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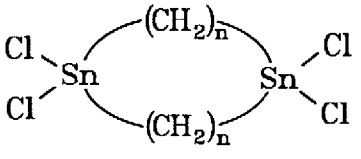
Macrocycles Containing Tin.
Ditopic, Tricyclic, Lewis Acidic Hosts with Four Binding Sites

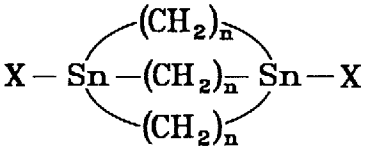
Michael T. Blanda and Martin Newcomb*
Department of Chemistry, Texas A&M University, College Station, Texas, 77843, USA

Summary: Preparation of the title class of anion-binding hosts is described, and the chloride binding properties of one host are reported.

The complexation of anions in organic media by multidentate, neutral, Lewis acidic hosts is a relatively young field of study.[1] Our contributions in this area have involved the development of macrocyclic[2] (**1**) and macrobicyclic[3] (**2**) hosts that contain Lewis acidic tin atoms as the binding sites. Low size selectivity was observed in chloride binding by macrocyclic hosts containing two binding sites,[2b] but substantial size selectivity in binding fluoride, chloride, and bromide anions was found in two-site macrobicycles.[3b,d] Solution ^{119}Sn NMR studies of bicyclic hosts binding anions in halogenated solvents[3b,d] as well as X-ray crystallographic and solid state ^{119}Sn NMR studies of bicycle-anion complexes[3c] demonstrate that anions are held in the cavities of the hosts; the selectivity apparently originates from the fit of the encrypted anion in the cavity. It was expected that the incorporation of additional binding sites into relatively rigid host superstructures would result in both stronger binding and higher selectivity. In this letter, we report examples of macrotricyclic species containing four tin atoms and studies of chloride complexation by one ditopic host that exhibits the expected enhancement in anion binding strength.



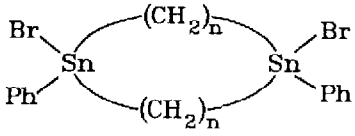
1: n = 8, 10, 12



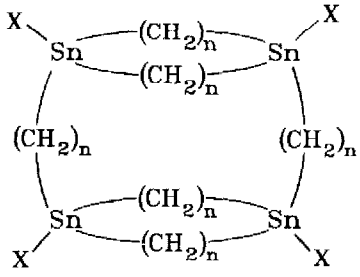
2: X=Cl or Br
n=6,7,8,10,12

Our approach to the synthesis of tin-containing hosts involves sequential addition of the linking polymethylene chains. Thus, one reactive site per tin atom was created by selective HX cleavage of phenyl groups from a bis(triphenylstannyl)alkane, and the resulting bis(halodiphenylstannyl)alkane was converted to a macrocycle by reaction with a di-Grignard reagent under relatively high dilution condi-

tions.[2a] Repeating the sequence on macrocycles containing linking polymethylene chains of 6, 7, 8, 10, or 12 units gave macrobicyclic compounds.[3d] For the small macrocyclic compounds **3** and **4**, reaction with a di-Grignard reagent in somewhat more concentrated solutions resulted in the formation of macrotricycles **5** and **6** as the major products isolated by preparative reverse-phase chromatography.[4] Treatment of the tetra-tin tricycle **6** with HCl gave host **7** in essentially quantitative yield.[5]



3: n = 4
4: n = 5



5: n=4, X=Ph
6: n=5, X=Ph
7: n=5, X=Cl

The chloride binding properties of host **7** in solution were studied by ^{119}Sn NMR spectroscopy. In $CDCl_3$ solutions, the signal from triorganotin chlorides is observed at about δ 150, and the signal from a stannate $(R_3SnCl_2)^-$ in $CDCl_3$ is observed in the vicinity of δ -60.[3d] For the macrobicyclic hosts **2** that bind only one halide ion, the signal for the complexed tin atoms was found midway between these values.[3d] When aliquots of tetrahexylammonium chloride solution were added to a $CDCl_3$ solution containing host **7** and NMR spectra were recorded, the limiting chemical shift for the complex was at δ 87. The figure shows the saturation curves obtained for Bu_3SnCl, macrobicycle **2** (n = 12), and host **7**. The break in the saturation curve for **7** at a guest to host ratio of about 1:1 not only shows that the host forms a 1:1 complex with chloride but also indicates that the binding constant is relatively large. The asymptotic value in the saturation study of δ 87, about one fourth of the total change in chemical shift expected for conversion of stannanes to stannates, confirms that a 1:1 complex is formed. Further, the lack of change in the chemical shift in NMR spectra of **7** in the presence of excess chloride shows that any interaction between the 1:1 complex and a second chloride anion is very weak.

A single ^{119}Sn NMR signal was observed from all solutions containing host **7** and chloride which shows that the four tin atoms in the host bind the anion either simultaneously or in an NMR-fast, time averaged manner. Exchange of free host and the 1:1 complex also was quite rapid. In the absence of added chloride, the ^{119}Sn NMR spectrum of **7** was complex due to slow conformational changes in solution, and it was difficult to estimate the natural T_2 for this species. Nevertheless, using a conservative estimate of 0.0005 s for T_2 of free host **7**, line shape simulations[6] of spectra containing one and two equivalents of chloride revealed that noticeable line broadening due to exchange would have been apparent if the rate constant for exchange was 1×10^6 s^{-1} or less at 20 °C.

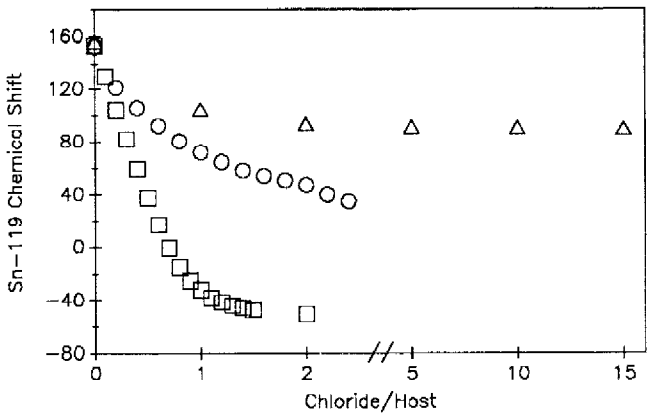


Figure. Titration Curves for Bu_3SnCl (□), bicycle **2** (n = 12) (○), and host **7** (△) in $CDCl_3$.

The chloride binding behavior of macrotricyclic host **7** is unique in comparison to that seen with the macrocyclic and macrobicyclic species we have previously studied. Specifically, fast exchange of free host and complex was observed with the macrocyclic hosts **1**, but these species showed only limited cooperative effects of the binding sites and bound two chloride anions strongly.[2b] On the other hand, for the bicyclic hosts **2** that formed 1:1 complexes with chloride, exchange of free host and complex by dissociation of the bound chloride from the cavity tended to be a slow process;[3d] indeed, in the bicycle that bound chloride most strongly, the rate constant for dissociation of chloride from the cavity of the complex was on the order of 1×10^4 s^{-1}, and the chloride selectivity for hosts **2** was found to originate predominantly in the rates of dissociation of the complexes.[3d] That the tricyclic host **7** forms a 1:1 complex with chloride while rapid equilibration between free host and the complex is maintained suggests that the propensity for forming the 1:1 complex may result more from the cooperative binding of the guest by the multiple binding sites than from a simple structure-controlled exclusion of additional guests.

The formation constant for the 1:1 complex of **7** and chloride was determined by an iterative Hildebrand-Benesi treatment.[7] At 20 °C, the binding constant in $CDCl_3$ was 500 M^{-1}. This represents an increase in binding energy in $CDCl_3$ solution of 2.0 kcal/mol over that found for the strongest binding bicyclic host (**2**, n = 8).[3d] It is noteworthy that this binding constant is also substantially greater than that for Bu_3SnCl binding chloride. Previously, we observed that, although the bicyclic hosts **2** could bind chloride selectively, the largest binding constant was no greater than that of Bu_3SnCl,[3d] and we ascribed this behavior in part to the fact that hosts **2** apparently bind chloride with only one Lewis acidic site. The substantial increase in the binding constant for host **7** complexing chloride is additional evidence that the multiple Lewis acid sites in **7** act in a cooperative manner.

In summary, the strong binding of chloride by host **7** coupled with its propensity to form only a 1:1 complex with chloride suggest that the Lewis acidic sites in the ditopic host are properly oriented for binding an included guest. In our continuing efforts with four site, Lewis acidic hosts, we plan to vary

the length of the spacers between the two binding regions defined by the macrocyclic subunits to give a series of ditopic hosts. Given the unique chloride binding features of host **7**, we expect that the macrotricycles reported here are the progenitors of a series of interesting anion and donor binding agents.

Acknowledgment: We thank the Office of Naval Research for financial support. We thank Mr. W. M. Cates for assistance in the preparation of **5** and Dr. J. H. Horner for helpful discussions.

References and Notes

1. Recent examples include the following. Jung, M. E.; Xia, H. *Tetrahedron Lett.* **1988**, *29*, 297-300. Wuest, J. D.; Zacharie, B. *J. Am. Chem. Soc.* **1987**, *109*, 4714-4715. Katz, H. E. *Organometallics* **1987**, *6*, 1134-1136. Swami, K.; Hutchinson, J. P.; Kuivila, H. G.; Zubieta, J. A. *Ibid.* **1984**, *3*, 1687-1694. Gielen, M.; Jurkschat, K.; Mahieu, B.; Apers, D. *J. Organometal. Chem.* **1985**, 286, 145-151.
2. (a) Azuma, Y.; Newcomb, M. *Organometallics* **1984**, *3*, 9-14. (b) Newcomb, M.; Madonik, A. M.; Blanda, M. T.; Judice, J. K. *Ibid.* **1987**, *6*, 145-150.
3. (a) Newcomb, M.; Horner, J. H.; Blanda, M. T.; *J. Am. Chem. Soc.* **1987**, *109*, 7878-7879. (b) Newcomb, M.; Blanda, M. T. *Tetrahedron Lett.* **1988**, *29*, 4261-4264. (c) Newcomb, M.; Horner, J. H.; Blanda, M. T.; Squattrito, P. J. *J. Am. Chem. Soc.* **1989**, *111*, 0000. (d) Blanda, M. T.; Horner, J. H.; Newcomb, M., submitted for publication.
4. In a representative procedure, a solution of **4**[3d] (4 mmol) in 500 mL of THF under nitrogen was stirred at room temperature as a solution of the di-Grignard reagent from 1,5-dibromopentane in THF (500 mL, 0.012 M) was added over a period of 2 h. The mixture was stirred for an additional 6 h at room temperature. Approximately half of the THF was distilled from the reaction mixture at reduced pressure, and the remaining solution was diluted with 200 mL of ether. The mixture was washed with satd NH_4Cl soln, satd KF soln, and satd NaCl soln. The organic phase was dried ($MgSO_4$) and distilled at reduced pressure to give a residue that was purified by reverse-phase chromatography (LiChroprep® RP-18, THF/MeOH elution) to give **6**. Recrystallization from THF/MeOH gave **6** (mp > 220 °C) in 10% yield. Product **5** had mp 176-178 °C.
   The macrotricycles were characterized as follows. Compound **5**: ^{13}C NMR (50 MHz, $CDCl_3$, ref. Me_4Si) δ 9.42, 10.29, 29.43, 31.43, 128.0, 128.2, 136.4, 142.5; ^{119}Sn NMR (149 MHz, $CDCl_3$, ref. Me_4Sn) δ −44.2; Anal. for $C_{48}H_{68}Sn_4$, calcd: C, 51.48; H, 6.12; found: C, 51.90; H, 6.14. Compound **6**: ^{13}C NMR (50 MHz, $CDCl_3$, ref. Me_4Si) δ 10.84, 11.68, 27.0, 27.1, 37.3, 40.9, 128.5, 128.6, 136.7, 142.3; ^{119}Sn NMR (149 MHz, $CDCl_3$, ref. Me_4Sn) δ −44.2; Anal. for $C_{54}H_{80}Sn_4$, calcd: C, 53.89; H, 6.70; found: C, 53.73; H, 6.81. (Analyses performed by Galbraith Laboratories, Inc.)
   The structure of **5** was confirmed by X-ray crystallography; the results (submitted for the referees) will be published. Crystals of **6** were not suitable for X-ray analysis. The structure of **6** was deduced from (1) the analogy in the reactions forming **5** and **6**, (2) the analogy in HPLC retention times of **5** and **6**, (3) the high symmetry of **6** indicated by NMR spectroscopy (one ^{119}Sn signal, ten ^{13}C signals), (4) analysis, and (5) conversion of **6** to **7** which displayed similar high symmetry by NMR spectroscopy.
5. Tetraphenyl tricycle **6** was converted to host **7** by treatment with a standardized solution of HCl in CH_2Cl_2 by the same method as reported for the cleavage reactions leading to bicyclic hosts **2**.[3d] The crude product was recrystallized from $CHCl_3$/hexanes to give **7** (mp > 220 °C) in 98% yield. The product had the following spectral properties: ^{13}C NMR (50 MHz, $CDCl_3$, ref. Me_4Si) δ 18.5, 19.0, 24.7, 25.8, 37.0, 36.9; ^{119}Sn NMR (149 MHz, $CDCl_3$, ref. Me_4Sn) δ 158.3 (major), 162.5 (minor). The ^{119}Sn NMR spectra in the presence of chloride contained one sharp peak, see text. Crystals of **7** were not suitable for X-ray analysis.
6. ^{119}Sn NMR spectra were obtained at 149.5 MHz. The spectra were simulated with a two site exchange model; see Sandström, J. *Dynamic NMR Spectroscopy*; Academic: London, 1982; pp 12-15.
7. The NMR adaptation of the Hildebrand-Benesi treatment[8] and the iterative program have been described.[3d] ^{119}Sn NMR spectra of five solutions of host **7** and tetrahexylammonium chloride in $CDCl_3$ were obtained and analyzed. The resulting calculated chemical shift for the 1:1 complex was δ 87, the same as that found experimentally in the saturation study.
8. Connors, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; Wiley-Interscience: New York, 1987; pp 24-28.

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