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FULL PAPER

Macrocyclic ligand design. A synthetic, solvent extraction, computational and NMR study of the effect of cryptand flexibility on sodium ion affinity †

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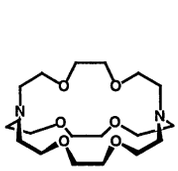
The rigidity of a series of cryptands incorporating an N_2O_6-donor has been shown to have a marked effect on the ability of such species to complex sodium ions. X-Ray and associated computational investigations, including molecular mechanics, semi-empirical (AM1) and *ab initio* (density functional) studies, coupled with the results of sodium picrate extraction experiments and NMR studies, have been employed to probe the conformational aspects influencing sodium ion complexation along the ligand series. It is concluded that the ease with which a cryptand is able to adopt an *endo–endo* conformation is an important factor affecting the occurrence of inclusive metal-ion binding in these systems.

Introduction

Polyether cryptands were among the first fully synthetic supramolecular host molecules to be synthesised and their metal complexation behaviour has been studied in considerable detail, with applications in catalysis, separations and in chemical sensors being reported.[1–3] A large number of such cryptands have now been prepared[4] and characteristically they exhibit affinities for 'hard' metal ions such as the alkali and alkaline earths; the latter ions bind *via* electrostatic interaction with the dipolar ether functions, replacing solvent molecules from the co-ordination sphere of the metal. Relative to their single-ring analogues, bicyclic cryptands usually exhibit higher formation constants for metal binding that can involve both favourable entropy and/or enthalpy terms—depending on the system—a phenomenon known as the *Cryptate Effect*.[5–8]

Cryptands, along with their two dimensional analogues, the crown ethers, were the first cyclic ligands shown to be capable of discriminating between ions from each of the above groups. For example, the 'classical' cryptand **1** (2.2.2) has long been known to bind potassium ions selectively in the presence of other alkali metal ions.[5,9,10] Such selectivity is characteristic of many cryptands and largely depends on the number (and type) of donor atoms present, as well as on the spatial and electronic complementarity of the cryptand's cavity for the metal ion involved. The incorporation of rigidity in such systems, in the form of fused benzo substituents, has been demonstrated to enhance metal ion selectivity in particular cases by introducing an element of preorganisation through restricting the possible conformations that can be adopted. In this manner, better complementarity between cavity and metal may be achieved.[11] Nevertheless, to achieve optimal binding properties, it is important to obtain just the right balance between flexibility (which lowers the energy barrier to complexation and decomplexation) and rigidity (which confers selectivity, but can result in inhibition of the ingress of a metal ion into the cavity).[12] The balance between rigidity and flexibility and its effect on the complexation behaviour of cryptands is a central theme of the work now presented. For this purpose, and as part of on-going research aimed at developing and understanding new systems for metal ion recognition,[13] we have investigated the Na^+ complexation behaviour of the cryptands **2**–**4** incorporating a gradation in steric rigidity (and perhaps cavity size—see later) and compared their behaviour with the flexible system **1**; 2.2.2.[9,10]



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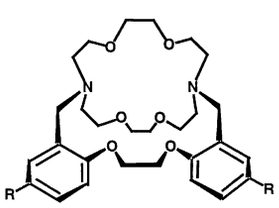

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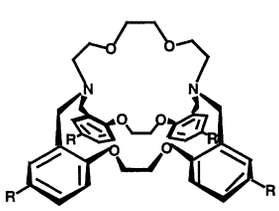

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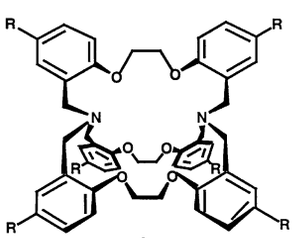

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Results and discussion

Cryptand **1** (2.2.2) and cryptands **2**–**4** each share a common N_2O_6 donor set, with the final member, **4**, having a total of six rigid benzo groups as part of its framework; in theory, the nitrogen atoms in cryptands such as these can have their lone

† Electronic supplementary information (ESI) available: tables of ^1H and ^{13}C NMR induced chemical shifts. See http://www.rsc.org/suppdata/dt/b1/b102585f/

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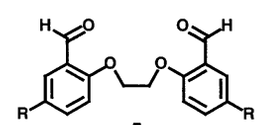
pairs pointing either in or out of the cavity, leading to possible *endo–endo*, *exo–exo* isomerism (or even *endo–exo* isomerism).[14]

By analogy with the published behaviour of **1** (2.2.2) and related all-aliphatic derivatives,[5] it was anticipated that **2**–**4** might show a gradation in binding affinities for an alkali metal (such as sodium). In turn, this would allow a systematic evaluation of steric influences (and, in particular, increasing steric rigidity) on complexation behaviour—while noting that there is also a gradation in the hardness of the oxygen donors along the series, as aromatic–aliphatic ethers replace all-aliphatic ones. Further, it is expected that there will be a gradation in ligand solvation energy along the ligand series as bulky benzo substituents are replaced by aliphatic moieties. Ligand desolvation terms have been demonstrated to play a significant role in influencing the relative free energies of complex formation for a number of related azacrown ligand series.[15]

In a prior investigation,[16] we reported the preparation and characterisation (including an X-ray structure and a preliminary computational study) of the free cage **4** (R = H). The structure showed that the bridgehead nitrogen lone pairs are orientated *exo*, with the benzylic methylene groups directed into the cage. In this configuration, a very restricted volume remains for inclusion of a guest in the cavity. The preference of this cage for an *exo–exo* arrangement was postulated to reflect steric influences associated with the partial-rigidity and bulkiness of the benzylic linkages present (the bridgehead essentially corresponds to a substituted tribenzylamine).

Cage synthesis

The synthesis of **4** (R = H), as reported previously,[16] involves the 1 : 1 Schiff base condensation of dialdehyde **5** (R = H) and related diamine precursor **6** (R = H) followed by *in situ* sodium borohydride reduction of the intermediate diimine to yield the corresponding diaza macrocycle **7** (R = H). Double *N*-alkylation of this species with 2,2′-(ethylenedioxy)bis-(benzyl chloride) **8** (R = H) in dry acetonitrile in the presence of sodium or caesium carbonate gave **4** (R = H) in 42 percent yield. Overall, the strategy employed is generally similar to that used previously by Bradshaw *et al.*[17] for other cryptand syntheses.



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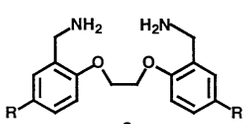

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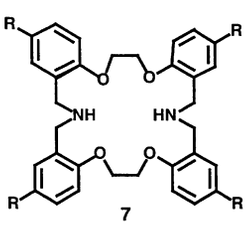

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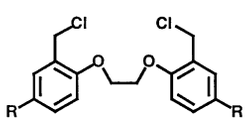

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In the present study the preparation of the more lipophilic cryptand **4** (R = *t*-Bu) followed that used for **4** (R = H),[16] except that the dialdehyde precursor was the *tert*-butyl derivative 1,2-bis(4-*tert*-butyl-2-formylphenoxy)ethane, **5** (R = *t*-Bu).[18] The required diamine **6** (R = *t*-Bu) was obtained in two steps from the dialdehyde **5** (R = *t*-Bu); treatment of the latter with hydroxylamine in refluxing ethanol produced the corresponding dioxime which was then reduced to **6** (R = *t*-Bu) in 77 percent yield using lithium aluminium hydride in refluxing tetrahydrofuran. As before, condensation of the dialdehyde and diamine, followed by sodium borohydride reduction, produced macrocycle **7** (R = *t*-Bu). The dichloro derivative **8** (R = *t*-Bu) required for cage formation was also prepared from the dialdehyde **5** (R = *t*-Bu) in two steps using standard functional group interconversions; namely, borohydride reduction of the dialdehyde **5** (R = *t*-Bu) to give the corresponding dialcohol in 96 percent yield. This was then converted to the dichloro derivative **8** (R = *t*-Bu) in 98 percent yield by treatment with thionyl chloride in refluxing dichloromethane. The synthesis of **4** (R = *t*-Bu) involved dissolving the dichloro derivative **8** (R = *t*-Bu) and **7** (R = *t*-Bu) in a 1 : 1 mixture of toluene and acetonitrile and adding this solution dropwise over one hour to a suspension of caesium carbonate in the same mixed solvent at 40 °C. The reaction mixture was then heated under reflux for 72 hours to give **4** (R = *t*-Bu) in 85 percent yield.

The first of the cryptands of intermediate geometry, **2** (R = H or *t*-Bu), were synthesised by bis-alkylation of commercially available 1,10-diaza-18-crown-6 using the appropriately substituted dichloride of type **8** (R = H or *t*-Bu) in the presence of sodium or caesium carbonate in acetonitrile. The products were obtained in yields of 11 and 65 percent, respectively, after a somewhat tedious purification procedure in each case (see Experimental section).

In an alternative synthesis of **2** (R = *t*-Bu), paralleling a procedure reported by Bradshaw *et al.*[19] for the synthesis of a related cryptand, the final ligand 'strap' was constructed by bis-alkylation of ethylene glycol ditosylate with the required bis(*N,N′*-methylenephenolate) derivative of 1,10-diaza-18-crown-6. For this purpose *N,N′*-bis(4-*tert*-butylphenyl-2-ylmethyl)diaza-18-crown-6 was prepared by means of a Mannich reaction between 1,10-diaza-18-crown-6, 4-*tert*-butylphenol and paraformaldehyde.[20] This product was then converted to the disodium salt by treatment with sodium ethoxide in tetrahydrofuran/ethanol. Reaction with ethylene glycol ditosylate then yielded **2** (R = *t*-Bu) in 82 percent yield. Although this two-reaction sequence gave **2** (R = *t*-Bu) in slightly lower overall yield based on the precursor macrocycle than the one-step procedure described above (59 percent overall compared to 65 percent for the previous case), the two-step route proved more convenient since it produced a more readily purified crude product than obtained from the first procedure.

The synthesis of **3** (R = H) involved bis-alkylation of the N_2O_4-macrocycle **7** (R = H) using triethylene glycol ditosylate under basic conditions. However, an initial attempt using sodium carbonate as base led instead to the isolation of a spiro-derivative of **7** in which dialkylation (that is, quaternisation) had occurred at a single ring nitrogen. It is postulated that complexation of sodium ion may have inhibited the triethylene glycol moiety from spanning the co-ordination cavity and alkylating the second nitrogen atom in this case. In order to circumvent this possibility, triethylamine was employed as the base. The subsequent synthesis then gave the desired product, **3** (R = H), in 28 percent yield.

Two alternative synthetic routes to **3** (R = *t*-Bu) were developed. The first followed that just described and involved reaction of the macrocyclic diamine **7** (R = *t*-Bu) with triethylene glycol ditosylate, caesium carbonate and tetrabutylammonium bromide in refluxing toluene/acetonitrile (1 : 1). After purification, **3** (R = *t*-Bu) was isolated in 35 percent yield. The second procedure involved the initial synthesis of the diaza-crown **9** (R = *t*-Bu) using essentially the same methodology as employed for **7** (R = *t*-Bu); see Experimental section. Double *n*-alkylation of this crown with the dichloride **8** (R = *t*-Bu) in acetonitrile containing a suspension of caesium carbonate yielded **3** (R = *t*-Bu) in 70 percent yield after purification.

Variable temperature NMR study

In a previous study, Lehn *et al.*[10] have used variable temperature NMR studies of **1** (2.2.2) in $CDCl_3$ to investigate an interconversion process believed to involve two forms of d_3-symmetry in which the geminal NCH_2 protons of this cryptand are in different environments; this likely involves a twisting

Table 1 2.2.2 cage torsion angles (degrees)

Compound	N–C	C–C	C–O	O–C	C–C
(*2.2.2*)·2BH_3[a] (2-symmetry) (*exo–exo*)	60, −179	−93	177	178	65
	(60, −179)	*(−93)*	*(177)*	*(178)*	
	59, 178	173	149	−176	70
	61, −58	*−73*	*176*	*−154*	
	69, −58	−73	176	−154	70
	59, 178	*173*	*149*	*−176*	
1 (2.2.2)[a] (*1*-symmetry) (*exo–exo*)	79, −156	69	−167	180	175
	84, −145	*68*	*−94*	*−175*	
	82, −152	77	−90	−174	178
	86, −144	*69*	*−174*	*172*	
	73, −161	67	−109	−178	−179
	72, −159	*69*	*−155*	*176*	
(2.2.2)·2H^+[b] (*1*-symmetry) (*endo–endo*)	77, −156(2)	51(2)	168(2)	180(2)	−78(2)
	−72(2), 161(2)	*−53(2)*	*−78(2)*	*−152(2)*	
	73(2), −162(1)	53(2)	168(2)	−178(2)	−78(2)
	−73(2), 161(2)	*−51(2)*	*−76(2)*	*−153(2)*	
	77(2), −156(2)	52(2)	169(1)	−178(1)	−81(2)
	−72(2), 160(1)	*−49(2)*	*−81(2)*	*−149(2)*	
[Na(2.2.2)]$^+$[c] (*32*-symmetry) (*endo–endo*)	105, −130	13	−130	156	−40
	(105, −130)	*(13)*	*(−130)* (×3)	*156*	
[K(2.2.2)]$^+$[d] (*2*-symmetry) (*endo–endo*) (chirality of this and the above Na^+ adduct inverted)	64.3, −169.0	57.6	−172.5	−179.3	−49.6
	65.4, −168.2	*55.0*	*−169.9*	*−178.1*	
	65.4, −168.2	55.0	−169.9	−178.1	−49.6
	64.3, −169.0	*57.6*	*−172.5*	*−179.3*	
	65.2, −167.0	55.9	−170.4	−177.8	
	(65.2, −167.0)	*(55.9)*	*(−170.4)*	*(−177.8)*	*−52.5*
[NaL]$^+$ (L = **3**, R = H)[e] (the 2.2.2. string)	100(3), −155(3)	55(4)	72(4)	180(3)	63(3)
	90(3), −150(3)	*58(3)*	*71(3)*	*−179(2)*	

Representative conformations found in structures incorporating ligand **1** (2.2.2) are presented. Presentation is in the form of the torsions throughout each of the three strings in each complex, on two lines, thus:

(C,C)N–C–C–O–C
|
(C,C)N–C–C–O–C

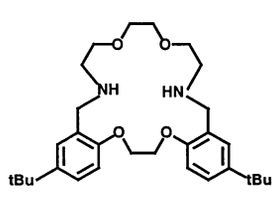
Chiralities are presented in a common basis as far as possible; in designating the compounds, any substitution at the nitrogens is shown. Standard uncertainities are cited where accessible. [a] Ref. 25. [b] Ref. 26. [c] Ref. 32; another (disordered) example is found as the iodide in ref. 30. [d] Ref. 31; the conformations of the Rb, Cs analogues are closely similar — see ref. 29. [e] This work.

around the N···N axis of the cage. Indeed, consideration of torsions in the strings of the cage in a variety of its forms, as tabulated in Table 1, suggests a variety of possible pathways for such twists. The free energy of activation ($\Delta G^{\ddagger}$) was determined to be 27.2 kJ mol^{-1} for this process. In the present investigation, a similar ^1H NMR variable temperature study was carried out for the six-benzo substituted cryptand, **4** (R = H), in $CDCl_3$. For this system a two-site interchange process was also identified with a $\Delta G^{\ddagger}$ value of ≈ 63 kJ mol^{-1}. This significantly higher value relative to that reported for 2.2.2 is in keeping with the reduced conformational flexibility expected for **4** (R = H).

Metal ion extraction experiments

There are now many reports of the solvent extraction of alkali metal picrates from water into an immiscible organic phase containing a polyether crown or cryptand ligand.[21] In such studies, the complexed alkali metal is transferred to the organic phase as an ion-pair with the picrate anion. The intense yellow colour of the picrate ion makes spectrophotometric determination of the degree of extraction into the organic phase possible. The use of picrate almost always results in higher metal partition coefficients than occurs with simple inorganic anions such as chloride or nitrate. This is because the efficiency of metal ion transfer is significantly influenced by the hydration energy of the anion present,[8,22] with picrate being weakly hydrated.

In the present study comparative solvent extractions of sodium picrate from an aqueous phase to a chloroform phase incorporating cryptands **2**–**4** (R = H) and **1** (2.2.2) have been undertaken. The more lipophilic systems **2**–**4** (R = *t*-Bu) were also synthesised with the aim of carrying out parallel extraction experiments (together with the NMR induced shift studies discussed below). However, preliminary experiments indicated that there is a tendency for these *tert*-butyl derivatives [especially **4** (R = *t*-Bu)] to extract picric acid under the conditions employed for the metal extractions—a problem that does not occur for the lower-lipophilic systems with R = H. In view of this, no results for the systems with R = *t*-Bu are presented here. The results of the sodium picrate extraction (water/chloroform) experiments for **2**–**4** (R = H) and **1** (2.2.2) are summarised in Fig. 1. While no extraction was observed for **4** (R = H) under the conditions employed, as the flexibility increases along the series **3** (R = H), **2** (R = H) and **1** (2.2.2) these cryptands become progressively better extractants of Na^+.



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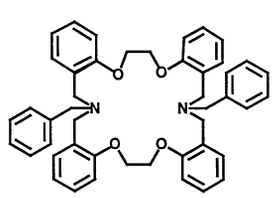

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Despite the inability of cryptand **4** (R = H) to extract Na^+, in a separate series of experiments the corresponding monocyclic precursor **7** (R = H) was found to be a good extractant for this ion—in contradistinction to the behaviour predicted from (sole) consideration of the cryptate effect. Further, it was

Table 2 Calculated *endo–endo* − *exo–exo* conformational preferences for cryptands **1** (2.2.2) and **2**–**4** (R = H)

	MM3 Δ Steric energy/kJ mol^{-1}	AM1 Δ H_f/kJ mol^{-1}	Local DFT Δ Electronic energy/kJ mol^{-1}
4 *endo–endo* − *exo–exo*	−184.1	−113.0	−230.5[a]
3 *endo–endo* − *exo–exo*	−36.8	−12.6	−77.8[b]
2 *endo–endo* − *exo–exo*	−20.1	−7.9	−45.6[b]
1 *endo–endo* − *exo–exo*	−7.9	−3.8	−7.1[b]

[a] Single point calculations at the SVWN5/6-31G‡ level at the AM1 minimum. [b] Structure geometry optimised at the SVWN5/6-31G* level.

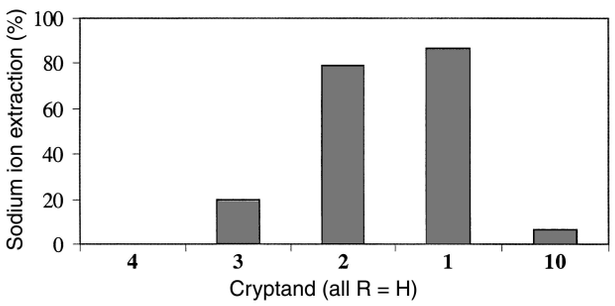

Fig. 1 Relative sodium picrate extraction by **1**, **2**–**4** (R = H) and **10** from water into chloroform (see Experimental section for details).

observed that the *N*,*N*′-dibenzyl derivative of **7** (R = H), namely **10** (R = H), a closer model for **4** (R = H), also extracts Na^+ (albeit only to the extent of 6 percent) under the same conditions employed for **1**–**4** (Fig. 1). Even though **10** contains fewer potential donors than **4** (R = H), it is significant that it is still able to extract sodium while **4** does not. Clearly in **10** the nitrogen atoms are free to interconvert between their *endo*- and *exo*-orientations and the observed ability of **10** to extract Na^+ suggests that the tribenzylamine moieties participate in binding to this ion—in contrast to the situation for **4** (R = H) which, as mentioned already, appears to favour the adoption of an *exo–exo* arrangement of its bridgehead nitrogens (with an associated sterically crowded cryptand cavity).[16] The above observations are thus in accord with the lower accessibility of the *endo–endo* form of cryptand **4** (R = H) inhibiting the inclusive co-ordination of a sodium ion.

In view of the above results for sodium with **2**–**4** (R = H) and **1** (2.2.2), it was of interest to examine whether similar patterns would be maintained for the adjacent Group 1 metal ions, lithium and potassium. Accordingly, further solvent extraction experiments involving these metal picrates were instigated using related conditions to those employed for sodium picrate. Within experimental error, no extraction was again observed for **4** (R = H) with either of these metal salts. As before, extraction was observed to occur in both cases for **2** and **3** (R = H), with the degree of extraction again increasing on passing from **2** (R = H) to **3** (R = H) for each metal system. That is, the Li^+ and K^+ extraction patterns along the series **2**–**4** (R = H) showed the same overall trend as occurs for Na^+ (Fig. 1). Further, in the case of K^+, flexible 2.2.2 was once again observed to be the most efficient extraction reagent along the cryptand series (in parallel to the results from the Na^+ extraction experiments); however, this was not the case for Li^+. For this ion, the extraction efficiency of 2.2.2 was lower than found for **2** (R = H). While the origin of this is uncertain, it presumably reflects the poorer complementarity of lithium (relative to sodium or potassium) for the cavity of 2.2.2. In accord with this observation, it has been well documented previously that the thermodynamic stability of the lithium complex is significantly lower than that of the corresponding sodium or potassium complex.[5,23]

Computational studies for metal-free cryptands

In view of the above results, comparative gas-phase computational investigations of the effect of bridgehead nitrogen configuration on the overall cage conformations for **1** and **2**–**4** (R = H) were undertaken (without symmetry restriction) using molecular mechanics (MM3), semi-empirical MO (AM1) and local-density functional (SVWN5/VN*) methods. Calculations were run using Spartan[24] running on an SGI Power Challenge. Specifically, geometry optimisations were performed in order to obtain the energy differences between the respective minimised *endo–endo* and *exo–exo* structures. The results are summarised in Table 2. All three computational methods are in reasonable agreement and confirm that **4** (R = H) is the least flexible followed by **3** (R = H), **2** (R = H) then **1** (2.2.2). That is, the respective *endo–endo* conformers become progressively more accessible along the series given by **4**, **3**, **2** (all R = H) and **1** (2.2.2). As mentioned already, the X-ray structure of **4** (R = H)[16] shows that it has an *exo–exo* arrangement of its nitrogens while in the corresponding solid state structure of **1**[25] they are *endo–endo* (as is this cryptand in its diprotonated form).[26] Table 1 tabulates the detailed conformations of the associated strings of this cage in a variety of uncomplexed and complexed structures for comparison with the corresponding aliphatic string in the sodium complex of **3** (R = H) investigated as part of the present study (see below). Clearly, the degree of 'preparedness' of **1** (2.2.2) for co-ordination can differ greatly—presumably in response to the respective associated environments.

The relatively high calculated enthalpic difference between the *endo–endo* and *exo–exo* forms of **4** (R = H) (Table 2) indicates that adoption of the *endo–endo* form is clearly not favoured. As mentioned already, the configurational inflexibility of **4** (R = H) appears largely as a reflection of the presence of the bulky tribenzylamine bridgehead groups, with their semi-rigid N–C–C–C torsion angles. In contrast, the calculated energy difference between the minimised *endo–endo* and *exo–exo* structures of 2.2.2 is small using all three computational techniques, confirming the previous observations that inversion of the bridgehead nitrogen atoms in 2.2.2 between the *exo–exo*, *exo–endo* and *endo–endo* forms is facile.[10,27] Clearly, the computational results for the unbound cryptands also confirm that configurational flexibility increases along the series **4**, **3**, **2** (all R = H) and **1**.

Computational studies on selected metal-containing cryptands

A series of local (SVWN5/VN*) and non-local (pBP86/VN*) density functional calculations on selected cryptand complexes of Li^+, Na^+ and K^+ have been performed using Spartan, with little structural variation being observed between the two methods. In an attempt to provide chemically reasonable starting geometries on which to base the calculations, attempts were made to grow crystals of alkali metal–cage complexes of **2**–**4** (R = H) that were suitable for X-ray analysis but, in general, these attempts were unsuccessful. Nevertheless, poor quality crystals of [NaL]picrate·CH_2Cl_2 where L = **3** (R = H) were obtained (from dichloromethane) which, subjected to a single crystal X-ray study, yielded results definitive of the gross conformation and atom connectivity within the complex. The structure (Fig. 2) clearly shows that the bridgehead nitrogens adopt *endo–endo* configurations and that these nitrogens are weakly co-ordinating, with Na–N distances of 2.85(4) and 2.95(4) Å. All six of the oxygen donors are co-ordinated to the

Table 3 The sodium environment, $[NaL]^+$ (L = **3**, R = H)

Atom	*r*	O(8b)	O(8c)	O(3a′)	O(8b′)	O(8c′)
O(3a)	2.33(2)	104.2(9)	109.5(9)	69.1(8)	83.6(8)	165.2(9)
O(8b)	2.52(3)		105(1)	173.3(9)	66.4(9)	90.2(8)
O(8c)	2.53(2)			79.4(8)	166.0(8)	62.9(8)
O(3a′)	2.44(3)				111(1)	96.5(9)
O(8b′)	2.62(2)					105.4(9)
O(8c′)	2.59(2)					

Na · · · N(0,0′) are 2.85(4), 2.95(4) Å. *r* (Å) is the Na–O distance; other entries are the angles (degrees) subtended by the relevant atoms at the head of the row and column.

Table 4 L = **3** (R = H) torsion angles (degrees)

Compound	N–C	C–C	C–C	C–O	O–C	C–C
4 (R = H)[a]	−80(4), 152(3)	170(4)	4(5)	−169(3)	171(3)	−61(3)
	−88(4), 148(3)	*167(3)*	*3(5)*	*−147(3)*	*−178(3)*	
	−77(3), 156(3)	157(3)	11(5)	−171(4)	174(3)	−64(4)
	−77(3), 159(3)	*167(3)*	*10(6)*	*−165(4)*	*170(4)*	
	−75(4), 160(3)	162(3)	5(5)	−166(7)	172(7)	−64(3)
	−74(4), 165(3)	*156(4)*	*7(6)*	*−165(3)*	*176(3)*	
$[NaL]^+$ (L = **3**, R = H)[b]	81(3), −171(3)	73(4)	−9(4)	147(3)	−157(3)	−76(4)
(the 3.2.3 strings)	*67(4), −174(3)*	*74(3)*	*2(3)*	*148(3)*	*−176(3)*	
	80(4), −172(3)	61(5)	−1(6)	132(4)	−172(4)	−60(5)
	75(4), −165(3)	*74(4)*	*−1(5)*	*148(4)*	*−166(3)*	

Presentation as in Table 1. [a] Ref. 16. [b] This work.

Table 5 Metal–donor atom contacts from non-local density functional calculations for the complexes of **3** (R = H)

	Calculated (mean) metal–donor contacts/Å			
	Aliphatic ether–M	Aromatic ether–M	N–M	Pauling metal radius/Å
Li^+	2.09[a,b]	2.74[b]	3.20	0.60
Na^+	2.44[a]	2.63[b]	3.06	0.95
K^+	2.700[a]	2.87[b]	3.08	1.33

[a] Range of metal–aliphatic ether contacts (Å) from CSDS: Li–O, 1.72–2.65 Å (mean 2.03 Å); Na–O, 1.95–3.21 Å (mean 2.48 Å); K–O, 2.36–3.41 Å (2.83 Å). [b] Range of metal–aromatic ether contacts (Å) from CSDS: Li–O, 2.007–2.54 Å (mean 2.11 Å)—see text; Na–O, 2.27–3.00 Å (mean 2.523 Å); K–O, 2.61–3.21 Å (mean 2.84 Å).

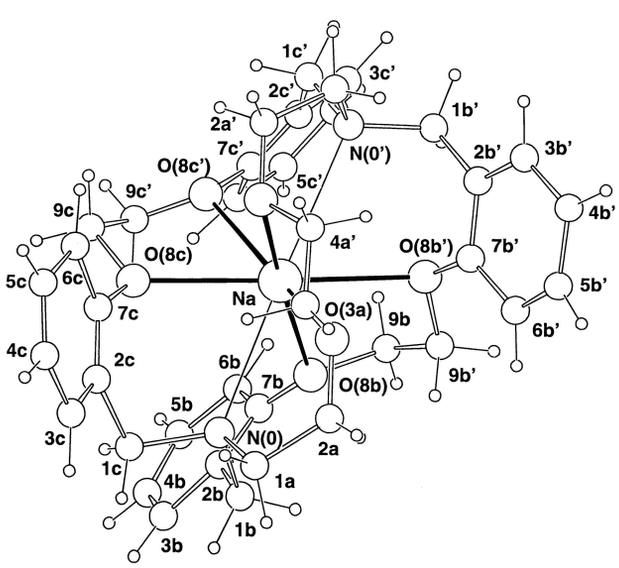

Fig. 2 Projection of the $[NaL]^+$ (L = **3**, R = H) cation down its *quasi*-2 axis.

sodium (Table 3) with a mean bond length of 2.5(1) Å [range: 2.33(2)–2.62(2) Å]. The conformations of the two 3.2.3 type strings of the present structure differ from those previously described in ligand **4** (the latter having overall *quasi*-3 symmetry) (Table 4) and, similarly, the conformation of the 2.2.2 string is likewise unusual, the free 2.2.2 ligand conformations (Table 1) again not being immediately precursive of that of the complex at this level of detail. The present complex cation has overall *quasi*-2 symmetry as is evident in its projection down that *quasi*-axis in Fig. 2.

This X-ray determination provided a basis for setting the starting structures for the calculations on the Li^+, Na^+ and K^+ complexes incorporating L = **3** (R = H). A comparison between the non-local-density functional minimised structure and the (crude) X-ray data for the above sodium complex indicated that reasonable accord (RMS differences: bond lengths = 0.078 Å, angles = 4.95°, torsion angles = 5.45°) between the two structures was present. All calculations were run using the pBP86 functional and the VN* numeral basis set. The largest differences between the calculated and X-ray bond and torsion angles appear to be associated with the disorder found in the positions of individual carbons attached to the bridgehead nitrogens.

As well as for the Na^+ complex **3** (R = H), geometry optimisations were also performed for the corresponding Li^+ and K^+ species. Table 5 provides a comparison of selected mean metal–donor contact data for the minimised structures with related data from the Cambridge Structural Database System (Version 5.19) (CSDS).[28] The (mean) calculated aliphatic and aryloxy (the latter refers to ethers in which one aryl and one aliphatic group is attached to the oxygen) ether to metal values for the Na^+ and K^+ species all fall centrally in the observed range for bonds of similar type listed in the CSDS, with the individual contacts each lying well within the respective ranges. However,

this is not the case for the lithium complex. While the aliphatic ether to Li^+ contacts all lie within the 'normal' range (Table 5), the mean value from Li^+ to the aromatic ether donors falls very significantly above the corresponding literature range. This result is perhaps best interpreted as implying that the lithium ion is 'too small' for **3** (R = H) and that, as a consequence, there is a tendency for the (weaker) aromatic ether donors to not participate in binding to this metal. In this context, the calculated energies of the respective metal complexes of **3** (R = H), after subtracting the energy of the cryptand and the particular metal ion (and ignoring basic effects such as BSSE), were found to fall in the order $Li^+ > Na^+ > K^+$—in keeping with lithium being the least strongly bound of these three metals.

In part to provide additional validation of the above studies, a set of parallel density functional calculations were undertaken for the Li^+, Na^+ and K^+ complexes of **1** (2.2.2) for which solution thermodynamic stability data have long been available[5] along with precise crystal structures for the sodium and potassium complexes;[29–32] with the X-ray structure[30] of the sodium complex again forming the basis for the starting geometries for each calculation. In the case of the sodium and potassium complexes, the minimised geometries were in each case quite close to those found in the corresponding X-ray structures.[30,33] Clearly both of these metal ions are accommodated well by **1**. For the smaller lithium, as inferred previously, it was anticipated that the conformational flexibility of the cryptand arising from its all-aliphatic nature would allow this ion to also occupy the central cavity but that its 'fit' would be poor. The calculated structure is in accord with this expectation: a very non-symmetric geometry was predicted with two long (mean: 3.14 Å) and one short (2.16 Å) Li–O contacts, with the respective Li–N distances being 2.19 Å and 4.05 Å. While this (gas phase) result is thus in strong accord with the previous assumption[5] that there will be poor complementarity between the Li^+ ion and the cavity of this cryptand, it needs to be emphasised that the solution behaviour will of course involve a dynamic equilibrium over a range of conformations/configurations and possible solvation patterns—as demonstrated already for the alkali metal complexes of this ligand using the molecular dynamics technique,[34–36] and the experimental data, presented in Table 1.

In parallel to the published data for the experimentally determined[5] stability constants of the 1 : 1 (metal : 2.2.2) complexes in solution, the calculated gas-phase stabilities of the complexes investigated in the present study also follow a similar order of $Li^+ < Na^+ < K^+$.

NMR induced chemical shift studies

Using the more lipophilic derivatives **2** (R = *t*-Bu) and **4** (R = *t*-Bu) together with **1** (2.2.2) it has proved possible to obtain ^1H and ^{13}C NMR induced chemical shift data for complex formation of each of these species with selected alkali metal nitrates. A stoichiometric amount of the respective alkali metal nitrates was added to each of the above cryptands dissolved in dimethylformamide-d_7 (*ca.* 0.10 mol dm^{-3}) held in the NMR tube. Despite the use of the more chloroform soluble derivatives of **2** and **4** with R = *t*-Bu, under the conditions employed metal complex precipitation was found to occur in the presence of the heavier alkali metals, thus limiting the range of the studies involving these latter systems.

While quite low induced shifts were observed for the interaction of Li^+ with the flexible cryptand **1** (in keeping with a weak interaction occurring), shifts in the presence of both Na^+ and K^+ were generally higher in accord with the enhanced binding occurring for 2.2.2 with these ions[5,37] while the corresponding shifts in the presence of Rb^+ and Cs^+ tended once again to be lower. This pattern is thus in general agreement with that reported[5] for the binding affinities of **1** towards these alkali metals.

In contrast to the above, the Li^+ and Na^+ induced shifts in both the ^1H and ^{13}C NMR spectra of the least flexible system **4** (R = *t*-Bu) in dimethylformamide-d_6 were uniformly minimal, amounting to not more than 0.02 ppm in the ^1H spectrum and 0.53 ppm in the ^{13}C spectrum. Such a result is thus in complete accord with our earlier conclusions that the rigidity of this ligand system inhibits metal binding. Unfortunately, as mentioned above, low solubilities prevented shifts being obtained for the remaining alkali metals but little interaction with **4** (R = *t*-Bu) is expected in these cases also.

The induced chemical shifts for cryptand **2** (R = *t*-Bu), of intermediate flexibility, in the presence of Li^+, Na^+ and K^+ again followed the expected pattern. Minimal shifts [up to ±0.01 ppm (^1H) and −0.14 ppm (^{13}C)] were induced by Li^+ while both Na^+ and K^+ yielded significant shifts [up to +0.51 ppm (^1H) and +3.91 ppm (^{13}C) for Na^+ and up to −0.29 (^1H) and +3.72 ppm (^{13}C) for K^+] in the case of particular resonances. Again, such behaviour is in full accord with the results discussed above.

Concluding remarks

A series of computational and experimental studies has been performed to probe the effect of increasing rigidity on the conformational freedom of the diaza-polyether cryptands **1** and **2**–**4** (R = H). Clearly, both sets of results are in good agreement concerning the effect that increasing benzylamine incorporation has on the topological rigidity of the cryptands investigated, namely, that increasing the number of benzyl substituents on the bridgehead amine atoms hinders the adoption of an *endo–endo* nitrogen conformation and in doing so impedes metal ion complexation.

Experimental

^1H and ^{13}C NMR spectra were determined on a Bruker AM300 spectrometer at 300 and 75 MHz, respectively. The ^1H NMR variable temperature study was performed using the literature procedure.[38] Electrospray (ES) ionisation, electron impact (EI) and liquid secondary ion (LSI) mass spectra were recorded on a Kraytos M25RFA or a Bruker APEX 47e spectrometer, while plasma desorption (PD) spectra were obtained on a Bio-Ion 20R instrument from Applied Biosystems. Melting points are uncorrected. Unless stated otherwise, chromatographic separations were performed using vacuum-assisted elution on Merck silica gel 60H F_{254}, 60 mesh (63–230 μm). Dialdehydes **5** (R = H)[39] and **5** (R = *t*-Bu)[18] together with the dichloro precursor **8** (R = H),[16] macrocycle **7** (R = H),[16] cryptand **4** (R = H),[16] triethylene glycol tritosylate[40] and *N*,*N*′-bis(4-*tert*-butylphenol-2-ylmethyl)diaza-18-crown-6[20] were prepared by the published procedures.

Macrocycle and cryptand synthesis

Cryptand 2 (R = H). 1,10-Diaza-18-crown-6 (218 mg, 0.83 mmol), dichloride **8** (R = H)[16] (258 mg, 8.3 mmol) and sodium carbonate (670 mg, 6.3 mmol) were stirred in HPLC grade acetonitrile (20 cm^3) at room temperature for 48 h. The solvent was then evaporated, dichloromethane added and the resulting suspension filtered. The precipitate was washed thoroughly with dichloromethane (2 × 20 cm^3) and the combined organic fractions evaporated on a rotary evaporator. The resulting oil was chromatographed (silica, eluent 5% methanol/chloroform) to yield cryptand **2** (R = H) as a colourless solid (45 mg, 11%), mp 137–139 °C. HR-MS (LSI) (M + H^+) found 501.2971. $C_{28}H_{41}O_6N_2$ requires 501.2964. ^1H-NMR ($CDCl_3$ at 320 K) $\delta \approx 2.5$ (br s), ≈2.6 (br s), ≈3.1 (br s), ≈3.5 (br s), ≈3.6 (br s), 4.40 (s, CH_2O, 4 H), 6.97 (dd, $J = 2$, 8 Hz, H-6′, 4 H), 7.09 (d, $J = 8$ Hz, H-3′, 4 H), 7.16 (dd, $J = 2$, 8 Hz, H-4′, 4 H). ^{13}C-NMR ($CDCl_3$ at 320 K) δ 51.4, 56.0, 65.9, 66.8, 68.8, 114.8, 122.0, 126.9, 129.6, 132.4, 157.4.

Cryptand 3 (R = H). A mixture of triethylamine (660 mg, 6.5 mmol), **7** (R = H)[16] (265 mg, 0.52 mmol) and triethylene glycol ditosylate[40] (240 mg, 0.552 mmol) were dissolved in AR toluene (20 cm^3). The mixture was heated at 95 °C under a nitrogen atmosphere for 8 days. The solvent was evaporated and the dark brown mixture partitioned between dichloromethane (20 cm^3) and water (20 cm^3). Further extraction with dichloromethane (20 cm^3) followed by routine work-up yielded a dark brown oil, which was passed down a chromatography column (alumina, eluted with dichloromethane). Concentration of the eluent yielded **3** (R = H) as a colourless solid which was collected by filtration and was washed with acetone; yield 90 mg (28%); mp 224–227 °C. HR-MS (LSI) ($M + H^+$) found 625.3265. $C_{38}H_{45}N_2O_6$ requires 625.3277. ^{1}H-NMR ($CDCl_3$) δ 2.94 (t, J = 6 Hz, CH_2N, 4 H), 3.51 (s, CH_2O, 4 H), 3.69 (t, J = 6 Hz, CH_2O, 4 H), 3.84 (d, J_{ab} = 15 Hz, $ArCH_aCH_bN$, 4 H), 4.19 (d, J_{ab} = 15 Hz, $ArCH_aCH_bN$, 4 H), 4.31 (s, CH_2O, 4 H), 6.91 (d, J = 8 Hz, H-6′, 4 H), 7.02 (t, J = 7 Hz, H-4′, 4 H), 7.21 (t, J = 8 Hz, H-5′, 4 H), 7.73 (d, J = 7, H-3′, 4 H). ^{13}C NMR ($CDCl_3$) δ 51.9, 52.3, 67.3, 69.0, 71.5, 112.2, 121.3, 127.3, 129.6, 129.7, 156.5.

Dibenzylated macrocycle 10. A mixture of caesium carbonate (383 mg, 1.18 mmol), benzyl chloride (55 mg, 0.43 mmol) and **7** (R = H) (93 mg, 0.18 mmol) in acetonitrile (CaH_2 dried) (20 cm^3) was heated at reflux under nitrogen for 24 h. The solvent was removed to yield a yellow solid. This was partitioned between water (30 cm^3) and dichloromethane (20 cm^3) and the pH of the aqueous phase was adjusted to 14 with NaOH solution (0.1 mol dm^{-3}). The dichloromethane layer was separated and the aqueous layer was again extracted with dichloromethane (3 × 20 cm^3). The organic layers were combined, dried over anhydrous sodium sulfate, and the solvent was removed on a rotary evaporator to yield **10** as a yellow solid (120 mg, 95%); mp 215 °C (Found: C, 79.6; H, 6.6; N, 4.15. Calc. for $C_{46}H_{46}N_2O_4$: C, 79.97; H, 6.71; N, 4.05%). ^{1}H-NMR ($CDCl_3$) δ 3.79 (s, 4H, $ArCH_2$), 3.87 (s, 8H, $ArCH_2N$), 4.25 (s, 8H, CH_2O), 6.85–7.91 (m, arom). ^{13}C-NMR ($CDCl_3$) δ 52.21 ($ArCH_2$), 59.02 (CH_2N), 66.40 (CH_2O), 111.3, 121.3, 126.6, 127.1, 128.0, 128.1, 128.3, 129.1, 140.2 (arom).

1,2-Bis(4-*tert*-butyl-2-formylphenoxy)ethane dioxime. Hydroxylamine hydrochloride (10.82 g, 0.156 mol) was dissolved in aqueous NaOH (8.18 g, 0.205 mol in 40 cm^3 of water). The neutralised hydroxylamine solution was added to 1,2-bis(4-*tert*-butyl-2-formylphenoxy)ethane (8.22 g, 21.5 mmol) in absolute ethanol (100 cm^3) contained in a 250 cm^3 one-necked round-bottomed flask equipped with magnetic stirring and a reflux condenser. The resulting clear solution was refluxed for 5 h (a white precipitate gradually formed). The reaction mixture was cooled to room temperature, poured into HCl (2 mol dm^{-3}, 350 cm^3), and allowed to stand in a refrigerator overnight. The white precipitate of 1,2-bis(4-*tert*-butyl-2-formylphenoxy)ethane dioxime that formed was filtered off and dried in a vacuum oven at 75 °C; yield 7.33 g (17.4 mmol, 81%); mp > 250 °C (Found: C, 70.1; H, 7.7; N, 6.6. Calc. for $C_{24}H_{32}N_2O_4$: C, 69.88; H, 7.82; N, 6.79%). MS (PD) m/z = 412.2 (M^+). ^{1}H-NMR (DMSO-d_6): δ 8.26 (s, 2H, C*H*-NOH), 7.68 (d, 2H, J = 3 Hz, arom. 3-*H*), 7.37 (dd, 2H, J = 3 Hz, J = 9 Hz, arom. 5-*H*), 6.90 (d, 2H, J = 9 Hz, arom. 6-*H*), 4.35 (s, 4H, OCH_2CH_2O), 1.24 [s, 18H, $C(CH_3)_3$]. ^{13}C-NMR (DMSO-d_6) δ 153.98, 143.46, 143.10, 127.80, 121.71, 120.60, 112.92, 67.28, 33.87, 31.22.

1,2-Bis(4-*tert*-butyl-2-aminomethylphenoxy)ethane 6 (R = *t*-Bu). 1,2-Bis(4-*tert*-butyl-2-formylphenoxy)ethane dioxime (7.26 g, 17.6 mmol) (see above) was dissolved in dry tetrahydrofuran (150 cm^3) under N_2 in a 250 cm^3 one-necked round-bottomed flask equipped with magnetic stirring and a reflux condenser. The clear solution was cooled to 0 °C in an ice bath. Lithium aluminium hydride (6.66 g, 0.175 mol) was added (gas evolution) and the reaction was stirred at 0 °C for 10 min after which it was allowed to warm to room temperature. The solution was refluxed for 4 h, then stirred at 50 °C for 16 h after which it was allowed to cool to room temperature. Water (7 cm^3) was added, followed by 20% NaOH (7 cm^3) and then more water (7 cm^3) to quench the reaction. The granular precipitate thus formed was filtered off and washed with dichloromethane (3 × 50 cm^3); the combined filtrates were evaporated, and the residue was taken up in dichloromethane (250 cm^3) and washed with NaOH (4 mol dm^{-3}, 2 × 50 cm^3), water (2 × 50 cm^3) and dried (anhydrous Na_2SO_4). Evaporation of the solvent gave a yellow solid which was taken up in ethanol (100 cm^3); aqueous 60% HPF_6 (20 cm^3) was then added. The solution was then held at 5 °C for 2 h. The crystals that formed were filtered off and recrystallised from absolute ethanol to give the monohexafluorophosphate salt of 1,2-bis(4-*tert*-butyl-2-aminomethylphenoxy)ethane **6** (R = *t*-Bu) as colourless needles; yield 7.15 g (77%); mp > 250 °C. The following procedure was employed to produce the free amine. The hexafluorophosphate salt (1.55 g, 2.02 mmol) was suspended in dichloromethane (100 cm^3) and NaOH solution (6 mol dm^{-3}, 40 cm^3) was added. The resulting two-phase system was stirred vigorously for 60 min, after which the phases were separated. The aqueous phase was extracted with dichloromethane (50 cm^3), and the combined organic phases were washed with NaOH solution (6 mol dm^{-3}, 20 cm^3) then water (2 × 50 cm^3). The chloroform phase was separated and dried (anhydrous Na_2SO_4), then evaporated to give 1,2-bis(4-*tert*-butyl-2-aminomethylphenoxy)ethane **6** (R = *t*-Bu) as a white crystalline solid; yield 1.08 g (96%); mp 106–108 °C (Found: C, 75.3; H, 9.8; N, 7.3. Calc. for $C_{24}H_{36}N_2O_2$: C, 74.96; H, 9.44; N, 7.28%). MS (PD) m/z = 384.9 (M^+). ^{1}H-NMR ($CDCl_3$) δ 7.29 (d, 2H, J = 3 Hz, arom. 3-*H*), 7.26 (dd, 2H, J_1 = 3 Hz, J_2 = 9 Hz, arom. 5-*H*), 6.78 (d, 2H, J = 9 Hz, arom. 6-*H*), 4.40 (s, 4H, OCH_2CH_2O), 3.86 (s, 4H, CH_2NH_2), 1.98 (br s, 4H, CH_2NH_2), 1.34 [s, 18H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.19, 143.82, 131.16, 126.08, 124.58, 110.86, 66.63, 43.00, 34.11, 31.69.

1,2-Bis(4-*tert*-butyl-2-chloromethylphenoxy)ethane 8 (R = *t*-Bu). 1,2-Bis(4-*tert*-butyl-2-hydroxymethylphenoxy)ethane (850 mg, 2.21 mmol) was dissolved under N_2 in dry dichloromethane (50 cm^3) in a 100 cm^3 one-necked round-bottomed flask equipped with magnetic stirring and a dropping funnel. The clear solution was cooled to −78 °C using a solid CO_2/acetone cooling bath. Thionyl chloride (1.5 cm^3 ≈245 mg, 20.6 mmol) was added dropwise and the reaction solution was allowed to warm to room temperature over a period of 45 min. The reaction solution was heated at reflux for 10 min then stirred without heating for 30 min after which it was cooled in an ice bath. Water (15 cm^3) was then added slowly to quench the reaction solution. The mixture was allowed to warm to room temperature and the phases were separated. The aqueous phase was extracted with dichloromethane (50 cm^3) and the combined organic phases were washed with water (2 × 100 cm^3), dried (anhydrous Na_2SO_4), and evaporated to give the product 1,2-bis(4-*tert*-butyl-2-chloromethylphenoxy)ethane **8** (R = *t*-Bu) as a white crystalline solid; yield 91 mg (98%) (Found: C, 67.9, H, 7.3. Calc. for $C_{24}H_{32}Cl_2O_2$: C, 68.40, H, 7.65%). MS (PD) m/z = 421.8 (M^+). ^{1}H-NMR ($CDCl_3$) δ 7.35 (d, 2H, J = 3 Hz, arom. 3-*H*), 7.30 (dd, 2H, J_1 = 3 Hz, J_2 = 9 Hz, arom. 5-*H*), 6.89 (d, 2H, J = 9 Hz, arom. 6-*H*), 4.62 (s, 4H, CH_2Cl), 4.39 (s, 4H, CH_2O), 1.29 [s, 18H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.28, 143.99, 127.75, 126.75, 125.64, 111.83, 67.21, 42.03, 34.14, 31.43.

Cryptand 2 (R = *t*-Bu). *Method 1.* Caesium carbonate (13.78 g, 42.3 mmol) was suspended in dry acetonitrile (60 cm^3) in a 250 cm^3 three-necked round-bottomed flask equipped with magnetic stirring, a nitrogen bubbler and two 100 cm^3 dropping

funnels. 1,2-Bis(4-*tert*-butyl-2-chloromethylphenoxy)ethane **8** (R = *t*-Bu) (900 mg, 2.14 mmol) was dissolved in dry acetonitrile (60 cm^3) and transferred to the first dropping funnel, while 1,10-diaza-18-crown-6 (553 mg, 2.11 mmol) was dissolved in dry acetonitrile (60 cm^3) and transferred to the second dropping funnel. The two solutions were added dropwise simultaneously to the reaction vessel over 45 min, and the resulting suspension was stirred at room temperature for 72 h. The reaction mixture was filtered to remove undissoled salts, these were washed with acetonitrile, and the filtered solution was evaporated under vacuum to give a residue which was subjected to column chromatography on deactivated silica gel (column packed in dichloromethane–ethanol–concentrated aqueous ammonia 200 : 15 : 1, gradient elution from dichloromethane–methanol–conc. aqueous ammonia 200 : 15 : 1 to 200 : 22 : 2). Evaporation of the relevant fraction gave a colourless oil, which hardened upon standing. The oil was redissolved in redistilled chloroform (100 cm^3) and subjected to continuous extraction with distilled water (using a continuous extractor for liquid–liquid extraction by upward displacement) for two days. The phases were separated, and toluene (100 cm^3) was added to the organic phase. The solvent was removed under vacuum (with concurrent drying by azeotropic distillation of the toluene). After drying in a vacuum at 60 °C, the uncomplexed cryptand **2** (R = *t*-Bu) was obtained as a colourless glass which crystallised upon standing to give a low-melting white solid; yield 840 mg (65%).

Method 2. The macrocyclic Mannich base, *N*,*N*′-bis(4-*tert*-butylphenol-2-ylmethyl)diaza-18-crown-6 [20] (1.16 g, 1.98 mmol), was dissolved in dry tetrahydrofuran (50 cm^3) in a 100 cm^3 round-bottomed flask under N_2 and treated with a solution of sodium (93 mg, 4.04 mmol) in dry ethanol (4 cm^3). The solution, which at first became clear, soon turned cloudy, and a white powder precipitated from the reaction mixture. This was redissolved by the addition of dry ethanol (20 cm^3) and the resulting solution was stirred at room temperature for 20 min. The solvent was evaporated under vacuum, and the resulting semisolid was redissolved in dry dimethylformamide (50 cm^3) with gentle heating; ethylene glycol distosylate (741 mg, 2.00 mmol) was added. The resulting solution was heated at the reflux for 24 h, the solvent was evaporated under vacuum, and the resulting oily residue was purified by column chromatography (SiO_2; eluent dichloromethane–methanol–triethylamine 50 : 5 : 1) to give a yellowish oil, which was purified by continuous extraction with distilled water as described in Method 1 (see above) to give the product **2** (R = *t*-Bu) as a white low-melting crystalline solid; yield 1.00 g (82%) (Found: C, 70.5; H. 9.1; N, 4.7. Calc. for $C_{36}H_{56}N_2O_6$: C, 70.55; H, 9.21; N, 4.57%). MS (PD) $m/z = 637.5$ ($M + Na^+$). ^{1}H-NMR ($CDCl_3$) δ 7.45 (d, 2H, $J = 3$ Hz, arom. 3-*H*), 7.20 (dd, 2H, $J_1 = 3$ Hz, $J_2 = 9$ Hz, arom. 5-*H*), 6.81 (d, 2H, $J = 9$ Hz, arom. 6-*H*), 4.32 (s, 4H, $ArOCH_2$), 3.89 (s, 4H, $ArCH_2N$), 3.56 (m, 16H, CH_2OCH_2), 2.96 [symm. m, 8H, $ArCH_2NCH_2$], 1.31 [s, 18H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$): δ 154.60, 143.56, 128.64, 127.85, 124.13, 111.28, 70.48, 69.85, 67.13, 54.63, 52.33, 34.00, 31.47.

Macrocycle 7 (R = *t*-Bu). Bis(4-*tert*-butyl-2-aminomethylphenoxy)ethane **6** (R = *t*-Bu) (794 mg, 2.06 mmol) in dry methanol (50 cm^3) and 1,2-bis(4-*tert*-butyl-2-formylphenoxy)-ethane **5** (R = *t*-Bu) (788 mg, 2.06 mmol) in dry methanol were added dropwise simultaneously into methanol (50 cm^3) and 3X molecular sieves (10 cm^3) (under N_2) in a 250 cm^3 three-necked round-bottomed flask equipped with magnetic stirring, two 50 cm^3 dropping funnels, and a reflux condenser. After complete addition (1 h), the solution was refluxed for 2 h, whereupon $NaBH_4$ (500 mg, 13.2 mmol) was added and the reaction solution was heated at reflux for 90 min. The reaction mixture was filtered through Celite to remove the molecular sieves, the solvent was removed, and the residue was taken up in dichloromethane (200 cm^3) and washed with NaOH (2 mol dm^{-3}, 50 cm^3), water (50 cm^3), saturated aqueous NaCl (50 cm^3) and then evaporated to give **7** (R = *t*-Bu) as a white powder; yield 1.44 g (95%); mp 219–220 °C.

Although this material was sufficiently pure for further reactions, an analytical sample was prepared by chromatography (deactivated SiO_2, gradient elution from 5% methanol in dichloromethane to 10% methanol in dichloromethane) (Found: C, 78.6; H, 9.1. Calc. for $C_{48}H_{66}N_2O_4$: C, 78.43; H, 9.05%). HR-MS (EI) (M^+) found 734.5017. $C_{48}H_{66}N_2O_4$ requires 734.5023. ^{1}H-NMR ($CDCl_3$) δ 7.81 (d, 4H, $J = 3$ Hz, arom. 3-*H*), 7.17 (dd, 4H, $J_1 = 3$ Hz, $J_2 = 9$ Hz, arom. 5-*H*), 6.81 (d, 4H, $J = 9$ Hz, arom. 6-*H*), 4.24 (s, 8H, CH_2CH_2O), 4.17 [d, 4H, $J_{a,b} = 15$ Hz, $Ar(CH_aH_b)N$], 3.84 [d, 4H, $J_{a,b} = 15$ Hz, $Ar(CH_aH_b)N$], 3.65 (t, 4H, $J = 6$ Hz, NCH_2CH_2O), 3.50 (s, 4H, $CH_2OCH_2CH_2O$), 2.93 (t, 4H, $J = 6$ Hz, NCH_2CH_2O), 1.30 [s, 36H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.14, 143.57, 128.70, 124.27, 111.05, 66.37, 49.34, 34.14, 31.54.

Cryptand 3 (R = *t*-Bu). *Method 1.* Tetrabutylammonium bromide (25 mg) was added to caesium carbonate (5.0 g, 15 mmol) suspended in a 1 : 1 mixture of dry toluene and dry acetonitrile (50 cm^3) under N_2 contained in a 500 cm^3 three-necked round-bottomed flask equipped with magnetic stirring, a reflux condenser and two 100 cm^3 dropping funnels. The macrocyclic diamine **7** (R = *t*-Bu) (432 mg, 0.59 mmol) in toluene–acetonitrile (1 : 1, 80 cm^3) was placed in one of the dropping funnels, while triethylene glycol ditosylate (270 mg, 5.89 mmol) in toluene–acetonitrile (1 : 1, 80 cm^3) was placed in the other. The caesium carbonate suspension was heated to reflux with stirring and the above two solutions were added dropwise simultaneously over a period of $2\frac{1}{2}$ h. The reaction mixture was refluxed for 72 h, after which it was allowed to cool to room temperature and filtered through a sintered glass funnel. The residue on the filter was washed with dichloromethane (2 × 50 cm^3). Evaporation of the combined filtrates gave an oily residue, which was taken up in dichloromethane (200 cm^3) and washed with water (3 × 100 cm^3), dried ($CaCl_2$), and evaporated under vacuum. The residue was purified by chromatography (SiO_2, eluent 5% methanol in dichloromethane) to give **3** (R = *t*-Bu) as a white low-melting crystalline solid which was dried on a vacuum line then crystallised from cyclohexane; yield 170 mg (35%).

Method 2. Caesium carbonate (5.40 g, 16.6 mmol) was suspended in dry acetonitrile (50 cm^3) under N_2 in a 250 cm^3 three-necked round-bottomed flask equipped with a magnetic stirrer, a reflux condenser and two dropping funnels. The suspension was warmed to 45 °C on an oil bath. 1,2-Bis(4-*tert*-butyl-2-chloromethylphenoxy)ethane **8** (R = *t*-Bu) (436 mg, 1.03 mmol) was dissolved in dry acetonitrile (50 cm^3) and placed in the first dropping funnel, while macrocycle **9** (534 mg, 1.07 mmol) dissolved in dry acetonitrile (50 cm^3) was placed in the second. The two solutions were added dropwise simultaneously to the reaction solution over 1 h. The resulting reaction mixture was stirred at 45 °C for a further 48 h and then refluxed for 3 h. The reaction mixture was filtered hot, after which the solvent was removed under vacuum. The residue that remained was dissolved in the minimum amount of dichloromethane and chromatographed on deactivated silica (SiO_2, packed with dichloromethane–methanol–triethylamine 50 : 5 : 1 and gradient eluted from dichloromethane–methanol 25 : 1 to dichloromethane–methanol–triethylamine 50 : 5 : 2). The resulting residue was redissolved in chloroform (100 cm^3) and subjected to continuous extraction with distilled water (using a continuous extractor for liquid–liquid extraction by upward displacement) for two days. The phases were then separated, and toluene (100 cm^3) was added to the organic phase. The solvent was removed under vacuum (with concurrent drying by azeotropic distillation of the toluene). After drying under vacuum at 60 °C, the uncomplexed cryptand **3** (R = *t*-Bu) was obtained as

a colourless glass; yield 612 mg (70%) (Found: C, 76.4; H, 9.1; N, 3.35. Calc. for $C_{54}H_{76}N_2O_6$: C, 76.38; H, 9.02; N, 3.30%). MS (PD) m/z = 871.9 ($M + Na^+$). ^{1}H-NMR ($CDCl_3$) δ 7.81 (d, 4H, J = 3 Hz, arom. 3-*H*), 7.17 (dd, 4H, J_1 = 3 Hz, J_2 = 9 Hz, arom. 5-*H*), 6.81 (d, 4H, J = 9 Hz, arom. 6-*H*), 4.24 (s, 8H, OCH_2-CH_2O), 4.17 [d, 4H, J = 15 Hz, $RN(CH^{\alpha}H^{\beta})_2$], 3.84 [d, 4H, J = 15 Hz, $RN(CH^{\alpha}H^{\beta})_2$], 3.65 (t, 4H, J = 6 Hz, NCH_2CH_2O), 3.50 (s, 4H, $CH_2OCH_2CH_2OCH_2$), 2.93 (t, 4H, J = 6 Hz, NCH_2CH_2O), 1.30 [s, 36H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.39, 143.95, 128.91, 126.23, 123.65, 111.78, 71.65, 68.84, 67.46, 52.01, 51.94, 34.14, 31.57.

Cryptand 4 (R = *t*-Bu). Caesium carbonate (5.0 g, 15 mmol) was suspended in a 1 : 1 mixture of dry toluene and dry acetonitrile (100 cm^3) under N_2 in a 500 cm^3 three-necked round-bottomed flask equipped with magnetic stirring, a reflux condenser and two 100 cm^3 dropping funnels. The reaction mixture was heated to 40 °C on an oil bath, and the macrocyclic diamine **7** (R = *t*-Bu) (520 mg, 0.69 mmol) in toluene–acetonitrile (1 : 1, 100 cm^3) was placed in one dropping funnel, while 1,2-bis(4-*tert*-butyl-2-chloromethylphenoxy)-ethane **8** (R = *t*-Bu) (303 mg, 0.72 mmol) in toluene–acetonitrile (1 : 1, 100 cm^3) was placed in the other. The two solutions were added dropwise simultaneously over 1 h after which the reaction mixture was refluxed for 72 h. Upon allowing the solution to cool to room temperature, the reaction mixture was filtered, and the residue on the filter was washed with dichloromethane (2 × 50 cm^3). The combined filtrates were evaporated under vacuum and the residue that remained was taken up in dichloromethane (300 cm^3) and this solution washed with water (3 × 100 cm^3). The organic layer was separated, dried ($CaCl_2$), and evaporated under vacuum to give **4** (R = *t*-Bu) as a white microcrystalline solid, which was dried under vacuum at 80 °C for 48 h; yield 637 mg (85%); mp > 275 °C (Found: C, 79.85; H, 9.07; N, 2.28. Calc. for $C_{72}H_{96}N_2O_6$: C, 79.66; H, 8.91; N, 2.58%). HR-MS (EI) (M^+) found 1084.7255. $C_{72}H_{96}N_2O_6$ requires 1084.7268. ^{1}H-NMR ($CDCl_3$) δ 8.18 (d, 6H, J = 3 Hz, arom. 3-*H*), 7.15 (dd, 6H, J_1 = 3 Hz, J_2 = 9 Hz, arom. 5-*H*), 6.78 (d, 6H, J = 9 Hz, arom. 6-*H*), 4.22 (s, 12H, OCH_2CH_2O), 3.99 [s, 12H, $N(CH_2)_3$], 1.28 [s, 54H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.05, 143.65, 128.26, 124.30, 123.02, 110.13, 66.15, 52.82, 34.22, 31.68.

1,2-Bis(4-*tert*-butyl-2-hydroxymethylphenoxy)ethane. 1,2-Bis-(4-*tert*-butyl-2-formylphenoxy)ethane **5** (R = *t*-Bu) (1.12 g, 2.94 mmol) was dissolved in dry ethanol (40 cm^3) in a 100 cm^3 one-necked round-bottomed flask and $NaBH_4$ (640 mg, 17 mmol) was added. The clear solution was refluxed for 90 min, water (100 cm^3) was added, and the resulting mixture was refluxed for 5 min. After cooling the reaction mixture to room temperature, it was extracted with ethylacetate (2 × 100 cm^3); the combined organic extracts were washed with $NaHCO_3$ (2 × 100 cm^3) and water (100 cm^3), then dried (anhydrous Na_2SO_4). Evaporation of the solvent gave 1,2-bis(4-*tert*-butyl-2-hydroxymethylphenoxy)ethane as white crystals; yield 1.09 g (2.82 mmol, 96%); mp 123–124 °C (Found: C, 74.34; H, 9.10. Calc. for $C_{24}H_{34}O_4$: C, 74.58; H, 8.87%). MS (EI): m/z = 386 (M^+). ^{1}H-NMR ($CDCl_3$) δ 7.28 (d, 2H, J = Hz, arom. 3-*H*), 7.24 (dd, 2H, J_1 = 3 Hz, J_2 = 9 Hz, arom. 5-*H*), 6.84 (d, 2H, J = 9 Hz, arom. 6-*H*), 4.63 (s, 4H, CH_2OH), 4.37 (s, 4H, CH_2CH_2O), 3.20 (br s, 2H, CH_2OH), 1.27 [s, 18H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.16, 144.26, 128.98, 126.83, 125.50, 66.93, 62.08, 34.14, 31.43.

Unsymmetrical macrocycle 9. Dry methanol (50 cm^3) and 3X molecular sieves (20 cm^3) were placed in a 500 cm^3 three-necked round-bottomed flask equipped with two 100 cm^3 dropping funnels, a reflux condenser and magnetic stirring. The mixture was warmed to 50 °C (under N_2) on an oil bath. 1,2-Bis(4-*tert*-butyl-2-formylphenoxy)ethane **5** (R = *t*-Bu) (1.95 g, 5.10 mmol) in dry methanol (70 cm^3) was placed in one dropping funnel, while 1,2-bis(2-aminoethoxy)ethane (0.76 g, 5.15 mmol) in dry methanol (70 cm^3) was placed in the other. The solutions were added dropwise simultaneously over a period of 50 min and the reaction mixture was then refluxed for 2 h. $NaBH_4$ pellets (1.29 g, 34 mmol) were added, and the resulting suspension was refluxed for a further 5 h, after which it was filtered through a bed of Celite to remove the molecular sieves. The latter were washed with dichloromethane (2 × 50 cm^3) and the combined filtrates were evaporated in a rotary evaporator. The resulting oily residue was redissolved in dichloromethane (200 cm^3) which was washed with water (2 × 100 cm^3). Toluene (100 cm^3) was added to the organic phase and the solvent was removed under vacuum (with concurrent drying by azeotropic distillation of the toluene) to give the macrocycle as a colourless residue; yield 2.34 g (92%).

Analytically pure material was obtained by subjecting the above product to chromatography (either deactivated basic Al_2O_3 with gradient elution from dichloromethane to 10% methanol in dichloromethane or SiO_2 using dichloromethane–methanol–triethylamine 50 : 3 : 1 as eluent). The relevant fractions were evaporated under high vacuum, and the residue redissolved in chloroform. The chloroform solution was subjected to continuous extraction with distilled water (using a continuous extractor for liquid–liquid extraction by upward displacement) for 72 h. The phases were separated, and toluene (100 cm^3) was added to the organic phase. The solvent was removed under vacuum (with concurrent drying by azeotropic distillation of the toluene). After drying under vacuum at 60 °C for 72 h, the product was obtained as a colourless glass (Found: C, 71.9; H, 9.2; N, 5.5. Calc. for $C_{30}H_{46}N_2O_4$: C, 72.25; H, 9.30; N, 5.62%). MS (PD) m/z = 498.8 (M^+). ^{1}H-NMR ($CDCl_3$) δ 7.30 (d, 2H, J = 3 H, arom. 3-*H*), 7.25 (dd, 2H, J_1 = 3 Hz, J_2 = 9 Hz, arom. 5-*H*), 6.85 (d, 2H, J = 9 Hz, arom. 6-*H*), 4.37 (s, 4H, OCH_2CH_2O), 3.87 (s, 4H, $CH_2OCH_2CH_2$-OCH_2), 3.64 (t, 4H, J = 5 Hz, NCH_2CH_2O), 3.54 (s, 4H, $ArCH_2NH$), 3.10 (br s, 2H, N*H*), 2.77 (t, 4H, J = 5 Hz, OCH_2-CH_2NH), 1.30 [s, 18H, $C(CH_3)_3$]. ^{13}C-NMR ($CDCl_3$) δ 154.77, 143.86, 127.80, 127.66, 125.04, 111.91, 70.07, 67.46, 49.64, 48.18, 33.93, 31.36.

Picrate extraction experiments

The extraction experiments were performed in 15 cm^3 sealed glass vials which were shaken on an oscillating shaker for 2 h (at 22 °C) at 120 cycles per min. The extractions involved an aqueous source phase (3 cm^3) and a chloroform organic phase (3 cm^3). The aqueous phase was a standard solution of sodium picrate which was prepared in distilled, deionised water by neutralising (pH = 7.00 ± 0.05) an aqueous solution of picric acid with sodium hydroxide solution (0.1 mol dm^{-3}). The concentration of this standard solution (0.81 mmol dm^{-3}) was accurately determined using the aqueous molar absorptivity of sodium picrate (ε_{356nm} = 1.45 × 10^4 mol^{-1} dm^3).[41] The chloroform phase contained an accurately known concentration of ligand (≈1 mmol dm^{-3}). As part of each set of experiments, control experiments (×3) using chloroform alone were also run. The chloroform used for all extraction experiments was first distilled and then saturated with water prior to use.

After equilibration had been established, the concentration of picrate in the aqueous phase was determined by spectrophotometry. The percent extraction was calculated as (moles of picrate in chloroform)/(moles of picrate corresponding to 100% extraction).[42] All spectrophotometric determinations were performed using a Hewlett Packard 8451A Diode Array spectrophotometer. All extractions were performed in triplicate with the variation in the metal extraction being less than ±10%. Comparative extraction experiments were run in parallel under identical conditions.

NMR induced chemical shift and relaxation studies

^{1}H and ^{13}C NMR spectra for these studies were obtained on a Varian Unity 400 spectrometer at 400 and 100 MHz, respectively. The cryptand was dissolved in dimethylformamide-d_7 (0.5 cm^3) and placed in a 5 mm (o.d.) NMR tube. The cryptand concentration was *ca.* 0.10 mol dm^{-3} in each case. To obtain the induced chemical shift data, a stoichiometric amount of the required metal nitrate was added directly to the tube containing the cryptand solution and the mixture was shaken until complete dissolution had ocurred. All metal nitrates from lithium to caesium dissolved in the solution containing **1** (2.2.2), while rubidium and caesium nitrates yielded precipitates when added to the solution containing **2** (R = *t*-Bu) and potassium, rubidium and caesium nitrates also produced a precipitate on addition to the **4** (R = *t*-Bu) solution.

Crystallographic data

[NaL](picrate)·CH_2Cl_2 (L = **3** (R = H)) ≡ $C_{44}H_{48}N_5NaO_{13}$·CH_2Cl_2, M = 961.8. Triclinic, space group $P\bar{1}$ (C_i^1, no. 2), a = 12.299(10), b = 14.264(11), c = 15.32(2) Å, α = 63.29(8), β = 81.12(9), γ = 77.38(6)°, V = 2338 Å^3. D_c (Z = 2) = 1.36$_6$ g cm^{-3}. μ_{Mo} = 2.2 cm^{-1}; specimen (capillary): 0.30 × 0.12 × 0.43 mm (no correction). Full sphere of single counter instrument room temperature (T *ca.* 295 K) data ($2\theta_{max}$ = 44°, $2\theta/\theta$ scan mode; monochromatic Mo Kα radiation λ = 0.7107$_3$ Å) = 10081 reflections, merging to 5782 (R_{int} = 0.066) (no absorption correction), 1228 ($I > 3\sigma(I)$) considered 'observed' and used in the full-matrix least-squares refinement (isotropic non-hydrogen thermal parameter forms, (x, y, z, U_{iso})$_H$ constrained at estimates; CH_2Cl_2 modelled as disordered, constrained geometry). Conventional R, R_W (statistical weights) on $|F|$ 0.13, 0.14. Xtal 3.4 program system.[43]

CCDC reference number 164829.

See http://www.rsc.org/suppdata/dt/b1/b102585f/ for crystallographic data in CIF or other electronic format.

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References

1 L. F. Lindoy, *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press, Cambridge, 1989.
2 B. Dietrich, P. Viout and J.-M. Lehn, *Macrocyclic Chemistry*, VCH, Weinheim, 1993.
3 *Macrocyclic Compounds in Analytical Chemistry*, ed. Yu. A. Zolotov, Wiley, New York, 1997.
4 G. W. Gokel, *Crown Ethers and Cryptands*, in Monographs in Supramolecular Chemistry, ed. J. F. Stoddart, Royal Society of Chemistry, Cambridge, 1992; R. M. Izatt, P. Pawlak, J. S. Bradshaw and R. L. Bruening, *Chem. Rev.*, 1995, **95**, 2529; B. Dietrich, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vögtle, Pergamon Press, Oxford, 1996, vol. 1, pp. 153–211.
5 J.-M. Lehn and J. P. Sauvage, *J. Am. Chem. Soc.*, 1975, **97**, 6700.
6 E. Kauffmann, J.-M. Lehn and J.-P. Sauvage, *Helv. Chim. Acta*, 1976, **59**, 1099.
7 H.-J. Buschmann, *Inorg. Chim. Acta*, 1987, **134**, 225 and refs. therein; F. Marsicano, R. D. Hancock and A. McGowan, *J. Coord. Chem.*, 1992, **25**, 85.
8 B. G. Cox and H. Schneider, *Coordination and Transport Properties of Macrocyclic Compounds in Solution*, Elsevier, Amsterdam, 1992.
9 B. Dietrich, J.-M. Lehn and J. P. Sauvage, *Chem. Commun.*, 1970, 1055.
10 B. Dietrich, J.-M. Lehn, J. P. Sauvage and J. Blanzat, *Tetrahedron*, 1973, **29**, 1629.
11 X. X. Zhang, R. M. Izatt, J. S. Bradshaw and K. E. Krakowiak, *Coord. Chem. Rev.*, 1998, **174**, 179.
12 J.-M. Lehn, *Acc. Chem. Res.*, 1978, **2**, 49; C. Detellier, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vögtle, Pergamon Press, Oxford, 1996, vol. 1, pp. 357–375.
13 T. W. Hambley, L. F. Lindoy, J. R. Reimers, P. Turner, G. Wei and A. N. Widmer-Cooper, *J. Chem. Soc., Dalton Trans.*, 2001, 614 and refs. therein.
14 R. W. Alder and S. P. East, *Chem. Rev.*, 1996, **96**, 2097.
15 H.-J. Buschmann, E. Schollmeyer, R. Trueltzsch and J. Beger, *Thermochim. Acta*, 1993, **213**, 11; V. P. Solov'ev, N. N. Strakhova, O. A. Raevsky, V. Ruediger and H.-J. Schneider, *J. Org. Chem.*, 1996, **61**, 5221; A. Thaler, R. Bergter, T. Ossowski, B. G. Cox and H. Schneider, *Inorg. Chim. Acta*, 1999, **285**, 1; H.-J. Buschmann and E. Schollmeyer, *J. Inclusion Phenom. Macrocyclic Chem.*, 2000, **38**, 85.
16 I. M. Atkinson, L. F. Lindoy, O. A. Matthews, G. V. Meehan, A. N. Sobolev and A. H. White, *Aust. J. Chem.*, 1994, **47**, 1155.
17 K. E. Krakowiak, J. S. Bradshaw and D. J. Zamecka-Krakowiak, *Chem. Rev.*, 1989, **89**, 929; K. E. Krakowiak and J. S. Bradshaw, *J. Org. Chem.*, 1991, **56**, 3723.
18 L. F. Lindoy, G. V. Meehan and N. Svenstrup, *Synthesis*, 1998, 1029.
19 A. V. Bordunov, N. K. Dalley, X. Kou, J. S. Bradshaw and V. N. Pastushok, *J. Heterocyclic Chem.*, 1996, **33**, 933.
20 K. W. Chi, H.-C. Wei, T. Kottke and R. J. Lagow, *J. Org. Chem.*, 1996, **61**, 5684.
21 See, for example: U. Olsher, H. Feinberg, F. Frolow and G. Shoham, *Pure Appl. Chem.*, 1996, **68**, 1195; F. Arnaud-Neu, Z. Asfari, B. Souley and J. Vicens, *An. Quim. Int. Ed.*, 1997, **93**, 404; E. Makrlik and P. Vanura, *J. Radioanal. Nucl. Chem.*, 1997, **223**, 229; A. P. Marchang, S. Alihoxzic, A. S. McKim, K. A. Kumar, K. Mlinaric-Majerski, T. Sumanovac and S. G. Bott, *Tetrahedron Lett.*, 1998, **39**, 1861; A. P. Marchand, A. S. McKim and K. A. Kumar, *Tetrahedron*, 1998, **54**, 13 421; C. Hamamci, H. Hosgoren and S. Erdogan, *Talanta*, 1998, **47**, 229; A. P. Marchang and H.-S. Chong, *Tetrahedron*, 1999, **55**, 9697; G. G. Talanova, N. S. A. Elkarim, V. S. Talanov, R. E. Hanes, H.-S. Hwang, A. R. Bartsch and R. D. Rogers, *J. Am. Chem. Soc.*, 1999, **121**, 11 281.
22 J. D. Lamb, J. J. Christensen, S. R. Izatt, K. Bedke, M. S. Astin and R. M. Izatt, *J. Am. Chem. Soc.*, 1980, **102**, 3399; V. V. Yakshin, V. M. Abashkin and B. N. Laskorin, *Dokl. Akad. Nauk SSSR*, 1980, **252**, 273; G. G. Talanova, K. B. Yatsimirskii and A. H. Ziemanis, *Dokl. Akad. Nauk SSSR*, 1991, **319**, 12 145; U. Olsher, M. G. Hankins, D. Y. Kim and R. A. Bartsch, *J. Am. Chem. Soc.*, 1993, **115**, 3370.
23 H.-J. Buschmann, *Inorg. Chim. Acta*, 1986, **125**, 31.
24 Spartan Version 4.0, Wavefunction, Inc., 18401 Von Karman Ave., #370 Irvine, CA 92715, USA.
25 B. Metz, D. Moras and R. Weiss, *J. Chem. Soc., Perkin Trans. 2*, 1976, 423.
26 L. R. MacGillivray and J. L. Atwood, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1828.
27 R. Geue, S. H. Jacobson and R. Pizer, *J. Am. Chem. Soc.*, 1986, **108**, 1150 and refs. therein.
28 F. H. Allen, *Chem. Des. Automat. News*, 1993, **8**, 1.
29 B. Mertz, D. Moras and R. Weiss, *Chem. Commun.*, 1971, 444.
30 D. Moras and R. Weiss, *Acta Crystallogr., Sect. B*, 1973, **29**, 396.
31 D. Moras, B. Metz and R. Weiss, *Acta Crystallogr., Sect. B*, 1973, **29**, 383.
32 F. J. Tehan, B. L. Barnett and J. L. Dye, *J. Am. Chem. Soc.*, 1979, **96**, 7203.
33 D. Moras, B. Metz and R. Weiss, *Acta Crystallogr., Sect. B*, 1973, **29**, 386.
34 G. Wipff and P. Kollman, *Nouv. J. Chim.*, 1985, **9**, 457.
35 P. Auffinger and G. Wipff, *J. Incl. Phenom. Mol. Recognit. Chem.*, 1991, **11**, 71.
36 G. Wipff, *J. Coord. Chem.*, 1992, **27**, 7; L. Troxler and G. Wipff, *J. Am. Chem. Soc.*, 1994, **116**, 1468.
37 J. Gutknecht, H. Schneider and J. Stroka, *Inorg. Chem.*, 1978, **17**, 3326; G. Anderegg, *Helv. Chim. Acta*, 1975, **58**, 1218.
38 J. Sandstrom, *Dynamic NMR Spectroscopy*, Academic Press, New York, 1982.
39 L. G. Armstrong and L. F. Lindoy, *Inorg. Chem.*, 1975, **14**, 1322.
40 J. Dale and P. O. Kristiansen, *Acta Chem. Scand.*, 1972, **26**, 1471.
41 Y. Takeda and H. Goto, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 1920.
42 G. W. Gokel, *Chem. Soc. Rev.*, 1992, 39.
43 S. R. Hall, G. S. D. King and J. M. Stewart (Editors), *The Xtal 3.4 Users' Manual*, University of Western Australia, Lamb, Perth, 1995.