4.4 *N,N-Dimethyl-tert-butyl-m-xylyl-tetraamide (receptor **R8**)*

A solution of *N′*-methyl-2,2′-diaminodiethylamine (1.17 g, 10 mmol) and triethylamine (2.22 g, 22 mmol) in CH_2Cl_2 (400 ml) and a solution of 5-*tert*-butylisophthaloyl dichloride (2.58 g, 10 mmol) in CH_2Cl_2 were simultaneously added to stirring CH_2Cl_2 (500 ml) and allowed to react for 6 h under N_2 atmosphere at 0°C. The resulting mixture was further stirred overnight at room temperature. The solvent was evaporated and the residue was redissolved in CH_2Cl_2 (100 ml). The organic phase was washed with H_2O (1 × 100 ml), dried over $MgSO_4$ and concentrated. The product was purified by column chromatography (Al_2O_3, 2% methanol in CH_2Cl_2) to yield neutral amide **R8** (1.7 g, 2.8 mmol, 55%) as a white powder. Analytical data: Anal. Calcd for $C_{34}H_{50}N_6O_4$: 67.30; H, 8.31; N, 13.85. Found: C, 67.43; H, 8.52; N, 14.04. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ: 8.23 (s, 2H, Ar*H*), 7.70 (b, 8H, N*H* and Ar*H*), 3.58 (b, 8H, CH_2), 2.58 (s, 6H, CH_3), 2.50 (t, 8H, NCH_2), 2.12 (s, 18H, CH_3).

2.5 *Distribution experiments*

Liquid–liquid contacting experiments were carried out in 2 ml flip-top plastic vials. All samples were run in duplicate. The initial aqueous phase consisted of 10 mM $NaNO_3$, 0.1 mM Na_2SO_4 spiked at an activity level of 0.45–1.0 μCi/ml of $^{35}SO_4^{2-}$ as Na_2SO_4. The organic phase was $CHCl_3$ containing 10 mM purified Aliquat 336N and an appropriate concentration (0.1–10 mM) of one of the eight receptors being investigated. Equal volume ratios of 0.25 ml of organic and aqueous phases were hand-shaken a few times, then contacted at 25°C for 2–4 h by tumbling end-over-end at 40 rpm using a Glass-Col rotating wheel. The vials were then centrifuged at 3000 rpm for 5 min to separate the phases. A 100 μl sub sample was removed from each phase and added to individual 20 ml plastic scintillation vials containing 5 ml Ultima Gold XR scintillation cocktail. The samples were hand-shaken and placed in the dark for 60 min prior to counting. The sulphate distribution ratio (D_{SO_4}) was determined as the ratio of the $^{35}SO_4^{2-}$ activities in the organic and aqueous phases.

The precision of the sulphate distribution ratios was carefully estimated in order to eliminate bias in the modelling. Given the nature of the techniques employed, the combined precision due to volumetric transfers, sampling and laboratory-temperature variation in the employed techniques generally falls in the 5–10% range. This was confirmed with replicate determinations for each data point having $D_{SO_4} \geq 10^{-4}$, whose average error was found to be ±6.3%. For lower values of D_{SO_4}, where tracer liquid-scintillation count rates approached background (corresponding to $D_{SO_4} \approx 2.0 \times 10^{-5}$), the replicate error worsened considerably. For computational purposes, the precision error was taken to be ±6.3% for $D_{SO_4} \geq 10^{-4}$ and ±27.5% for lower D_{SO_4} values. Values of D_{SO_4} less than 10^{-5} were rejected.

2.6 *Equilibrium modelling*

The liquid–liquid distribution data were analysed with the aid of the program SXLSQI (*52*). This program makes it convenient to set up equilibrium problems in liquid–liquid systems by allowing the user to define the stoichiometry of an equilibrium between reactant species (in our case, aqueous ions and organic-phase extractant molecules) and postulated product species (in our case, ion pairs and extraction complexes in the organic phase). As is typically required, simultaneous multiple equilibria may be treated, which includes interphase distribution and homogeneous reactions in either phase. The postulated equilibria and their corresponding $\log K$ values formally used by SXLSQI in this paper, Equations (1)–(4), are given

Table 1. Formal ion-pair extraction equilibria used in the SXLSQI modelling.

Equation	Name	Equation no.
$Q^+ + NO_3^- \overset{K_1}{\rightleftharpoons} \overline{QNO_3}$	Quat nitrate extraction	(1)
$2Q^+ + SO_4^{2-} \overset{K_2}{\rightleftharpoons} \overline{Q_2SO_4}$	Quat sulphate extraction	(2)
$2Q^+ + SO_4^{2-} + \overline{R} \overset{K_3}{\rightleftharpoons} \overline{Q_2RSO_4}$	Quat sulphate extraction by one receptor molecule	(3)
$2Q^+ + SO_4^{2-} + 2\overline{R} \overset{K_4}{\rightleftharpoons} \overline{Q_2R_2SO_4}$	Quat sulphate extraction by two receptor molecules	(4)

Notes: Q represents the cation of Aliquat 336N, and the species R represents an anion receptor. Overbars denote species in the organic phase.

in Table 1; see Section 3 for the explanation for these choices. The ion-exchange and binding reactions of actual interest here, as shown in Table 2, must be obtained from appropriate subtractions of equilibria in Table 1 and are not used directly by SXLSQI.

Thermodynamic equilibrium constants K_{1-10} are defined on the molarity scale and corrected to infinite dilution. They are given as activity quotients in the standard mass-action formalism. For example, the exchange equilibrium constant corresponding to Equation (5) in Table 2 would be defined as

$$K_5 = \frac{[Q_2SO_4]_{org}\, g_{Q_2SO_4}[NO_3]_{aq}^2 g_{NO_3}^2}{[QNO_3]_{org}^2\, g_{QNO_3}^2 [SO_4^{2-}]_{aq} g_{SO_4}}, \qquad (5a)$$

where g represents a molarity-scale activity coefficient. In the fitting calculations performed by SXLSQI and the more general program SXFIT (*53*), all organic-phase and aqueous-phase activity coefficients are estimated using, respectively, the Pitzer treatment (*54*) and the Hildebrand–Scott treatment (*55*). Input parameters needed for the activity-coefficient calculations, phase-volume changes and concentration-scale interconversions (*56*, *57*) are shown in Table 3.

Mathematically, the problem to be solved amounts to the simultaneous solution of the equilibrium-quotient expressions for each postulated equilibrium and the conservation-of-mass expressions for each system component appearing in the equilibria. In the present modelling, which is typical, the variables are the initial concentrations of reactant species, and the user supplies the values for each data point. Adjustable parameters are the log K values corresponding to the postulated equilibria; the user supplies initial estimates. Other parameters (some of which are also potentially adjustable) and constants must also be supplied by the user; this is described in greater detail below. This combination of information fully defines the mathematical problem, allowing the program to numerically calculate the concentrations of all of the species at equilibrium for each data point. From the equilibrium concentrations, experimental observables are calculated, which are most often the equilibrium concentrations themselves or distribution ratios. A refinement cycle is completed when the program has calculated the value of the observable for each data point in the input set, and the goodness of fit is then determined.

The SXLSQI program employs the least-squares criterion and reports the goodness of fit in terms of an agreement factor σ (*51*), which here is a weighted root-mean-square deviation of the distribution ratios D_{SO_4} calculated from the model vs. the experimental value of D_{SO_4}. It is defined according to

$$\sigma = \left[\sum w_i (Y_i - Y_{c,i})^2 / (N_o - N_p)\right]^{1/2}, \qquad (11)$$

where Y_i is the ith experimentally observed quantity (i.e. $\log D_{SO_4}$), $Y_{c,i}$ is the corresponding quantity calculated from

Table 2. Derived anion-exchange and anion-binding equilibria.

Equation	Name	Equation no.
$2\overline{QNO_3} + SO_4^{2-} \overset{K_5}{\rightleftharpoons} \overline{Q_2SO_4} + 2NO_3^-$	Quat nitrate–sulphate exchange	(5)
$2\overline{QNO_3} + SO_4^{2-} + \overline{R} \overset{K_6}{\rightleftharpoons} \overline{Q_2RSO_4} + 2NO_3^-$	Quat nitrate–sulphate exchange 1:1 receptor–sulphate complex	(6)
$2\overline{QNO_3} + SO_4^{2-} + 2\overline{R} \overset{K_7}{\rightleftharpoons} \overline{Q_2R_2SO_4} + 2NO_3^-$	Quat nitrate–sulphate exchange 2:1 receptor–sulphate complex	(7)
$\overline{R} + \overline{Q_2SO_4} \overset{K_8}{\rightleftharpoons} \overline{Q_2RSO_4}$	Homogeneous sulphate binding 1:1 receptor–sulphate complex	(8)
$2\overline{R} + \overline{Q_2SO_4} \overset{K_9}{\rightleftharpoons} \overline{Q_2R_2SO_4}$	Homogeneous sulphate binding 2:1 receptor–sulphate complex	(9)
$\overline{R} + \overline{Q_2RSO_4} \overset{K_{10}}{\rightleftharpoons} \overline{Q_2R_2SO_4}$	Homogeneous sulphate binding add second receptor	(10)

Notes: Q represents the cation of Aliquat 336N, and the species R represents an anion receptor. Overbars denote species in the organic phase.

Table 3. Summary of parameters used in SXLSQI modelling.

Species	V_0 ($cm^3\,mol^{-1}$)	S_v* ($cm^3\,l^{1/2}\,mol^{-3/2}$)		
Masson coefficients[a]				
Q^+	−340.88	−11.263		
Na^+	−1.21	1.203		
H^+	0.00	0.000		
NO_3^-	29.33	0.543		
SO_4^{2-}	13.94	9.754		
Species	$\beta^{(0)}$	$\beta^{(1)}$	C^{Φ}	α_1
Pitzer parameters[b]				
QNO_3	−0.01540	0.1120	−0.000030	2.0
Q_2SO_4	0.04088	0.6585	−0.000581	2.0
$NaNO_3$	0.00680	0.1783	−0.000720	2.0
Na_2SO_4	0.01958	1.1130	0.002487	2.0
HNO_3	0.11190	0.3686	0.002470	2.0
Species	Molecular wt	Molar volume ($cm^3\,mol^{-1}$)	Dielectric constant	Solubility parameters ($cal^{1/2}\,cm^{-3/2}$)
Other parameters[c]				
R1	715.67	405.5		11.87
R2	572.54	327.6		11.83
R3	1059.79	423.7		12.20
R4	732.79	445.6		11.74
R5	909.189	714.0		10.19
R6	428.62	335.6		10.83
R7	933.18	607.8		12.57
R8	606.798	484.4		11.25
$CHCl_3$	119.4	80.013	4.806	9.234
A336N	430.72	431		
Na^+	22.990	−1.2		
H^+	1.0079	0.0		
NO_3^-	62.005	29.0		
SO_4^{2-}	96.05	14.9		

Notes: Q represents the cation of Aliquat 336N, and the species **R** represent the different anion receptors.
[a] Masson coefficients account for the small volume changes of the aqueous phase as electrolyte concentrations vary. Values taken from Ref. (*56*).
[b] Pitzer parameters taken from Ref. (*54*) allow SXLSQI to estimate the aqueous-phase ionic activity coefficients.
[c] Molar volumes for organic species were estimated from group parameters from Ref. (*57*) or were interpolated from similar molecules found in the same reference as were the Hildebrand solubility parameters. Values for inorganic ions were taken to be approximately equal to V_0.

the model being tested, w_i is the weighting factor defined as the reciprocal of the square of the estimated uncertainty of Y_i, N_o is the number of observations, and N_p is the number of adjustable parameters (i.e. $\log K$ values). Given how the weighting is defined, the value of σ will approach unity when the error of fitting is equal to the estimated experimental error. For this to be true and the fitting to be unbiased, the precision of each data point must be reasonably well estimated. Multiple refinement cycles provide final converged estimates of the $\log K$ parameters when the minimum value of σ is reached within a user-defined tolerance.

3. Results and discussion

3.1 Anion exchange by quaternary ammonium nitrate alone

Extraction of sulphate by the quaternary ammonium nitrate salt Aliquat 336N (denoted as QNO_3 in equations) used alone in chloroform was characterised so as to confirm the expected anion-exchange behaviour and to provide the equilibrium constant for the baseline exchange reaction. A series of equilibrations was performed in which the organic-phase concentration of Aliquat 336N was varied at fixed 10 mM aqueous sodium nitrate and 0.1 mM sodium sulphate concentrations (Figure 2). The same aqueous composition was then used in all subsequent receptor experiments. Overall, sulphate distribution ratios (D_{SO_4}) are low, as expected. In fact, the value of D_{SO_4} obtained with 10 mM Aliquat 336N is at or below the limit of detection ($D_{SO_4} \approx 2.0 \times 10^{-5}$), and only by raising the Aliquat 336N concentration was it possible to measure D_{SO_4} reliably in the absence of an anion receptor. Simple linear behaviour was obtained at higher concentrations, involving a second-power dependence on the concentration of Aliquat 336N present in the organic phase. More precisely, the corresponding linear regression with equal

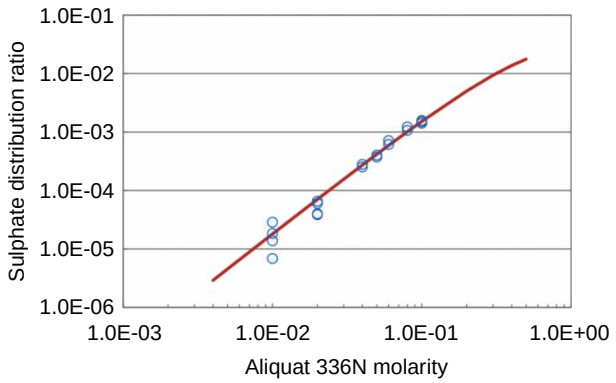


Figure 2. Dependence of the sulphate distribution ratio (D_{SO_4}) on the Aliquat 336N molarity in chloroform. The points represent the experimental data, and the solid line is the SXLSQI fit using the simple anion-exchange model given by Equation (5) and the parameters shown in Tables 3 and 4. In the experiment, Aliquat 336N solutions in chloroform were equilibrated at 25°C and 1:1 phase ratio with an aqueous phase containing 10 mM sodium nitrate and 0.1 mM sodium sulphate traced with $^{35}SO_4^{2-}$. The solid curve is extrapolated to lower and higher Aliquat N concentrations. Worsening precision is evident as the values of D_{SO_4} fall below 10^{-4} towards the limit of detection ($D_{SO_4} \approx 2.0 \times 10^{-5}$).

weighting (on the log–log scale) was found to be $\log D_{SO_4} = 2.073(78) \log[QNO_3]_{org} - 0.713(117)$, where values in parentheses represent standard errors for the slope and intercept and $[QNO_3]$ is equated with the analytical concentration of Aliquat 336N; $r^2 = 0.975$. At 10 mM Aliquat 336N, the concentration used in the receptor experiments, the sulphate distribution ratio D_{SO_4} due to the anion exchanger alone is $1.38(10) \times 10^{-5}$, as given by the linear regression. From exchange of a divalent aqueous anion for two organic-phase univalent anions, the value of D_{SO_4} can be expected to fall with the second power of the aqueous nitrate concentration (see below). However, since the D_{SO_4} values were so low already, no experiments at higher aqueous nitrate concentration were performed.

To interpret the power dependence (slope = 2) observed in Figure 2, it is convenient to rearrange the standard equilibrium quotient Equation (5a) corresponding to the anion-exchange equilibrium Equation (5) as follows. Defining the sulphate distribution ratio as $D_{SO_4} = [SO_4^{2-}]_{org}/[SO_4^{2-}]_{aq}$ and taking the anion-exchange process in Equation (5) as the only process occurring, the expression for the distribution ratio in terms of discrete species becomes $D_{SO_4} = [Q_2SO_4]_{org}/[SO_4^{2-}]_{aq}$. Substituting this expression for D_{SO_4} in Equation (5a) and rearranging in a logarithmic form gives

$$\log D_{SO_4} = 2 \log [QNO_3]_{org} - 2 \log [NO_3^-]_{aq} + \log (K_5 G^{-1}), \quad (5b)$$

where G is the quotient of activity coefficients shown in Equation (5a). Assuming the experimental design assures the constancy of G, graphical analysis of the dependence of $\log D_{SO_4}$ on $\log[QNO_3]_{org}$ and $\log [NO_3^-]_{aq}$ is expected to show slopes of 2 and −2, respectively. The assumption of constant G is in fact good in the present case, as aqueous concentrations are fixed, and the organic-phase concentrations are kept low (see also below), though the program SXLSQI calculates the activity coefficients regardless. To simplify the data analysis, the initial aqueous sodium sulphate concentration was kept low and constant at 0.1 mM in all experiments. With low loading assured (<0.004%), the concentrations of $[QNO_3]_{org}$ and $[NO_3^-]_{aq}$ in Equation (5b) can be safely equated with their initial values.

Whereas the sulphate distribution ratio D_{SO_4} represents a standard measure of the extent of removal of sulphate from the aqueous phase with practical meaning in terms of performing a separation, the separation factor ($S_{SO_4/NO_3} = D_{SO_4}/D_{NO_3}$) provides a more formal measure of selectivity. The extraction will be sulphate or nitrate selective depending on whether S_{SO_4/NO_3} is, respectively, greater or less than 1. In general, values of S_{SO_4/NO_3} calculated from the data in Figure 2 were very low with Aliquat 336N used alone and followed a first-power dependence on its concentration with unweighted linear regression $\log S_{SO_4/NO_3} = 1.073(78) \log [QNO_3]_{org} - 2.713(117)$; $r^2 = 0.912$. From the regression, $S_{SO_4/NO_3} = 1.38 \times 10^{-5}$ at 10 mM Aliquat 336N in the organic phase and 10 mM sodium nitrate concentration in the aqueous phase, and it increases by an order of magnitude at 100 mM Aliquat 336N.

Although the process occurring is anion exchange, it was formally modelled as a competitive ion-pair extraction. As currently written, the program SXLSQI does not have the capability to model anion-exchange processes directly. However, an essentially equivalent formal model is to suppose that the quaternary ammonium salts of nitrate and sulphate exist initially in the aqueous phase and are both extracted into the organic phase with high extraction constants, respectively, $\log K_1$ and $\log K_2$. The net extraction, given by Equation (5), is the anion-exchange process being considered with corresponding $\log K_5 = \log K_2 - 2 \log K_1$. The absolute values of $\log K_1$ and $\log K_2$ cannot be determined independently from the data, as they are mutually dependent parameters (constant difference). However, the absolute values of these parameters are not material to the exchange reactions of interest as long as they are high enough that the quaternary ammonium salts would be highly partitioned to the solvent phase. To set the values of $\log K_1$ and $\log K_2$ as shown in Table 4, $\log K_1$ was fixed while the best value of $\log K_2$ was determined by least-squares refinement. The actual two-dimensional parameter space was then mapped out using a series of such refinements in which $\log K_1$ was incrementally increased from 4 up to 10. It was found that the

Table 4. Constants obtained from SXLSQI fitting.

	Aliquat 336N alone[a]		Aliquat 336N + receptor[b]		
Receptor	$\log K_1$ (reference)	$\log K_2$	$\log K_3$	$\log K_4$	Agreement factor σ
R1	8.500	12.353 (13)	17.13 (2)	18.11 (0.40)	1.376
R2	8.500	12.353 (13)	15.89 (3)	17.45 (0.14)	1.034
R3	8.500	12.353 (13)	14.96 (14)	17.90 (0.13)[c]	0.875
R4	8.500	12.353 (13)	16.84 (5)	18.11 (0.50)	2.890
R5	8.500	12.353 (13)	14.45 (1.23)	18.29 (0.13)[c]	2.984
R6	8.500	12.353 (13)	15.99 (9)	18.15 (0.13)	2.156
R7	8.500	12.353 (13)	16.77 (4)	18.59 (0.22)	1.988
R8	8.500	12.353 (13)	15.62 (1)	17.69 (0.12)	1.489

Notes: Entries in this table correspond to output from SXLSQI corresponding to fits of the data shown in Figures 2 and 3. Parentheses indicate uncertainties to the number of digits shown.

[a] Values of $\log K_1$ and $\log K_2$ were determined as described in the text based on fitting sulphate exchange data in the absence of anion receptors (Figure 2). Choosing $\log K_1 = 8.5$ as reference, $\log K_2 = 12.353 \pm 0.013$ with $\sigma = 1.8124$.

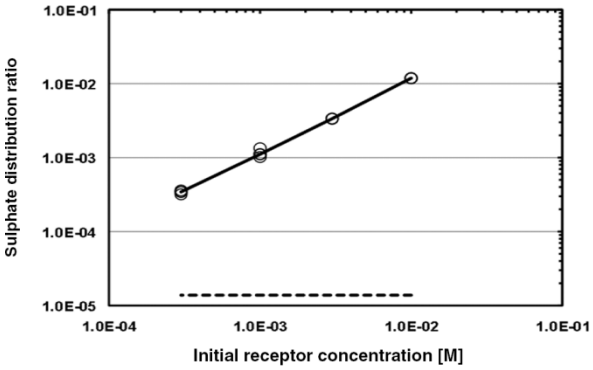
[b] Values of $\log K_1$ and $\log K_2$ were fixed while refining $\log K_3$ and $\log K_4$ in fitting the sulphate distribution data with increasing receptor concentration (Figure 3).

[c] Because of a fluctuating convergence point in refinement, $\log K_3$ was automatically refined for fixed values of $\log K_4$. The value of $\log K_4$ shown gave the minimum agreement factor on refining $\log K_3$. Uncertainty values of $\log K_4$ were taken to be ± 0.13, noting that the uncertainty of $\log K_4$ levels off at approximately this value for low values of $\log K_3$.

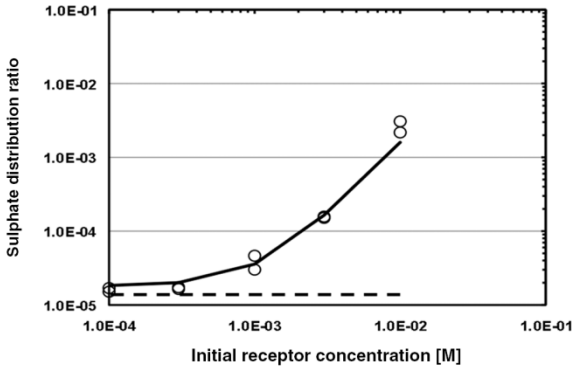
goodness of fit given by the agreement factor σ (Equation (11)) improved as the value of $\log K_1$ was raised to approximately 6, where the values for σ and for $\log K_2$ started to level off. The agreement factor continued to decrease gradually as the value of $\log K_1$ increased thereafter; however, the improvements were slight, and a value of 8.5 for $\log K_1$ was arbitrarily adopted as a reference. This gave $\log K_2 = 12.353 \pm 0.013$ with $\sigma = 1.8124$ and $\log K_5 = -4.647 \pm 0.013$. It is important to note that all values of $\log K_{2-4}$ are referenced to the arbitrary value of $\log K_1 = 8.5$. When its value is subtracted (multiplied by two) to obtain the anion-exchange constants of interest (i.e. $\log K_5$, $\log K_6$ and $\log K_7$) and homogeneous binding constants (i.e. $\log K_{8-10}$) as discussed in Section 3.2, its absolute value becomes immaterial. The reasonably good agreement between this simple anion-exchange model and the data may be inferred from an inspection of Figure 2. Extrapolation of the curves to higher concentrations of Aliquat 336N shows curvature, which is indicative of activity-coefficient effects.

The agreement between the simple anion-exchange model given by Equation (5) and the data shown in Figure 2 support the model assumption that neutral monomer species QNO_3 and Q_2SO_4 dominate under the conditions of the present work. Not only was the statistical agreement satisfactory ($\sigma = 1.8$), but the expected second-power dependence on $[QNO_3]_{org}$ from Equation (5b) is observed (slope = 2.07). While our conditions were chosen carefully to foster this ideal behaviour, we felt it prudent to consider the possible effect of aggregation on the extraction behaviour in the light of the tendency of lipophilic salts in low-polarity solvents to aggregate to dimers and higher oligomers, including reverse micelles (*48*). Several cases may be considered and individually ruled out. Since so little sulphate is extracted, we start our examination of them by assuming that no organic-phase species will have more than one sulphate anion. Typically, an already-aggregated state of the extractant tends to give slopes lower than 2 in plots of reagent dependence similar to that shown in Figure 2. If in the first case we have higher-order aggregates of the form $(QNO_3)_n$ that incorporate sulphate to give species of the form $(Q_2SO_4)(QNO_3)_{n-2}$, a slope of 1 is expected (case of constant aggregation). On a similar basis, one may rule out a second case in which aggregates of the form $(QNO_3)_n$ deaggregate upon exchange with sulphate to give monomer species Q_2SO_4, since here a slope of $2/n$ is expected. Finally, for the case where Aliquat 336N exists as monomers QNO_3 that aggregate on exchange with sulphate to give species of the form $(Q_2SO_4)(QNO_3)_{n-2}$, a slope of n is expected. While not observed in the present instance, we encountered this situation previously in the case of pertechnetate exchange with nitrate (*58*). Thus, while all possible scenarios cannot be ruled out, on the basis of this latter precedent and the above case analysis, we suggest that a slope of 2 represents a unique and diagnostic case for the simplest anion-exchange process involving monomeric species, as defined by Equation (5).

Although there appear to be no literature data on quaternary ammonium nitrate and sulphate salts in chloroform, the extraction behaviour of other quaternary ammonium salts in organic solvents, including chloroform (*59–62*), is sufficiently well understood to have further confidence in our model assumptions. In chloroform ($\varepsilon = 4.806$ at 20°C (*63*)) and other low-permittivity diluents, quaternary ammonium salts are generally expected to exist as ion pairs, except at high dilution (*64*). Conductance measurements have in fact shown that closely related methyltrioctyl and methyltridecyl ammonium chloride salts exist primarily in the form of



R1



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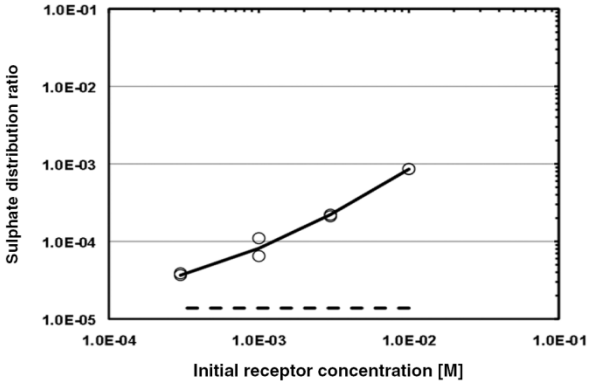

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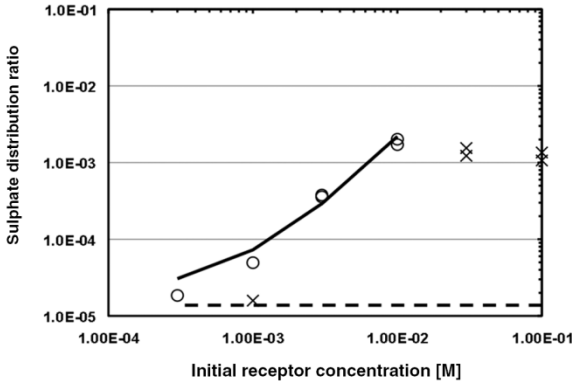

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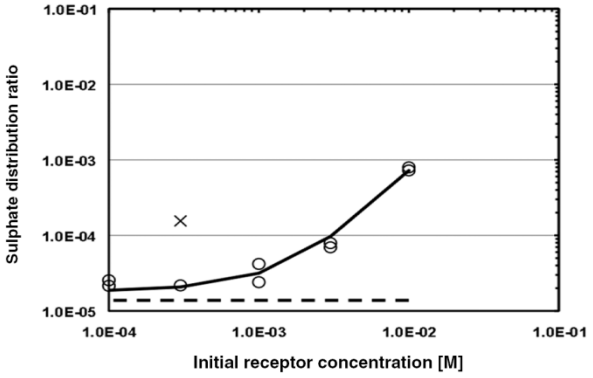
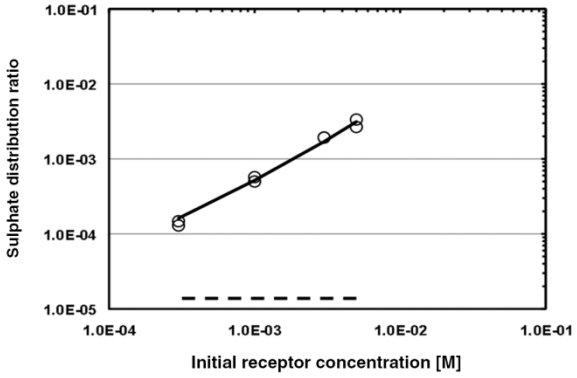
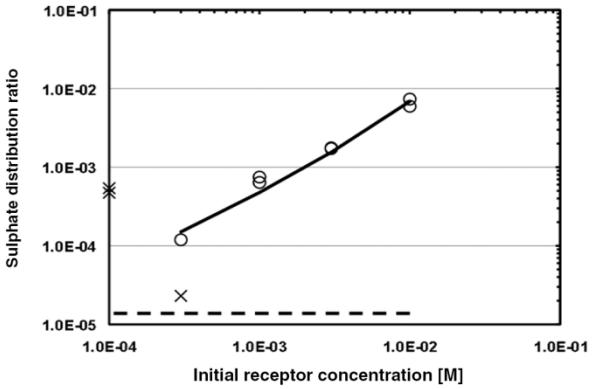


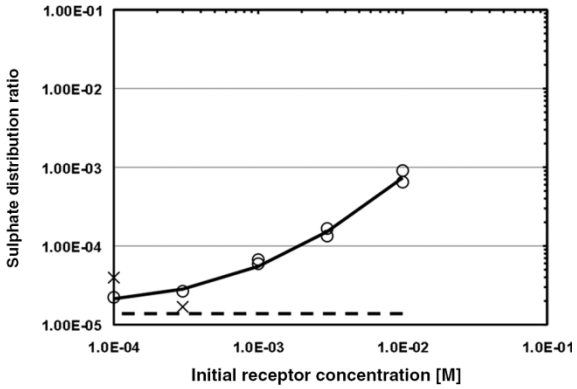
R3



R7



R4



R8

ion pairs in chloroform (*62*). The partition ratio of methyltrioctyl ammonium chloride from water is high ($P_{QCl} = [Q]_{org}/[Q]_{aq} \approx 3000$ at 10 mM), and its concentration dependence was shown to be consistent with ion pairs of methyltrioctyl ammonium chloride down to 1.5×10^{-4} M in chloroform (*61*). The partitioning was also found to obey the mass action given by the form of Equation (1) as an ion-pair extraction, where the anion is chloride. The logarithm of the ion-pair extraction constant for methyltrioctyl ammonium chloride from water to chloroform is 7.07 (*61*), a finding that supports the reasonable, albeit arbitrarily chosen, value $\log K_1 = 8.5$ used in Table 4 for Aliquat 336N. Activity coefficients for methyltrioctyl and methyltridecyl ammonium chloride salts at 10 mM in chloroform are close to unity ($g_{QCl} = 0.92$) (*62*). Finally, aggregation of the salts of Aliquat 336 in our system can be assumed to be negligible based on vapour-phase osmometry results on methyltrioctyl and methyltridecyl ammonium chloride salts in chloroform (*59*, *62*). Although lipophilic salts in organic solvents have long been known to aggregate, the three long chains on the Aliquat 336 cation minimise this effect (*48*). Chloroform is especially forgiving as well, owing to its good solvating ability towards anions (*13*). While the literature data discussed here pertain to the chloride salts of Aliquat 336 and methyltrioctyl and methyltridecyl ammonium cations, the nitrate and sulphate forms are likely neutral monomeric species under the present dilute conditions, and the fact that reasonably good fits were obtained tends to support this simple picture. Generally, quaternary ammonium salt partitioning, aggregation and ion-pair dissociation all increase as the charge density of the anion decreases (*48*). Tridodecylammonium salts of a variety of anions remain unaggregated in chloroform, even for large iodide and thiocyanate anions. The tendency of the sulphate salt to aggregate is expected to be small, owing to the low dipole moment of a single Q_2SO_4 monomer.

3.2 Enhanced anion exchange by receptors added to quaternary ammonium nitrate

Addition of up to 10 mM of any of the eight receptors to the 10 mM solution of Aliquat 336N in chloroform markedly enhances the extraction of sulphate as shown by the plots in Figure 3. This is immediately interpreted as implying that all the receptors used are selective in binding sulphate vs. nitrate, because nitrate-binding selectivity would be expected to result in *decreased* sulphate extraction on addition of the anion receptor. Sulphate selectivity would normally be expected in view of its higher charge density and resultant increased H-bond acceptor strength relative to nitrate. In addition, sulphate with its 12 potential H-bond acceptor sites vs. 6 for nitrate (*65*) would present a greater number of potential multipoint interactions for sufficiently flexible multidentate H-bond donors. One should still bear in mind that the sulphate selectivity in this context is *binding* selectivity vs. *extraction* selectivity. This distinction is highlighted by our modelling studies, where the extraction equilibria responsible for the enhanced sulphate extraction are derived and then used to estimate the homogeneous binding constants by subtraction of the evaluated anion-exchange equilibrium given in Equation (5). However, prior to turning to this discussion, it is helpful first to compare the various distribution ratios and separation factors to survey *extraction* selectivity.

Table 5 lists the maximum sulphate distribution ratios, separation factors and enhancement factors for each receptor at 10 mM in the presence of 10 mM Aliquat 336N. Given that the nitrate distribution ratio D_{NO_3} by design equals 1 at 10 mM Aliquat 336N in the organic phase and 10 mM sodium nitrate in the aqueous phase, the extraction separation factor S_{SO_4/NO_3} may be equated with D_{SO_4} in the present case. Although S_{SO_4/NO_3} therefore increases markedly upon addition of the receptors, it may be seen from Table 5 that S_{SO_4/NO_3} with any of the receptors is still less than unity under the conditions employed, reaching a maximum of only 1.18×10^{-2} with receptor **R1**. That is, the extraction is still formally nitrate selective (i.e. $S_{SO_4/NO_3} < 1$) under the best of the conditions tested. However, given that D_{SO_4} and S_{SO_4/NO_3} may be increased (not necessarily equally) by appropriate increases in reagent concentrations, subject to solubility limits, higher extraction performance may be readily obtained by design. For example, we showed earlier that a value of D_{SO_3} greater than 1 with a higher value of S_{SO_4/NO_3} (0.163) could be achieved with 100 mM of Aliquat 336N and 100 mM **R2** in toluene (*10*).

Casual inspection of the plots in Figure 3 and data given in Table 5 shows that the enhancements on adding up to 10 mM receptor are quite significant, reaching nearly three orders of magnitude for the fluorinated calix[5]pyrrole **R1**. For quantitative comparison, an enhancement

Figure 3. Observed and calculated sulphate distribution ratios (D_{SO_4}) as a function of the concentrations of eight macrocyclic anion receptors (**R1**–**R8**) in combination with 10 mM Aliquat 336N in $CHCl_3$. The dashed line corresponds to the distribution ratio for 10 mM Aliquat 336N used without receptor ($D_{SO_4} \approx 1.38 \times 10^{-5}$). The aqueous phase consisted of 0.1 mM Na_2SO_4 and 10 mM $NaNO_3$. The points represent the experimental data, while the solid line is the SXLSQI fit using the formal model given by Equations (1)–(4) in Table 1 and the parameters listed in Tables 3 and 4. Points shown with ' × ' symbols on plots were not included in the data fitting; most of these are outliers, except for the points above 10^{-2} M **R6**, in which case a third phase was observed.

Table 5. Enhancement of sulphate extraction by lipophilic anion receptors.

Receptor	$D_{SO_4} = S_{SO_4/NO_3}$[a]	Enhancement factor[b]	$C\log P$ (octanol/H_2O)[c]	$\log P$ ($CHCl_3/H_2O$)[d]	Steepest slope[e]
R1	1.18×10^{-2}	855	11.7	11.5	1.0
R2	8.59×10^{-4}	62	9.4	9.3	1.1
R3	7.61×10^{-4}	55	14.6	14.2	1.9
R4	6.65×10^{-3}	482	13.2	13.1	1.1
R5	2.62×10^{-3}	190	22.1	23.5	2.3
R6	1.86×10^{-3}	135	7.3	7.7	1.8
R7	6.85×10^{-3}[f]	496	6.3	5.4	1.1
R8	7.77×10^{-4}	56	4.5	4.7	1.4

Notes: Systems contained 10 mM Aliquat 336N (QNO_3) and 10 mM receptor (**R**) in the chloroform phase and 10 mM $NaNO_3$ and 0.1 mM Na_2SO_4 in the aqueous phase; the phase ratio was 1:1 and $T = 25 \pm 0.5$°C.

[a] Average of two values; the value of the separation factor S_{SO_4/NO_3} is the same as D_{SO_4}, since $D_{NO_3} = 1$ at 10 mM Aliquat 336N.

[b] Calculated as the ratio $D_{SO_4,Q+R}/D_{SO_4,Q}$, corresponding to quaternary ammonium salt plus receptor vs. quaternary ammonium salt used alone; $D_{SO_4,Q}$ is taken as 1.38×10^{-5} (from the linear regression described in the text).

[c] $C\log P$ values were calculated using the chemical properties $C\log P$ algorithm of the program ChemBioDraw Ultra (CambridgeSoft, v11.0.1).

[d] Calculated from $\log(P_{CHCl_3,W}/P_{Oct,W}) + C\log P$ by estimating the ratio $(P_{CHCl_3,W}/P_{Oct,W})$ using Hildebrand solubility parameters and molar volumes corresponding to the receptors, octanol and chloroform (Table 3).

[e] Graphical determination.

[f] From extrapolation by linear regression; value could not be obtained experimentally at 10 mM due to solubility limitations.

factor may be defined as the value of the sulphate distribution ratio obtained with the combination of quaternary ammonium salt and anion receptor ($D_{SO_4,Q+R}$) divided by the value of the sulphate distribution ratio obtained with the quaternary ammonium salt used alone ($D_{SO_4,Q}$). Table 5 lists the distribution ratios $D_{SO_4,Q+R}$ and corresponding enhancement factors observed at 10 mM receptor concentration. It is likely that the enhancement factors may be equated with the so-called synergistic factors, defined as $D_{SO_4,Q+R}/(D_{SO_4,Q} + D_{SO_4,R})$, where $D_{SO_4,R}$ is the sulphate distribution ratio obtained with the receptor used alone. However, we were unable to determine these values, due to the limited solubility of the receptors in the absence of Aliquat 336N and to their exceedingly low $D_{SO_4,R}$ values.

An analysis of the lipophilicity of the receptors shows that relative differences in their partitioning to the aqueous phase cannot account for the differences in their effectiveness in enhancing sulphate extraction. In simplest terms, receptor lipophilicity would be expected to be a factor in our systems if more than ~10% of the initial organic-phase concentration partitions to the aqueous phase. On the contrary, the receptors may all be considered to be predominantly distributed to the organic phase, as shown by an estimation of their partition ratios ($P = [R]_{org}/[R]_{aq}$). These were obtained via a calculation of $C\log P$ values, corresponding to the logarithm of the octanol–water partition constants based on the fragment method of Hansch and Leo (*66*). From the $C\log P$ estimates shown in Table 5, it may be seen that the receptors are sufficiently lipophilic that the small concentration loss to the aqueous phase is negligible. As a further check, the values of $C\log P$ were converted to the corresponding logarithm of chloroform–water partition constants using the Hildebrand solubility parameters and molar volumes given in Table 3 (*57*). It may be seen that the partition ratios are changed little, and on this basis it is concluded that no more than 0.01% of any of the receptors is expected to be partitioned to the aqueous phase from chloroform. Moreover, by inspection (Table 5), one may see that there is no correlation between the enhancement factor and $\log P$. Thus, while the lipophilicity of the receptors varies widely in absolute magnitude, all of them are strongly lipophilic, to the point where the differences in lipophilicity cannot account for the variations in extraction enhancement efficiency. We were thus led to conclude that differences in sulphate binding are responsible for the observed disparities in extraction enhancement.

Taken as a measure of sulphate binding, the enhancement factors shown in Table 5 allow insights regarding the effect of the receptor structure on the extraction process to be drawn; this can be done without considering stoichiometry, a matter that will be considered further below. From the enhancement factors, the strongest receptors are apparently **R1**, **R4** and **R7**. As seen previously (*10*), the tetraamide macrocycle **R7** bearing two dansyl groups is remarkably effective, and this may be contrasted with rather weak enhancement by its dimethyl analogue **R8**. The latter receptor system bears two *t*-butyl groups needed to raise the lipophilicity from a $C\log P$ value of 0.15 that would be expected for its unsubstituted analogue (i.e. without its *t*-butyl groups) up to the value of 4.5 estimated for **R8** (Table 5). We earlier found the unsubstituted analogue to be completely inactive in sulphate enhancement (*10*), which we now suggest is in fact due to its poor lipophilicity.

The extraction enhancements shown in Table 5 show significant effects of ring size and substitution among the calixpyrroles tested. The fluorinated calix[5]pyrrole **R1** is

much stronger than the smaller fluorinated calix[4]pyrrole **R2** in chloroform. This may simply reflect the stronger interaction of a flexible donor with a greater number of H-bond donor groups and an acceptor with a multiplicity (12 sites, two each on O—S—O edges of the sulphate tetrahedron (*65*)) of H-bond acceptor sites. However, the relative advantage of **R1** is apparently solvent-dependent and disappears in toluene (*10*), whence **R1** and **R2** are similarly strong. Interestingly, the brominated calix[4]-pyrrole **R3** has comparable strength to the fluorinated analogue **R2**, and both are among the weakest receptors tested. Moreover, the parent calix[4]pyrrole **R6** is stronger than either its fluorinated or brominated analogues. Rather than suggest that halogenation lowers anion binding, we prefer to speculate that the sulphate complex of **R6** may be gaining extra stability owing to its demonstrated ability to accept a cation within the bowl-like cavity formed upon anion binding (*42–44*). In this case, the co-complexed cation would presumably be the Aliquat 336 cation (assuming it is bound). Although the Aliquat 336 cation has not been studied in this regard, methylalkylimidizolium cations have been shown by X-ray crystallography and NMR spectroscopic analyses to occupy the bowl formed when the calix[4]pyrrole binds an anion (*42*). It seems possible, then, that the apparent binding strength of **R6** reflects the same phenomenon of cation dependence characterised in previous binding studies (*44*). Further experiments will be required to elucidate this interesting question.

Finally, it is seen that the nature of the substitution at the *meso* carbons in the family of fluorinated calix[4]pyrroles can influence the apparent enhancement for sulphate in competition with nitrate. The octamethyl derivative **R2** performs relatively weakly under the present conditions. However, substitution of the *meso* carbons by *n*-butyl or spiro-cyclohexyl groups serves to boost the enhancement factor. This is rationalised in terms of a conformational effect on the calixpyrrole, which prefers the *1,3-alt* conformation in its unbound state and has to rearrange to the *cone* conformation for binding (*38*). However, it may also be that the alkyl substitution on the *meso* carbons increases the amphiphilic nature of the *cone* conformation, stabilizing the $Q_2R_nSO_4$ species in concert with the two quaternary ammonium cations that are also associated with the sulphate complex. That is, this species bearing two Aliquat 336 cations and one or two receptor molecules may begin to take on properties of an incipient reverse micelle, wherein the surfactant-like behaviour of the receptors serves to control the apparent sulphate binding behaviour in this system. Again, further study will be needed to confirm or refute this supposition.

Graphical inspection of the enhancement behaviour shown in Figure 3 leads us to suggest that each extracted sulphate anion is bound by one or two receptor molecules, depending on the structure of the receptor. To predict the form of the extraction curve, one may consider that a receptor R combined with Aliquat 336N in chloroform results in formation of an organic-phase sulphate complex $Q_2R_nSO_4$. Table 2 shows the two applicable equilibria, Equations (6) and (7). For the present, we consider that nitrate binding is weak and can be neglected, although this issue will be examined further below. Given that anion exchange occurs in the background independently according to Equation (5), the sulphate distribution ratio takes the form

$$D_{SO_4} = \frac{[\overline{Q_2SO_4}] + [\overline{Q_2RSO_4}] + [\overline{Q_2R_2SO_4}]}{[SO_4^{2-}]_{aq}}. \qquad (12)$$

Substituting the appropriate equilibrium quotient for each organic-phase sulphate species and rearranging gives

$$D_{SO_4} = \left(\frac{[\overline{QNO_3}]^2}{[NO_3^-]^2}\right)(K_5' + K_6'[\overline{R}] + K_7'[\overline{R}]^2), \qquad (13)$$

where overbars denote organic-phase species and the equilibrium constants K_n' are conditional constants equal to the product of K_n and the appropriate activity-coefficient ratio G_n. Since the sulphate concentration is low, all concentrations in this expression may be equated with their initial values. (Since D_{SO_4} did not exceed 1.2×10^{-2} in any experiment, the loading of the receptor would be $<0.1\%$ even with the most conservative assumption of three receptors per sulphate.) It may be seen that D_{SO_4} has a possible quadratic dependence on the receptor concentration. In logarithmic form, Equation (12) has the form

$$\log D_{SO_4} = 2\log[\overline{QNO_3}] - 2\log[NO_3^-] + \log(K_5' + K_6'[\overline{R}] + K_7'[\overline{R}]^2). \qquad (14)$$

This expression predicts the same dependence on organic-phase Aliquat 336N and aqueous-phase nitrate concentration obtained with pure anion exchange (i.e. without receptor as given by Equation (5b)). As the receptor concentration increases from very low values, D_{SO_4} should rise gradually from the value 1.38×10^{-5} obtained with Aliquat 336N used alone. When D_{SO4} is approximately an order of magnitude higher, say, above 2×10^{-4}, the last term in Equation (14) becomes approximately, $\log\left(K_6^1[\overline{R}] + K_7^1[\overline{R}]^2\right)$, and thus, one expects nonlinearity with line-segment slopes in the range 1–2.

As shown in Table 5, the limiting slopes of the curves in Figure 3 in fact fall in the range 1–2, thus providing support for the postulate that each sulphate molecule is bound by one or two molecules of the anion receptor. It may be noted that the three strongest receptors, **R1**, **R4** and **R7**, all exhibit slopes at or near 1.0 over their entire concentration range, suggesting the predominance

of 1:1 binding under the experimental conditions. In these cases, sandwich formation would appear to be less favourable, owing to factors such as more complete inclusion and H-bond donation in the first receptor molecule and steric inhibition of the approach of a second receptor.

In contrast to the above, three of the receptors, **R3**, **R5** and **R6**, exhibit pronounced curvature in their plots, reaching slopes of approximately 2 as they increase in concentration to 10 mM. For these receptors, all calix[4]pyrroles, enhancement is practically negligible until they reach a concentration of 1 mM or greater. Receptor **R8**, a more lipophilic derivative of the parent tetraamide macrocycle known to form a sandwich structure with sulphate (*36*), exhibits a slope of 1.4, leading us to suggest it displays a similar binding tendency in solution.

As shown in Figure 3, the extraction curves for the various receptors added to Aliquat 336N in chloroform are readily fit by SXLSQI using the simple formal model defined in Table 1. This model postulates the organic-phase sulphate complexes Q_2RSO_4 and $Q_2R_2SO_4$ in agreement with the graphical analysis presented above. Only two fitting parameters were employed, namely $\log K_3$ and $\log K_4$, where $\log K_1$ and $\log K_2$, which had been determined in the previous section, were held constant. These constants are listed in Table 4 together with their precision estimates and the overall agreement factors for each system. In general, the statistics of fitting embodied in σ were satisfactory, given the limited number of data points in each set and the significant scatter as the D_{SO_4} values decreased towards the limit of measurement.

The derived constants for the anion-exchange and binding equilibria of interest as summarised in Table 6 reflect the qualitative analysis described above based on the observed graphical behaviour of the plots. The subtractions required to produce each constant are given in the column headers. The constants $\log K_6$ and $\log K_7$ correspond to the anion-exchange equilibria as enhanced by a receptor via complexation of the sulphate anion in the organic phase. The constants $\log K_8$ and $\log K_9$ correspond to the homogeneous binding constants for sulphate, and $\log K_{10}$ is the stepwise constant for addition of the second receptor molecule to the 1:1 complex. Values for the first binding constant $\log K_8$ fall in the range 2.1–4.8, which may be considered typical for many anion-binding reactions in organic solvents. Values of $\log K_{10}$, corresponding to the *apparent* addition of a second receptor molecule, fall in the range 1.0–3.8. The qualifying word 'apparent' is used here in connection with the constants corresponding to the species $Q_2R_2SO_4$ (i.e. $\log K_4$, $\log K_7$, $\log K_9$ and $\log K_{10}$), in that they may be underestimated and should therefore be considered tentative until the question of competitive nitrate binding is definitively resolved (see below). For six of the receptors, $\log K_{10} < \log K_8$; **R3** and **R5** seem to be exceptions, but the large errors preclude a definite conclusion. As shown in the qualitative analysis above, the strongest 1:1 binding occurs with receptors **R1**, **R4** and **R7**, and the apparent addition of the second receptor is more than two and a half orders of magnitude weaker. All of the other receptors have comparable 1:1 binding strengths with a varying apparent ability to engage in sandwich formation.

Although the agreement of the model with the sulphate extraction behaviour observed in our survey of receptors as anion-exchange synergists is encouraging, the model as yet does not include competitive nitrate binding. Nitrate is typically bound weakly by anion receptors, justifying its tentative neglect in the present model. However, its binding may not actually be negligible. As anecdotal evidence, we note that the solubility of **R2** in toluene increases in the presence of Aliquat 336N, making it possible to reach 100 mM of **R2** in toluene (*10*). However, it is also to be noted that nitrate binding in chloroform would be expected to be much weaker.

Although quantifying the potential effect of nitrate binding is desirable, this was made difficult by virtue of the fact that the model already agrees fairly well with the data and that the number of adjustable parameters (i.e. 2) is

Table 6. Derived constants corresponding to anion-exchange and anion-binding equilibria.

Receptor	$\log K_5 = \log K_2 - 2\log K_1$	$\log K_6 = \log K_3 - 2\log K_1$	$\log K_7 = \log K_4 - 2\log K_1$	$\log K_8 = \log K_3 - \log K_2$	$\log K_9 = \log K_4 - \log K_2$	$\log K_{10} = \log K_4 - \log K_3$
R1	−4.65 (1)	0.13 (3)	1.1 (4)	4.78 (2)	5.8 (4)	1.0 (4)
R2	−4.65 (1)	−1.11 (4)	0.4 (1)	3.53 (4)	5.1 (1)	1.6 (1)
R3	−4.65 (1)	−2.04 (14)	0.9 (1)	2.61 (14)	5.6 (1)	2.9 (2)
R4	−4.65 (1)	−0.16 (6)	1.1 (5)	4.49 (5)	5.8 (5)	1.3 (5)
R5	−4.65 (1)	−2.6 (1.2)	1.3 (1)	2.1 (1.2)	5.9 (1)	3.8 (1.2)
R6	−4.65 (1)	−1.01 (9)	1.2 (1)	3.64 (9)	5.8 (1)	2.2 (2)
R7	−4.65 (1)	−0.23 (5)	1.6 (2)	4.42 (4)	6.2 (2)	1.8 (2)
R8	−4.65 (1)	−1.38 (12)	0.7 (1)	3.27 (11)	5.3 (1)	2.1 (2)

Notes: Values of $\log K$ shown in this table correspond to derived constants of interest according to the relations shown in the heading, using values of $\log K_{1-4}$ taken from Table 4. Parentheses indicate uncertainties to the number of digits shown. Corresponding equilibria are defined in Table 2.

already large with respect to the limited range of the survey data. Therefore, it is not possible to refine productively the model with a third species such as $QRNO_3$. That is, the present survey data do not allow determination of the nitrate binding constants. Nevertheless, it is possible to make a few observations about the effect of nitrate binding. First, it is clear from Equation (14) that significant nitrate binding has a mathematical impact on $\log D_{SO_4}$ by decreasing the free organic-phase QNO_3 and R concentrations. In the limit that the receptor is $\geq 90\%$ in the form of the 1:1 nitrate complex $QRNO_3$ (nitrate binding constant $\geq 10^4$), Equations (6) and (7) would effectively become

$$\overline{QRNO_3} + \overline{QNO_3} + SO_4^{2-} \rightleftharpoons \overline{Q_2RSO_4} + 2NO_3^-, \quad (15)$$

$$2\overline{QRNO_3} + SO_4^{2-} \rightleftharpoons \overline{Q_2R_2SO_4} + 2NO_3^-. \quad (16)$$

A log–log representation of the equilibrium quotient for Equation (15) predicts a dependence of $\log D_{SO_4}$ on the term $\log [\overline{R}]_{Tot}([\overline{Q}]_{Tot} - [\overline{R}]_{Tot})$, where the subscript 'Tot' refers to the total concentration of either anion receptor or Aliquat 336N in the organic phase. This dependence will lead to pronounced nonlinearity as the anion receptor concentration is increased. In fact, considering the first derivative with respect to total receptor concentration leads to the prediction that $\log D_{SO_4}$ will reach a maximum at a receptor concentration of 5 mM and then decrease. This behaviour is not observed. Thus, it is likely that only a minor fraction of the receptor molecules could be engaged in nitrate binding. With regard to Equation (16), a log–log analysis leads to a dependence of $\log D_{SO_4}$ on the term $\log [\overline{R}]^2_{Tot}$, meaning that for receptors exhibiting a tendency for sulphate sandwich formation, nitrate binding would still produce a second-power dependence (slope = 2) on receptor concentration. Therefore, estimates of $\log K_4$, $\log K_7$, $\log K_9$ and $\log K_{10}$ from SXLSQI fitting (Table 6) may be underestimated and should be considered tentative or 'apparent' values until the question of nitrate binding is definitively resolved.

The above expectations regarding the potential nitrate-binding effect were confirmed by a sensitivity check performed using SXLSQI. In this procedure, the refinement of $\log K_3$ and $\log K_4$ was performed as before, except for the formal addition of the organic-phase species $QRNO_3$ to the model with a corresponding homogeneous complexation constant ($\log K$ value) fixed at a value of 2.0. This complexation constant is considered conservatively high, corresponding to approximately half of the anion receptor being bound to nitrate at a receptor concentration of 1 mM in the presence of 10 mM Aliquat 336N in the organic phase. For six receptors (all except **R3** and **R5**), it was found that the data could be fit just as well (approximately unchanged agreement factors) with the inclusion of nitrate competition for the reason that the value of $\log K_4$ increases to compensate for it. In terms of the derived constants, the obtained $\log K_6$ values minimally increased by only 0.1–0.3 in the competitive model, while the obtained $\log K_7$ values were significantly increased by 1.0–1.7. For receptors **R3** and **R5**, the receptors having plots with the most pronounced curvature and the lowest 1:1 binding constants (Table 6), the fitting was decidedly worse with inclusion of nitrate competition, which can be safely neglected. Overall, if nitrate competition is important in this system, its effect would be to make $\log K_6$ and $\log K_8$ slightly underestimated and $\log K_7$, $\log K_9$ and $\log K_{10}$ significantly underestimated. This question is being resolved in current investigations.

4. Conclusions

In this work, survey data have been presented showing that two representative families of lipophilic macrocyclic anion receptors produce marked enhancements in the liquid–liquid anion exchange of sulphate in the presence of competing nitrate. The systems examined included tetraamide macrocycles and calixpyrroles bearing a variety of substituents. The anion receptors were combined at 0.1–10 mM in chloroform with 10 mM of the commercial long-chain quaternary ammonium nitrate salt Aliquat 336N with formula $CH_3(C_{8,10}H_{17,21})_3N^+NO_3^-$, and the aqueous phase contained 10 mM of sodium nitrate and 0.1 mM of sodium sulphate traced with $^{35}SO_4^{2-}$. Qualitatively, the comparative data show that macrocycle substituent effects have a strong influence on the ability of a given receptor framework to enhance sulphate extraction. For example, the dansyl N-substituents on the tetraamide macrocycles appear particularly effective. Among the calix[4]pyrroles, a surprise is that fluorination or bromination of each of the pyrrole C—H positions apparently weakens extraction, contrary to the expectation that the electron-withdrawing effect of the halogen substituents should enhance anion binding via stronger H-bonds. Such effects suggest that interactions other than simple H-bond strength are operative in this system. One possibility that bears further investigation is that the quaternary ammonium cation may be playing a role in the context of the supramolecular structure of the organic-phase complex.

In accordance with the major goal of this work, equilibrium-modelling results show that the extraction enhancement may be directly attributed to the complexation of sulphate by the anion receptors in the organic phase. The model development revealed simple behaviour of the quaternary ammonium nitrate salt in acting as a liquid–liquid anion exchanger. As expected, from known solvation thermodynamics, sulphate exchange for two nitrate anions is weak and, in fact, barely detectable under the conditions of the survey. However, addition of the receptors at up to equal concentration to the quaternary

ammonium salt in chloroform increases extraction by up to three orders of magnitude through formation of sulphate complexes of the stoichiometry Q_2RSO_4 and $Q_2R_2SO_4$, where Q is the quaternary ammonium ion and R is the receptor. Provisional extraction and binding constants corresponding to the formation of these two species are reported. However, the role of the competitive binding of nitrate in the model remains to be resolved, and this will require collecting and analysing more extensive data sets on selected receptors. Although the binding of nitrate appears to be fortuitously weak and thus only a minor influence in the present case, the role of competition due to other common matrix anions such as chloride is in general expected to be important and will need to be closely examined in making progress in understanding synergised anion exchange.

Within the context of the growing literature on anion binding by abiotic receptors, the reported binding constants have additional significance of being rare, if not sole, examples of sulphate binding constants in chloroform. Indeed, we were unable to find a reported sulphate binding constant in this solvent or in the related solvents dichloromethane or 1,2-dichloroethane, though hydrogen sulphate-binding constants are known. For example, two 2,5-diamidothiophene macrocycles each featuring two pyrrole units in dry 1,2-dichlorethane have been examined by UV/vis titrations, revealing apparent hydrogen sulphate binding constants of $1.89(10) \times 10^4$ and $1.74(80) \times 10^3$ and corresponding hydrogen sulphate–nitrate selectivity factors of 1.7 and 7.4 (*67*). Bisthiourea tweezers bind sulphate with formation of 1:1 and 1:2 sulphate–receptor complexes in water-saturated nitrobenzene as measured by NMR and polarography, but no binding constants were reported (*68*). It should be appreciated that, owing to the low dielectric constant of chloroform, any binding constant for the doubly charged sulphate anion will entail ion-pairing that must be defined, and water can be expected to play a significant role if it is present. Thus, comparisons of binding constants for this anion, and indeed any anion, in chloroform or related solvents cannot be readily compared without controlling for these aspects. That is to say, an understanding of anion-binding phenomena in solution must take into account the supramolecular nature of the reactant and product species.

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