# MACROCYCLES CONTAINING TIN. A SMALL, EXCLUSIVE HOST FOR THE FLUORIDE ION

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Summary: The binding properties of macrobicyclic host 1 in solution were studied by NMR spectroscopy; host 1 maintains structural integrity in the presence of halide anions and binds fluoride ion strongly while it excludes all other halides.

Molecular recognition of anionic guests by multidentate, Lewis acidic hosts in organic media has been observed in only limited cases.[1] Further, neutral, macrocyclic receptors for anions or bases have just begun to receive attention.[2,3] We recently reported the synthesis and chloride anion binding properties of a series of Lewis acidic macrobicyclic hosts (1-4) containing bridgehead tin atoms.[3] Hosts 2 and 3 bound chloride more strongly than host 4, presumably reflecting a better "fit" of the chloride ion in the cavities of 2 and 3; thus, size selectivity in the binding of chloride was demonstrated. The behavior of host 1 in the presence of chloride was perhaps more noteworthy since this species showed no apparent complexation with chloride.[3]

$$Cl-Sn \overset{-(CH_2)_n-}{\underset{-(CH_2)_n-}{\overline{-(CH_2)_n-}}} Sn-Cl$$
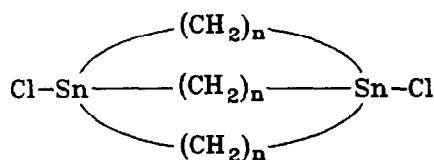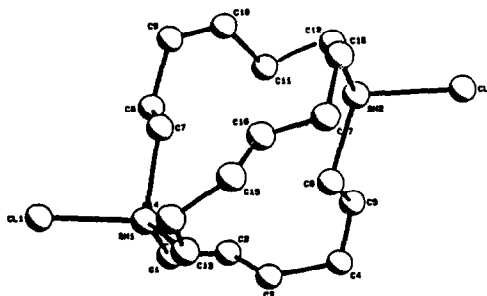
1:n=6, 2:n=8, 3:n=10, 4:n=12

Figure 1. X-ray crystal structure of 1.

In this communication we report further studies of the interesting host 1.[4] This compound was found to be Lewis acidic exclusively towards the small fluoride anion which it complexed strongly; it exhibited no Lewis acidic properties towards other halide ions. The remarkable binding selectivity of 1 and the apparent stability of the tin-chlorine bonds in 1 in the presence of other halides support our conclusion[3] that hosts 1-4 complex halide ions by inclusion within the cavity.

For the series of hosts 1-4, molecular models had suggested the possibility of inclusion of chloride into the cavities of 2-4 but not into that of 1. An X-ray crystal structure of 1 confirmed the prediction of the models (Figure 1).[5] In the solid state, the molecule is

a crude sphere with a tin-tin distance of 5.25 Å. Assuming a tin atom radius of 1.4 Å,[6] the chloride ion (diameter ca. 3.6 Å)[6] should not fit between the tin atoms, but inclusion of the fluoride anion (diameter ca. 2.6 Å)[6] might be expected.

The binding properties of the tin-containing hosts in solution are conveniently studied by ^{119}Sn NMR spectroscopy since tin species typically experience about a 200 ppm upfield chemical shift upon conversion from a four-coordinate stannane to a pentavalent stannate.[7] Careful NMR[8a] studies of the potential binding of chloride by 1 were performed to confirm of our earlier observation. When solutions of host 1 in CDCl$_3$ were treated with tetrahexylammonium chloride, the ^{119}Sn signal from 1 at δ 148.5 remained sharp and unshifted. Ultimately, solutions containing a five-fold excess of chloride (0.41 M) were studied. Spectra were recorded at 30 and -50 °C to guarantee that at least one set of studies was performed outside of the range of dynamic NMR behavior. From the 30 °C spectra, assuming the fast exchange limit, the amount of complexed host 1 was less than 0.5%, and the binding constant for Eq 1 must be less than 0.003 M^{-1}. From the -50 °C spectra (signal to noise - 50:1), assuming the slow exchange limit, the amount of complex (expected at δ 0-30[3]) was less than 2%, and K_{eq} must be less than 0.01 M^{-1}. For comparison, host 2 binds chloride strongly under these conditions (K_{eq} - 20-50 M^{-1})[3]; the reduction in cavity size from 2 to 1 leads to a reduction in binding energy of chloride of at least 3.7 (-50 °C) or 5.5 (30 °C) kcal/mol.

$$\text{Host} + \text{X}^- \overset{K}{\rightleftharpoons} [\text{Host--X}]^- \quad (1)$$
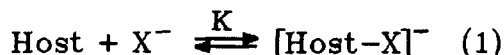
Similar behavior was observed in the ^{119}Sn NMR spectra of CDCl$_3$ solutions of 1 containing 0.41 M bromide and 0.41 M iodide. As expected, the signal from 1 was unaffected in its chemical shift and line-shape showing that there was no detectable binding of these halides. When these solutions were allowed to stand for two days, the ^{119}Sn from 1 remained unchanged indicating that the tin-chlorine bond in 1 was stable over this time period. In simple mono-halo tin compounds, the tin-halogen bonds are labile.[9]

Dramatically different behavior was observed in the ^{119}Sn NMR spectra of 1 in the presence of tetrabutylammonium fluoride. Upon addition of increments of the fluoride salt, the signal from uncomplexed 1 at δ 148.5 was reduced in intensity and a new doublet centered at δ -6.5, with a ^{119}Sn-^{19}F coupling constant of 1090 (± 50) Hz, was observed. Figure 2 shows spectra of 1 containing about 0.4 and 0.5 equivalents of fluoride per mole of host. It is noteworthy that the ^{119}Sn NMR spectra were unchanged upon standing for several days at room temperature; specifically, there was no new signal in the region of the uncomplexed host. This shows that host 1 maintained its structural identity, and the fluoride ions did not replace chloride despite the rapid complexation--decomplexation.

For comparisons to a simple model, the ^{119}Sn NMR spectra of mixtures of tributyltin chloride (5) and tetrabutylammonium fluoride were studied. Since the halogens are freely exchanging under these conditions, the identity of the tin species cannot be rigorously assigned, but qualitative conclusions are warranted. Upon incremental additions of the fluoride salt to a CDCl$_3$ solution of 5, the signal (initially at δ 156) remained sharp but shifted smoothly upfield. With ca 2 equivalents of fluoride present, the signal was at δ -30.7 although this did not appear to be the final limiting chemical shift.
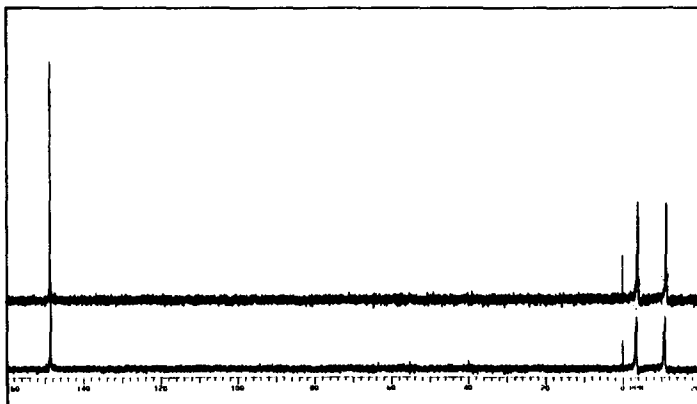
Figure 2. ^{119}Sn NMR spectra in CDCl$_3$ of 1 with 0.4 (lower) and 0.5 (upper) equivalents of tetrabutylammonium fluoride.

The host 1-Fl$^-$ complex could also be observed by ^{19}F NMR spectroscopy.[8b] A solution containing ionic fluoride shows a very broad signal centered at δ -88.6. In the presence of limiting host 1, the ^{19}F spectrum was complex, containing three significant sets of sharp peaks. A signal at δ -76.1 was readily assigned to the 1-F$^-$ complex based on the ^{119}Sn and ^{117}Sn satellites with coupling constants of ca 1100 Hz. A signal at δ -89.1 was assigned to free fluoride, and a signal at δ -75.5 was not assigned.

Since sharp NMR peaks were observed in the slow exchange limit for the host 1-F$^-$ complex at 30 °C in the ^{119}Sn spectra, limiting values for the rate constants for complexation can be calculated. Line-shape analysis[10] showed that the (presumed) first-order rate of decomplexation (k_r) must be less than 100 s^{-1} based on the signals for the free and complexed host in the ^{119}Sn spectrum and the sharp doublet signals of the complex. In contrast, the rate constant for exchange in binding of model 5 to fluoride must be greater than 8 x 10^5 s^{-1} based on the observed fast exchange in the NMR spectra of 5--fluoride mixtures.

Despite the substantial reduction in the rates of complexation-decomplexation of fluoride by host 1, which we attribute to steric interactions involving the hydrocarbon rings, the binding constant remained high. Using the ^{119}Sn and ^{19}F spectra of one sample of 1 and fluoride, the ratio of complexed to free species for both host and fluoride were determined. The binding constant at 30 °C was 100 or 200 M^{-1} depending upon the assignment of the fluoride signal at δ -75.5. Thus, host 1 binds F$^-$ at least five orders of magnitude more strongly than it binds chloride or, apparently, any other donor. The impressive binding selectivity of host 1 is more apparent when one compares these results with those for the acyclic model 5. For 5--fluoride mixtures, the binding constant at 30 °C was ca 220 M^{-1}, similar to that for 1. The binding constant for 5 with chloride ion, however, is also large (20 M^{-1}).[12]

There is a striking parallel between our observations with the macrocyclic Lewis acidic hosts 1-4 and the cation binding properties of their basic counterparts, the well-studied crown ethers, cryptands etc. Specifically, the proper fit of a guest within the cavity of the host can lead to selective complexation such as we observed in the binding of chloride by 2-4, but substantially greater size-selective effects exist when a small guest fits a cavity and its larger homologues are excluded. Thus, in its binding of fluoride, host 1 resembles,

for example, small-cavity, lithium- and sodium-specific spherands reported by Cram.[14] We ex-
pect that other properties of the cation-binding hosts will also be paralleled by anion bind-
ing hosts.

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   ppm downfield from external Me₄Sn. (b) ^{19}F NMR spectra were obtained on a Varian XL-
   400 spectrometer at 376 MHz; chemical shifts are reported in ppm relative to external
   1,1,1-triflurotoluene which was defined as δ 0.
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    plexed species that were in the expected range (δ -53 for F⁻ and δ -62 for Cl⁻).
13. A simple computer program was written which used the double-reciprocal (Hildebrand-
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