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ARTICLE TYPE

Synthesis and inclusion properties of C_3-symmetric triazole derivatives based on hexahomotrioxacalix[3]arene

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A series of metal ion receptors *cone*-7,15,23-tri-*tert*-butyl-25,26,27-tris{[1*H*-(1-arylmethyl)(1,2,3-triazolyl)]-4-methoxy} andhexahomotrioxacalix[3]arenes *cone*-**3**–*cone*-**5** have been synthesized from 7,15,23-tri-*tert*-butyl-25,26,27-tris(propargyloxy)hexahomotrioxacalix[3]arene **2** *via* Click chemistry. The complexation properties of the receptors *cone*-**3**–*cone*-**5** toward the selected binding of heavy metal and transition metal ions have been evaluated. The structure of *cone*-**3** was elucidated by single-crystal X-ray crystallography.

Introduction

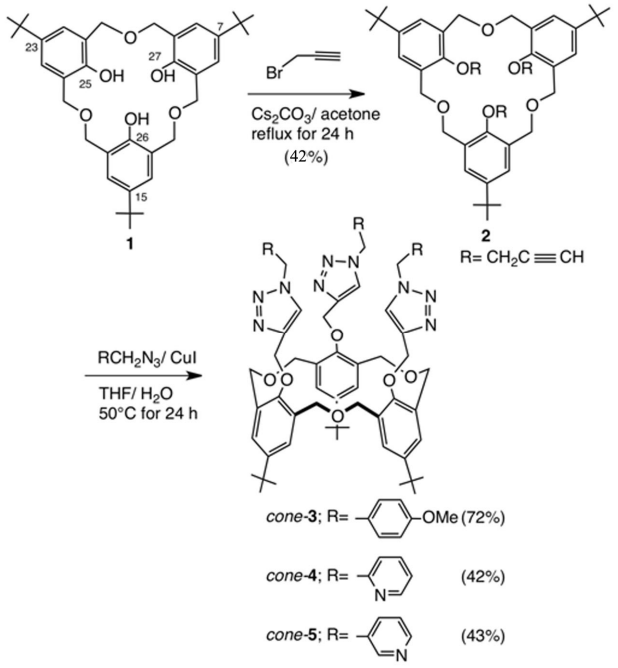
Over the last few decades, the development of artificial receptors for ion recognition, complexation and transportation has proved to be an important topic in both environmental and supramolecular chemistry.[1] Calixarenes and their derivatives are macrocyclic compounds possessing a hydrophobic cavity, which can bind various organic, inorganic or biological molecules and be widely used as convenient and versatile building blocks in supramolecular chemistry.[2] They can be modified to give rise to a great variety of derivatives with tuneable binding properties. For example, calix[4]arene derivatives incorporating crown ethers, amides, esters, and carboxylic acid groups have been shown to selectively extract metal ions.[3] Hexahomotrioxacalix[3]arene is related to calix[4]arene and 18-crown-6 ether; it has a three-dimensional cavity with a potentially C_3-symmetric structure, and is attractive to supramolecular chemists as a receptor for metal cations,[4] ammonium cations,[5] and fullerene derivatives.[6] Introduction of larger alkyl groups on the phenolic oxygens of calix[4]arenes led to a situation where the OR groups cannot rotate through the annulus.[7] Although there exist four possible conformational isomers in calix[4]arenes, *viz.* cone, partial-cone, 1,2-alternate and 1,3-alternate, only two different conformational isomers, "cone" and "partial-cone", should be expected in hexahomotrioxacalix[3]arene. Thus, the conformational isomerism should be much simpler in *O*-alkylated hexahomotrioxacalix[3]arenes. Shinkai *et al* reported the conformer distribution of the hexahomotrioxacalix[3]arene ligand set, and found that the partial-cone is sterically less crowded than the cone and therefore formed predominantly regardless of the *O*-alkylation conditions.[7d] The cone form results only in the presence of a templating metal such as NaH which strongly interacts with the phenolic oxygens, with substituent groups such as ethoxycarbonylmethyl or *N,N*-diethylamino- carbonylmethyl groups present in the reaction system.[8]

Recently the application of Cu(I)-catalyzed 1,3-dipolar cycloaddition of an azide and a terminal alkyne (CuAAC 'click' reaction) has provided a straightforward molecular linking strategy which has been adopted in a wide range of applications in the biological, materials, and medicinal chemistry areas.[9] The properties of the 1,2,3-triazole moiety as the linker in multivalent derivatives can be exploited for the binding of cations, such as in the accelerated catalysis of the "click" reaction by *in situ* formation of copper complexes. The coordination chemistry of triazoles has also been investigated through the formation of transition metal complexes of a range of bis-triazoles.[10] In calixarene chemistry, the copper-catalyzed 1,2,3-triazole was first exploited for the functionalization of the calixarene scaffold by Zhao and co-workers in 2005.[11] More relevant to this work has been the incorporation of functionalized triazoles on to a tailored calixarene scaffold for the selective binding of various metal cations.[12] Very recently, we also have developed a series of triazole-derived chemosensors for selective binding of heavy metal ions based on calixarene scaffolds.[13] For example, chemosensors derived from hexahomotrioxacalix[3]arene exhibited a highly selective affinity for the Pb^{2+} cation through enhancement of the monomer emission of pyrene in both organic and organic/aqueous solution,[13a] whereas a similar outcome was observed for the Zn^{2+} ion only in a purely organic medium.[13b] Indeed, triazole-appended receptors also have a strong affinity for other heavy metal ions such as Cu^{2+} and Hg^{2+}, and substantial binding constants have been evidenced by slightly changing the fluorescence properties of the pyrene in different solvents. Interestingly, Rao *et al* reported a calix[4]arene sensor[12f] which incorporated two potential binding sites: one bistriazole binding pocket and another consisting of two Schiff base groups functionalised with hydroxymethyl groups. The Rao system appeared extremely sensitive and was selective towards the sensing of Zn^{2+} over other tested divalent metal ions. However, ^{1}H NMR studies revealed that Zn^{2+} only binds at the Schiff base site. Similar studies were conducted by Xie and co-workers[14] by attaching pyridin-2′-yl-1,2,3-triazole fluorophores to *β*-cyclodextrin and calix[4]arene, and their observations indicated that chemical modification of a calixarene represents an effective and versatile way of producing receptors with

highly selective ion-binding properties. Even minor changes in the regioselective functionalization or conformation of the chemically modified calixarenes can be associated with dramatic changes in the complexation properties. As a part of our research on the construction of calixarene-derived chemosensors, we herein report the synthesis and characterisation of a series of triazole derivatives based on hexahomotrioxacalix[3]arenes fixed in the cone conformation using *O*-propargyl groups, together with their binding properties towards heavy- and transition-metal ions.

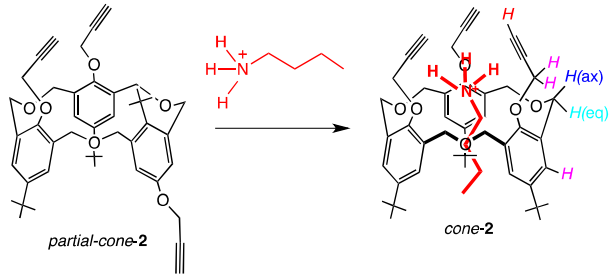
Results and Discussion

A series of triazole derivatives based on hexahomotrioxacalix[3]arene was synthesized by the method shown in *Scheme 1*.



Scheme 1 Synthesis of triazole derivatives based on hexahomotrioxacalix[3]arene with the cone conformation, *cone*-**3**–**5**.

Reaction of the calix[3]arene **1** with propargyl bromide in the presence of Cs_2CO_3 afforded **2** in 42% yield.[13a] The ^{1}H NMR spectrum of **2** shows two singlets for the *tert*-butyl protons at δ 1.22 and 1.27 ppm (relative intensity 2:1) and multiplet signals for the bridging methylene protons in the region of δ 4.0 to 4.85 ppm. Furthermore, the resonances of the aromatic protons appeared at δ 7.23 and 7.30 ppm, consistent with **2** adopting a partial-cone structure. In order to confirm whether compound **2** can be converted from *partial-cone* to *cone* structure, ^{1}H NMR titration experiments of **2** with *n*-$BuNH_3ClO_4$ were carried out in a solution of $CDCl_3/CD_3CN$ (10:1 v/v). The partial ^{1}H NMR spectra of **2** in the absence and presence of *n*-$BuNH_3ClO_4$ are shown in *Fig. 1*. Upon interaction with *n*-$BuNH_3^+$, the bridging methylene protons (H_{ax} and H_{eq}) clearly appeared at δ 4.98 and 4.29 ppm, and the aromatic protons also shifted to a single peak at δ 7.30 ppm. The ^{1}H NMR changes indicated that the *O*-propargyl conformation of **2** also allowed oxygen-through-the-annulus rotation on interaction with the C_3 symmetry structure of *n*-$BuNH_3^+$ and thus interconversion from *partial-cone* to *cone* structure of **2** had occurred (*Scheme 2*). On the other hand, the X-ray crystal structure of **2**[13a] (*Fig. 2*) revealed that there are two different conformations in the unit cell (1:1 ratio), and that one exhibits a classical partial-cone structure (*Fig. 2a*) while the other exhibits an intermediate between partial-cone and cone structure (*Fig. 2b*).



Scheme 2 Complexation of **2** with *n*-$BuNH_3ClO_4$.

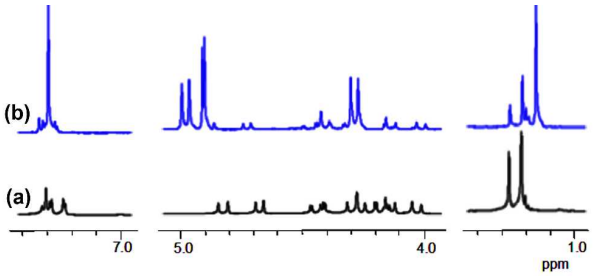


Fig. 1 (a) Partial ^{1}H NMR spectra of **2** in a $CDCl_3/CD_3CN$ (10:1 v/v) solution and (b) in the presence of 1.0 equiv of *n*-$BuNH_3ClO_4$.

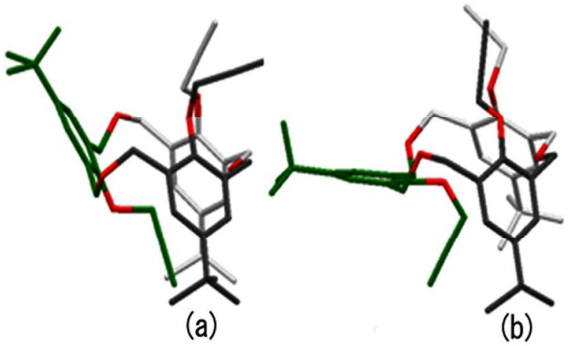


Fig. 2 The X-ray structure of **2** with two different conformations in the unit cell.[13a]

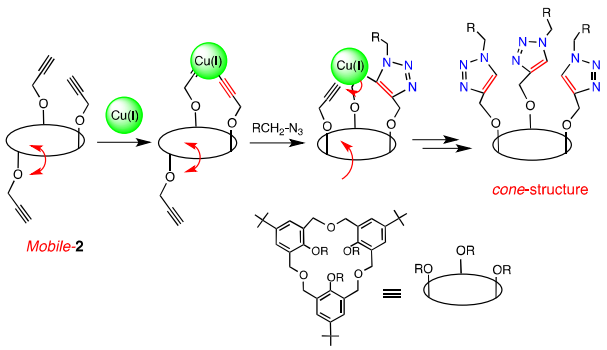
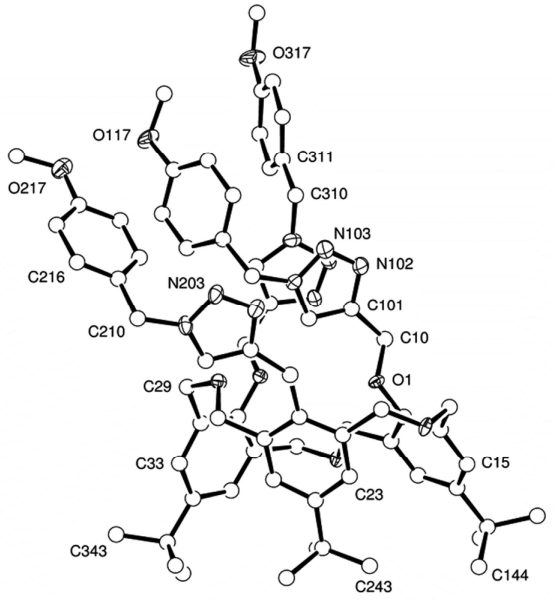
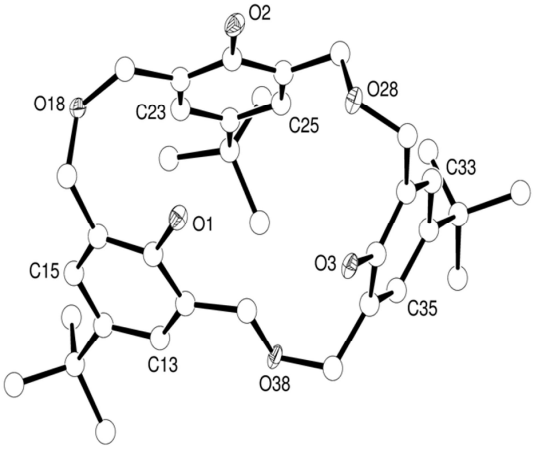


Fig. 3 Plausible reaction pathways for hexahomotrioxacalix[3]arene derivatives from mobile-structure to cone-structure by the Cu(I) catalysed 'click' reaction.

Following on from these observations, we reasoned that the template effect of the Cu(I) ions should play an important role in the formation of cone products of hexahomotrioxacalix-[3]arene (*Fig. 3*).[15] We then showed that a series of *cone* conformations of triazole derivatives based on hexahomotrioxacalix[3]arene, *cone*-**3**–*cone*-**5**, could be synthesized by the Cu(I)-catalyzed 1,3-dipolar cycloaddition reaction of **2** with azides under click conditions with yields of 72, 42 and 43 %, respectively. The ^{1}H NMR spectrum of *cone*-**3**, for example, showed a singlet for the *tert*-butyl protons at δ 1.08 ppm, and singlets for ArOCH_2-triazole and triazole-CH_2-4-methoxybenzene at δ 4.55 and 5.29 ppm, respectively, indicating a C_3-symmetrical cone structure for this compound. Moreover, single crystal X-ray diffraction analysis of cone-**3** confirmed its conformation (but distorted considerably from C_3-symmetry) as shown in *Fig. 4*. The calixarene ring forms a 'flattened cone' shape, with the phenolic O atoms O(1) and O(3) pointing inwards towards the centre of the ring, and the third O atom, O(2), pointing outwards.



(a)



(b)

Fig. 4 X-ray structure of compound *cone*-**3** showing (a) the whole molecule, and (b) the upper-rim groups, viewed on to the calix-ring plane. The thermal ellipsoids of the O and N atoms are drawn at the 50% probability level; C atoms are drawn as spheres and hydrogen atoms have been omitted for clarity.

Similarly, the ^{1}H NMR spectra of compounds *cone*-**4** and *cone*-**5** also suggest that the pyridine triazole derivatives adopt the cone conformation. Interestingly, the chemical shift of the protons on the triazole rings of *cone*-**3**–*cone*-**5** appeared at δ 7.61, 7.85, and 7.77 ppm, respectively; the different chemical shifts of these protons may be attributed to the interaction of the pyridine nitrogen atom with the triazole protons. For example, in *cone*-**4**, there are two cavities, *i.e.* rings of nitrogen-rich groups, in the lower rim substituents; one is formed from the nitrogen atoms of the triazole ring in each chain, and the other from the nitrogen atoms of the three pyridine rings. These artificial receptors, which have electronic donor and acceptor moieties in their structure, can form intra- or inter-molecular hydrogen bonds, depending partly on the solvent. For example, DMSO, MeCN, and THF are potential acceptor molecules with which the triazole C-H groups can form intermolecular hydrogen bonds. In other solvents, such as $CHCl_3$, intramolecular hydrogen bonds may be formed. It was thought that the geometric structure of compound *cone*-**4** might make it feasible, in $CHCl_3$, to form intramolecular hydrogen bonds between the hydrogen atom of the triazole ring and the nitrogen atom of the pyridine. This appears likely since the chemical shifts of the protons on the triazole rings move downfield.

In order to investigate the ionophoric affinities of the compounds *cone*-**3**–*cone*-**5** for cations, the extraction ability was determined by solvent extraction from the aqueous phase to the organic phase (methylene dichloride). The results are summarized in *Fig. 5,* and we see that compounds *cone*-**3**–*cone*-**5** showed high extractability towards Ag^+, Cu^{2+}, Pb^{2+} and Hg^{2+} cations. This pronounced extractability for Ag^+ has not been observed with other triazole-modified calixarene-derived compounds.[12, 13a,b] The association constants of receptors *cone*-**3**–*cone*-**5** for the picrates of silver cations were determined in CH_2Cl_2/THF (99:1, v/v) according to the Benesi-Hildebrand equation,[16] and were calculated, for complexation with Ag^+, to be 3.2 × 10^3, 2.1 × 10^4 and 4.7 × 10^3 M^{-1}, respectively. After addition of compounds *cone*-**3**–*cone*-**5** to the solution of picrate, the absorption maximum peak was shifted from 358 nm to 378 nm, indicating the formation of complexes.

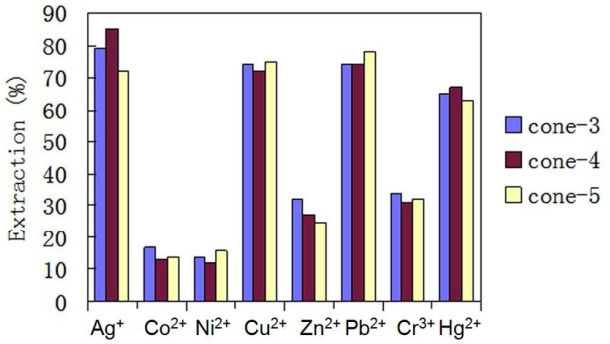


Fig. 5 Liquid-liquid extractability of compounds *cone*-**3**–*cone*-**5** with metal cations ([Host] = 1.25 × 10^{-4} mol in CH_2Cl_2, [Guest] = 1.25 × 10^{-4} mol in water at 25 °C).

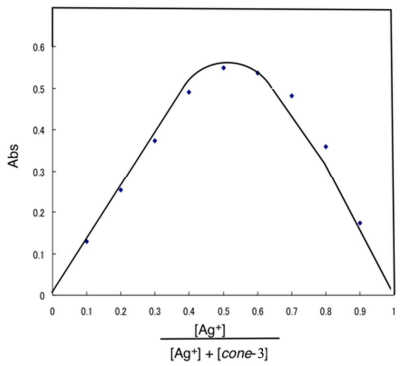


Fig. 6 Job plot for complexation of *cone*-**3** with Ag^+ ion

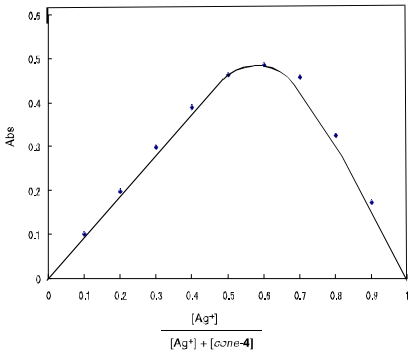


Fig. 7 Job plot for complexation of *cone*-**4** with Ag^+ ion

Due to the existence of three metal-binding sites including the parent cavities, triazole moieties as well as in the pyridine moieties, so, there are several possibilities for metal complexation in compounds **3–5** with guest molecules and 1:1 or 1:2 metal complexation might be possible. Therefore, two-phase picrate extraction (H_2O/CH_2Cl_2) using the continuous variation method was applied to determine the stoichiometry of the *cone*-**3** with Ag^+ ions. The percentage extraction for *cone*-**3** (Job plot) supports the formation of a 1:1 complex with Ag^+ cation, whilst that for *cone*-**4** indicates the formation of 1:2 complexes. Thus, the percentage extractions reach a maximum at 0.5 mole fraction when *cone*-**3** and the Ag^+ cation concentrations were varied systematically (*Fig. 6*), indicating that Ag^+ forms a 1:1 complex with *cone*-**3**. When *cone*-**4** and Ag^+ cation concentrations were changed systematically, the percentage extraction reached a maximum between 0.6 and 0.7 mole which indicated that *cone*-**4** formed a 1:2 complex with Ag^+ (*Fig. 7*). Interestingly, in the case of *cone*-**5**, 1:1 complexation with Ag^+ was observed in spite of the two different (triazolyl and pyridyl group) binding sites.

Furthermore, in order to look further into the binding properties of the receptors *cone*-**3**–*cone*-**5** with Ag^+, ^1H NMR titration experiments were carried out in CD_3CN solution. The partial chemical shift changes for compounds *cone*-**3**–*cone*-**5** on complexation with Ag^+ are illustrated in *Fig. 8*. For example, on gradual addition of Ag^+ salt to a solution of compound *cone*-**3** (*Fig. 8a*), the proton on the triazole ring showed a downfield shift of Δδ 0.15 ppm, from δ 7.61 to 7.76ppm, and the OCH_2-bridge linker protons were shifted upfield by Δδ 0.18 ppm (H_{ax}: from δ 4.48 to 4.30 ppm; H_{eq}: from δ 4.35 to 4.18 ppm). The spectral changes suggested that all three triazole moieties of *cone*-**3** and the parent cavity of hexahomotrioxacalix[3]arene were involved in the

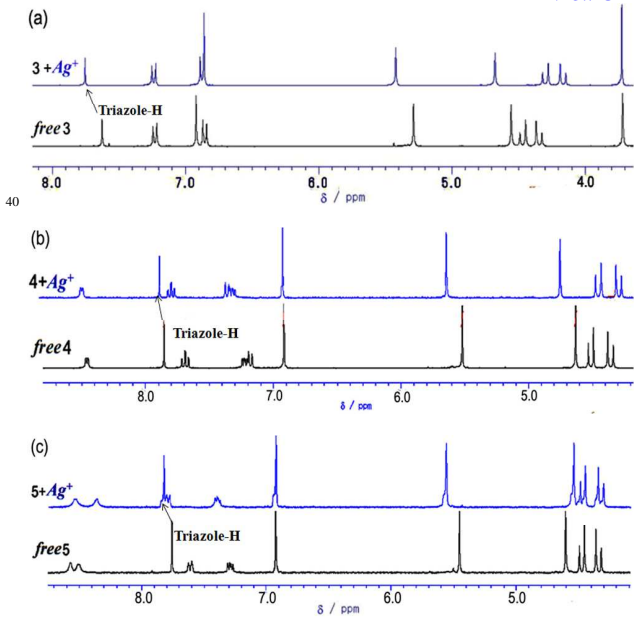


Fig. 8 Partial chemical shifts of compounds *cone*-**3**–*cone*-**5** (4×10^{-3} M) at 300 MHz in CD_3CN solution in the presence of 1.0 equiv. of $AgClO_4$.

complexation with Ag^+. Similarly, titration of 1.0 equiv of $AgClO_4$ with a solution of *cone*-**4** also caused immediate complexation as shown by the downfield shift of the triazole proton (Δδ 0.05 ppm). Moreover, the protons on the pyridine moieties were also shifted downfield (*Fig. 8b*), indicating that the nitrogen atoms not only of the triazole ring but also of the pyridine moieties were involved in the selective binding of Ag^+ cations. However, titration of 1.0 equiv of $AgClO_4$ with the solution of *cone*-**5** revealed no obvious chemical shift changes for the OCH_2-bridge linker protons, which have previously been used to track the complex behaviour of the calixarene with guest by measurement of the tilt angle of the parent cavity rings.[17] Interestingly, some of the protons on the pyridine moieties exhibited larger downfield shifts (while others shifted upfield) and accompany a slightly downfield shift of the triazole protons when $AgClO_4$ was added to the solution of receptor *cone*-**5** (*Fig. 8c*). This result suggested that the nitrogen-rich tri-ligand cavities formed by the pyridine moieties have a stronger affinity for Ag^+ than do the triazole groups alone.

Conclusions

A series of metal ion receptors *cone*-**3**–*cone*-**5** has been synthesized *via* click chemistry, and the binding of transition metal ions has been evaluated by solvent extraction from the aqueous to the organic phase (methylene dichloride) using ^1H NMR titration experiments. We have also demonstrated that the *O*-propargyl group of the flexible macrocycle **2**, on reaction with azides, gives tri-triazole alkylated products which adopt cone conformations. X-ray crystallographic and ^1H NMR spectra studies provided unambiguous information about the cone structures. The binding studies of *cone*-**3**–*cone*-**5** indicated that the nitrogen-rich tri-ligand cavities formed by both the triazole ring and the pyridine N atoms show selectivity for Ag^+, but the nitrogen atoms on the pyridine moieties appeared to have a stronger affinity for those cations. These results give some insight into the molecular design of new synthetic receptors for metal ions.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me_4Si as an internal reference. IR spectra were measured as KBr pellets on a Nippon Denshi JIR-AQ2OM spectrometer. UV-vis spectra were recorded on a Perkin Elmer Lambda 19 UV/VIS/NIR spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-01SA-2 spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5. Gas–liquid chromatograph (GLC) analyses were performed by Shimadzu gas chromatograph, GC-14A; silicone OV-1, 2 m; programmed temperature rise, 12°C min^{-1}; carrier gas nitrogen, 25 mL min^{-1}.

Materials. 7,15,23-tri-*tert*-Butylhexahomotrioxacalix[3]-arene **1** was prepared according to the previously reported procedure.[7a]

Preparation of 7,15,23-tri-*tert*-butyl-25,26,27-tris(propargyloxy)hexahomotrioxacalix[3]arene (2): A solution of hexahomotrioxacalix[3]arene (**1**) (0.3 g, 0.52 mmol) and Cs_2CO_3 (1.69 g, 5.2 mmol) in dry acetone (15 mL) was heated at reflux for 1 h. 3-Bromo-1-propyne (propargyl bromide) (0.62 g, 5.2 mmol) and dry acetone (10 mL) were added and the mixture was refluxed for 18 h. The solvent was evaporated and the residue partitioned between 10% HCl and CH_2Cl_2. The organic layer was separated and dried ($MgSO_4$) and the solvent was evaporated. The residue was dried to afford **2** as a colourless oil (0.15 g, 42%) which was recrystallized from $CHCl_3$/hexane (1:3, v/v) to afford the desired product **2** as colourless prisms, mp 106–108 °C; δ_H ($CDCl_3$): 1.22 (18H, s, *t*Bu), 1.27 (9H, s, *t*Bu), 1.98 (1H, t, *J*= 2.4 Hz, acetylene-*H*), 2.41 (2H, t, *J*= 2.4 Hz, acetylene-*H*), 2.87 (2H, s, ArO-CH_2-acetylene), 4.29 (4H, s, ArO-CH_2-acetylene), 4.0–4.85 (12H, m, ether bridge), 7.23 (2H, d, *J*= 2.4 Hz, Ar*H*), 7.30 (2H, d, *J*= 2.4 Hz, Ar*H*) and 7.31 (2H, s, Ar*H*); δ_C ($CDCl_3$): 31.39, 31.46, 34.26, 34.39, 60.087, 61.74, 64.25, 66.50, 69.33, 73.82, 75.04, 79.47, 80.05, 126.57, 128.21, 128.45, 130.14, 130.71, 131.77, 146.81, 146.93, 151.99 and 153.43; FAB: *m/z* 690 (M^+). Anal. calcd. for $C_{45}H_{54}O_6$ (690.9): C, 78.23; H, 7.88; Found: C, 78.48; H, 7.65%.

Preparation of *cone*-7,15,23-tri-*tert*-butyl-25,26,27-tris{[1*H*-(4-methoxybenzyl)(1,2,3-triazolyl)]-4-methoxy}hexahomotrioxacalix[3]arene (*cone*-3): Copper iodide (10 mg) was added to a solution of **2** (50 mg, 0.072 mmol) and 4-methoxybenzyl azide (73.5 mg, 0.45 mmol) in 15 mL THF/H_2O (2:1), and the mixture was heated at 50°C for 24 h. The resulting solution was cooled and diluted with water and extracted twice with $CHCl_3$. The organic layer was separated and dried ($MgSO_4$) and evaporated to give the solid crude product. The residue was eluted from a column chromatography of silica gel with hexane/ethyl acetate (v/v= 4:1) to give the desired product *cone*-**3** (64 mg, 72%) as colourless prisms [$CHCl_3$/hexane (1:3, v:v)], mp 147–149 °C; δ_H ($CDCl_3$): 1.07 (27H, s, *t*Bu), 3.71 (9H, s, O*Me*), 4.35 (6H, d, *J*= 13.1 Hz, ether bridge), 4.48 (6H, d, *J*= 13.1 Hz, ether bridge), 4.55 (6H, s, ArO-CH_2-triazole), 5.29 (6H, s, triazole-CH_2-Ar), 6.87 (6H, d, *J*=9.0 Hz, Ar*H*), 6.92 (6H, s, Ar*H*), 7.23 (6H, d, *J*= 9.0 Hz, Ar*H*) and 7.61 (3H, s, triazole-*H*); δ_C ($CDCl_3$): 31.43, 31.21, 53.36, 55.25, 67.33, 69.36, 114.27, 123.22, 126.10, 127.08, 129.78, 130.96, 144.31, 146.42, 152.07 and 159.74; FAB: *m/z* 1180.4739 (M^+). Anal. calcd. for $C_{69}H_{81}O_9N_9$ (1180.47): C, 70.21; H, 6.92; N, 10.68. Found: C, 70.38; H, 6.78; N, 10.54%.

Similarly, compounds *cone*-**4** and *cone*-**5** were prepared as described above in 42 and 43% yields, respectively.

***cone*-7,15,23-Tri-*tert*-butyl-25,26,27-tris{[1*H*-(2-pyridylmethyl)(1,2,3-triazolyl)]-4-methoxy} hexahomotrioxacalix[3]arene (*cone*-4)**: colourless prisms [$CHCl_3$/hexane (1:3, v:v)], mp 81–82 °C; δ_H ($CDCl_3$): 1.08 (27H, s, *t*Bu), 4.37 (6H, d, *J*= 13.7 Hz, ether bridge), 4.51 (6H, d, *J*= 13.7 Hz, ether bridge), 4.62 (6H, s, ArO-CH_2-triazole), 5.52 (6H, s, triazole-CH_2-2py), 6.91 (6H, s, Ar*H*), 7.20 (3H, d, *J*= 7.9 Hz, 2-py-H_3), 7.23 (3H, m, 2-py-H_5), 7.70 (3H, dd, *J*= 7.9, 7.2 Hz, 2-py-H_4), 7.85 (3H, s, triazole-*H*) and 8.48 (3H, d, *J*= 4.4 Hz, 2-py-H_6); δ_C ($CDCl_3$): 28.87, 31.64, 52.70, 64.72, 66.80, 119.83, 120.62, 122.03, 123.57, 128.45, 134.60, 141.70, 143.83, 147.05, 149.57 and 152.09; FAB: *m/z* 1093.35 (M^+). Anal. calcd. for $C_{63}H_{72}O_6N_{12}$ (1093.35): C, 69.21; H, 6.64; N, 15.37. Found: C, 69.16; H, 6.65; N, 15.59 %.

***cone*-7,15,23-Tri-*tert*-butyl-25,26,27-tris{[1*H*-(3-pyridylmethyl)(1,2,3-triazolyl)]-4-methoxy}-hexahomotrioxacalix[3]arene (*cone*-5)** : colourless prisms [$CHCl_3$/hexane (1:3, v:v)], mp 77–78 °C; δ_H ($CDCl_3$): 1.09 (27H, s, *t*Bu), 4.34 (6H, d, *J*= 13.4 Hz, ether bridge), 4.48 (6H, d, *J*= 13.4, ether bridge), 4.60 (6H, s, ArO-CH_2-triazole), 5.46 (6H, s, triazole-CH_2-3py), 6.92 (6H, s, Ar*H*), 7.30 (3H, m, 3-py-H_5), 7.61 (3H, d, *J*= 7.5 Hz, 3-py-H_4), 7.77 (3H, s, triazole-*H*), 8.50 (3H, d, *J*= 4.4 Hz, 3-py-H_6) and 8.58 (3H, broad s, 3-py-H_2); δ_C ($CDCl_3$): 28.83, 31.63, 48.71, 64.67, 66.83, 121.01, 121.17, 121.22, 123.73, 128.28, 133.35, 141.94, 143.97, 146.83, 147.38 and 149.57; FAB: *m/z* 1093.35 (M^+). Anal. calcd. for $C_{63}H_{72}O_6N_{12}$ (1093.35): C, 69.21; H, 6.64; N, 15.37. Found: C, 69.37 H, 6.53; N, 15.27 %.

Stoichiometry of metal complexation

The method of continuous variation was employed to determine the stoichiometry in complexes of hosts *cone*-**3**–*cone*-**5**. Two-phase solvent extraction was carried out between aqueous picrates (5 mL, [metal picrate] = 2×10^{-4} M) and host (5 mL, [host] = 2×10^{-4} M in CH_2Cl_2). The molar ratios of the both host and metal picrate were varied from 0 to 1, while the total concentration was kept at several constant levels. The two-phase mixture in a glass tube immersed in a thermostated water bath at 25 °C was shaken at 300 strokes per min for 1 h and then kept, at the same temperature, for 2 h, allowing the complete separation of the two phases. The absorbance of each solution was determined by UV spectroscopy (λ= 290 nm). Job plots were generated by plotting the extracted [M^+] *versus* the mole fraction of metal.

^{1}H NMR complexation experiments

To a CD_3CN solution (5×10^{-3} M) of *cone*-**3**–*cone*-**5** in the NMR tube was added a CD_3CN solution (5×10^{-3} M) of

$AgSO_3CF_3$. The spectrum was recorded after addition and the temperature of the NMR probe was kept constant at 27 °C. The association constant K_{ass} was calculated by non-linear fitting analysis of the observed chemical shift changes of the ArOCH_2-triazole protons.[18]

Extraction experiments

Metal picrates (2.5×10^{-4} M) were prepared *in situ* by dissolving the metal hydroxide (0.01 mol) in 2.5×10^{-4} M picric acid (100 mL); triply-distilled water was used for all aqueous solutions. Two-phase solvent extraction was carried out between water (5 mL, [metal picrate] = 2.5×10^{-4} M) and CH_2Cl_2 (5 mL, [ionophore] = 2.5×10^{-4} M). The two-phase mixture was shaken in a stoppered flask for 2 h at 25 °C. We confirmed that this period was sufficient to attain the distribution equilibrium. This was repeated 3 times, and the solutions were left standing until phase separation was complete. The extractability was determined spectrophotochemically from the decrease in the absorbance of the picrate ion in the aqueous phase, as described by Pedersen.[19]

Crystallographic analysis of *cone*-3

Crystal data: $C_{69}H_{81}N_9O_9$, M = 1180.4. Monoclinic, space group $P2_1/c$ (no. 14), a = 29.7377(12), b = 9.6031(6), c = 22.5784(9) Å, β = 104.967(4) °, V = 6229.1(5) Å^3. Z = 4, Dc = 1.259 g cm^{-3}, F(000) = 2520, T = 140(1) K, μ(Mo-Kα) = 0.8 cm^{-1}, λ(Mo-Kα) = 0.71069 Å.

Crystals are long, colourless plates. From a sample under oil, one, *ca* 1.0 x 0.28 x 0.03 mm, was mounted on a glass fibre and fixed in the cold nitrogen stream on an Oxford Diffraction Xcalibur-3 CCD diffractometer equipped with Mo-Kα radiation and graphite monochromator. Intensity data were measured by thin-slice ω- and φ-scans. Total no. of reflections recorded, to θ_{max} = 20°, was 63509 of which 5787 were unique (Rint = 0.157); 4332 were 'observed' with $I > 2\sigma_I$.

Data were processed using the CrysAlisPro-CCD and -RED[20] programs. The structure was determined by the direct methods routines in the SHELXS program[21] and refined by full-matrix least-squares methods, on F^2's, in SHELXL[21]. The non-hydrogen atoms were refined with anisotropic thermal parameters (but from a rather limited data-set, some thermal parameters appeared barely acceptable). Hydrogen atoms were included in idealised positions and their Uiso values were set to ride on the Ueq values of the parent carbon atoms. At the conclusion of the refinement, wR_2 = 0.144 and R_1 = 0.126[21] for all 5787 reflections weighted $w = [\sigma^2(F_o^2) + (0.0620P)^2]^{-1}$ with $P = (F_o^2 + 2F_c^2)/3$; for the 'observed' data only, R_1 = 0.076.

In the final difference map, the highest peak (*ca* 0.6 eÅ^{-3}) was near H(205).

Scattering factors for neutral atoms were taken from reference 22. Computer programs used in this analysis have been noted above, and were run through WinGX[23] on a Dell Precision 370 PC at the University of East Anglia.

Crystallographic data (excluding structure factors) for *cone*-**3** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 886164. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: 144-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

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Notes and references

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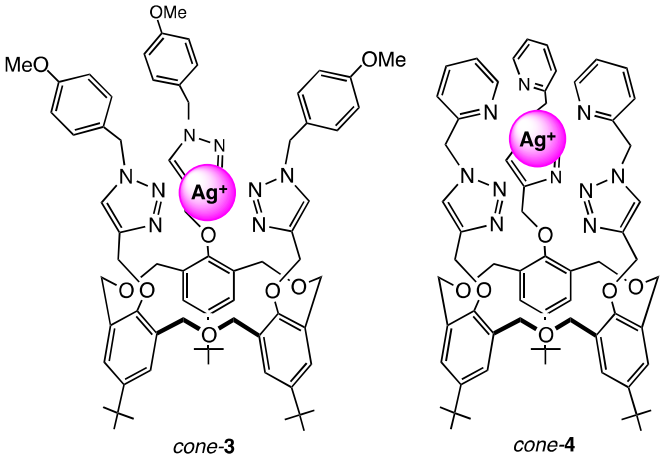

Binding modes of *cone*-**3** and *cone*-**4** with Ag^{+}