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Novel dual-host approach in ion pair extraction: a simple tripodal nitrate host facilitates $CsNO_3$ transfer to 1,2-dichloroethane by a large crown ether

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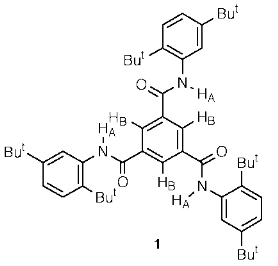
The readily available benzene-1,3,5-tricarboxamide 1 enhances $CsNO_3$ extraction by tetrabenzo-24-crown-8 *via* hydrogen bonding to the nitrate anion, as demonstrated by NMR and electrospray ionization mass spectrometry.

Considerable effort has been expended toward developing host molecules for recognition of cations[1] and, more recently, anions.[2] Surprisingly little attention, though, has been given to recognition of targeted ion pairs,[3] despite potential applications.[4] Historically, ion-pair extraction of alkali and alkaline earth metal salts[5] has tended to be weak, owing to unfavorable dehydration–resolvation energetics for co-extraction of the common inorganic anions.[6,7] This effect simply reflects the normal electrostatic 'bias'[7b] disfavoring small, charge-dense anions (Hofmeister series).[8] Although various successful approaches have been developed to circumvent this 'anion problem',[5a,9] it was our thought that the combination of an anion host with a cation host would represent a singular advance by making anion transfer to the organic phase both more favorable and selective.[10] The idea was shown to work under some conditions in supported liquid membranes,[11] whereas we sought simpler and more synthetically accessible anion receptors as the key to widespread application. Nitrate represents an ion of particular significance in separation chemistry,[4] and certain of its salts, especially $CsNO_3$, are important components of nuclear waste.[4a] However, few designed nitrate receptors have been reported,[12] and neutral lipophilic nitrate hosts are rare.[12a,b] We now report that crown ether extraction of $CsNO_3$ is increased by a simple tripodal host that directly binds nitrate ion through amide N–H hydrogen bonds.

The anion host **1** and controls **2** and **3** were synthesized by standard methods from the corresponding anilines and acid chlorides.[13] The chosen benzene-1,3,5-tricarboxamide skeleton combines the desired C_3 symmetry environment for recognition of the nitrate anion with synthetic ease and flexibility. Amides and ureas have been employed in anion host–guest chemistry.[2,14–17] Moreover, the potential for variation of the aniline moiety allows 'tuning' of the electronic and steric contributions to the binding, as well as solubility and hydrophobicity. Tetrabenzo-24-crown-8[18] was used as the cation host because it effectively complexes the caesium cation[19] in 1,2-dichloroethane, while keeping the encapsulated Cs^+ cation and the NO_3^- anion fully dissociated.[20]



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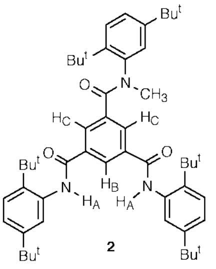

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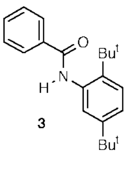

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The distribution results[21] (Fig. 1) show that amides **1** and **2** (but not monoamide **3**) enhance the extraction of $CsNO_3$ by tetrabenzo-24-crown-8. At 10 mM, tripodal amide **1** enhances the extraction by a factor of 1.9 ($D_{Cs} = 6.3 \times 10^{-3}$ for **1** *vs.* 3.3×10^{-3} for the crown-only experiment), whereas the same concentration of bipodal amide **2** enhances Cs extraction by a factor of 1.3 ($D_{Cs} = 4.2 \times 10^{-3}$). The enhancement is dependent on the amide concentration, as expected (Fig. 1). No extraction was detected with the amides alone ($D_{Cs} < 2 \times 10^{-5}$).

The nitrate binding affinities of **1** and **2** were determined by ^1H NMR titrations with $(Bu_4N)NO_3$ in 1,2-dichloroethane-d_4. Non-linear regression analysis[22] of the binding isotherms[23] obtained from the downfield chemical shift changes for the N–H amide (H_A) resonances ($\Delta\delta$ N–H), as well as for the *ortho* C–H aromatic (H_B) resonances ($\Delta\delta$ C–H), gave 1:1 association constants (K_a) of 250 M^{-1} for the formation of $\mathbf{1}\cdot NO_3^-$ *vs.* 23 M^{-1} for $\mathbf{2}\cdot NO_3^-$ (Table 1). For the diamide **2**, both H_A and H_B gave significant downfield shift changes, while the H_C chemical shift remained virtually constant. This is indicative of nitrate complexation by two hydrogen bonds.[16] In contrast, $\mathbf{1}\cdot NO_3^-$ exhibited a single downfield-shifted resonance for H_B, suggest-

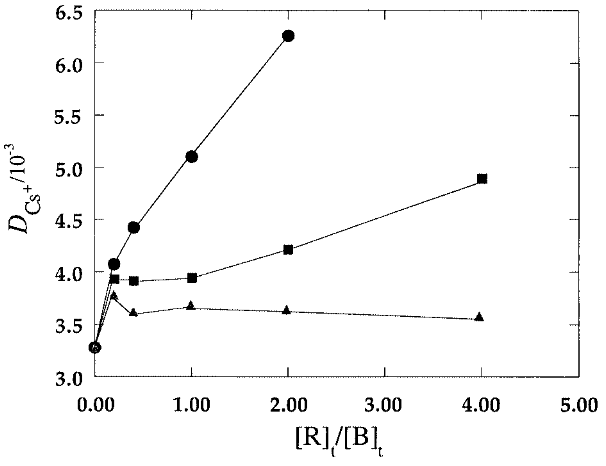

Fig. 1 Plot of D_{Cs} *vs.* $[R]_t/[B]_t$ at 25 °C, where $[R]_t$ is the total amide (R = **1**–**3**) concentration and $[B]_t$ is the total crown concentration (5 mM): (●) **1**, (■) **2** and (▲) **3**. Errors are estimated to be < 5%.

Table 1 Chemical shift changes, association constants, and ΔG^o values at 18.1 °C for $\mathbf{1}\cdot NO_3^-$ and $\mathbf{2}\cdot NO_3^-$ formation

Compound	δ_H(N–H)	δ_H(2-C–H)	K_a/M^{-1}	ΔG^o/kJ mol^{-1}
1	8.01	8.61		
$\mathbf{1}\cdot[NO_3^-]$	9.32	8.78	250[a]	−13.4
2	7.58	8.22		
$\mathbf{2}\cdot[NO_3^-]$	9.54	8.75	23[a]	−7.5

[a] Errors are estimated to be < 5%.

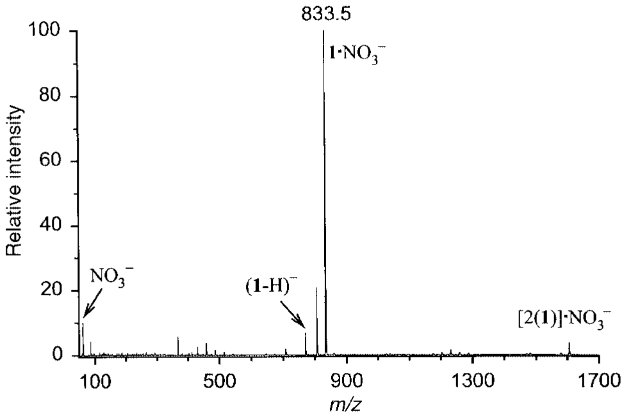

Fig. 2 Negative ion electrospray ionization mass spectrum for **1**·NO$_3^-$ in extraction solvent. The peak at *m/z* 806.5 corresponds to **1**·Cl$^-$ (ref. 25). The results were reproduced in solutions of **1** and (Bu$_4$N)NO$_3$.

ing participation of all three N–H groups, whether by pairs in fast equilibrium or in concert.

Negative ion mode electrospray ionization mass spectrometry[24] confirms the ^{1}H NMR conclusion of a 1:1 **1**·NO$_3^-$ complexation stoichiometry (*m/z* = 833.5; Fig. 2). Receptor **2** also gave a peak corresponding to **2**·NO$_3^-$, but with a lower intensity. No evidence for **3**·NO$_3^-$ was observed.

Based on these observations, and taking into consideration the ten-fold higher K_a for **1**·NO$_3^-$ *vs.* **2**·NO$_3^-$, which cannot be attributed solely to the statistical factor (3), we suggest that a contribution of the third amide group in **1**·NO$_3^-$ is primarily responsible for the higher extraction enhancement for **1** *vs.* **2**. The ^{1}H NMR association constants would ideally imply extraction enhancements of 3.5 and 1.2, respectively, which are consistent with the actual values of 1.9 and 1.3.[26]

In conclusion, the present results demonstrate the viability of employing two simple host molecules for transporting a selected salt *vs.* targeting only a single ion. The extraction enhancement obtained sets the ground for further research into using different hosts and target guest systems, as well as in elucidating aspects of speciation, selectivity, and structure of the supramolecular complexes involved.

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26 The enhancement factors are approximated as $1 + K_a[\mathrm{R}]_t$ assuming formation of 1:1 **R**·NO$_3^-$ complexes. Probable aggregation of **R** or formation of **R**·crown complexes would be expected to reduce the enhancement and to be stronger for **1** than for **2**.

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