Synthesis of Cationic Organometallic Calixarene Hosts by Direct Metalation of the Outer Face

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Complexation of the aromatic rings of various calix[4]arenes to transition metal containing moieties results in significant changes to the solubility, acidity and host–guest properties of the macrocycles.

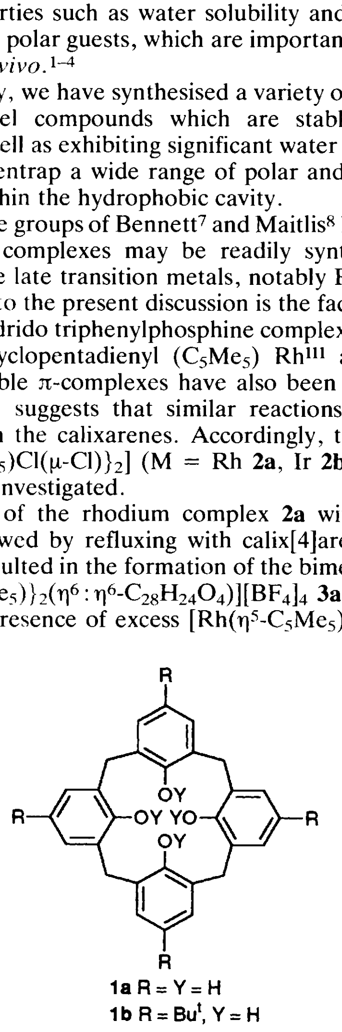
One of the most exciting areas in current supramolecular chemistry concerns the synthesis of artificial enzyme mimics based upon macrocyclic hosts such as the calix[*n*]arenes **1** and cyclodextrins which possess large, hydrophobic cavities suitable for the inclusion of potential substrates.[1–4] Our work has been directed towards the synthesis of calixarene-based bowlic host molecules in which a catalytically or redox active metal centre is either embedded within, or is in close proximity to the hydrophobic cavity of a calixarene. To achieve this goal without the interference of solvent or other potential guest molecules the possibility of direct covalent attachment of transition metals to the calixarene aromatic rings was investigated.

Shinkai and coworkers have reported the synthesis of neutral π-chromium tricarbonyl complexes of **1c** ($R = H$, $Y = Pr^n$) in which the metal binds to the outer face of the calixarene, and have demonstrated their use in chemical modification of the host molecules.[5,6] However, these air-sensitive metal complexes are only formed under forcing conditions (130 °C) in conjunction with a very limited range of especially rigid, unhindered calix[4]arenes and are unlikely to display properties such as water solubility and the ability to accommodate polar guests, which are important in mimicking conditions *in vivo*.[1–4]

Accordingly, we have synthesised a variety of more robust, cationic model compounds which are stable to air and moisture as well as exhibiting significant water solubility, and are likely to entrap a wide range of polar and anionic guest molecules within the hydrophobic cavity.

Work by the groups of Bennett[7] and Maitlis[8] has shown that stable arene complexes may be readily synthesised for a number of the late transition metals, notably Ru, Rh and Ir. Of relevance to the present discussion is the fact that in many cases [*e.g.* hydrido triphenylphosphine complexes of Ru^{II} and pentamethylcyclopentadienyl (C_5Me_5) Rh^{III} and Ir^{III} fragments][9,10] stable π-complexes have also been obtained with phenol which suggests that similar reactions may also be observed with the calixarenes. Accordingly, the reaction of $[\{M(\eta^5\text{-}C_5Me_5)Cl(\mu\text{-}Cl)\}_2]$ (M = Rh **2a**, Ir **2b**)[11] with calixarenes **1** was investigated.

Treatment of the rhodium complex **2a** with $Ag[BF_4]$ in acetone followed by refluxing with calix[4]arene **1a** in neat CF_3CO_2H resulted in the formation of the bimetallic complex $[\{Rh(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{28}H_{24}O_4)][BF_4]_4$ **3a** in 95% yield, even in the presence of excess $[Rh(\eta^5\text{-}C_5Me_5)(acetone)_3]^{2+}$. The formulation of **3a** was confirmed by a FAB mass spectrum which clearly indicated a molecular cation peak at *m/z* 898 as well as a smaller signal at *m/z* 985 corresponding to the cation in (**3a**) associated with one tetrafluoroborate anion. The ^1H NMR spectrum of the complex demonstrated two pairs of signals for the aromatic rings (δ 7.17, d, 6.77, t and 7.02, d, 6.61, t) correspnding to the unbound and bound faces of the calixarene, respectively. The observation of a single AB quartet (δ 4.27 and 3.42, $^2J = 12.8$ Hz), assigned to the bridging methylenic protons of the macrocycle, suggests that the two metal centers occupy faces on opposite sides of the molecule and that the calixarene adopts the characteristic cone conformation.



1a R = Y = H
1b R = Bu^t, Y = H
1c R = H, Y = Pr^n

Previous reports[10] have noted that the related C_5Me_5 rhodium π-phenol complexes $[Rh(\eta^5\text{-}C_5Me_5)(\eta^6\text{-}PhOH)][PF_6]_2$ tend to deprotonate, forming $[\{Rh(\eta^5\text{-}C_5Me_5)\}_2(\eta^6\text{-}PhO\text{-}H\cdots O(\eta^6\text{-})Ph)][PF_6]_3$. Under the conditions employed in the present work, however, the calixarene oxygen atoms are fully protonated due to the presence of CF_3CO_2H (a signal due to the OH protons was located in the ^1H NMR spectrum of **3a** as an extremely broad resonance at *ca.* 5.3 ppm, while the infrared spectrum demonstrated a broad band assigned to $\nu(OH)$ at 3420 cm^{-1}). The broadness and high field chemical shift of the OH NMR signal suggests that the hydroxylic protons in **3a** may be relatively acidic and only loosely associated with the cationic complex. Treatment of **3a** with excess Na_2CO_3 in acetone resulted in the loss of two protons to form the dicationic complex $[\{Rh(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{28}H_{22}O_4)][BF_4]_2$ **4a**. This contrasts to free *p-tert*-butylcalix[4]arene which is deprotonated twice only by strong bases such as LiH.[12] In the case of **4a** the two hydroxylic protons are clearly observed in the ^1H NMR spectrum as a sharp peak at δ 10.28, close to the chemical shift of the OH protons in free calix[4]arene.[1] There is also a marked upfield shift in the position of the higher field aromatic resonances suggesting that it is the bound phenolic residues which are deprotonated, resulting in the formation of a bis(oxocyclohexadienyl) type ligand.

If **1a** is refluxed in acetone with $[Rh(\eta^5\text{-}C_5Me_5)(acetone)_3]^{2+}$ in the presence of only a few drops of CF_3CO_2H a yellow precipitate of a further compound, **5a**, is obtained exhibiting a similar ^1H NMR spectrum to **3a** with chemical shifts of the aromatic rings and high field methylenic signal intermediate between those of **3a** and **4a**. The majority of resonances in the spectrum of **5a** were split into pairs (*e.g.* for the C_5Me_5 rings singlets at δ 2.16 and 2.15 were observed) suggesting an asymmetric complex in which there is a slight difference between the two coordinated rings. This data, in conjunction with the less acidic conditions employed in the synthesis of **5a** leads us to formulate the complex as the singly deprotonated trication $[\{Rh(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{28}H_{23}O_4)][BF_4]_3$. This formulation was confirmed by addition of aqueous $H[BF_4]$ to an NMR sample of **5a**, which resulted in the complete conversion of **5a** into **3a**. This significant enhancement in calixarene acidity suggests that the new metalated host molecules may display an extensive range of complexation chemistry in their own right.

Reaction of the iridium complex **2b** with **1a** in acetone/CF_3CO_2H results in the formation of the iridium analogue of **3a**, $[\{Ir(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{28}H_{24}O_4)][BF_4]_4$ **3b** in 56% yield. Interestingly however, reaction of **2b** (pre-treated with

$Ag[BF_4]$) with **1a** in neat CF_3CO_2H resulted in the surprising isolation of the tetrametallic species $[\{Ir(\eta^5\text{-}C_5Me_5)\}_4(\eta^6:\eta^6:\eta^6:\eta^6\text{-}C_{28}H_{22}O_4)][BF_4]_6$ **6b** in 76% yield, even in the presence of a 1 : 1 molar ratio of **2b** to **1a**. Calix[4]arene is extremely poorly soluble in CF_3CO_2H and a significant quantity of the undissolved macrocycle was recovered at the end of the reaction suggesting that the primary metalation step is rate limiting under these conditions. The FAB mass spectrum of **6b** exhibited peaks corresponding to calix[4]arene coordinated to one, two, three and four C_5Me_5 Ir fragments whilst the symmetrical nature of the product was clearly indicated by its ^1H NMR spectrum which exhibited a single set of resonances for the calixarene ligand at similar chemical shift to those assigned to the coordinated faces of **3b**. The observation of the characteristic AB pattern for the methylenic bridges indicates a cone conformation.[1]

Reaction of complexes **2** in neat CF_3CO_2H with the more sterically hindered *p-tert*-butylcalix[4]arene **1b** again led, in almost quantitative yield, to the bimetallic complexes $[\{M(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{44}H_{56}O_4)][BF_4]_4$ (M = Rh **7a**, Ir **7b**), related to **3a** and **3b**. Tetrametallic species were not formed even in the presence of excess metal complex. Complexes **7** were characterised as described above and exist solely in the cone conformation. In the case of **7b** the ^1H NMR spectrum exhibited a relatively sharp signal at δ 7.38 assigned to the hydroxy protons of the calixarene integrating for 4H, whereas the analogous signal for the rhodium analogue was extremely broad.

Consistent with the high acidity observed for **3**, slow crystallisation of complexes **7** from NO_2CH_3–Et_2O gave two new species, **8a** and **8b**, exhibiting ^1H NMR spectra similar to that of **5a** suggesting them to be the triply charged cationic complexes $[\{M(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{44}H_{55}O_4)][BF_4]_3$. In confirmation the iridium complex **8b** as a diethyl ether–nitromethane solvate was characterised by a single crystal X-ray structure determination, Fig. 1.[7] The structure of **8b**·Et_2O·NO_2Me is an excellent illustration of the type of host–guest interaction which make this class of compounds of interest. The calix[4]arene host adopts the cone conformation with the two iridium centers situated upon opposite sides of the macrocycle. Deeply embedded within the hydrophobic cavity is a molecule of diethyl ether exhibiting close contacts from the terminus of the solvent to the calixarene aromatic rings, C(1)S···ring centroids of 3.53, 3.62, 3.69 and 3.83 Å to rings C, D, A and B, respectively. Calculated hydrogen atom positions suggest that the -Me moiety C(1)S is orientated such as to form weak C–H···π hydrogen bonds with the unmetalated aromatic rings (B, D) whilst avoiding the partially positively charged coordinated decks. The hydrogen bonding network at the calixarene oxygen atoms is asymmetric with short contacts from O(b) to O(a) and O(c) of 2.52 and 2.64 Å, respectively, whilst longer bonds are formed to O(d); O(d)···O(a), O(c) 2.71 and 2.76 Å. These distances are shorter than those observed for the longest O···O contact in the sodium salt of the *p-tert*-butylcalix[4]arene monoanion (2.92 Å)[12] where the oxygen atoms are not bridged by a proton, whilst the distances between hydrogen bonded oxygen atoms in the latter structure are significantly less than in **8b** (2.43–2.58 Å). This evidence suggests that crystallographic disorder results in either O(a) or O(c) being deprotonated with little effect on the crystal packing. Consistent with an oxocyclohexadienyl description for the coordinated decks of the calixarene ligand, the C(1)–O distance is markedly shorter for rings A and C, 1.30 Å av., than the unmetallated rings B and D, 1.37 Å av.

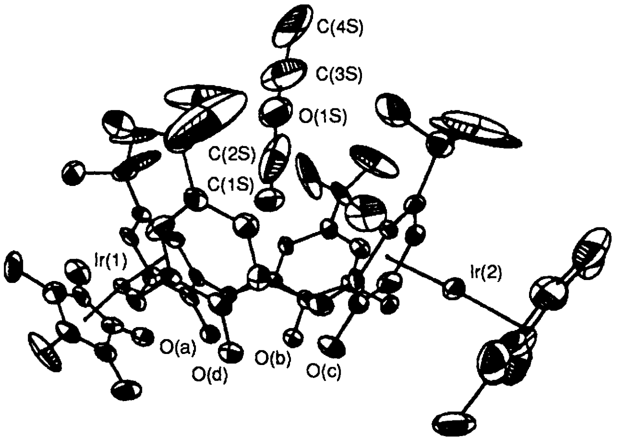


Fig. 1 X-Ray crystal structure of the molecular cation in $[\{Ir(\eta^5\text{-}C_5Me_5)\}_2(\eta^6:\eta^6\text{-}C_{44}H_{56}O_4)][BF_4]_3$·$Et_2O$·$NO_2Me$ along with the included molecule of diethyl ether

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Footnote

† *Crystal data* for $C_{64}H_{86}O_4Ir_2$·$3BF_4$·$C_4H_{10}O$·NO_2CH_3, Mw 1699.36, colourless block, monoclinic, $P2_1/a$, $a = 19.670(6)$, $b = 14.211(1)$, $c = 27.655(5)$ Å, $\beta = 108.62(2)°$, $V = 7325$ Å^3, $Z = 4$, $D_c = 1.55$ g cm^{-3}, $\mu = 37.61$ cm^{-1}. Of 13862 data collected on an Enraf-Nonius CAD4 diffractometer (Mo-Kα, 2θ = 4–50° at 20 °C) 5338 unique reflections were judged observed $[I > 3\sigma(I)]$. Data were corrected for Lorentz, polarisation and absorption effects (ψ-scans). The structure was solved by direct methods (SHELX86[13]) and refined by alternating least squares and difference Fourier techniques (SHELX76[14]). The nitromethane solvent molecule was found to be disordered over two possible sets of positions about the central nitrogen. The final refinement converged with $R = 0.057$, $R_w = 0.076$.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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