

# Synthesis and chloride binding properties of a Lewis acidic tetratin(IV) calixarene

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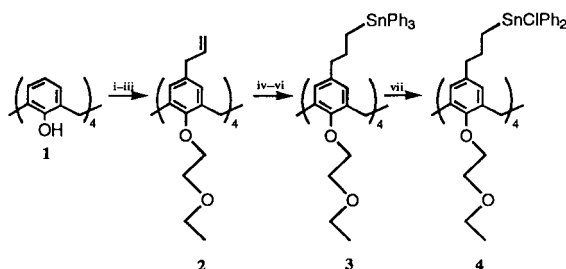
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The Lewis acidic calix[4]arene with four covalently attached diphenylmonochlorotin(IV) centers was synthesized and its stannate complex with chloride was studied by  $^{119}\text{Sn}$  NMR.

The supramolecular chemistry of anions including their detection, sequestration and transportation by calixarenes is an emerging area of research involving this versatile class of receptor molecules.<sup>1</sup> Compared to their positively charged counterparts, anions are inherently more difficult to bind due to their relatively larger ionic radii, higher solvation energies and diverse topologies.<sup>2</sup> Even with these formidable obstacles, calixarenes with incorporated hydrogen bond donors (*e.g.* ureas, amides and alcohols)<sup>3</sup> or electron-deficient metal centers (*e.g.* metallocenes and metal complexes)<sup>4</sup> have been synthesized which selectively bind different types of anions. Recently, there has been an increased interest in designing heteroditopic ligands for the simultaneous complexation of anions and cations suitable for extraction or transportation of metal salts. Since calixarenes can be functionalized on both their upper and lower rims, they are attractive molecular scaffolds for constructing heteroditopic hosts. Common design features of previously reported bifunctional calixarenes are hydrogen bond donors for anion complexation and crown ether or ester groups for cation recognition.<sup>5</sup> In this context, we report the synthesis and chloride-binding properties of a neutral, heteroditopic calixarene containing covalently attached Lewis acidic tin atoms for anion binding and ether oxygens for cation binding.

Incorporation of main group metals, particularly tin, represents a relatively unexplored area of calixarene chemistry. Two of the reported three examples are actually complexes containing mono- and ditin(II) centers wherein the calixarenes served as oxoligands.<sup>6a,b</sup> The lone example of a covalently attached tin(IV)-containing calixarene utilizes the tin atoms as the bridge between adjacent aromatic rings.<sup>6c</sup> The relatively longer C–Sn bonds allowed this compound to adopt a nearly planar geometry, thereby destroying the chalice-like structure.

The neutral Lewis acidic tetrastannacalix[4]arene host **4** was synthesized as outlined in Scheme 1.†‡ The principal starting material for the synthesis was the *de-tert*-butylated calix[4]arene **1**, which was readily obtained in multigram batches from literature procedures.<sup>7</sup> The dealkylated calixarene was used so that the Lewis acidic tin atoms could be appended to the upper rim. Alkylation of the lower rim of **1** with allyl bromide yielded



**Scheme 1** Reagents and conditions: i, NaH, allyl bromide; ii, *N,N*-diethylaniline, heat; iii, NaH, 2-bromoethylethyl ether; iv, 9-BBN, H<sub>2</sub>O<sub>2</sub>, NaOH; v, Ph<sub>3</sub>P, CCl<sub>4</sub>; vi, Ph<sub>3</sub>SnSnPh<sub>3</sub>, Li; vii, HCl, CH<sub>2</sub>Cl<sub>2</sub>.

the tetraallyl ether (85%), which when heated to 215 °C underwent a Claisen rearrangement that transferred the allyl groups to the upper rim (71%).<sup>7</sup>

The cone conformation in the calix[4]arene framework of **2** was then fixed by appending ethoxyethyl groups on to the lower rim of the rearranged tetraallyltetrahydroxycalixarene (58%).<sup>8</sup> These ether groups were used to create a prototypical cation binding site for three reasons: (i) they were inert to the conditions of the subsequent reactions, (ii) their cation-binding properties were already known<sup>9</sup> and (iii) their conformational influence on the calixarene was predictable. Hydroboration of the double bonds in **2** with 9-BBN produced the tetraol (28%) which was converted to the corresponding tetrachloride by treatment with Ph<sub>3</sub>P/CCl<sub>4</sub> (82%). The tetratin compound **3** was obtained by reacting the tetrachloride with Ph<sub>3</sub>SnLi (40%).<sup>10</sup> The  $^{119}\text{Sn}$  NMR spectrum of **3** contained only one signal at  $\delta$  –101.27, which indicated that the four tins were equivalent in solution. Without the inductive effects of an electron withdrawing group, the tin atoms are not acidic enough to complex chloride ions, thus host **4** was obtained after careful treatment of **3** with anhydrous HCl at –78 °C (90%). The  $^{119}\text{Sn}$  NMR spectrum of **4** also contained just a single signal at  $\delta$  +14.75 which is within the range of typical Ph<sub>2</sub>RSnCl species.<sup>11a</sup> What ultimately motivated us to employ the 3-carbon spacer group on the upper rim was the fact that the order of reactivity in this reaction is Ph > Bn > R.<sup>11b</sup> This meant that at least a 2-carbon spacer had to separate the tin atoms from the aromatic rings on which they were attached so that regiochemical control could be achieved in the chlorination reaction.

The chloride complexing properties of **4** were investigated in CDCl<sub>3</sub> by using  $^{119}\text{Sn}$  NMR to observe the change from the tetravalent uncomplexed, stannane species to the pentavalent geometry of the stannate complex.<sup>11b,12</sup> Initial binding studies were restricted to chloride binding in order to eliminate complications introduced by ligand exchange at the tin atoms. The stoichiometry of the complex was determined by the method of continuous variation (Job plot).<sup>13</sup> This method is particularly useful for systems under rapid exchange conditions and can be adapted easily to  $^{119}\text{Sn}$  NMR data.<sup>12</sup> The experiment required analysis of several solutions of **4** and Bu<sub>4</sub>NCl prepared such that the mole fractions changed, but the concentration was constant. A plot of ( $\Delta\delta X_{\text{H}}$ ) vs.  $X_{\text{H}}$ , where  $\Delta\delta = (\delta_{\text{obs}} - \delta_{\text{H}})$ , produced a parabolic curve that maximized at  $X_{\text{H}} = 0.25$ , indicating that each tin atom acted independently in the formation of a 4:1 (Cl:**4**) stannate complex. This result is not surprising, since the tin atoms are not structurally preorganized in a well-defined binding site that would facilitate cooperative binding.

Chloride association constants for **4** were determined by the Benesi–Hildebrand method as adapted to  $^{119}\text{Sn}$  NMR data as shown in eqn. (1).<sup>12</sup>

$$(\delta_{\text{obs}} - \delta_{\text{H}})^{-1} = (\delta_{\text{C}} - \delta_{\text{H}})^{-1} + (K_{\text{eq}}(\delta_{\text{C}} - \delta_{\text{H}}))^{-1} [\text{Cl}^-] \quad (1)$$

The rate of exchange between the free host and complex was rapid on the NMR time scale, over the temperature range of –20 to +50 °C, as evidenced by a single weighted-average signal that was observed to shift from its initial value for the free host ( $\delta$  +14.35) to higher field strengths upon the addition of

chloride. For example, the signal for Cl<sup>-</sup>/host = 4 was observed at  $\delta$  -171.93 and continued to shift slightly further upfield with the addition of 8, 12, 16 and 20 equiv. of Cl<sup>-</sup>. The total displacement ( $\delta_{\text{obs}} - \delta_{\text{host}}$ ) was 207 ppm, with 90% displacement occurring at the addition 4 equiv. of Cl<sup>-</sup>. This behavior is characteristic of weak binding, which was confirmed by the small  $K_{\text{eq}}$  values that ranged from a high of 52 M<sup>-1</sup> at 253 K to a low of 13 M<sup>-1</sup> at 328 K, with intermediate values of 25 and 33 M<sup>-1</sup> at 295 and 273 K, respectively. Not only are these values similar to acyclic ditin model compounds,<sup>14</sup> they were anticipated since the tin atoms in **4** lack any preorganization and cooperative binding.

We are currently investigating the simultaneous ion pair complexing properties of **4** with NaCl as the metal salt. These studies are based on previous results that demonstrated that the ethoxyethyl ether groups were selective for sodium ions even though the percent extraction is relatively low.<sup>9</sup>

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## Notes and references

† All new compounds were characterized by <sup>1</sup>H (400 MHz), <sup>13</sup>C (100 MHz) and <sup>119</sup>Sn (149 MHz) NMR spectroscopy and elemental analysis. Internal standards for NMR spectra were tetramethylsilane (<sup>1</sup>H and <sup>13</sup>C) and tetramethyltin (<sup>119</sup>Sn).

<sup>119</sup>Sn Job plot experiments: Aliquots from 0.1 M stock CDCl<sub>3</sub> solutions of **4** and Bu<sub>4</sub>NCl were mixed so that the mole fractions of each changed, but the total concentration of all species in solution remained constant. Spectra were acquired at 295 K (149 MHz) on samples containing mole fractions of **4** ranging from 0.1 to 0.8.

Binding constants: Equilibrium constants were determined by the Benesi-Hildebrand method, wherein a large excess of guest species was present relative to the amount of host. In these experiments, aliquots of a 1.72 M solution of Bu<sub>4</sub>NCl were added to 0.780 ml (0.071 mmol) of a 0.091 M solution of **4** in 1 ml volumetric flasks. The solutions were mixed thoroughly and transferred to an NMR tube. Binding constants were determined at 328, 295, 273 and 253 K.

‡ Selected data for **2**:  $\delta_{\text{C}}(\text{CDCl}_3)$  15.29, 30.72, 39.36, 66.32, 69.63, 73.10, 114.82, 128.30, 133.11, 134.63, 138.22, 154.47. For tetraol:  $\delta_{\text{C}}(\text{CDCl}_3)$  15.25, 30.51, 31.22, 33.89, 61.86, 66.28, 69.61, 73.14, 127.87, 134.52, 135.11, 153.99.  $\delta_{\text{C}}(\text{CDCl}_3)$  15.28, 30.70, 31.91, 34.07, 44.17, 66.31, 69.65, 73.14, 128.12, 133.95, 134.68, 154.41. For **3**:  $\delta_{\text{C}}(\text{CDCl}_3)$  10.53, 15.31, 28.62, 30.83, 39.47, 66.29, 69.64, 72.93, 128.09, 128.43, 128.77, 134.34, 135.12, 137.04, 139.08, 154.32;  $\delta_{\text{Sn}}$  -101.24. For **4**:  $\delta_{\text{C}}(\text{CDCl}_3)$  15.21,

16.89, 27.42, 30.69, 37.88, 38.79, 64.71, 68.64, 72.03, 127.69, 128.33, 128.77, 133.92, 134.86, 136.77, 138.59, 154.03.  $\delta_{\text{Sn}}(\text{CDCl}_3)$  +14.75.

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