ChemComm
FEATURE ARTICLE

Laying traps for elusive prey: recent advances in the non-covalent binding of anions

Jerry L. Atwood,*[a] K. Travis Holman[a] and Jonathan W. Steed*[b]

[a] *Department of Chemistry, University of Missouri-Columbia, Columbia, MO 65211, USA*
[b] *Department of Chemistry, King's College London, Strand, London, UK WC2R 2LS*

The structure and function of a new class of host molecules for the supramolecular complexation of anionic guest species are analysed within the context of other recent advances in the field. In particular, organometallic hosts based upon the calixarenes, and the related macrocycle cyclotriveratrylene (CTV), are examined. X-Ray crystallographic results clearly demonstrate the inclusion of anionic guest species such as BF_4^-, I^-, $CF_3SO_3^-$, ReO_4^- *etc.* within the ostensibly electron-rich bowl-shaped cavities of both types of host as a result of cooperative effects arising from the presence of two or more metal centres arranged around a common binding pocket. Solution radiochemical studies show that hosts based upon CTV in particular are selective for large tetrahedral anions such as MO_4^- (M = Tc, Re). It is anticipated that the ability to discriminate between anions on a size and shape selective basis by means of manipulation of host cavity dimensions will pave the way towards new sensor devices and methods of environmental waste remediation.

Introduction

With the advent of macrocyclic ligands such as the crown ethers, cryptands and an enormous range of other multidentate hosts, supramolecular cation coordination chemistry has progressed rapidly.[1–4] In comparison, progress in the non-covalent complexation of anions has been more slow, probably as a consequence of the large ionic radii of anions, high free energy of solvation and the wide variety of topologies encountered, resulting in great difficulty in designing multidentate receptors with appropriately situated Lewis-acidic or other acceptor sites. In recent years, however, increasing attention has focused upon supramolecular anion complexation,[5–23] perhaps not in little part because of the important environmental consequences of the presence of excess nutrients such as nitrate and phosphate.[24–27] Also relevant are anionic products of nuclear fuel reprocessing such as $^{99}TcO_4^-$,[27,28] as well as the extreme importance of anionic substrates in biochemistry.[29]

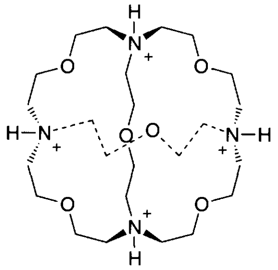
One of the problems which most plagues chemists involved in the design and synthesis of anion hosts, however, is that of introducing *anion selectivity*. Factors such as anion size and topology, charge density, hydrogen-bond donor/acceptor properties and Lewis-basic character must all be considered and such properties are often less easily defined than in analogous examples in cation complexation.[5] Recent X-ray crystallographic studies have demonstrated that, in nature, the *selective* binding of anions such as phosphate and sulfate is achieved by complex hydrogen-bond donor/acceptor arrays.[30–32] It still remains to be seen if such arrays may be duplicated with the same success in a synthetic system.

Several comprehensive reviews of recent progress in various forms of multidentate anion complexation have been published and the interested reader is referred to these works as a primary source for further reading.[33–35] A book dealing solely with the topic of anion complexation is also planned.[5] The purpose of this account is to survey some new methods of anion complexation, most notably those involving the calixarenes and other polycyclic, aromatic hosts, as a means towards introduction of anion selectivity and to introduce our own work on organometallic macrocyclic hosts based upon the calixarenes and other bowl-shaped molecules.[36–41]

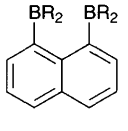
Historical Perspective

One of the earliest reports of anion complexation dates back to 1967 (the same year as the first reports of the alkali-metal complexation properties of the crown ethers[42]) and involves the chelation of the bidentate Lewis acids $X_2B(CH_2)_2BX_2$ **1** (X = F, Cl) to methoxide ions.[43] In the following year Park and Simmons described the size selective binding of halide ions by *in,in*-1,11-diazabicyclo[9.9.9]nonacosane and related bicyclic, bidentate ammonium ion based receptors.[44] After these early results, however, it was not until 1976 that work by Graf and Lehn upon related tetraprotonated, tricyclic, spheroidal cryptands such as **2** demonstrated a high affinity for Cl^- and Br^-.[45] This work was followed by the synthesis of a cylindrical bis(tren) macrocycle selective for linear anions such as azide[46] and recently, by even larger cyclophane receptors capable of encompassing large carboxylate anions such as terephthalate.[47] Since then work upon macrocyclic polyammonium based receptors related to cryptands and spherands has progressed rapidly[5,7,8,33–35,48–50] and includes the binding of biologically important anions such as ATP and anionic transition-metal species such as MCl_4^{2-} (M = Pd, Pt). Recent work has also demonstrated that macrotricyclic zwitterions involving macrotricyclic borane–amine adducts may act as electrically neutral anion hosts, thus eliminating the need for competition of the guest with the counter ions of the host.[6]

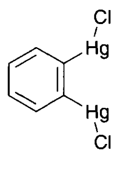
Uncharged, bidentate Lewis acids related to **1** have also received considerable attention. In particular receptors such as those based upon the 1,8-diborylnaphthalene unit **3**[18,33-35,51] and the *o*-phenylenedimercurials **4**[20,52] have been shown to readily chelate hydride and halide anions. A recent report deals with carborane supported cyclic *o*-dimercurials which represent anion complexation analogues of the crown ethers.[9] Reinhoudt and coworkers have also recently reported a range of neutral uranyl salene complexes which form novel hosts for a range of anions, notably H_2PO_4, incorporating both Lewis-acidic and hydrogen-bond acceptor sites.[10–12]



2



3



4

The Calixarenes

The calixarenes are a class of phenolic macrocycles more generally termed [1_n]metacyclophanes consisting of four or more phenolic units bridged by methylenic spacer groups, Fig. 1.[53,54] With an electron-rich molecular cavity and 'lower rim' consisting of a cyclic array of oxygen donors, the calixarenes are, in general, much more suited to cation complexation that the binding of anions, and indeed numerous such examples have been reported.[55–58] Only a single report involving the binding of an anion by a native calixarene has appeared, involving the inclusion of a methyl sulfate anion in the solid state within the cavity of [*p*-sulfonatocalix[4]arene]$^{5-}$. This inclusion of an 'anion by an anion' is, however, a weak interaction based solely upon hydrophobic considerations and does not represent a significant attraction.[59] The calixarenes do, however, represent a synthetically malleable framework upon which charged, Lewis-acidic or hydrogen-bond donor or acceptor functionalities may be placed in order to design anion binding hosts of very specific dimensions and selectivities.

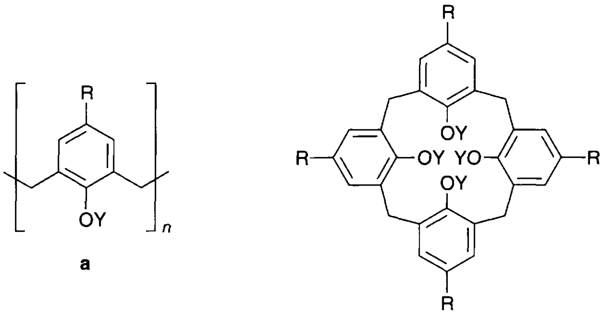
Recently Puddephatt and coworkers have developed a series of rigid, resorcinol-based calixarene ligands (L) such as **5**, incorporating trivalent phosphorous substituents. Reaction of these macrocycles with complexes of the coinage metals such as $[\{M(CCPh)\}_n]$ (M = Cu, Ag) in the presence of pyridinium chloride gives the metal complexes $[C_5H_5NH][M_4(L)(\mu Cl)_4(\mu_n\text{-}Cl)]$ (n = 3, M = Cu **6a**; n = 4, M = Ag **6b**). In the case of **6a** the guest chloride anion bridges across three of the four copper centres, but is too small to adopt the full μ_4-binding mode possible in the rigid cavity. The guest anion in **6a** may be selectively exchanged for bromide or iodide by addition of the appropriate alkali-metal halides and, in the case of the iodide salt, the guest iodide anion then adopts the full μ_4-I symmetrically bridging mode. In the case of the silver complex **6b** the presence of the larger metal ion enables even chloride to bridge symmetrically between the four metal centres.[17,60]

As part of a research programme aimed at the design of new spectroelectrochemical sensory reagents for anions, Beer and coworkers have recently reported a range of calixarene-based hosts containing electrochemically active cobaltocenium, ferrocene or tris(bipyridyl)ruthenium moieties in conjunction with amide NH groups,[13–15] as well as a range of related non-calixarene species.[61–63] Solution electrochemical and ^{1}H NMR measurements indicate a significant selectivity of these hosts for $H_2PO_4^-$ even over tenfold excesses of HSO_4^- and Cl^-. Also, competition experiments between calixarene and non-calixarene hosts indicate that the former possess a higher affinity for dihydrogen phosphate.[14] These same workers have also developed fluorescent sensors for chloride and phosphate based upon porphyrin and other N-donor macrocycle moieties.[64,65] Related work, especially involving biologically important polyanions, has been carried out by Czarnik.[66]

Within our own group we have recently embarked upon a programme of research aimed at the synthesis of new anion hosts, incorporating redox-active transition-metal centres by direct attachment of cationic metal ions to the calixarene aromatic rings. It is anticipated that such materials will have application in environmental waste remediation and in the sensing of environmental pollutants. We reasoned that the reaction of calixarenes with cationic metal centres may well result in cationic hosts displaying not only anion complexation affinity, but also important properties such as air- and moisture-stability, water solubility and synthetic accessibility under relatively mild conditions.

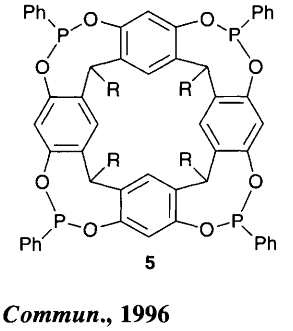
There is ample literature precedent for the stability and facile synthesis of arene compounds of the second- and third-row late transition metals, notably Ru, Os, Rh and Ir,[67–69] and indeed in many cases [*e.g.* hydrido triphenylphosphine complexes of Ru and pentamethylcyclopentadienyl and norbornadiene compounds of Rh and Ir] stable π complexes are formed with phenol, suggesting that analogous chemistry may also exist for the calixarenes.[73–75] Also, Shinkai and coworkers have reported a range of neutral π-chromium tricarbonyl complexes of especially rigidified calix[4]arene *n*-propyl ethers.[70–72] While useful in connection with calixarene modification by nucleophilic addition reactions at the metallated rings, these materials have not been studied with a view to anion complexation and it seems unlikely that these electron-rich chromium(0) species will display any significant anion coordination behaviour.

We began very simply with the reaction of *p*-*tert*-butylcalix[4]arene **7a** with the chloride-bridged dimer complexes $[\{M(\eta^5\text{-}C_5Me_5)Cl(\mu\text{-}Cl)\}_2]$ (M = Rh **8a**, Ir **8b**),[76] pretreated with silver salts according to the reaction shown in Scheme 1. This strategy was immediately successful in as much as the bimetallic hosts $[\{M(\eta^5\text{-}C_5Me_5)\}_2(p\text{-}tert\text{-butylcalix[4]arene})][BF_4]_4$ (M = Rh **9a**, Ir **9b**) were produced in excellent yield.[37] Unfortunately, as the X-ray crystal structure of the deprotonated analogue of **9b** revealed, none of the tetrafluoroborate anions are included within the calixarene bowl (Fig. 2), but rather they occupy lattice voids to either side of the metal centres, while the narrow molecular cavity is filled by a molecule of diethyl ether in a fashion more reminiscent of classical calixarene inclusion chemistry.[53,54] This lack of anion inclusion is unsurprising given the relatively electron-rich nature of the calixarene cavity, formed from four aromatic rings, and it was deemed necessary to metallate all four rings, as well as to reduce the steric bulk at the upper rim of the cavity, in order to maximize the possibility of anion inclusion.



R = Bu^t, Y = H, **7a**
R = Y = H, **7b**
R = H, Y = Et, **7c**

Fig. 1 Generalized structures of the calix[n]arenes **a** (n = 4–8) and calix[4]arenes **b**



5

$$[\{MLCl(\mu\text{-}Cl)\}_2] + AgX \xrightarrow[-AgCl]{Me_2CO} [ML(Me_2CO)_3]^{2+} \xrightarrow[\substack{CF_3CO_2H,\ reflux \\ -acetone}]{+L'} [(ML)_nL']^{m+}$$

M = Ru, Rh, Ir
L = C_6H_6, *p*-$MeC_6H_4CHMe_2$, C_6Me_6, C_5Me_5
L′ = calix[4]arene, *p*-*tert*-butylcalix[4]arene, *p*-*tert*-butylcalix[5]arene, CTV *etc.*
X = BF_4, PF_6, CF_3SO_3, $^1/_2SO_4$
n = 1–4, m = 2–6

Scheme 1 General synthesis of metallated host compounds[67–69]

Under mild conditions (refluxing acetone in the presence of CF_3CO_2H) analogous results were obtained for the debutylated calixarene **7b** (which possesses a less sterically congested cavity), giving the bimetallic host $[\{Ir(\eta^5\text{-}C_5Me_5)\}_2(calix[4]arene)]^{4+}$ for which an X-ray crystal structure demonstrating the inclusion of a $-CF_3$ substituent of the neutral silver complex $[\{Ag(\mu\text{-}O_2CCF_3)\}_2]$ (present as a result of the use of excess silver salt in the early stages of the reaction, Scheme 1) was obtained.[77] While surprising, this result was unproductive from the point of view of anion complexation. However, under more forcing conditions (refluxing CF_3CO_2H) we were able to cleanly isolate the tetrametallic complex $[\{Ir(\eta^5\text{-}C_5Me_5)\}_4(calix[4]arene - 2H)][BF_4]_6$ **10**.[37] The fact that this material has only a 6+ (as opposed to 8+) charge is a result of the high acidity of two of the phenolic oxygen atoms of the metallated calixarene. High acidity of at least one phenolic proton was also noted for complexes of type **9** and even related phenol species.[73–75] More importantly, however, the X-ray crystal structure of **10** revealed the inclusion of one of the BF_4^- anions deeply within the calixarene bowl with F(1A)···C contacts as low as 2.91, Å demonstrating that the calixarene cavity is ideally suited to the inclusion of the small, tetrahedral tetrafluoroborate anion. Furthermore, in contrast to the shallow methylsulfate inclusion observed for $[p\text{-sulfonatocalix}[4]arene]^{5-}$ in which the methyl substituent lies between 4.15 and 5.03 Å from the four calixarene oxygen atoms,[59] the intracavity fluorine atom F(1A) is situated only 2.58 Å from the plane containing the four phenolic oxygen atoms with F(1A)···O distances in the range 3.12–3.25 Å, demonstrating conclusively that the interaction in this case is of electrostatic origin, between an electron-deficient host and an electron-rich guest. Indeed, there is ample precedent for the build-up of partial positive charge upon the carbon atoms of coordinated unsaturated hydrocarbons.[78,79]

Reaction of **7b** with the ruthenium complex $[\{Ru(\eta^6\text{-}p\text{-}MeC_6H_4CHMe_2)Cl(\mu\text{-}Cl)\}_2]$ **11** which is isoelectronic with complexes **8**, as in Scheme 1 also resulted in the clean isolation of tetrametallic complexes, namely $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_4(calix[4]arene - 2H)][BF_4]_6$ **12a**.[36] As with complex **10**, the X-ray crystal structure of **12a** demonstrates that one of the BF_4^- anions is found deeply embedded within the calixarene cavity (Fig. 3) with F(1A)···$O_{phenolic}$ distances of 3.23–3.37 Å. The fluorine atom F(1A) lies 2.70 Å above the plane of the phenolic oxygen atoms, whilst the shortest F(1A)···C distance is to C(1A) and C(1D), 2.85 Å, compared with distances > 3.10 Å for the remaining, non-included anions, clearly suggesting a cooperative effect arising from the proximity of the four metallated rings. Also noteworthy are the low crystallographic thermal parameters of the included anion. The small, near-spherical shape of BF_4^- often results in a very high degree of thermal motion even in the solid state. In contrast, the included anion in both **10** and **12a** exhibits thermal motion similar to the much less mobile atoms of the host, emphasizing the tight fit of the anion into the intracavity void.

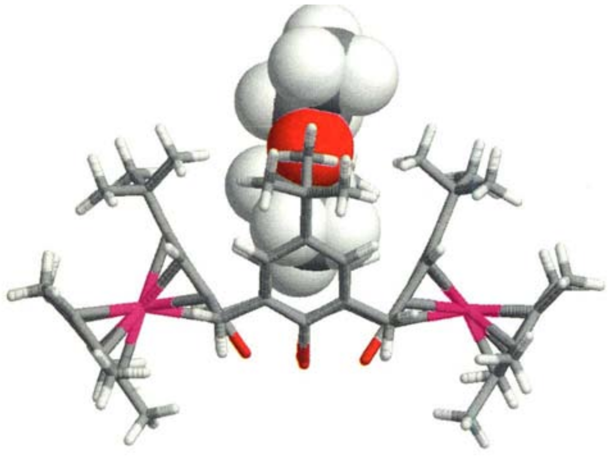
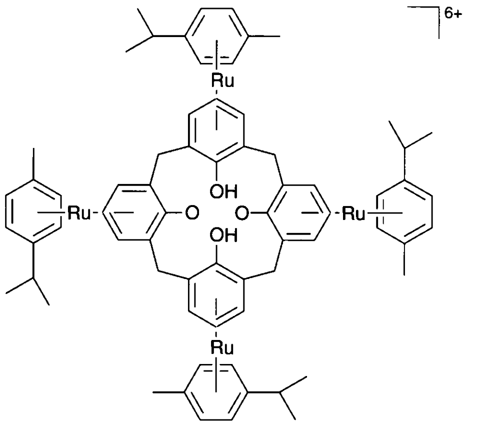


Fig. 2 X-Ray crystal structure of the bimetallic host $[\{Ir(\eta^5\text{-}C_5Me_5)\}_2(p\text{-}tert\text{-}butylcalix[4]arene - H)][BF_4]_3{\cdot}Et_2O{\cdot}MeNO_2$ showing the inclusion of a neutral solvent molecule

Substitution of $Ag[CF_3SO_3]$ and $Ag_2[SO_4]$ in place of $Ag[BF_4]$ resulted in the ready synthesis of the analogous triflate and hydrogen sulfate species $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_4(calix[4]arene - 2H)]X_6$ ($X = CF_3SO_3$ **12b**, $X = HSO_4$ **12c**). Complex **12b** in particular has proved versatile since it may be cleanly prepared in exceptionally high yield (*ca.* 85%) and the triflate counter ion is readily exchanged for other anions such as Cl^-, Br^-, I^-, $H_2PO_4^-$, SCN^-, HSO_4^-, ReO_4^- *etc.* as their tetraalkylammonium salts in polar solvents such as nitromethane or dimethylformamide, or with alkali-metal salts in water, although a number of these salts are highly insoluble precluding the synthesis of X-ray diffraction quality crystals.

In solution, preliminary radiochemical studies also indicate some selectivity of **12b** for the radioisotope $^{99}TcO_4^-$ over the triflate anion, possibly as a consequence of the size of the cavity in host **12** which may well be more suited to the inclusion of tetrahedral or spherical rather than cylindrical anions, as evidenced by the structure of **12a**.[36] In particular, the iodide salt $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_4(calix[4]arene - 2H)]I_6$ has been crystallographically characterized and, as expected, contains an iodide anion (again exhibiting low thermal motion) within the



12

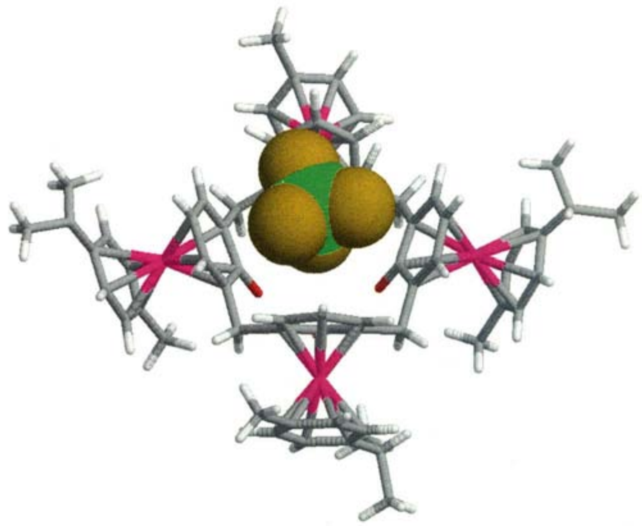


Fig. 3 X-Ray crystal structure of the tetrametallic host $[\{Ru(\eta^6\text{-}p\text{-}MeC_6H_4CHMe_2)\}_4(calix[4]arene - 2H)]^{6+}$ showing the included BF_4^- anion

calixarene cavity.[77] The closest iodide–carbon approach is to C(4B) at the upper rim of the calixarene, I(1)···C(4B) 3.73 Å, whilst the height of the iodide anion above the plane of the phenolic oxygen atoms of 4.00 Å is consistent with the large ionic radius of I^- and suggests that iodide is slightly too large a guest to fit comfortably within the calix[4]arene cavity. It should be noted, however, that the iodide penetrates the cavity more deeply than the central (*i.e.* boron) atom of the BF_4^- anion in **12a** (the boron is situated at 4.11 Å above the plane of the phenolic oxygen atoms) and the penetration is still markedly deeper than those based solely upon hydrophobic interactions.[59]

Interestingly, the synthesis of tetrametallic complexes of type **12** is not general, and is strongly dependent upon the choice of silver salt added. For example, attempts to make analogues of **12** containing phosphate and carboxylate anions have resulted only in the isolation of bimetallic species such as $[\{Ru(\eta^6\text{-arene})\}_2(\text{calix[4]arene})][H(CF_3CO_2)_2]_4$ **13** (arene = *p*-cymene, hexamethylbenzene) related to complexes **9**. Bimetallic compounds were also obtained from the reaction of **10** and $Ag[BF_4]$ with calix[4]arene ethyl ether **7c**. Overall these results suggest that the formation of tetrametallic complexes capable of anion complexation is sensitive both to subtle ion-pairing effects and to the stereochemistry about the calixarene as a whole.

Given the apparently excellent fit of tetrahedral anions within the calix[4]arene cavity we attempted the reaction of the iridium complex **8b** with *p-tert*-butylcalix[5]arene, which possesses a larger cavity than its tetrameric analogue **7a**. As with **7a** we were unable to metallate all of the aromatic rings of the macrocycle; however, the isolated product $[\{Ir(\eta^5\text{-}C_5Me_5)\}_3(p\text{-}tert\text{-butylcalix[5]arene} - H)][BF_4]_5$ did exhibit anion inclusion by virtue of two of the three metallated rings of the macrocycle (rings C and D, Fig. 4) adjacent to one another. In this case the included tetrafluoroborate anion is situated asymmetrically in the large calix[5]arene cavity, close to the rings C and D, with relatively long F···C contacts in the region of 2.95 Å.[41] This result serves to illustrate that it is not necessary to metallate all the rings of the calixarene hosts in order to observe anion binding, but inclusion within the calixarene cavity is not observed unless at least two transition- metal containing moieties are adjacent to one another and hence able to exert a cooperative effect, favouring intracavity inclusion.

A number of attempts have been made to metallate various other calixarenes and their derivatives with some degree of success. Notably, the bimetallic species $[\{Ir(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{32}H_{30}O_4N_4Me_8)]^{6+}$ derived from the diprotonated form of the Mannich base dimethylaminomethylcalix[4]arene[58] has been synthesized, offering increased promise for anion complexation as a consequence of the $-NHMe_2^+$ potential anion binding sites.[80] A bimetallic calix[4]resorcarene derivative, $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_2(\text{calix[4]resorcarene}-2H)][BF_4]_2$, has also been synthesized and its X-ray crystal structure determined, Fig. 5. While this bimetallic complex does not bind anions as a consequence of its narrow molecular cavity, it does offer scope for further variation of the host size and shape in order to fine-tune anion selectivity.[80]

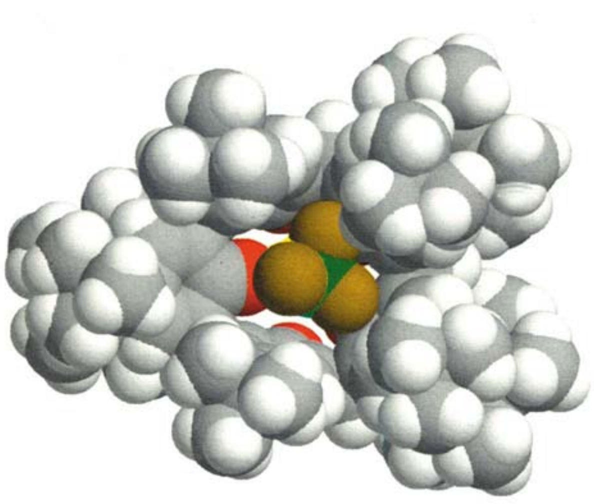


Fig. 4 Tetrafluoroborate inclusion within a calix[5]arene derivative

Cyclotriveratrylene

Another bowl-shaped macrocycle which contains electron-rich aromatic rings liable to act as good ligands for transition metals, is the trimeric veratrole derivative cyclotriveratrylene (CTV) **14**.[81–85] Solid-state inclusion complexes of CTV have been known for many years but have always been of the channel variety with neutral guest molecules occupying lattice voids between stacks of hosts. The wide, shallow CTV cavity in these materials is occupied by the base of another CTV unit.[82,83] We reasoned that attachment of transition-metal centres to the outer surface of CTV in the same way as the calixarenes should result in potential anion complexation hosts, and furthermore, should prevent the stacking of one CTV unit into another in the solid state, thus modifying the inclusion chemistry of CTV.

In practice, reaction of the chloro complexes **8b** and **11** with $Ag[BF_4]$ and CTV in a similar way to that outlined in Scheme 1 resulted in the clean isolation of a wide range of mono-, di- and tri-metallated CTV compounds $[\{Ru(\eta^6\text{-arene})_n\}(CTV)]^{2n+}$ (arene = *p*-cymene, n = 1 **15**, 2 **16**, 3 **17**; arene = benzene, n = 1 or 3; arene = hexamethylbenzene, n = 1) and $[\{Ir(\eta^5\text{-}C_5Me_5)\}_n(CTV)]^{2n+}$ (n = 1 **18**, 2 **19**, 3 **20**) with the number of metal centres (and hence charge of the cation) essentially dependent solely upon the relative stoichiometries of starting materials added at the beginning of the reaction.[38–40] Furthermore, these materials proved to be more readily handled than their calixarene analogues, being generally more soluble in polar organic solvents and not subject to deprotonation.

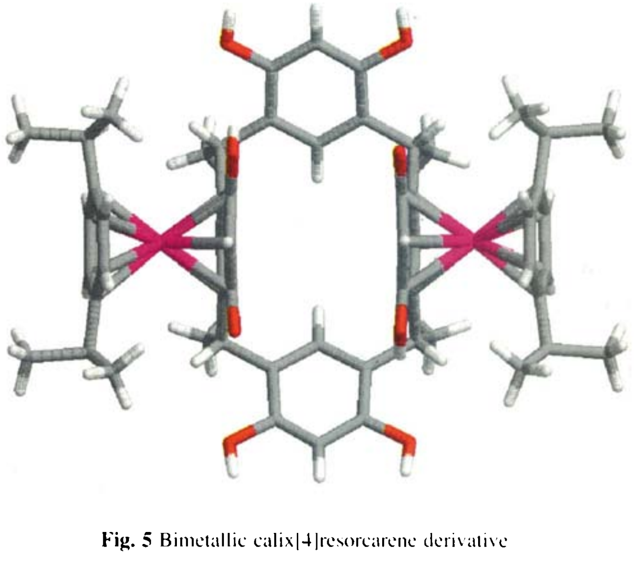
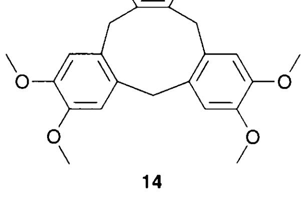


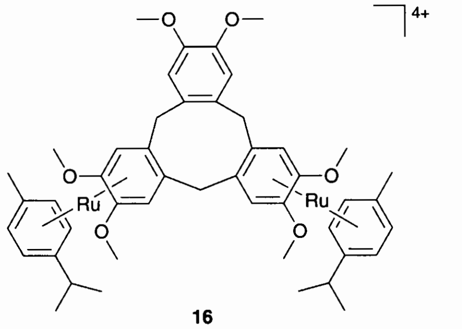
Fig. 5 Bimetallic calix[4]resorcarene derivative



14

A range of the monometallic complexes of types **15** and **18** have been synthesized with various counter anions. The results of X-ray crystal structure determinations indicate that as expected, only neutral solvent molecules are included within the CTV cavity. The one exception is the $[H(CF_3CO_2)_2]^-$ salt $[Ru(\eta^6\text{-}MeC_6H_4CHMe_2)(\eta^6\text{-}CTV)][H(CF_3CO_2)_2]_2$ **15b** which exhibits the inclusion of the CF_3 substituent of one of the $[H(CF_3CO_2)_2]^-$ anions within the CTV cavity. Anion–cation contacts are long, however (upwards of 3.3 Å), clearly indicative of a hydrophobic type interaction rather than true anion binding.[39]

The situation is very different, however, for the bi- and trimetallic CTV complexes of type **16**, **17**, **19** and **20** which act as true anion hosts in the same way as their calixarene analogues. In the case of the bimetallic complex $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_2(\eta^6:\eta^6\text{-}CTV)]^{4+}$ **16** we have characterized both the triflate and mixed perrhenate/triflate salts by X-ray crystallography, Fig. 6, as well as the tetrafluoroborate salt of the analogous iridium complex $[\{Ir(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}CTV)][BF_4]_4$ **19a**. In the case of $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_2(\eta^6:\eta^6\text{-}CTV)][CF_3SO_3]_4$ **16a** the triflate guest is firmly embedded within the CTV cavity with the negatively charged sulfonate head group seated between the two metallated rings whilst the hydrophobic–CF_3 substituent lies at the centre of the cavity. The closest $-SO_3\cdots$CTV contact, O(2)···C(2B), of 2.95(1) Å is relatively long in comparison to those observed for **12a**, reflecting the shallowness of the CTV bowl, which is not ideally suited to the triflate anion, and the presence of only two metal centres.[40]



16

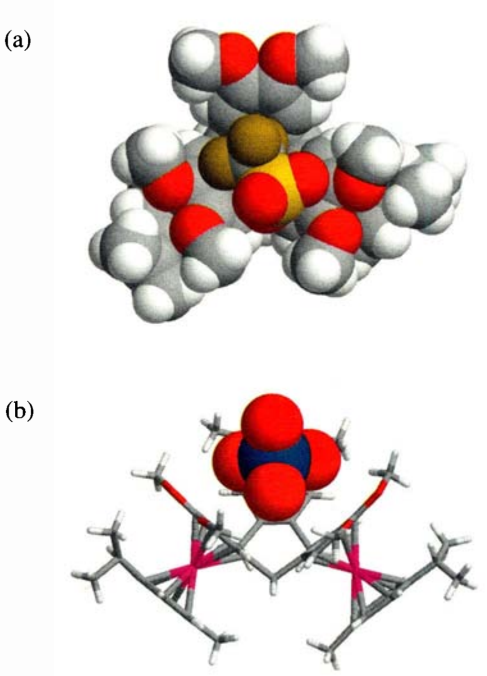


Fig. 6 X-Ray crystal structure of the bimetallic host **16** with included anionic guests (*a*) trifluoromethanesulfonate, (*b*) perrhenate

Metathesis of **16a** with $[NBu^n{}_4][ReO_4]$ results in the isolation of the perrhenate salt $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_2(\eta^6:\eta^6\text{-}CTV)][ReO_4]_4$ **16b** as a poorly crystalline powder. In the presence of a limited quantity of $[NBu^n{}_4][ReO_4]$, however, single crystals of a mixed anion complex $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_2(\eta^6:\eta^6\text{-}CTV)][ReO_4]_3[CF_3SO_3]$ **16c** may be obtained.[40] Once again the structure clearly demonstrates the binding of the ReO_4^- ion within the CTV cavity, slightly displaced from the pseudo-threefold axis of the CTV ligand towards the two metallated rings. This result is especially important because of the close relationship between $[ReO_4]^-$ and the isoelectronic pertechnetate ion, $[TcO_4]^-$. The radioisotope ^{99}Tc ($t_{1/2}$ 2.13 × 10^5 y) is formed in high fission yield (6.13% from ^{235}U) and, during nuclear fuel reprocessing, is converted to $[^{99}TcO_4]^-$ by aqueous nitric acid. Releases from the nuclear fuel cycle as well as atomic weapons testing and use of ^{99}Mo pertechnetate generators in medical applications all contribute to the presence of ^{99}Tc in the environment, where it is concentrated in the food chain by absorption into lichens which are in turn consumed by grazing animals such as reindeer.[27,28] One of the potential applications of selective anion complexation hosts is the removal of such dangerous contaminants and it is clear that the design of hosts with anion complementary cavity dimensions may well lead to such selectivity.

A number of radiochemical studies have been carried out upon host **16** which have demonstrated a marked selectivity of the wide CTV bowl for large, tetrahedral anions such as MO_4^-. In particular, competition studies with 3–10-fold excesses of Cl^-, NO_3^-, SO_4^{2-} and ClO_4^- over $^{188}ReO_4^-$ in two-phase extraction experiments (saline–nitromethane) indicate that the extractability of the perrhenate anion is inhibited only by ClO_4^-, which is structurally very similar. The fact that SO_4^{2-} has little effect in spite of its tetrahedral shape and higher negative charge may be attributable to its high free energy of hydration, encouraging it to remain within the aqueous layer. Most surprisingly of all, direct competition studies between $^{188}ReO_4^-$ and $^{99m}TcO_4^-$ suggest a small but statistically significant difference in the extractability of the two anions by host **16** (71 *vs.* 84%).[40] It is possible that the rigid CTV bowl is somewhat better suited to the inclusion of TcO_4^- than the rhenium analogue, in spite of the relatively small size difference between the two. The situation may well be significantly affected by the different hydrated radii of the anions.

The anion binding properties of host **16** (as the triflate salt) were also investigated by means of cyclic voltammetry. In the absence of any externally added anion, the cyclic voltammogram (CV) of **16** displayed two irreversible reduction waves, −670 and −825 mV. A slight, concentration dependent, cathodic shift was noted for $[NBu_4][ReO_4]$ with the reduction wave at −825 mV especially, shifting to −809 mV. Strikingly, however, addition of the HSO_4^- anion in molar ratios increasing from 1 : 10 to 2 : 1 caused a marked change in the appearace of the CV, such that both reduction waves merged into a single, irreversible peak at −753 mV. A significant effect was also noted for the addition of $[NBu_4][H_2PO_4]$ with a net cathodic shift of 43 mV for the second reduction wave, gradually increasing over the same range of molar ratios. These results are typical of the redox potential shifts noted by Beer and coworkers for systems based upon the Co^{3+}–Co^{2+} couple in cobaltocenium derivatives.[13,15]

The fact that the most striking effects on the CV are obtained from large, tetrahedral anions such as $H_2PO_4^-$ and HSO_4^- strongly supports the contention that these anions are bound within the macrocyclic cavity, which is of complementary dimensions to these anions (little effect was observed upon addition of Cl^-, I^- or BPh_4^-). This contention is also supported by the radiochemical data reported above. While a smaller effect is noted for ReO_4^-, it is important to note the difference in solvent between the cyclic voltammetric and radiochemical experiments. It is highly probable that the affinity of the host for the target anions is significantly influenced by solvation effects. Thus, in saline–nitromethane little sulfate selectivity is noted, whereas HSO_4^- exerts a strong influence in MeCN solution, as may be expected from the high affinity of the hydrogen sulfate anion for aqueous media. It is likely that the opposite effect is in evidence for ReO_4^-. It should be noted that the effect of the HSO_4^- anion on the CV of **16** may also result in part from its high acidity, though this is not the case with $H_2PO_4^-$.

The inclusion of the tetrahedral $[ReO_4]^-$ in **16c** is also related to the structure observed for the bimetallic iridium complex **19a**, with the smaller $[BF_4]^-$ anion situated even more asymmetrically in the wide CTV cavity. The size mismatch between the small anion and large CTV cavity is further exemplified by the trimetallic species $[\{Ru(\eta^6\text{-}MeC_6H_4CHMe_2)\}_3(\eta^6:\eta^6:\eta^6\text{-CTV})][BF_4]_6$ **17a**.[38] In the solid state the complex belongs to the cubic space group $Pa\bar{3}$, with the hexacation situated upon a threefold rotation axis, implying that the CTV host adopts its full C_{3v} symmetry (as opposed to C_s observed for the free ligand) as a result of reduced repulsion between the aromatic rings and/or steric effects arising from the presence of the bulky cymene ligands. However, there is room for only one tetrafluoroborate anion within the central cavity and rather than lie in the centre of the CTV bowl, on the threefold rotation axis, the entire guest is disordered over three sites, each similar to the single intracavity anion binding site in **19a**. A similar off-axis binding of BF_4^- within the large CTV bowl is observed for the iridium analogue $[\{Ir(\eta^5\text{-}C_5Me_5)\}_3(\eta^6:\eta^6:\eta^6\text{-CTV})][BF_4]_6$ **20**, although fortunately the complex is crystallographically ordered, Fig. 7.[39]

Conclusions

This survey has demonstrated both the generality and the ready synthesis of anion complexation hosts based on the previously unprecedented inclusion of anionic guests within an ostensibly electron-rich macrocyclic cavity. From these results four general statements may be made.

(*i*) Anion binding occurs in hosts containing two or more cationic transition-metal centres bound to adjacent rings of polyaromatic macrocycles.

(*ii*) Anion inclusion is favoured by an open cavity that is not severely sterically hindered.

(*iii*) Size compatibility between anion and host also favours cooperativity between metal centres and hence tight binding.

(*iv*) Host–guest interactions are strongly influenced by additional factors, notably anion solvation energy within the medium of study and the magnitude of the electrostatic charge on the host and anion

Given these rules it should now be possible to design anion complexation hosts specific to particular target anions (*e.g.* $H_2PO_4^-$, TcO_4^-, ATP *etc.*) and apply them to real anion sensing and binding applications in the field.

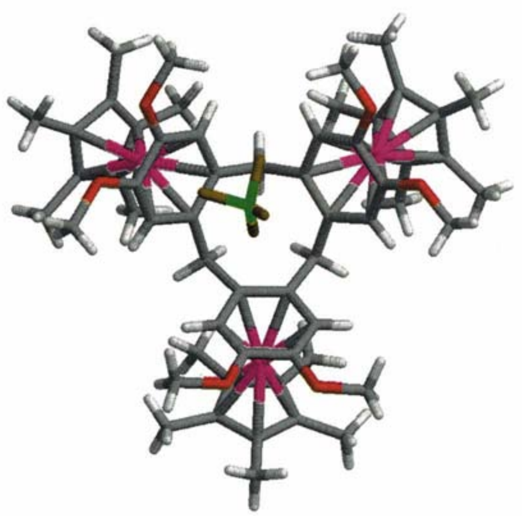


Fig. 7 X-Ray crystal structure of the trimetallic host **20** showing the off-centre position of the included tetrafluoroborate anion

Acknowledgments

We are indebted to our coworkers whose names appear in the references, with whom it has been a great pleasure to be associated. We are also extremely grateful to the continued support of the US National Science Foundation, the University of Missouri–Columbia and NATO for providing the funding without which this work would not be possible.

Jerry Atwood was born in Missouri, where he received a B.S. In 1964. Following the Ph.D. from the University of Illinois in 1968, he took a position as Assistant Professor at the University of Alabama. He rose to the position of University Research Professor in 1987 and moved to the University of Missouri–Columbia as Professor and Chair in 1994. His research interests currently are based on supramolecular chemistry, and they comprise both fundamental studies and applications to industrial and environmental chemistry. He is founder and co-editor of the journal *Supramolecular Chemistry* and was recently appointed as an Associate Editor for *Chemical Communications*.

Jonathan Steed was born in Wimbledon, England. He received his B.Sc. in 1990 and Ph.D. three years later from University College London, under Dr Derek A. Tocher. In 1993 he joined the group of Professor Jerry L. Atwood at the University of Alabama and, more recently, at the University of Missouri–Columbia, as a NATO Postdoctoral fellow. Since September 1995 he has held the post of Lecturer in Inorganic and Supramolecular Chemistry at King's College London. His interests include the application of inorganic and organometallic chemistry to supramolecular systems as well as more conventional aspects of transition-metal coordination chemistry.

Travis Holman obtained his Bachelors degree from St Mary's University in Halifax, Nova Scotia. He is currently a Ph.D. candidate in Inorganic Supramolecular Chemistry at the University of Missouri–Columbia.

References

1 C. J. Pedersen, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1021.

2 K. B. Mertes and J.-M. Lehn, Multidentate Macrocyclic and Macropolycyclic Ligands, in *Comprehensive Coordination Chemistry*, ed. G. Wilkinson, R. Gillard and J. A. McCleverty, Pergamon, Oxford, 1987, vol. 2, pp. 915–957.

3 J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 89.

4 *Cation Binding by Macrocycles*, ed Y. Inoue and G. W. Gokel, Marcel Dekker, New York, 1991.

5 *The Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James and E. Garcia-España, VCH, 1997, to be published.

6 K. Worm, F. P. Schmidtchen, A. Schier, A. Schafer and M. Hesse, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 327.

7 A. Bencini, A. Bianchi, P. Dapporto, E. Garcia-España, M. Micheloni, P. Paoletti and P. Paoli, *J. Chem. Soc., Chem. Commun.*, 1990, 753.

8 A. Bencini, A. Bianchi, P. Dapporto, E. Garcia-España, M. Micheloni, J. A. Ramirez, P. Paoletti and P. Paoli, *Inorg. Chem.*, 1992, **31**, 1902.

9 X. Yang, C. B. Knobler, Z. Zheng and M. F. Hawthorne, *J. Am. Chem. Soc.*, 1994, **116**, 7142.

10 D. M. Rudkevich, W. Verboom and D. N. Reinhoudt, *J. Org. Chem.*, 1994, **59**, 3683.

11 D. M. Rudkevich, Z. Brzozka, M. J. Palys, H. C. Visser, W. Verboom and D. N. Reinhoudt, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 467.

12 D. M. Rudkevich, W. Verboom, Z. Brzozka, M. J. Palys, W. P. R. V. Stauthamer, G. J. van Hummel, S. M. Franken, S. Harkema, J. F. J. Engbersen and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1994, **116**, 4341.

13 P. D. Beer, Z. Chen, A. J. Goulden, A. Graydon, S. E. Stokes and T. Wear, *J. Chem. Soc., Chem. Commun.*, 1993, 1834.

14 P. D. Beer, Z. Chen, A. J. Goulden, A. Grieve, D. Hesek, F. Szemes and T. Wear, *J. Chem. Soc., Chem. Commun.*, 1994, 1269.

15 P. D. Beer, M. G. B. Drew, C. Hazlewood, D. Hesek, J. Hodacova and S. E. Stokes, *J. Chem. Soc., Chem. Commun.*, 1993, 229.

16 S. E. Brown, J. E. Coates, C. J. Easton, S. J. van Eyk, S. F. Lincoln, B. L. May, M. A. Stile, C. B. Whalland and M. L. Williams, *J. Chem. Soc., Chem. Commun.*, 1994, 47.

17 W. Xu, J. J. Vittal and R. J. Puddephatt, *J. Am. Chem. Soc.*, 1993, **115**, 6456.

18 H. E. Katz, *J. Org. Chem.*, 1989, **54**, 2179.

19 M. T. Reetz, C. M. Niemeyer and K. Harms, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1472.

20 J. D. Wuest and B. Zacharie, *J. Am. Chem. Soc.*, 1987, **109**, 4714.

21 M. Newcomb, J. H. Horner, M. T. Blanda and P. J. Squattrito, *J. Am. Chem. Soc.*, 1989, **111**, 6294.

22 K. Tamao, T. Hayashi, Y. Ito and M. Shiro, *J. Am. Chem. Soc.*, 1990, **112**, 2422.

23 R. G. Gymer, *Chemistry: An Ecological Approach*, Harper and Row, New York, 1973.

24 C. F. Mason, *Biology of Freshwater Pollution*, 2nd edn., Longman, New York, 1991.

25 A. Sfriso and B. Pavoni, *Environmental Technol.*, 1994, **15**, 1.

26 C. Glidewell, *Chem. Br.*, 1990, **26**, 137.

27 M. Kubota, *Radiochim. Acta*, 1993, **63**, 91.

28 E. Holm, *Radiochim. Acta*, 1993, **63**, 57.

29 L. G. Lange III, J. F. Riordan and B. L. Vallè, *Biochemistry*, 1974, **13**, 4361.

30 H. Luecke and F. A. Quiocho, *Nature*, 1990, **347**, 402.

31 J. W. Pflugrath and F. A. Quiocho, *Nature*, 1985, **314**, 257.

32 J. J. He and F. A. Quiocho, *Science*, 1991, **251**, 1479.

33 H. E. Katz, in *Inclusion Chemistry*, ed. J. L. Atwood, J. E. D. Davies and D. D. MacNicol, Oxford University Press, Oxford, 1991, vol. 4, ch. 9.

34 B. Dietrich, *Pure Appl. Chem.*, 1993, **7**, 1457.

35 B. Dietrich, in *Inclusion Chemistry*, ed. J. L. Atwood, J. E. D. Davies and D. D. MacNicol, Academic Press, New York, 1984, vol. 2, p. 373.

36 J. W. Steed, R. K. Juneja and J. L. Atwood, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2456.

37 J. W. Steed, R. K. Juneja, R. S. Burkhalter and J. L. Atwood, *J. Chem. Soc., Chem. Commun.*, 1994, 2205.

38 J. W. Steed, P. C. Junk, J. L. Atwood, M. J. Barnes, C. L. Raston and R. S. Burkhalter, *J. Am. Chem. Soc.*, 1994, **116**, 10346.

39 J. W. Steed, K. T. Holman, M. M. Halihan, J. Montgomery, R. S. Burkhalter, S. S. Jurisson and J. L. Atwood, submitted for publication.

40 K. T. Holman, M. M. Halihan, J. W. Steed, S. S. Juisson and J. L. Atwood, *J. Am. Chem. Soc.*, 1995, **117**, 7848.

41 J. W. Steed, C. P. Johnson, R. K. Juneja, R. S. Burkhalter and J. L. Atwood, *Supramol. Chem.*, 1996, **6**, 235.

42 C. J. Pedersen, *J. Am. Chem. Soc.*, 1967, **89**, 7017.

43 D. F. Shriver and M. J. Ballas, *J. Am. Chem. Soc.*, 1967, **89**, 1078.

44 C. H. Park and H. E. Simmons, *J. Am. Chem. Soc.*, 1968, **90**, 2431.

45 E. Graf and J.-M. Lehn, *J. Am. Chem. Soc.*, 1976, **98**, 6403.

46 B. Dietrich, J. Guihem, J.-M. Lehn, C. Pascard and E. Sonveaux, *Helv. Chim. Acta*, 1984, **67**, 91.

47 J.-M. Lehn, R. Méric, J.-P. Vigneron, I. Bkouche-Waksman and C. Pascard, *J. Chem. Soc., Chem. Commun.*, 1991, 62.

48 M. W. Hosseini and J.-M. Lehn, *Helv. Chim. Acta*, 1986, **69**, 587.

49 M. W. Hosseini, J.-M. Lehn, S. R. Duff, K. Gu and M. P. Mertes, *J. Org. Chem.*, 1987, **52**, 1662.

50 F. P. Schmidtchen, *Chem. Ber.*, 1981, **114**, 597.

51 H. E. Katz, *J. Org. Chem.*, 1985, **50**, 5027.

52 A. L. Beauchamp, M. J. Olivier, J. D. Wuest and B. Zacharie, *J. Am. Chem. Soc.*, 1986, **108**, 73.

53 C. D. Gutsche, *Calixarenes*, The Royal Society of Chemistry, Cambridge, 1989.

54 *Calixarenes: A Versatile Class of Macrocyclic Compound*, ed. J. Vicens and V. Bohmer, Kluhwer, Dordrecht, 1991.

55 J. L. Atwood, in *Cation Binding by Macrocycles*, ed. Y. Inoue and G. W. Gokel, Marcel Dekker, New York, 1991.

56 S. Shinkai, H. Koreshi, K. Ueda, T. Arimura and O. Manabe, *J. Am. Chem. Soc.*, 1987, **109**, 6371.

57 S. G. Bott, A. W. Coleman and J. L. Atwood, *J. Am. Chem. Soc.*, 1986, **108**, 1709.

58 C. D. Gutsche and K. C. Nam, *J. Am. Chem. Soc.*, 1988, **110**, 6153.

59 S. G. Bott, A. W. Coleman and J. L. Atwood, *J. Am. Chem. Soc.*, 1988, **110**, 610.

60 W. Xu, J. P. Rourke, J. J. Vittal and R. J. Puddephatt, *Inorg. Chem.*, 1995, **34**, 323.

61 P. D. Beer, Z. Chen, M. G. B. Drew, J. Klingston, M. Ogden and P. Spencer, *J. Chem. Soc., Chem. Commun.*, 1993, 1046.

62 P. D. Beer, C. Hazlewood, D. Hesek, J. Hodacova and S. E. Stokes, *J. Chem. Soc., Dalton Trans.*, 1993, 1327.

63 P. D. Beer, D. Hesek, J. Hodacova and S. E. Stokes, *J. Chem. Soc., Chem. Commun.*, 1992, 270.

64 P. D. Beer, M. G. B. Drew, D. Hesek and R. Jagessar, *J. Chem. Soc., Chem. Commun.*, 1995, 1187.

65 P. D. Beer and F. Szemes, *J. Chem. Soc., Chem. Commun.*, 1995, 2245.

66 A. W. Czarnik, *Acc. Chem. Res.*, 1994, **27**, 302.

67 M. A. Bennett and T. W. Matheson, *J. Organomet. Chem.*, 1979, **175**, 87.

68 C. White and P. M. Maitlis, *J. Chem. Soc. A*, 1971, 3322.

69 P. J. Fagan, M. D. Ward and J. C. Calabrese, *J. Am. Chem. Soc.*, 1989, **111**, 1698.

70 H. Iki, T. Kikuchi and S. Shinkai, *J. Chem. Soc., Perkin Trans. 1*, 1992, 669.

71 T. Kikuchi, H. Iki, H. Tsuzuki and S. Shinkai, *Supramol. Chem.*, 1993, **1**, 103.

72 H. Iki, T. Kikuchi and S. Shinkai, *J. Chem. Soc., Perkin Trans. 1*, 1993, 205.

73 D. J. Cole-Hamilton, R. J. Young and G. Wilkinson, *J. Chem. Soc., Dalton Trans.*, 1976, 1995.

74 C. White, S. J. Thompson and P. M. Maitlis, *J. Organomet. Chem.*, 1977, **127**, 415.

75 M. Green and T. A. Kuc, *J. Chem. Soc., Dalton Trans.*, 1972, 832.

76 J. W. Kang, K. Moseley and P. M. Maitlis, *J. Am. Chem. Soc.*, 1969, **91**, 5970.

77 J. W. Steed and J. L. Atwood, unpublished work.

78 S. G. Davies, M. L. H. Green and D. M. P. Mingos, *Tetrahedron*, 1978, **34**, 3047.

79 D. Astruc, *Top. Curr. Chem.*, 1991, **160**, 47.

80 J. W. Steed, K. T. Holman and J. L. Atwood, manuscript in preparation.

81 J. W. Steed, H. Zhang and J. L. Atwood, *Supramol. Chem.*, 1996, **7**, 37.

82 H. Zhang and J. L. Atwood, *J. Crystallogr. Spec. Res.*, 1990, **20**, 465.

83 A. Collet, *Tetrahedron*, 1987, **43**, 5725.

84 S. Cerrini, E. Giglio, F. Mazza and N. V. Pavel, *Acta Crystallogr., Sect. B*, 1979, **35**, 2605.

85 G. I. Birnbaum, D. D. Klug, J. A. Ripmeester and J. S. Tse, *Can. J. Chem.*, 1985, **63**, 3258.

Received, 7th February 1996; 6/00890I