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A bis-triazacyclononane tris-pyridyl N₉-azacryptand 'Beer Can' receptor for complexation of alkali metal and lead(II) cations

Asha Brown,^[a] Thanthapatra Bunchuay,^[a] Christopher G. Crane,^[a] Nicholas G. White,^[b] Amber L. Thompson^[a] and Paul D. Beer^{*[a]}

Abstract: A new bis-triazacyclononane tris-pyridyl N₉-azacryptand ligand is synthesised via a convenient one-pot [2 + 3] condensation reaction between triazacyclononane and 2,6-bis(bromomethyl) pyridine in the presence of M₂CO₃ (M = Na, K). The proton, lithium, sodium, potassium and lead(II) complexes of the ligand are characterised in the solid state. A preliminary solution-phase competition experiment indicates that the cryptand ligand preferentially binds lead(II) in the presence of sodium, calcium, potassium and zinc cations in methanol solution.

Introduction

Cryptands are a class of cage-like polycyclic host molecules, first synthesised during the late 1960s, which played a central historical role in the advent of supramolecular chemistry.^[1] The early diaza polyether cryptand ligands were shown to be capable of binding spherical alkali metal and alkaline earth metal cations^[2,3] with unprecedented thermodynamic and kinetic stabilities, and with unrivalled selectivities for complementary sized metal cationic guests. The remarkable complexation properties of cryptand ligands, collectively termed the 'cryptate effect' are elegantly exemplified by Lehn's prototypical diazapolyoxa cryptand 222.^[4,5] This receptor binds potassium cations^[6] selectively over sodium and rubidium,^[7,8] with stability constants which are several orders of magnitude greater than those observed for macrocyclic ligands such as crown ethers and the naturally occurring antibiotic valinomycin,^[9] and with an unusually slow kinetic rate of dissociation.[10] The high thermodynamic stability of metal cryptate complexes is enthalpic in origin, arising predominately from the high degree of preorganisation and low degree of solvation of the cryptand ligands;[11] the ligands' stringent selectivity preferences have often been attributed to size complementarity considerations^[12] but other factors such as ligand flexibility and the solvation enthalpy and coordination preferences of the guest are also recognised to have an important influence.[13-15]

Since the early work on metal cryptate complexes, numerous cryptand host systems have been developed for metal cations, as well as anions^[16,17] and organic guest molecules.^[18] The resulting cryptate systems have found varied applications, for example as phase transfer catalysts,^[19] anion-exchange column stationary phases,^[20] ionophores in ion-selective electrodes,^[21-23] inert cations for the stabilisation of unusual alkalide^[24,25], electride^[26] and homopolyatomic^[27-29] anions, and components of higher order rotaxane-based molecular muscles.^[30] Cryptands have also attracted interest as selective chelates for the detection and sequestration of toxic heavy metal cations such as Pb(II), which is a pernicious environmental pollutant as a consequence of the historical widespread industrial use of lead in the production of lead-acid batteries; paints, pigments and glazes; ammunitions; plumbing pipes, solder and fixtures; herbal medicines; and leaded fuels. Once ingested or inhaled by humans lead is known to accumulate in soft tissues including the liver, kidneys and brain, where it can bind to the phosphate, thiol and amide groups of nucleic acids,^[31] proteins^[32] and enzymes^[33] with severe toxicological effects, especially in young children.^[34] Efforts to control the industrial use of this toxic metal have led to declining levels of lead in the environment, food and the human blood stream over recent decades; however there is thought to be no safe exposure threshold, with even low exposure levels presenting a significant public health risk.^[35] Selective chelate forming compounds which can be used for the environmental detection and extraction of lead, as well as in the diagnosis and treatment of lead intoxication, are therefore highly attractive targets.[36,37]

Herein we report the convenient one-pot synthesis of a new bis-triazacyclononane tris-pyridyl N₉-azacryptand ligand which is shown to encapsulate alkali metal and divalent lead cations. The lithium, sodium, potassium and lead(II) complexes of the cryptand ligand are characterised in solution and in the solid state. Preliminary cation binding competition experiments indicate that the cryptand exclusively complexes Pb²⁺ and Na⁺ in the presence of Ca²⁺, Zn²⁺ and K⁺ cations in methanol solution.

Results and Discussion

The new cryptand ligand comprises two triazacyclononane (TACN) capping groups which are bridged by three pyridyl sidearms to form a rigid cage-like structure in which each of the nine nitrogen donor groups converges towards a central cation binding cavity. The cryptand was synthesised via a one-pot [2 + 3] condensation reaction between TACN and 2,6-bis(bromomethyl) pyridine in the presence of M₂CO₃ (M = Li, Na, K) in refluxing acetonitrile. Purification by column chromatography on neutral

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Scheme 1. One-pot synthesis of the alkali metal cryptate complexes $[M\,{\subset}\,1]^*{\cdot}\mathsf{PF}_6{}^-$

alumina followed by counteranion exchange afforded the alkali metal cryptate products as their hexafluorophosphate salts (Scheme 1).

Potassium templated reaction. For the reaction performed in the presence of K₂CO₃ a single product was isolated in 20% yield. The electrospray mass spectrum of this compound showed a single peak at m/z = 606.34, corresponding to the $[M - PF_6]^+$ ion for the potassium cryptate complex $[K \subset 1]^+ \cdot PF_6^-$. The ¹H NMR spectrum of this species in CD₃OD (Figure 1) reveals a diastereotopic splitting of the methylene proton signals H₃ and H₃', along with the appearance of four separate signals corresponding to the ethylene protons H_4 , H_4 ', H_5 and H_5 ', consistent with a helical cryptate structure with overall D_3 point group symmetry. Variable temperature ¹H NMR experiments in [D₆]DMSO revealed that coalescence of the diastereotopic methylene signals is not observed below 100 °C, suggesting a high kinetic barrier to conformational interconversion (Figure S3, ESI). There is no ¹H NMR evidence of any additional asymmetry between the two TACN capping groups or the three pyridyl side-arms, which is consistent with an endo binding mode in which the potassium cation resides centrally within the cryptand's cavity.



Figure 1. ¹H NMR spectrum (500 MHz; CD₃OD; 298 K) of the potassium cryptate complex [K \subset 1]⁺·PF₆⁻.

Sodium templated reaction. In contrast, when the reaction was carried out using Na₂CO₃ in place of K₂CO₃ the formation of two separate products was apparent from analysis of the crude ¹H NMR spectrum. After chromatographic purification each of these products were isolated in yields of 20% and 5% respectively. While both products were observed as $[1 + Na]^+$ and $[1 + Na]^{2+}$



ions by electrospray mass spectrometry, the two compounds are clearly distinguishable by differences in their ¹H NMR spectra. The ¹H NMR spectrum of the minor product is analogous to that of the product of the potassium-templated reaction, suggesting a helical sodium cryptate structure, $[Na \subset 1]^+ \cdot PF_6^-$, in which the cation is centrally located within the cavity (Figure 2(i)). The ¹H NMR spectrum of the major product reveals additional asymmetry

between the top and bottom of the molecule, with the methylene and ethylene protons appearing as four and eight separate signals respectively. Furthermore an extra proton signal is observed at 10.2 ppm with an integral value of 1. The 2-D COSY spectrum revealed through-bond coupling interactions between this proton and the ethylene and methylene protons, suggesting that the extra signal appears as a result of internal protonation of one of the bridgehead nitrogen atoms (Figure 2(ii)). This bridgehead nitrogen proton signal is consistently observed as a sharp singlet in the protic CD₃OD solvent, from which it is apparent that the rate of the hydrogen-deuterium exchange reaction is slower than the timescale of the NMR experiment. Kinetically slow proton transfer rates are a characteristic feature of azacryptand ligands which is thought to reflect the restricted conformational dynamics of these cage-like structures.[38,39] The major product was therefore assigned as the protonated sodium cryptate $[Na \subset 1 \cdot H]^{2+2} PF_6^{-}$. The sodium cation presumably does not interact with the protonated TACN group and is instead displaced from the centre of the cryptand cavity towards the neutral TACN group, forming a six-coordinate complex with the three nitrogen atoms of this non-protonated TACN group and the three pyridyl nitrogen atoms. This was later corroborated by solid state structural characterisation of the complex (vide infra). The ready protonation of the sodium cryptate structure presents a possible indication that the size and topology of the ligand's cavity does not constitute an optimal coordination environment for the sodium cation, which may prefer a lower coordination number and shorter $Na^{\scriptscriptstyle +}\!\!-\!\!N_{\text{TACN}}$ distances than can be achieved in the symmetrical nonacoordinate complex.

Lithium templated reaction. Substitution of K_2CO_3 or Na_2CO_3 for Li_2CO_3 in the cryptand forming reaction was observed to have a detrimental effect on the cryptate yield. Although small quantities of the protonated and non-protonated lithium cryptates $[Li \subset \mathbf{1} \cdot H]^{2+} \cdot 2X^-$ and $[Li \subset \mathbf{1}]^+ \cdot X^-$ were detected during analysis of the crude product mixture, we were unable to isolate pure samples of these minor products owing to their very low yields of

formation and suspected interconversion during chromatography. This was taken as evidence that lithium is an inferior template for the formation of the cryptand ligand as a result of poor complementarity between the small, hard lithium cation and the cryptand's cavity. In spite of this, X-ray quality crystals of the protonated complex $[\text{Li} \subset 1 \cdot \text{H}]^{2+} 2\text{Cl}^-$ were grown from a solution containing a mixture of products isolated from the lithium templated reaction, which allowed this complex to be characterised in the solid state (vide infra).

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Figure 2. ¹H NMR characterisation (500 MHz; CD₃OD; 298 K) of the sodium cryptate complexes: (i) comparative 1-D spectra of the symmetrical complex [Na \subset 1]⁺·PF₆⁻ (top) and monoprotonated complex [Na \subset 1·H]²⁺·2PF₆⁻ (bottom) and (ii) section of the 2-D COSY spectrum of the monoprotonated complex [Na \subset 1·H]²⁺·2PF₆⁻.

Solid state characterisation of alkali metal cryptate complexes

The complexes $[K \subset 1]^{+} \cdot PF_6^{-}$, $[Na \subset 1]^{+} \cdot CI^{-}$, $[Na \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$ and $[Li \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$ were characterised by X-ray crystallography in the solid state and their structures compared with that of the diprotonated free ligand, $[H_2 \cdot 1]^{2+} \cdot 2Br^{-} \cdot ^{[40,41]}$

Diprotonated free ligand. The solid state structure of the diprotonated free ligand [H₂·1]²⁺·2Br⁻ (Figure 3) confirms that the ligand skeleton adopts a D₃ symmetric helical conformation, as suggested by the solution ¹H NMR spectra of the cryptate complexes $[K \subset 1]^+ \cdot PF_6^-$ and $[Na \subset 1]^+ \cdot PF_6^-$. The two TACN capping groups are staggered with respect to each other and the pyridyl side-arms are twisted by 46-49° in the same sense with respect to the planes defined by the three nitrogen atoms in each TACN capping group. Despite possessing this conformational chirality, the ligand crystallised as a racemate in the monoclinic non-chiral space group P21/c. All of the nitrogen atoms adopt an endo conformation with their lone pairs converging towards the spheroidal cryptand cavity. The TACN NCCN torsion angles, Ψ (Figure 7d), are in the range 42.9(5)–49.0(6)°, which indicates a relatively strain-free staggered synclinal conformation about the C-C bonds. A proton can be seen to reside on one of the bridgehead nitrogen atoms in each TACN capping group. The large twist angle between these capping groups ($\phi = 47(2)^\circ$; see Figure 7c) helps to minimise electrostatic repulsions between the two cationic ammonium groups. The bromide counteranions are presumably too large to penetrate the cavity and are instead located externally, where they participate in a series of C-H—Br⁻ short contacts with the CH₂ groups of the cryptand ligand and the dichloromethane solvent molecules.

 $[K \subset 1]^+ \cdot PF_6^-$. The potassium cryptate $[K \subset 1]^+ \cdot PF_6^-$ was similarly observed to crystallise as a racemate in the monoclinic space group P21/c. The asymmetric unit contains two crystallographically independent potassium cryptate complexes which have inverted helicities but otherwise appear to show minimal structural variations. Measurements have been taken from just one of the two complexes, since the other was found to incorporate significantly more disorder. In agreement with the ¹H NMR spectral assignment of the potassium cryptate, the metal cation is centrally located within the cavity, residing just 0.002 Å above the plane of the three N_{py} nitrogen donor atoms and forming an almost linear 178° angle with the centroids of the two TACN groups (Figure 4a). The cation can be seen to interact with the full complement of nine nitrogen donor atoms in a distorted tricapped trigonal prismatic coordination geometry. The K⁺-N_{TACN} distances (2.855(4)-2.933(4) Å; mean = 2.895 Å) and K⁺-N_{py} distances (2.710(3)-2.738(3) Å; mean = 2.725 Å) are 5-13% smaller than the sum of the ionic and van der Waals radii of nine-coordinate potassium and nitrogen (3.10 Å).[42,43] Assuming that the enthalpic gain is maximised when the cation-donor atom distances are approximately equal to the sum of their ionic and van der Waals radii, the short K^+ — N_{py} distances suggest that the volume of the cryptand's cavity may be slightly too small to accommodate the K⁺ cation without some unfavourable overlap of electron clouds.

In comparison to the diprotonated free ligand, the cryptand ligand is contracted along the C₃ axis and expanded in the perpendicular plane in order to optimally accommodate the potassium cation: this can be seen from the smaller TACN centroid–to–centroid distance (4.66 Å), and greater N_{py}–N_{py} distances (4.654(4)–4.780(5) Å; mean = 4.72 Å) compared to those observed in the structure of $[H_2 \cdot 1]^{2+} \cdot 2B^{-}$. There is a corresponding increase in the magnitude of the mean TACN NCCN torsion angle, Ψ , but the twist angle, φ , is comparable in the structures of $[H_2 \cdot 1]^{2+} \cdot 2B^{-}$ and $[K \subset 1]^+ \cdot PF_6^-$ (Figure 7 and Table 1).

 $[Na \subset 1]^+ \cdot CI^-$. The cryptate complex $[Na \subset 1]^+ \cdot CI^-$ crystallised in the centrosymmetric space group $P\overline{1}$. The asymmetric unit contains two sodium cryptate complexes which are structurally almost identical. In each complex the sodium cation is centrally located within the cryptand cavity (Figure 4b), lying in the plane defined by the three pyridyl nitrogen atoms and intersecting the C_3 axis which connects the centroids of the three nitrogen atoms in each TACN capping group (\angle centroid–Na⁺–centroid: 179.4°

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Figure 3. Solid state structure of the diprotonated free ligand $[H_2 \cdot 1]^{2+} \cdot 2Br^-$. For clarity, solvent molecules, non-polar hydrogen atoms and the two bromide counteranions have been omitted.

and 179.7°). This allows the each cation to interact with the nine available nitrogen donor atoms in a distorted tricapped trigonal prismatic geometry, analogous to that observed in the structure of the potassium complex $[K \subset 1]^+ \cdot PF_6^-$. The Na⁺-N_{TACN} distances fall in the range 2.820(2)-2.869(2) Å (mean = 2.84 Å) and are comparable to the sum of the van der Waals and ionic radii for nitrogen and nonacoordinate Na⁺ (2.79 Å).[42,43], whereas shorter Na⁺--N_{pv} distances of 2.576(2)--2.611(2) Å (mean = 2.59 Å) are observed. The TACN centroid-centroid distances (4.54 Å and 4.57 Å) reveal that the ligand is compressed along the C_3 axis compared to both the diprotonated free ligand [H21]2+·2Br- and the potassium complex $[K \subset 1]^+ \cdot PF_6^-$. It can be seen from the N_{py} — N_{py} distances (4.468(4)–4.517(3) Å; mean = 4.49 Å) that this compression is accompanied by an expansion in the perpendicular plane compared to the diprotonated free ligand $[H_2 \cdot 1]^{2+} \cdot 2Br^{-}$, but the degree of expansion is smaller than that observed in the structure of the potassium complex $[K \subset 1]^+ PF_6^-$ (Table 1). An additional solid state structure of the complex $[Na \subset 1]^+ CF_3SO_3^-$ was also obtained. While the data are not of sufficient quality for discussion here, it is nevertheless apparent that the coordination environment of the sodium cation in this $[Na \subset 1]^+ \cdot CF_3SO_3^-$ structure does not significantly differ from that observed in the structure $[Na \subset 1]^+ \cdot CI^-$ (section S4, ESI).

[Na ⊂ 1·H]²⁺·2Cl⁻. The solid state structure of the protonated sodium complex $[Na \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$ is in the space group *Fdd*2. The asymmetric unit contains one cryptate complex in which the sodium cation is significantly displaced from the centre of the cryptand cavity towards one of the two TACN groups, residing 0.58 Å above the plane described by the three pyridyl nitrogen atoms (Figure 4c). The cation's coordination environment can be regarded as an irregular six-coordinate polyhedron comprising the three N_{py} donors (Na⁺--N_{py} distances: 2.461(3)-2.550(3) Å; mean = 2.51 Å) and the three nitrogen donors from the more proximal of the two TACN groups (Na⁺--NTACN distances: 2.478(3)-2.485(3) Å; mean = 2.48 Å). The three shorter Na*-N_{TACN} are noticeably shorter than the Na⁺-N_{TACN} distances observed in the complex $[Na \subset 1]^+ \cdot Cl^-$, while the three $Na^+ - N_{py}$ distances are roughly comparable. The longer Na⁺-NTACN distances (3.405(3)-3.525(3) Å; mean = 3.48 Å) are significantly beyond the sum of the van der Waals and ionic radii for nitrogen and nine-coordinate sodium (2.79 Å),[42,43] suggesting that the more distant TACN group does not participate in any coordinative interactions with the cation. The asymmetric location of the cation is fully consistent with the protonated structure $[Na \subset 1 \cdot H]^{2+} \cdot 2X^{-}$ which was assigned from the solution NMR data. The Fourier difference map revealed a convincing peak for the electron density associated with the presence of a proton on one of the three nitrogen atoms of the more distant, non-coordinating TACN group. In addition, the presence of electron density corresponding to two chloride counteranions per cryptate complex in the solid state structure provides further indirect evidence of N protonation of the ligand on the basis of charge balance considerations.

[Li ⊂ 1·H]²⁺·2CI⁻. X-ray quality crystals of the protonated lithium complex $[Li \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$ were obtained from a mixed solution containing both the protonated and non-protonated complexes. The data are of relatively low quality but it was possible to unambiguously determine the structure of the complex, which is similar to that of the protonated sodium complex $[Na \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$. The $[Li \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$ structure likewise crystallises in the orthorhombic space group Fdd2 and the asymmetric unit contains half of a cryptate complex; this is related to the other half by a rotation about the crystallographic two-fold axis, which coincides with one of the C2 axes of the cryptand ligand. The structure contains substantial disorder and it was therefore necessary to use two positions of equal occupancy to model the majority of the atoms in the cryptand ligand, and four positions for the chloride counteranions. The position of the lithium cation is significantly offset from the centre of the cage towards one of the two TACN capping groups, with a distance of 0.94 Å between the cation and the mean plane of the pyridyl nitrogen atoms (Figure 4d). The cation's coordination sphere can therefore be regarded as a highly distorted six-coordinate octahedron comprising the three pyridyl nitrogen atoms (mean Li⁺—N_{py} distance: 2.39 Å) and the three nitrogen atoms of the more proximal TACN group (mean

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Figure 4. Solid state structures of the potassium, sodium and lithium cryptate structures: a) $[K \subset 1]^+ \cdot PF_6^-$, b) $[Na \subset 1]^+ \cdot CI^-$, c) $[Na \subset 1 \cdot H]^{2+} \cdot 2CI^-$ and d) $[Li \subset 1 \cdot H]^{2+} \cdot 2CI^-$. For clarity, solvent molecules, counteranions and non-polar hydrogen atoms have been omitted; only one of the two independent complexes found within the asymmetric units for the $[Na \subset 1]^+ \cdot CI^-$ and $[K \subset 1]^+ \cdot CI^-$ structures are shown; and only one of the partially occupied positions used to model each atom in the cryptand ligand is shown for the $[Li \subset 1 \cdot H]^{2+} \cdot 2CI^-$ structure.

Li⁺—N_{TACN} distance: 2.23 Å). The comparatively large mean distance between the lithium cation and the more distant set of TACN nitrogen atoms (3.78 Å) suggests that the metal cation is not involved in any coordinative interactions with this TACN group. It therefore appears, by analogy with the structure of the [Na $\subset 1$ · H]²⁺·2Cl⁻ complex, that the more distant TACN group is protonated. Although the data are not of sufficient quality for the NH⁺ proton electron density to be unequivocally identified in the difference maps, its presence is supported by the offset position of the lithium cation, in combination with the presence of electron density equating to two chloride anions per cryptate complex in the unit cell. The ligand appears to be stretched in the direction of the C_3 axis in order to maximise the distance between the lithium cation and the cationic ammonium group; as a result it displays the largest TACN centroid-to-centroid distances, smallest Npy- N_{py} distances and second smallest twist angle between TACN capping groups of all the metal cryptate complexes (Table 1).

Lead (II) complexation. We reasoned that the azacryptand **1** may hold potential as a complementary host for the toxic divalent lead cation based on the following considerations: the ionic radius of the Pb(II) cation lies in between those of Na⁺ and K⁺,^[42] while Pb(II) also benefits from a higher divalent charge; the ligand's

exclusive provision of nitrogen donor groups should help to confer selectivity for Pb(II) over harder alkali metal cations; furthermore Pb(II) is known to form complexes with high coordination numbers of up to 10, and has been previously documented to bind to various azacryptand hosts^[44–48] as well as to macrocyclic ligands incorporating TACN^[49–52] and pyridyl^[50,52–56] donor groups. In order to test the ligand's capacity for lead encapsulation the potassium cryptate complex [K \subset 1]⁺·PF₆⁻ was heated in the presence of a threefold excess of Pb(NO₃)₂ in CH₃CN. During monitoring of the reaction by electrospray mass spectrometry, the



Scheme 2. Synthesis of the lead cryptate complex $[Pb \subset 1]^{2+.}2PF_6^-$.

previously been structurally characterised, [44,47,48,58,59] to the best

of our knowledge this is the first example of a nonacoordinate

Pb(II) N₉ azacryptand complex. X-ray quality single crystals of the

lead cryptate were grown from a sample prepared by treatment of

the potassium cryptate with excess Pb(OAc)₂, followed by

counteranion exchange using Amberlite IRA400 ion exchange

resin, which was expected to yield the product as a chloride salt,

 $[Pb \subset 1]^{2^+} 2Cl^-$. Upon solving the structure the lead cryptate was instead found to have crystallised with a disordered complex

counteranion. The counteranion was successfully modelled as a

mixture of [PbCl₄]²⁻ and [PbCl₃AcO]²⁻, both occupying the same crystallographic site with fractional occupancies of 0.38 and 0.62 respectively. However, we note that this is a tentative assignment

and there remains some ambiguity about the identities of the unusual counteranions in this structure (see Section, S4, ESI for more details). Some positional disorder was identified in the

structure of the cryptate complex, and this was accordingly modelled using two discrete positions for all of the atoms in the ligand. The measurements discussed here are taken solely from the major component of the model for the disordered cryptand ligand, which has a refined partial occupancy of 0.84. The cryptate structure reveals a symmetrically located Pb(II) cation which is coplanar with the three pyridyl nitrogen donors and co-linear with the

two TACN centroids (distance between cation and plane: 0.015 Å; ∠centroid–Pb²⁺–centroid: 179.7°), indicating a holodirected geometry with no evidence of any stereochemical lone pair

activity. The Pb²⁺—N_{py} (2.692(7)–2.732(6) Å; mean = 2.72 Å) and

Pb²⁺—N_{TACN} distances (2.751(9)–2.821(10) Å; mean = 2.77 Å)

are 3–8% shorter than the sum of the ionic and van der Waals radii of nonacoordinate lead(II) and nitrogen (2.90 Å).^[42,43] The TACN centroid-to-centroid distance (4.39 Å) is the shortest of

those observed in any of the five cryptate structures discussed

here while the relatively large N_{py}—N_{py} distances (4.665(10)-

4.783(10) Å; mean = 4.71 Å) are comparable to those observed

in the structure of the potassium cryptate complex.

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 $[1 + K]^+$ molecular ion (*m*/*z* = 606) gradually disappeared and was replaced by a new peak centred at *m*/*z* = 388 corresponding to the $[1 + Pb]^{2+}$ ion, suggesting that the Pb²⁺ cation slowly displaces the K⁺ cation from the cryptand's cavity, with the transmetallation reaction reaching completion within 48 hours. After counteranion exchange using Amberlite ion-exchange resin the lead cryptate complex $[Pb \subset 1]^{2+} \cdot 2PF_6^-$ was isolated in 65% yield (Scheme 2).



Figure 5. Comparative ¹H NMR spectra (500 MHz; CD₃OD; 298 K) of the lead cryptate complex $[Pb \subset 1]^{2+} \cdot 2PF_6^-$ (top) and potassium cryptate complex $[K \subset 1]^+ \cdot PF_6^-$ (bottom). *The observation of a double water peak is attributed to the presence of both H₂O and HOD.

The ¹H NMR spectrum of this lead cryptate is compared with that of the potassium cryptate in Figure 5. Significant downfield shifts in the aromatic pyridyl and methylene CH_2 proton signals occur upon displacement of K⁺ by the divalent Pb^{2+} cation. In addition satellites of the methylene proton signals are observed in the spectrum of the lead complex as a result of scalar coupling

interactions between the ¹H ²⁰⁷Pb (I = ½; 22% and abundance) nuclei. Similarly, satellites of the signals for the methylene and pyridyl carbon atoms area observed in the ¹³C NMR spectrum (Figure S13, ESI). There is no apparent desymmetrisation of the ¹H NMR spectrum upon Pb2+, complexation of suggesting а spherically symmetrical charge distribution around the cation, with no stereochemical activity from the 6s² lone electron pair,



as might be expected in a nonacoordinate Pb²⁺ complex.^[57] The lead complex was also characterised in the solid state (Figure 6). While a number of lead cryptate complexes have

Figure 6. Orthogonal views of the solid state structure of the the lead cryptate complex $[Pb \subset 1]^{2+}X^{2-}$. For clarity, hydrogen atoms and counteranions have been omitted.



Figure 7. Parameters used to evaluate the distortions in the cryptand host conformation which occur in the presence of different cations: a) TACN centroid-to-centroid distance, b) N_{py} - N_{py} distances, c) twist angle, ϕ , between the two TACN capping groups and d) TACN NCCN torsion angle, Ψ .

 Table 1. Selected distances and angles from the solid state structures of the proton and metal cryptate complexes $[H_21]^{2+2}Br$, $[Li \subset 1 \cdot H]^{2+2}Cl^-$, $[Na \subset 1]^+ \cdot Cl^-$, $[Na \subset 1]^+ \cdot Cl^-$, $[Na \subset 1]^{2+2}Cl^-$, $[K \subset 1]^+ \cdot PF_6^-$, and $[Pb \subset 1]^{2+2}X^{2-}$ (X²⁻ = 38% PbCl₄²⁻ 62% PbCl₃AcO²⁻).^[a]

	[H₂1]⁺·2Br⁻	$[Li \sub 1 \cdot H]^+ \cdot CI^{-[b]}$	[Na ⊂ 1]⁺·Cl⁻	[Na ⊂ 1 ·H]⁺·Cl⁻	$[K \subset 1]^+ \cdot C^{[c]}$	$[Pb {\subset} {\boldsymbol{1}}]^{2+ \cdot} X^{2-[d]}$
$R(M^{+})$ + $R_{vdW}(N)$ (Å) ^[e]	_	2.14	2.79	2.57	3.10	2.90
M—N _{py} distances (Å)	_	2.35(2)–2.42(2) mean: 2.39(0.03)	2.576(2)–2.611(2) mean: 2.59(0.01)	2.461(3) –2.550(3) mean: 2.51(0.05)	2.710(3)–2.738(3) mean: 2.73(0.01)	2.692(6) –2.732(6) mean: 2.72(0.02)
M—N _{TACN} distances (Å) ^[f]	_	2.14(2)–2.26(3) ^[g] mean: 2.23(0.10) ^[g]	2.820(2)–2.869(2) mean: 2.84(0.02)	2.478(3)–2.485(3) ^[g] mean: 2.48(0.00) ^[g]	2.879(4)–2.933(4) mean: 2.90(0.02)	2.751(9)–2.821(10) mean: 2.77(0.03)
		3.62(2)–3.87(3) ^[h] mean: 3.78(0.13) ^[h]		3.405(3)–3.525(3) ^[h] mean: 3.48(0.06) ^[h]		
TACN centroid– centroid distance (Å) ^[f]	5.21	4.91 ^[1] 5.04	4.57 [₪] 4.54	4.89	4.66	4.39
Mean N _{py} —N _{py} distance (Å) ^{[f],[k]}	4.02(0.06)	3.81(0.24)	4.49(0.02)	4.22(0.05)	4.72(0.06)	4.71(0.07)
Twist angle, ϕ (°) ^{[f],[k]}	47(2)	40(2)	41(1)	38(1)	48(2)	44(1)
Mean TACN NCCN torsion angle, Ψ (°) ^{[f],[k]}	46.2(2.1)	-	50.9(0.6)	49.8(1.6)) ^[g] 45.7(2.7) ^[h]	52.7(1.7)	54.8(1.9)

[a] Where individual values are reported, estimated standard errors are given in parentheses. Where mean values are reported, the standard deviation is given in parentheses. [b] The diffraction data for the crystal structure of the protonated lithium cryptate, $[Li \subset 1 \cdot H]^{2+} \cdot 2CI^-$ are not of sufficient quality to support a detailed analysis of bond lengths and angles, but ranges and mean values are provided. Measurements have been taken from both equally occupied components of the disorder model. The variance in the measured values of the NCCN torsion angles is deemed to be too large for meaningful analysis so this parameter is not included in the table. [c] All measurements for the structure of the potassium cryptate $[K \subset 1]^+ \cdot PF_6$ are taken from just one of the two crystallographically independent complexes contained within the asymmetric unit, since the other was found to contain significantly more disorder. [d] The positional disorder in the structure of the lead chelate [Pb \subset 1]²⁺ · X²⁻ was modelled using two discrete, fractionally occupied positions for all of the atoms in the ligand. Measurements are taken solely from the higher occupancy position, which has a refined partial occupancy of 84%. [e] The sum of the ionic and van der Waals radii of the metal cation and nitrogen.^[42,43] The values for the ionic radii are based on a coordination number of 9 for the [K \subset 1]⁺·PF₆⁻, [Na \subset 1]⁺·Cl⁻ and [Pb \subset 1]²⁺·X²⁻ structures, and a coordination number of 6 for the [Na \subset 1·H]²⁺·2Cl⁻ structures. [f] TACN centroid–centroid, N_{Py}–N_{Py} distances, twist angle, φ , between TACN apping groups and TACN NCCN torsion angle, Ψ , are defined in Figure 7. [g] Measured values refer to the metal cation. [h] Measured values refer to the more distant, protonated TACN group which is not coordinated to the metal cation. [h] Measured values refer to the more distant, protonated TACN NCCN torsion angle, Ψ , per cryptand ligand. The possible to measure three values for the twist angle

Preliminary Competition experiments. In order to obtain a qualitative estimate of the relative affinity of the cryptand **1** for Pb²⁺ compared to other cations a competition experiment was undertaken. Na⁺, K⁺, Zn²⁺ and Ca²⁺ cations were identified as potentially important competitors whose concentrations may typically exceed those of Pb²⁺ during environmental and biomedical applications of lead(II) chelation processes. A 2 mM solution of the potassium complex [K \subset **1**]⁺·PF₆⁻ in CD₃OD was

heated at reflux in the presence of one molar equivalent of Pb(NO₃)₂, Ca(ClO₄)₂, Zn(ClO₄)₂ and NaClO₄. After three days, analysis of the product distribution by electrospray mass spectrometry revealed three $[1 + Pb]^{2+}$ and $[1 + Pb + X]^+$ (X = ClO₄⁻, PF₆⁻) ions associated with the lead(II) cryptate complex, along with a $[1 + Na]^+$ ion. In contrast, the potassium, calcium and zinc complexes of the cryptand ligand were not detected (Figure 8). This provides a provisional indication that the

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cryptand's affinity for lead(II) compares favourably with those for potassium, calcium and zinc(II) cations, although it should be noted that mass spectrometry is not a quantitative analysis technique. The room temperature ¹H NMR spectrum of the reaction mixture was also recorded at the end-point of the reaction in order to quantify the relative concentrations of the lead(II) and sodium cryptate complexes, which each give rise to a characteristic set of ¹H NMR signals in CD₃OD. Analysis of the integral ratios revealed that the lead(II) cryptate complex is the major product of the competition experiment, while complexes of all other metal cations, including sodium, are only present as baseline impurities (Figure S15, supporting information).^[60] Two additional minor sets of peak are observed in the spectrum. These peaks are assigned to protonated forms of the free ligand, which are estimated to make up ~13% of the total product distribution.[61] The cryptand therefore appears to show a selectivity preference for complexation of divalent lead cations in the presence of a range of other mono- and di-cations.



Figure 8. Truncated sections of an electrospray mass spectrum used to analyse the product distribution at the end-point of the cation competition experiment. Only the lead and sodium cryptate complexes [Pb \subset 1]²⁺.2X and [Na \subset 1]⁺.X are detected from a multicomponent mixture containing Pb²⁺, Na⁺, K⁺, Ca²⁺ and Zn²⁺ cations. All identified ions which contain the cryptand ligand 1 are shown, and the full spectrum is provided as supporting information (Figure S14, ESI).

Conclusions

A new bis-triazacyclononane tris-pyridyl N₉-azacryptand 'Beer can' ligand was synthesised via a convenient one-pot [2 + 3] condensation reaction which is templated by sodium and potassium cations. The diprotonated free ligand [H2·1]+·2Br- and the metal cryptate complexes $[Li \subset 1 \cdot H]^+ \cdot 2CI^-$, $[Na \subset 1]^+ \cdot CI^-$, $[Na \subset 1 \cdot H]^{2+} \cdot 2CI^{-}$, $[K \subset 1]^{+} \cdot PF_{6}^{-}$, and $[Pb \subset 1]^{2+} \cdot 2X^{-}$ were structurally characterised in the solid state. The structures demonstrate that the highly preorganised cage-like ligand is capable of undergoing slight conformational distortions in order to optimally accommodate each cation. Preliminary metal cation binding competition experiments revealed that the new cryptand exclusively binds sodium and lead in the presence of potassium, zinc and calcium cations in methanol solution. Detailed quantitative investigations into the thermodynamic and kinetic aspects of the cryptand's metal cation binding properties are continuing in our laboratories.

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Entry for the Table of Contents (Please choose one layout)

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A new N₉-azacryptand 'Beer Can' receptor for metal cations is prepared by a convenient one-pot [2 + 3] condensation reaction which is templated by alkali metal cations.



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A bis-triazacyclononane tris-pyridyl N₉-azacryptand 'Beer Can' receptor for complexation of alkali metal and Pb(II) cations