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Towards promising oxoanion extractants: azacages and open-chain counterparts †

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The efficiency of a series of amino-azacryptands for encapsulation and extraction of the oxoanions pertechnetate and perrhenate from aqueous solution is investigated and compared with that of their open-chain counterparts. The aqueous formation constants for oxoanion association with the cryptands were determined by pH potentiometry and/or NMR, and X-ray analysis of single crystals provides evidence for encapsulation. The extractabilities could not be explained solely on the basis of ligand lipophilicity; the level of protonation also plays an important role.

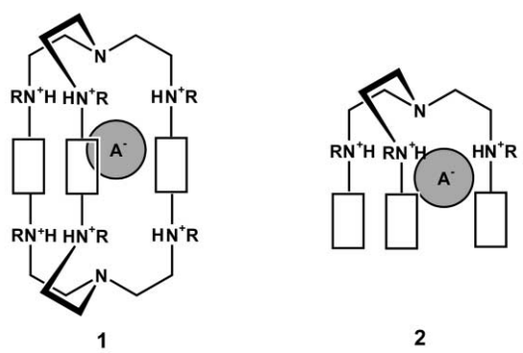
Introduction

Many high oxidation state, potentially toxic, metals and metalloids exist in the environment in oxoanionic form:[1] *e.g.*, those of arsenic, antimony, chromium, selenium among others. Recovery and recycling of such species can be problematic due to their high aqueous solubility. Thus, the challenging task of designing functional ligands for sequestration of oxoanions is of considerable interest in respect of applications in environmental monitoring and clean-up where oxoanions such as nitrate, phosphate, chromate, selenate and sulfate constitute persistent pollutants in soils and water.[2] There is also a specific concern about radionuclide build up in the form of soluble and bioavailable oxoanions such as pertechnetate in the neighbourhood of nuclear reprocessing plants. In addition oxoanion complexation is of particular interest in connection with radionuclide use in medical diagnostics and therapeutics because heavily used nuclides ^{99m}Tc and ^{188}Re are generated in isotonic solution in the form of perrhenate or pertechnetate MO_4^- anions; direct complexation of these species from the generator eluate would be a very desirable development.[3]

The first requirement for an efficient extraction process which can lead to separation and recovery of toxic or valuable material from effluent, aquifers or process streams is that the target anion should be well complexed by the ligand used so that the free energy of hydration can be overcome. In this connection the potentially encapsulating cryptand (**1**, see Scheme 1) or tripodand (**2**) ligands can have an advantage over simple open chain analogues because of host preorganisation together with the cooperative binding which results from a combination of convergent electrostatic field and focussed hydrogen bonding. The second requirement is that the solubility in the organic layer of both free protonated ligand and complex should be sizeable. Thus to make the most effective ligands for target oxoanions we need to design for appropriate size, shape, basicity and lipophilicity.[4]

Over recent years we have shown[5–8] that protonated forms of the aminocryptand hosts L^1 to L^3 (see Scheme 2) are effective complexants for oxoanions, especially tetrahedral oxoanions. These hosts are readily synthesised by borohydride reduction of the hexaimine products of [2 + 3] Schiff-base condensation of triamines and dicarbonyls.[5] X-Ray crystallographic studies demonstrate encapsulation of the target anions within the cavity of the hexaprotonated hosts, where they are tethered by a range of moderately strong hydrogen-bonding interactions, both direct (NH^+–$O_{oxoanion}$) and indirect (through water, furnished *via* remnant hydration of the oxoanion). The complexation constants for perchlorate are large enough to be measured, with some confidence, as in the range ≈ 2.3–3.5. It is noteworthy that previous studies of perchlorate complexation either record no complexation[9] or tentative values of the order of 1,[10,11] and some authors have continued to use perchlorate as a supposedly inert ionic strength medium for potentiometric studies of other anions.[12–14] Comparison of the crystallographic H-bond distances in the mononegatively charged perchlorate ion cryptate *versus* those of the dinegatively charged, but similarly sized selenate, chromate or thiosulfate anions does not show any noticeable overall shortening such as might accompany significant strengthening of the interaction. However, even the approximate estimation of complexation constants obtained *via* the NMR shift technique makes it clear that a charge-based selectivity exists,[7] which warrants careful potentiometric study of the dependence of complexation constant on electrostatic charge in both host and guest.

In recent studies we have examined the value of such aminocryptands with the tris(2-aminoethyl)amine (tren) scaffold as



Scheme 1

† Based on the presentation given at Dalton Discussion No. 5, 10–12th April 2003, Noordwijkerhout, The Netherlands.

Electronic supplementary information (ESI) available: loading experiments of the organic extracts with perrhenate. See http://www.rsc.org/suppdata/dt/b2/b210289g/

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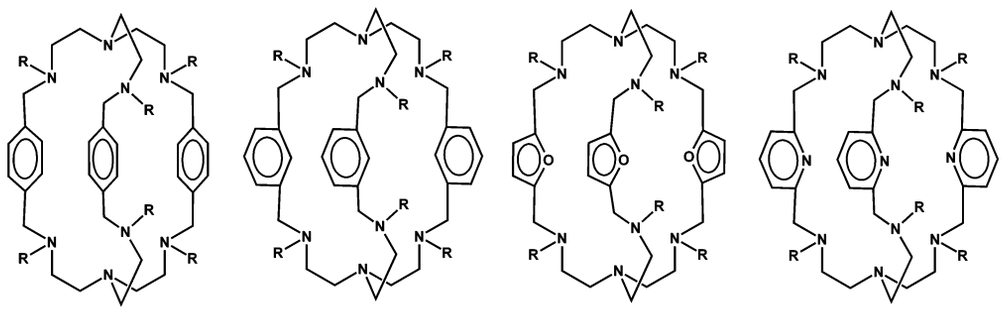
Table 1 Protonation constants for L^{2a} (R3Bm), $\log \beta \pm 1\sigma$ determined by pHmetry ($I = 0.1$ M OTs, $T = 298$ K)

(L,H)	1,1	1,2	1,3	1,4	1,5	1,6
$\log \beta$	9.83 ± 0.07	19 08 ± 0.04	27.66 ± 0.04	34.79 ± 0.04	41.18 ± 0.04	46.76 ± 0.05



Scheme 2

extractants for pertechnetate and perrhenate from aqueous solutions.[3] The efficiency of oxoanion extraction correlates primarily with the distinctive acid–base behaviour of the different aminocryptands. The highest extractabilities were achieved at pH values between 7 and 8 in which less highly protonated species dominate. These results indicate that both the increasing hydrophilicity caused by increased levels of protonation and the energetically unfavourable transfer of highly charged species from the aqueous into the organic phase allow only a weak extraction of the oxoanions from acidic solutions. In contrast to the situation under strongly acidic conditions where inclusive anion complexation is demonstrated, at neutral pH only peripherally bound anion complexes were structurally characterised.

Besides the aminocryptands, another promising approach for oxoanion complexation is based on the use of open-chain counterparts having the tripodal tren system as backbone functionalized by hydrogen bonding moieties, as amides, ureas or thioureas.[15–19] More recently, these compounds have been employed for nitrate extraction in a dual cation/anion strategy.[20–22] It is interesting to note that even the protonated tren unit itself gives well characterized complexes not only with halogenides[23–25] or dicarboxylates[26] but also with the oxoanions perchlorate[27] and molybdate.[28] In all cases the electrostatic interactions are associated with multiple hydrogen bonds.

In this paper we will illustrate the use of aminocryptands L^1 to L^4 to bind perrhenate and/or pertechnetate and to extract these ions into an organic phase. For the description of the complexation behaviour of the ligands aqueous formation or complexation constants have been measured by NMR and potentiometric methods and compared with X-ray crystallographic investigations of solid complexes, where available. The liquid–liquid extraction behaviour of the compounds will be discussed on the basis of these binding and structure studies and compared with related results of their open-chain counterparts L^5 to L^{12} (see Scheme 3). The functionalized tren derivatives have been synthesised *via* the Schiff-base route *via* reaction of tren with the corresponding aldehydes and subsequent borohydride reduction.

Results and discussion

Our previous work[6] on determination of the formation constants for the relatively weakly complexed mononegative anions perchlorate and nitrate demonstrates good agreement between values measured by NMR (at pH 3; all ligand present in the hexaprotonated form, *i.e.* only $H_6L^{6+}X^-$ considered) and potentiometric studies over the pH range 3 to 11 (ligand successively present at decreasing levels of protonation). The large, size excluded tosylate anion is used as the reference for these studies;[6,7,29] modification of the tosylate-medium ligand protonation constants in the presence of the anion of interest is indicative of host–guest interactions. The overall protonation constants for H_6L^{2a} in tosylate medium are given in Table 1. Inspection of the corresponding perchlorate data[6] showed that only at protonation levels above 5 was there significant deviation from the results for the tosyl calibrant, suggestive of anion complexation, *i.e.* in the presence of perchlorate, a slightly more basic pH is required to effect the reaction $H_6L^{6+} \longrightarrow H_5L^{5+} + H^+$. So it appears that, with perhaps some small contribution from the pentaprotonated host, only the hexaprotonated cryptand has the capability for complexation of this oxoanion.

We have now analysed, *via* both potentiometry and NMR, the complexation constants of protonated forms of L^2 with the target anion perrhenate. It can be seen (Tables 2 and 3) that these are significantly larger for ReO_4^- than for ClO_4^- at the hexaprotonated level of the host, and evidence of successful complexation of ReO_4^- at pentaprotonated level (*via* the NMR technique) and lower levels (*via* the potentiometric method) infers an overall stronger interaction than for perchlorate.

Use of the NMR shift technique[30] at constant pH (4 and 5.9) generates log *K* values (Table 3) in good agreement with those derived *via* potentiometric analysis over the range 3–11. The speciation plot, Fig. 1, illustrates that at higher pH there is

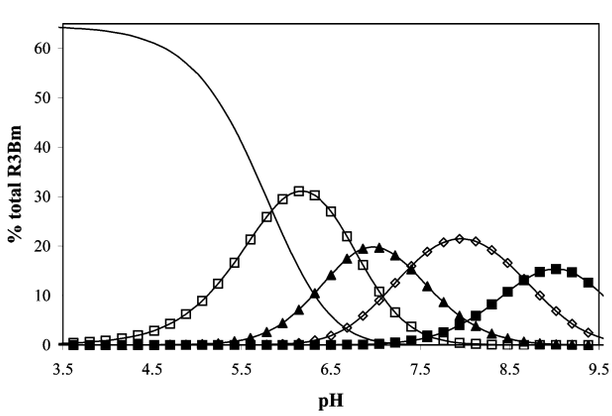
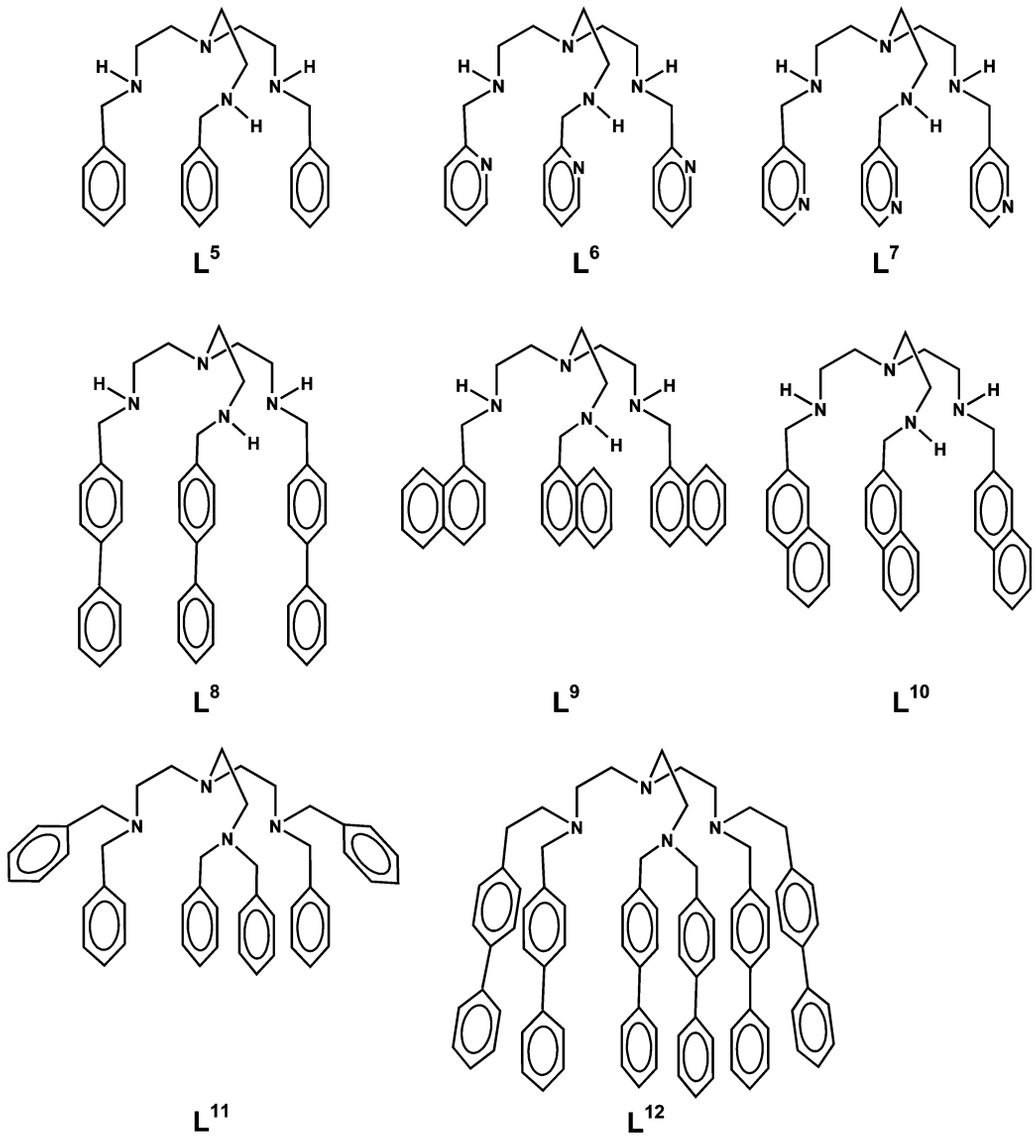


Fig. 1 Distribution of $H_xL^{2a}(ReO_4)^{(x-1)+}$ (x = 2–6) species as a function of pH. Calculated from the formation constants determined by pHmetry (Tables 1 and 2) for equimolar (1 mM) concentrations of L^{2a} and ReO_4^-. (—) $H_6L^{2a}ReO_4^{5+}$; (□) $H_5L^{2a}ReO_4^{4+}$; (▲) $H_4L^{2a}ReO_4^{3+}$; (◇) $H_3L^{2a}ReO_4^{2+}$ (■) $H_2L^{2a}ReO_4^+$.



Scheme 3

Table 2 Stepwise formation constants, log $K \pm 1\sigma$, for $H_xL^{2a}(ReO_4)^{(x-1)+}$ (x = 6–2) and $H_6L^{2a}(ClO_4)^{5+}$ determined by pHmetry (I = 0.1 M OTs, T = 298K)

Reaction	log K
$H_6L^{6+} + ReO_4^- \rightleftharpoons H_6LReO_4^{5+}$	3.71 ± 0.10
$H_5L^{5+} + ReO_4^- \rightleftharpoons H_5LReO_4^{4+}$	3.45 ± 0.09
$H_4L^{4+} + ReO_4^- \rightleftharpoons H_4LReO_4^{3+}$	3.06 ± 0.08
$H_3L^{3+} + ReO_4^- \rightleftharpoons H_6LReO_4^{2+}$	2.81 ± 0.07
$H_2L^{2+} + ReO_4^- \rightleftharpoons H_2LReO_4^{+}$	2.72 ± 0.07
$H_6L^{6+} + ReO_4^- \rightleftharpoons H_6LClO_4^{5+}$	3.24 ± 0.04

Table 3 Stepwise formation constants, log $K \pm 1\sigma$, for $H_6L^{2a}(ReO_4)^{5+}$ and $H_5L^{2a}(ReO_4)^{4+}$ determined by NMR (I = 0.1 M OTs)

Reaction	pH	log K
$H_6L^{6+} + ReO_4^- \rightleftharpoons H_6L\ ReO_4^{5+}$	4.00	3.76 ± 0.10
$H_5L^{5+} + ReO_4^- \rightleftharpoons H_5L\ ReO_4^{4+}$	5.90	3.66 ± 0.06

considerable overlap between anion complexes with the various protonation levels of the host and thus the fixed-pH NMR approach becomes less feasible in practice (*i.e.* the NMR shift can no longer be unambiguously ascribed to one particular species). However the potentiometrically derived complexation constants at protonation levels as low as two are still measurable, and show appreciable complexation of perrhenate. This suggests a possibility of successful extraction should the mononegatively charged perrhenate complex of the diprotonated host be sufficiently soluble in organic solvents. Unfortunately, we found no evidence for formation of the complex of the monoprotonated host, where charge neutrality should generate good organic solubility.

Structural studies

X-Ray crystallographic structure determination was attempted on a number of perrhenate complexes of *m*-xylyl, L^{2a}, and pyridine-spaced, L^{4a}, hosts at the hexaprotonated level. In the presence of excess perrhenate ion, the all-perrhenate complex of $[L^{2a}H_6]^{6+}$ was isolated from EtOH solution in the form of X-ray-quality crystals.

The structure (Fig. 2) of the $[L^{2a}H_6{\cdot}ReO_4]^{5+}$ cation is not dramatically different from that of the perchlorate analogue reported earlier,[6] although the symmetry of the anion site is lower. The included anion is tethered by a similar mix of direct NH^+–O_{anion} and indirect (water-mediated) H-bonds, and these are of similar bond length to those in the perchlorate case.[6] There are also H-bonds directed to anions held outside the cryptand cavity, some of which are just as short though not as numerous (see Table 4). As in the case of the perchlorate structure, one of the oxoanion O atoms, pointing in the direction of the bridgehead N, is not involved in H-bonding. However unlike the perchlorate structure, NH^+ donors from both ends

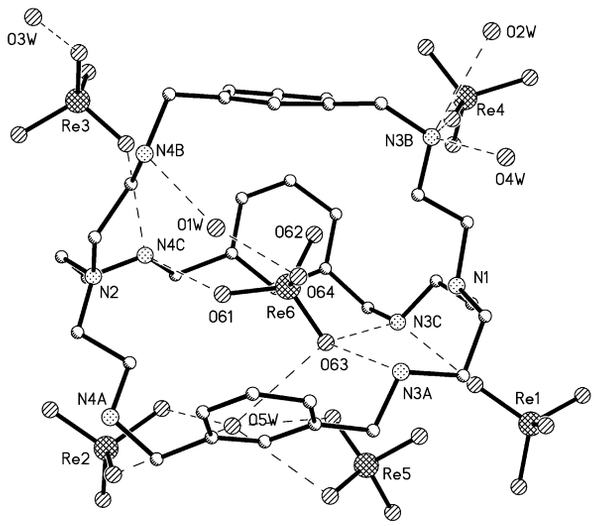


Fig. 2 Illustration of directed H-bond interactions in the $[L^{2a}H_6 \cdot ReO_4]^{5+}$ cation.

of the cryptand are involved in direct H-bonding to the anion. Also, as in many oxoanion structures we have examined, some of the shortest H-bonds involve the few molecules of hydrate water retained by the anion, which presumably have more freedom to position themselves for most efficient H-bonding. These often act as bridges [as shown in Fig. 2 for O(1W) between O(64) and N(4B)] between an oxoanion and a protonated amino group. The larger size and hence tighter cavity fit of the perrhenate anion (thermochemical radius[31] 260 pm for perrhenate *vs*. 240 pm for perchlorate) may partly explain the higher stability of the perrhenate complexes (*i.e*. for $[H_6L^2]^{6+}$ encapsulation of ReO_4^-, $\log K = 3.71$ and of ClO_4^-, $\log K = 3.24$) and thus suggest that the oxoanion is retained in the host cavity in solution.

An attempt was made to investigate competition between perchlorate and perrhenate for the cavity site, by altering the stoichiometric ratio used in synthesis. Single crystals isolated from solutions of 0.001 M $H_6L^{2a}(ClO_4)_6$ with ratios of added $KReO_4$ between 1 : 1 and 1 : 6 were examined by X-ray crystallography.[32] The perrhenate ion was always found in the cavity site although varying amounts of perchlorate, in response to stoichiometry, were present in the complex. The structure of the cation thus remained unchanged as the stoichiometric ratio altered, only the distribution of the counter ions varying.

In contrast, the oxoanion is not encapsulated within the cavity in the pyridine-spaced system (Fig. 3).[32] As often happens with this ligand[32–34] the host acts as a cleft rather than cavity-binder, retaining three perrhenate anions in each of the clefts formed between arms of the cryptand in the relatively open host conformation adopted. This applies to both of the unique cations in the unit cell (Fig. 3a,b). In solution, however, we found no evidence for a 1 : 3 cryptand : ReO_4^-species; the 1 : 1 model provides a good fit to the NMR experimental data. Given the lower basicity and hence weaker binding by this hexaprotonated ligand, as compared to the *m*-xylyl host (Table 5), we might expect that formation of any species with greater cryptand : oxoanion ratios would only be observed under conditions of very high anion excess (as seen previously in the L^{2a}–nitrate system[6]).

When measured by the NMR method, at fixed pH of 3, perrhenate complexation appears stronger than those of perchlorate or nitrate. Both the nitrate cryptate[34] of $L^{4a}H_6^{6+}$ and the perchlorate cryptate[33] of an octaprotonated version of this ligand have been shown to use a cleft, rather than cavity, oxoanion binding site. This cleft binding arrangement appears structurally adaptable, *e.g*. by alteration of the angle between

Table 4 Hydrogen bonds [Å]

$[(H_6L^{2a})(ReO_4)](ReO_4)_5 \cdot 5H_2O$

N3A ··· O63	2.99(2)	O1W ··· O53#1	2.97(2)
N3A ··· O52#1	2.75(2)	O1W ··· O5W#1	2.79(2)
N4A ··· O33#2	2.84(2)	O2W ··· O42#6	2.99(3)
N4A ··· O22#1	3.023(19)	O2W ··· O3W#5	2.82(2)
N4A ··· O14#3	2.881(17)	O3W ··· O12#4	2.95(2)
N3B ··· O44	3.05(2)	O3W ··· O34	3.04(3)
N3B ··· O4W	2.90(2)	O3W ··· O43#7	3.12(2)
N3B ··· O2W	2.85(2)	O4W ··· O14#1	3.19(2)
N4B ··· O1W	2.698(19)	O4W ··· O23#8	2.71(2)
N4B ··· O12#4	2.805(18)	O4W ··· O54#1	3.01(2)
N3C ··· O63	2.938(18)	O5W ··· O21	2.75(2)
N3C ··· O13	2.729(16)	O5W ··· O24	3.12(2)
N4C ··· O61	2.862(19)	O5W ··· O51	2.99(2)
N4C ··· O32	2.81(2)	O5W ··· O53	2.94(3)
O1W ··· O24#1	3.10(2)	O5W ··· O63	3.13(2)

$H_6L^{4a}(ReO_4)_6 \cdot H_6L^{4a}(ReO_4)_4(ClO_4)_2 \cdot 3H_2O$

N4A ··· O11$1	2.82 (1)	N13C ··· O54	2.81 (2)
N4A ··· O31$2	2.86 (2)	N13C ··· O72	3.12 (2)
N4A ··· O121	2.83 (1)	N13C ··· O114	2.92 (2)
N4B ··· O23$3	2.90 (2)	N13C ··· O113	3.01 (2)
N4B ··· O111	2.89 (2)	N13D ··· O33	2.85 (2)
N4C ··· O52	2.89 (2)	N13D ··· O42	3.13 (2)
N4C ··· O82	2.96 (2)	N13D ··· O44	3.14 (2)
N4C ··· O113	2.91 (2)	N13E ··· O12	2.71 (2)
N4D ··· O10@b	2.69 (4)	N13E ··· O73	2.86 (2)
N4D ··· O42	2.94 (2)	N13F ··· O12	2.88 (2)
N4D ··· O92	3.03 (3)	N13F ··· O24	3.01 (2)
N4D ··· O103a	3.06 (3)	N13F ··· O74	3.12 (2)
N4E ··· O33	3.10 (2)	O3W ··· N11E	3.29 (2)
N4E ··· O61	2.97 (2)	O1W ··· O94	2.83 (4)
N4E ··· O3W	2.86 (2)	O1W ··· O103a	2.92 (5)
N4F ··· O21$1	2.77 (2)	O1W ··· O104a	2.90 (4)
N4F ··· O71	2.73 (2)	O1W ··· O10#b	2.99 (5)
N13A ··· O34$4	3.02 (2)	O2W ··· O81$5	2.81 (2)
N13A ··· O64$4	2.79 (2)	O2W ··· O93$6	2.95 (3)
N13A ··· O123	3.02 (2)	O2W ··· O101$6a	3.03 (3)
N13B ··· O111	3.13 (2)	O2W ··· O3W	2.97 (3)
N13B ··· O123	2.95 (2)	O3W ··· O72	3.12 (2)

a and b refer to the two components of the disorder associated with the perrhenate anions. Symmetry transformations used to generate equivalent atoms: #1 $x + ½, -y, z + ½$. #2 $x, y - 1, z$. #3 $x - ½, -y, z + ½$. #4 $x, y, z + 1$. #5 $x + ½, 1 - y, -z + ½$. #6 $x + ½, 1 - y, z + ½$. #7 $-½ + x, 1 - y, ½ + z$. #8 $1 + x, y, z$. $1 $x, 1 + y, z$. $2 $½ + x, 1½ - y, z$. $3 $2 - x, 1 - y, ½ + z$. $4 $½ + x, ½ - y, z$. $5 $x, -1 + y, z$. $6 $1½ - x, -½ + y, ½ + z$.

the strands it can comfortably accommodate both the perchlorate ions and one larger perrhenate ion (Fig. 3a) suggesting, however, that some of the selectivity associated with the more rigid cavity binding conformations may be lost. The larger log *K* values recorded for perrhenate than for perchlorate complexation using the cleft conformation may indeed largely derive from more favourable desolvation effects.[31]

The studies described however all relate to highly protonated, often hexaprotonated, states of the host cryptands, and may not be directly relevant to behaviour at higher pH where charge neutrality of the anion/cryptate assembly permits its extraction into organic solvents. Previous work[3] has shown that in the tri- and di-protonated versions of the *p*-xylyl spaced ligand, the perrhenate ion is not encapsulated in the cryptand, at least in the solid state. Instead the cryptand host is held in a long and narrow conformation by intramolecular interactions including NH–N H-bonds between secondary amino functions.

The extraction studies described in the final section have been carried out under near-neutral pH conditions, where the cavity-binding conformation may not be the most favoured one, even for hosts like L^{2a} which have been shown[5] to make general use of it in both cation and anion coordination.

Table 5 Comparison of stepwise formation constants, log $K \pm 1\sigma$, for L^{2a} (R3Bm) and L^{4a} (R3P) with NO_3^-, ClO_4^- and ReO_4^- determined by pH and NMR titrations

	NO_3^-		ClO_4^-		ReO_4^-	
Species	NMR	pHmetry	NMR	pHmetry	NMR	pHmetry
H_6R3Bm^{6+}	3.74 ± 0.09 [a]	3.41 ± 0.06 [a]	3.53 ± 0.04 [a]	3.24 ± 0.06 [a]	3.76 ± 0.10 [b]	3.71 ± 0.10 [b]
H_5R3Bm^{5+}	not studied	2.53 ± 0.06 [c]	not studied	nd [d]	3.66 ± 0.05 [b]	3.45 ± 0.09 [b]
H_6R3P^{6+}	2.77 ± 0.08 [c]	2.67 ± 0.04 [c]	2.56 ± 0.08 [c]	nd [d]	3.20 ± 0.10 [b]	Not studied

[a] Ref. 6. [b] This work. [c] Ref. 34. [d] nd = no detectable complexation.

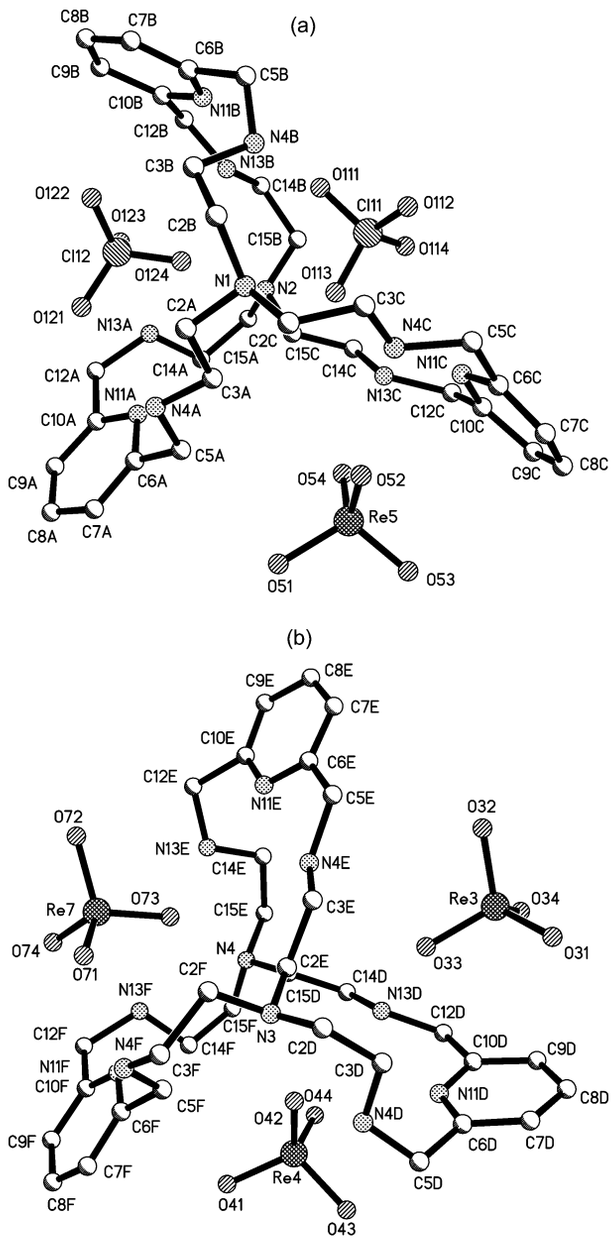


Fig. 3 Crystal structure of $H_6L^{4a}(ReO_4)_6 \cdot H_6L^{4a}(ReO_4)_4(ClO_4)_2 \cdot 3H_2O$ showing cleft binding of the oxoanions for two unique H_6L^{4a} cations.

Methylated cryptands

Despite relatively good complexation properties, the poor solubility in organic solvents of the secondary-amino cryptands adversely affects the capacity of these hosts to achieve transport of the oxoanionic targets from aqueous solution into non-polar media. This drew attention to the advantages of using N-substituted tertiary aminocryptands instead. The N–Me derivatives Me_6R3Bm, Me_6R3F and Me_6RP were synthesised by the standard method of treatment with formic acid /formaldehyde, and purified by size exclusion chromatography. Before use of L^{2b} and L^{4b} in extraction experiments, their basicity was monitored *via* potentiometric studies, in case substitution may have affected their protonation capacity. Cumulative $\Sigma\log K$ values show a small increase of acidity upon N-methylation (Table 6). This trend is in the expected direction, given the lower basicity of tertiary *versus* secondary amines.

Liquid–liquid extraction studies

The extraction behaviour of the azacages L^1 to L^4 and of the open-chain counterparts L^5 to L^{12} towards pertechnetate and/or perrhenate was studied using the extraction system $NaTcO_4$ or $NaReO_4$–buffer–H_2O/ ligand–$CHCl_3$. Fig. 4 shows an overview of the extraction strength for all the ligands studied at comparable experimental conditions (pH 7.4; = $c_{ReO_4^-,\ TcO_4^-}$ 1×10^{-4} M, $c_{ligand} = 1 \times 10^{-3}$ M). In all investigated cases TcO_4^- is slightly more readily extracted than ReO_4^-. This fact is a well-known finding for various extractant types and it is based on the higher lipophilicity of the pertechnetate anion.[31] Generally, the extractabilities for the aminocryptands are rather limited under the selected conditions, but a small increase could be found in the order $L^{1a} < L^{4a} < L^{2b} \approx L^{1b} < L^{3b} < L^{4b}$. In all cases the methylated derivatives lead to a significantly better extraction as compared to the unsubstituted analogues. The highest extraction was observed for the pyridine spaced hexamethylated aminocage L^{4b}. Amazingly, within the series of tripodal tren derivatives there are pronounced differences in the extraction properties; in some cases these are enhanced, and in other cases diminished, relative to the cages. The ligands L^5, L^8 and L^{11} give extractabilities between 16% and 26% for TcO_4^- which is comparable with the cages. In contrast, the tris(2-naphthyl) substituted ligand L^{10} extracts pertechnetate with the highest efficiency of all studied compounds, whereas L^7, L^9 and L^{12} show only a very weak tendency to transport this oxoanion into the organic phase.

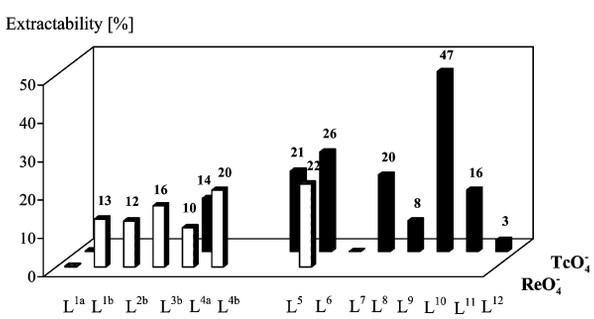


Fig. 4 Extractabilities of pertechnetate and perrhenate with azacages L^1–L^4 and tripodal counterparts L^5–L^{12} [$NaTcO_4$] or [$NaReO_4$] = 1×10^{-4} M; pH 7.4 (HEPES/NaOH buffer); [ligand] = 1×10^{-3} M in $CHCl_3$; shaking time 30 min; $T = 23 \pm 1$ °C.

For more information about the extraction equilibrium, the influence of pH on the extraction of the anions ReO_4^- and TcO_4^- by the various ligands was investigated. The studies with L^{4a}, L^{4b} and L^6 are presented in Fig. 5. With increasing pH, the extractabilities of these ligands increase. The maximum extraction is reached between pH 7 and 8, then decreases with

Table 6 Stepwise protonation constants, log $K \pm 1\sigma$, for cryptands, L^{2a}, L^{4a}, and their methylated derivatives determined by pHmetry (I = 0.1 M OTs, T = 298 K)

(L,H)	L^{2a}	L^{2b}	L^{4a}	L^{4b}
1,1	19.08 ± 0.07[a]	18.84 ± 0.09[a]	9.48 ± 0.07	18.94 ± 0.08[a]
1,2			8.80 ± 0.05	
1,3	8.58 ± 0.04	8.13 ± 0.09	7.76 ± 0.04	8.08 ± 0.08
1,4	7.13 ± 0.04	7.16 ± 0.07	7.10 ± 0.04	7.01 ± 0.09
1,5	6.39 ± 0.04	6.14 ± 0.07	6.46 ± 0.04	5.95 ± 0.09
1,6	5.58 ± 0.05	5.22 ± 0.08	5.76 ± 0.04	4.88 ± 0.11
Σlog K	46.76	45.49	45.36	44.86

[a] log β_2 (only 5 protons could be removed by titration in aqueous solution).

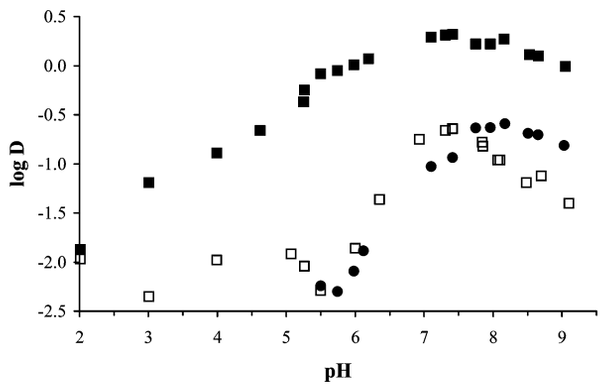


Fig. 5 Extraction of pertechnetate and perrhenate with L^{4a}, L^{4b} and L^6 as a function of pH. [$NaTcO_4$] (L^6, L^{4a}) or [$NaReO_4$] (L^{4b}) = 1×10^{-4} M; pH = 2.0–5.2 (NaOAc/HCl buffer); pH = 5.2–6.3 (MES/NaOH buffer); pH = 6.9–8.0 (HEPES/NaOH buffer); pH = 8.0–9.1 (TAPS/NaOH buffer); [L^{4a}, L^{4b}] = 1×10^{-3} M and [L^6] = 5×10^{-3} M in $CHCl_3$; shaking time 30 min; T = 23 ± 1 °C. (■) L^6, (●) L^{4a}, (□) L^{4b}.

increasing basic conditions in solution. This trend is in agreement with the changing protonation state of the ligands. At lower pH values the ligands will be more highly protonated, and thus more hydrophilic, leading to a decrease in the extraction ability from the aqueous into the organic phase. The higher extractabilities of L^{4b}, as compared to L^{4a} at pH 7.4, are consistent with the formation of more hydrophobic species for L^{4b}. As expected, these results support the interpretation that the aqueous–organic phase transfer is more favoured in the case of less highly charged cryptand–anion complex species, despite their lower formation constants in aqueous solution.

Generally, the effect of pH on the perrhenate extraction by the tripodal tren derivatives is less pronounced than in the case of the cages, as illustrated by ligand L^6. The reasons for this behaviour arise from both the lower number of protonation steps, and the smaller differences in the protonation constants.[35] Obviously, this behaviour does not strongly depend on the number and nature of the substituents.

To gain more information about the gradation of extractant lipophilicity, distribution measurements of the ligands have been performed between aqueous buffer solution (pH 7.4) and 1-octanol. The orders of increasing lipophilicity obtained for the cages are $L^{4a} \approx L^{4b} < L^{1a} < L^{3b} < L^{1b} < L^{2b}$ and for the tripodal counterparts $L^7 < L^6 < L^5 < L^{10} \approx L^{11} \approx L^{12}$. It is interesting to note that although the lowest lipophilicities were found for all the pyridine containing compounds, these ligands usually provide good extractabilities. In the case of the benzyl-, 2-naphthyl- and biphenyl-substituted tren derivatives, although these compounds are fully located in the 1-octanol phase, they exhibit a range of extraction efficiencies. One conclusion to be drawn from these studies is that the extraction ability of the investigated ligand cannot be explained solely on the basis of lipophilicity.

Further extraction studies were done to investigate the dependence on the extractant concentration. The aim of these experiments was to find the preferred composition of the extracted anion complexes. The results, as illustrated for the tripod structures L^5, L^6, L^8 and L^{10} to L^{12} in Fig. 6, reveal an essentially linear relationship between the distribution ratio, D, and the ligand concentration (pH 7.4, ligand excess). The slopes of the lines in the diagram are unity, indicating a 1 : 1 complex composition. Similar results were obtained for the remaining compounds. Loading experiments of the organic extracts with perrhenate for 1×10^{-3} M ligand solutions at pH 7.4 give maximum ligand to anion ratios of up to 1 : 3 of the species transferred into the organic phase.

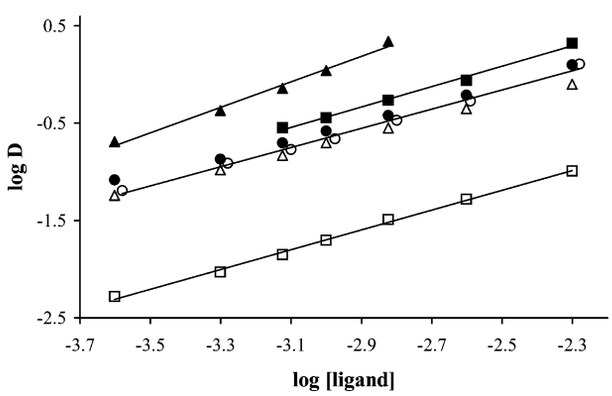


Fig. 6 Extraction of pertechnetate and perrhenate as a function of ligand concentration [$NaTcO_4$] or [$NaReO_4$] (L^6) = 1×10^{-4} M; pH = 7.4 (HEPES/NaOH buffer); [ligand] = 2.5×10^{-4} M–5×10^{-3} M in $CHCl_3$; shaking time 30 min; T = 23 ± 1 °C. (□) L^{12}, (△) L^{11}, (▲) L^{10}, (○) L^8, (■) L^6, (●) L^5.

Conclusions

On the basis of the extraction studies, both types of extractants, *i.e.* the aminocryptands and the tripodal tren derivatives, show that the behaviour is strongly influenced by spacer units and substitution. Obviously, the influential parameters for the phase transfer properties of the ligands are their basicity and levels of protonation. We have shown that extraction of TcO_4^- and ReO_4^- occurs at pH values at which the ligands are not highly protonated and consequently have only a weak tendency to form anion inclusion complexes in aqueous solution. This interpretation is in agreement with the aqueous complexation studies and crystal structure analyses.

Future planned work includes structural studies on the dependence of cryptand encapsulation on the level of protonation, and an investigation of the exceptionally good complexation properties of L^6.

Experimental

Syntheses

Ligands L^{1a}, L^{2a}, L^{3a}, and L^{4a} and their methylated derivatives, L^{1b}, L^{2b}, L^{3b}, and L^{4b} were prepared as follows:[36,37] 0.25 g of hexaamine cryptand and 25 g of paraformaldehyde were dissolved (with heating and stirrring) in 50 ml of formic acid. Once

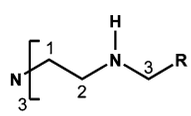
Table 7 Crystal data and structure refinements

Complex	$[(H_6L^{2a})(ReO_4)](ReO_4)_5 \cdot 5H_2O$	$H_6L^{4a}(ReO_4)_6 \cdot H_6L^{4a}(ReO_4)_4(ClO_4)_2 \cdot 3H_2O$
Empirical formula	$C_{36}H_{70}N_8O_{29}Re_6$	$C_{33}H_{59}N_{11}ClO_{25.5}Re_5$
M	2196.20	1984.36
T/K	150(2)	153(2)
λ/Å	0.71073	0.71073
Crystal system	Monoclinic	Orthorhombic
Space group	Pn (no. 7)	$Pna2_1$ (no. 33)
a/Å	14.8844(10)	30.9119(18)
b/Å	12.5582(8)	12.3210(7)
c/Å	16.5916(11)	27.4541(16)
β/°	112.7290(10)	90
V/Å^3	2860.5(3)	10456.3(10)
Z	2	8
$\rho_{calc.}$/Mg m^{-3}	2.550	2.521
μ/mm^{-1}	12.736	11.678
Refl. collected	33445	96679
Independent refl. [R_{int}]	12954 [0.0393]	18419 [0.0869]
$R1$, $wR2$ [$I>2\sigma(I)$]	0.0577, 0.1623	0.0586, 0.1629
$R1$, $wR2$ (all data)	0.0695, 0.1714	0.0679, 0.1695

dissolved, the mixture was refluxed under argon for five days (105 °C). After reflux, the mixture was brought to dryness, water (100 ml) was added and the resulting mixture was basified with KOH solution (4 g in 50 ml water). The alkaline solution was then extracted with chloroform (3 × 100 ml). The extracts were combined and evaporation produced a pale yellow oil. The oil was passed through a sephadex column using ethanol as the mobile phase. The fractions containing methylated cryptand were combined and the ethanol evaporated off producing clean hexamethyl cryptand.

Perrhenate complexes were made by treating an aqueous solution of the perchlorate complexes[6] with slight excess (1 : 7 ratio) of $KReO_4$, and allowing to crystallise over approximately 1 week in air. The first crop (yield 40–60%) was used for crystallography.

Ligands L^5 and L^6 were prepared as described elsewhere.[38,39] The general synthesis procedure for the tripodal tren derivatives was the following.



Ligands L^7 to L^{10}. To a solution of 2 mmol of the corresponding imine in 30 ml dry CH_2Cl_2 8 mmol KBH_4 was added. The mixture was stirred at room temperature overnight. After that time the mixture was poured into water and extracted with CH_2Cl_2. Then 10% NH_4Cl was added. The organic phase was washed with water, dried over $MgSO_4$ and evaporated.

Tris{2-[(3′-pyridylmethyl)amino]ethyl}amine L^7. Yellow oil (98%), $C_{24}H_{33}N_7$ (419.57); *m/z* (MALDI) 420 (M^+); $\delta_H(CDCl_3)$ 8.5–7.2 (4H, m, ArH); 3.73 (2H, s, H-3); 2.63 (2H, t, H-2); 2.55 (2H, t, H-1).

Tris{2-[(2′-naphthylmethyl)amino]ethyl}amine L^9. White solid (86%), mp 42 °C, $C_{39}H_{42}N_4$ (566.79); *m/z* (EI) 567 (M^+); $\delta_H(CDCl_3)$ 7.74 (5H, m, ArH); 7.38 (2H, m, ArH); 3.86 (2H, s, H-3); 2.72 (2H, t, H-2); 2.64 (2H, t, H-1).

Tris{2-[(1′-naphthylmethyl)amino]ethyl}amine L^{10}. Yellow oil (68%), $C_{39}H_{42}N_4$ (566.79); *m/z* (EI) 567 (M^+); $\delta_H(CDCl_3)$ 7.98 (1H, d, ArH); 7.82 (1H, d, ArH); 7.72 (1H, d, ArH); 7.48 (3H, m, ArH); 7.38 (1H, d, ArH); 4.09 (2H, s, H-3), 2.70 (2H, t, H-2); 2.59 (2H, t, H-1).

Tris{2-[(4′-phenyl)benzylamino]ethyl}amine L^8. White solid (97%), mp 87 °C, $C_{45}H_{48}N_4$ (644.90); *m/z* (EI) 645 (M^+); $\delta_H(CDCl_3)$ 7.5-7.3 (9H, m, ArH); 3.78 (2H, s, H-3); 2.77 (2H, t, H-2); 2.67 (2H, t, H-1).

Ligands L^{11} and L^{12}. To a solution of 1 mmol amine in 20 ml acetonitrile, 4 mmol K_2CO_3 and 4 mmol KI were added. The mixture was stirred under reflux for 15 minutes. After that time 3 mmol 4-bromomethylbenzene or 4-bromomethylbiphenyl in 10 ml acetonitrile was added to the mixture and stirred under reflux overnight. On cooling the mixture was evaporated to give an oil which was taken up in CH_2Cl_2. The CH_2Cl_2 phase was extracted with water and washed with 10% $Na_2S_2O_3$ solution and with water again. The organic phase was dried over $MgSO_4$. The solution was reduced in volume to give a white solid product which was recrystallized from ethylacetate/heptane 2 : 1.

Tris[2-(N,N-dibenzylamino)ethyl]amine L^{11}. White solid (89%), mp 50–53 °C, $C_{48}H_{54}N_4$(686.99); *m/z* (EI) 685 (M^+); $\delta_H(CDCl_3)$ 7.6–7.3 (10H, m, ArH); 4.65 (4H, s, H-3); 3.87 (2H, t, H-2); 3.65 (2H, t, H-1).

Tris{2[N,N-bis(4′-phenylbenzyl)amino]ethyl}amine L^{12}. White solid (92%), mp 125–126 °C, $C_{84}H_{78}N_4$ (1143.57); *m/z* (MALDI) 1145 (M^+); $\delta_H(CDCl_3)$ 7.8-7.3 (18H, m, ArH); 4.4–4.2 (4H, m, H-3); 3.65 (2H, t, H-2); 3.09 (2H, t, H-1).

Liquid–liquid extraction

The liquid–liquid extraction experiments were performed at 23 ± 1 °C in microcentrifuge tubes (2 cm^3) by means of mechanical shaking. The phase ratio $V_{(org)} : V_{(aq)}$ was 1 : 1 (0.5 cm^3 each). The shaking time was chosen as 30 minutes, because the extraction equilibrium was reached in all cases during this period. After extraction, all samples were centrifuged and the phases separated. The determination of the anion concentration in both phases was carried out radiometrically by β-radiation measurements of $^{99}TcO_4^-$ and $^{188}ReO_4^-$ in a liquid scintillation counter (LS 6000 LL/Beckman).

Lipophilicity data by UV/Vis spectroscopy

Information about the lipophilicity of the compounds has been obtained by distribution measurements in the water/1-octanol system. 0.001 M stock solutions of the ligands in buffer solution and 1-octanol, saturated with each other before use, were prepared. The experiments were performed with 0.0001 M solution of the ligands in aqueous solution (HEPES/NaOH, pH 7.4) and in 1-octanol. The phase ratio $V_{(org)} : V_{(aq)}$ was 1 : 1 (0.8 cm^3 each); the shaking period was 2 hours. After separation of both phases, the concentration of the ligands in the aqueous and organic phases was analyzed by UV/Vis spectroscopy (Lambda 2, Perkin-Elmer).

Solution equilibria

Potentiometric and NMR titrations were performed as described in detail in our previous work.[6] The reported oxoanion formation constants are conditional values, relative to those in tosylate medium (OTs).

X-Ray crystallography

Data collection and structure refinements are summarised in Table 7. Both data sets were collected on Bruker SMART 1000 diffractometers. The structures were solved by direct methods and refined by full-matrix least-squares on F^2 using all the data. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. All programs used in the structure solution and refinement were included in the SHELXTL package.[40]

In the case of $[(H_6L^{2a})(ReO_4)](ReO_4)_5 \cdot 5H_2O$, hydrogen atoms bonded to carbon or nitrogen were inserted at calculated positions using a riding model. The hydrogen atoms of the solvate water molecules were not located and were not included in the model.

A number of atoms in $H_6L^{4a}(ReO_4)_6 \cdot H_6L^{4a}(ReO_4)_4(ClO_4)_2 \cdot 3H_2O$ initially showed non-positive definite atomic displacement parameters and these were restrained using ISOR.[40] Hydrogen atoms bonded to carbon were inserted at calculated positions using a riding model but hydrogen atoms bonded to nitrogen or oxygen were not included in the refinement. One of the perrhenate anions is disordered over two sites and has been modelled as having equal occupancy for both sites.

CCDC reference numbers 195731 and 195732.

See http://www.rsc.org/suppdata/dt/b2/b210289g/ for crystallographic data in CIF or other electronic format.

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