H-6), 7.62 (s, 1 H, H-7), 3.08-2.98 (m, 4 H, H-8 and H-11), 1.93-1.88 (m, 4 H, H-9 and H-10); mass spectrum, *m/e* (relative intensity) 232 (M^+, 100).

1,2,3,4-Tetrahydro-6-methoxybenzo[*c*]phenanthrene. Further elution with pentane of the silicic acid column described in the preceding paragraph yielded 0.05 g (3%) of 1,2,3,4-tetrahydro-6-methoxybenzo[*c*]phenanthrene (**19**) (97% pure by GC/MS). Recrystallization from pentane gave 0.02 g of **19**, mp 96.2-96.5 °C: ^{1}H NMR (300 MHz) δ 8.79 (X part of ABX, 1 H, H-12, $J_{11,12} + J_{10,12} = 9.6$ Hz), 8.23 (d, 1 H, H-7, $J_{78} = 9.0$ Hz), 7.89 (X part of ABX, 1 H, H-9, $J_{9,10} + J_{9,11} = 9.5$ Hz), 7.67 (d, 1 H, H-8, $J_{78} = 9.0$ Hz), 7.58-7.50 (m, 2 H, H-10 and H-11), 6.77 (s, 1 H, H-5), 4.00 (s, 3 H, methoxy), 3.47 (t, 2 H, H-1, $J_{12} = 5.8$ Hz), 3.08 (t, 2 H, H-4, $J_{34} = 6.6$ Hz), 2.00-1.76 (m, 4 H, H-2 and H-3); mass spectrum, *m/e* (relative intensity) 262 (M^+, 100). Anal. Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92. Found: C, 87.10; H, 6.98.

Benz[*a*]anthracene (16). Treatment of 100 mg (0.43 mmol) of 8,9,10,11-tetrahydrobenz[*a*]anthracene with 215 mg (0.95 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 10 mL of refluxing dry benzene for 20 min gave, after chromatography on alumina, 90 mg (92%) of benz[*a*]anthracene (**16**), mp 158-161 °C. Recrystallization from methanol gave **16** with mp 161.0-161.8 °C (lit.[47] mp 160.5-161.0 °C): mass spectrum, *m/e* (relative intensity) 228 (M^+, 100).

Acknowledgment. This work was supported by Grant 1R15GM36083-01 from the National Institute of General Medical Sciences. We are grateful to the W. M. Keck Foundation and to Merck & Company, Inc. for grants that enabled the purchase of a 300-MHz NMR spectrometer and to the Camille and Henry Dreyfus Foundation and the PQ Corporation for grants that enabled the purchase of a GC/MS system. We are indebted to John Dykins, Director of the Mass Spectrometry Center of the Department of Chemistry at the University of Pennsylvania, for the high-resolution mass spectral measurements. We thank Dr. Clelia W. Mallory for many helpful discussions throughout the course of this work.

(47) Fieser, L. F.; Creech, H. J. *J. Am. Chem. Soc.* **1939**, *61*, 3502.

Macrocycles Containing Tin. Preparation of Macrobicyclic Lewis Acidic Hosts Containing Two Tin Atoms and ^{119}Sn NMR Studies of Their Chloride and Bromide Binding Properties in Solution

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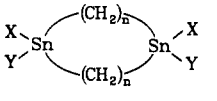
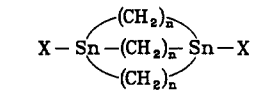
The preparation of eight symmetrical, macrobicyclic hosts containing two chloride- or bromide-substituted tin atoms at the bridgehead positions and linking chains of 6, 7, 8, 10, or 12 methylene groups are described. In solution, the smaller members exist as one isomer with the halogens outside of the cavity (out-out isomer), but the larger members exist as a mixture of the major out-out isomer and a minor in-out isomer that contains one halogen inside the cavity. Complexation of chloride anion by the five chloride-substituted hosts and of bromide anion by the three bromide-substituted hosts in halogenated solvents was studied by ^{119}Sn NMR spectroscopy. All of the bicyclic hosts that bind halide form complexes with 1:1 stoichiometry with a guest anion encrypted within the cavity of the host. Equilibrium constants for formation of the complexes were measured. Temperature-dependent dynamic NMR behavior was observed for four bicyclic hosts binding chloride and for one host binding bromide, and simulations of the spectra measured at various temperatures provided rate constants for binding guest anion within the cavity and for dissociation of the guest anion from the cavity. Arrhenius functions for these processes were calculated. Size-selective binding was observed in both chloride and bromide binding. For chloride complexation, the rate of formation of complexes at 20 °C increased monotonically as a function of the linking chain length, but the rate of dissociation did not.

The binding of anions and basic donors in organic media by multidentate Lewis acidic hosts is relatively unexplored.[1] Our group has studied the use of Lewis acidic tin atoms in macrocyclic[2] and macrobicyclic[3] compounds as hosts for anionic guests. Simple macrocycles containing two Lewis acidic sites (**1**) were found to bind chloride ion with little size selectivity,[2] but incorporation of a third linking chain between the acidic sites to give bicycles **2** provided hosts that bound chloride in a size-selective manner.[3a] This size-selective binding of chloride by hosts **2** and the anion-specific binding of fluoride ion by host **2a**[3b] suggested that bicyclic compounds included halide ions within their cavities, and this feature was confirmed in recent solid-state studies of a complex formed from host **2a** and tetrabutylammonium fluoride and a complex formed from host **2c** and benzyltriphenylphosphonium chloride.[4]



1: X=Y=Cl; n = 8, 10, 12
4: X=C_4H_9, Y=Cl, n=10



2: X=Cl 3: X=Br
a:n=6; b:n=7; c:n=8
d:n=10; e:n=12

(1) Recent examples include the following. Katz, H. E., submitted for publication. Jung, M. E.; Xia, H. *Tetrahedron Lett.* **1988**, *29*, 297-300. Wuest, J. D.; Zacharie, B. *J. Am. Chem. Soc.* **1987**, *109*, 4714-4715. Beauchamp, A. L.; Oliver, M. J.; Wuest, J. D.; Zacharie, B. *Organometallics* **1987**, *6*, 153-156. Katz, H. E. *Ibid.* **1987**, *6*, 1134-1136. Katz, H. E. *Ibid.* **1986**, *5*, 2308-2311. 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. Organomet. Chem.* **1985**, *286*, 145-151.

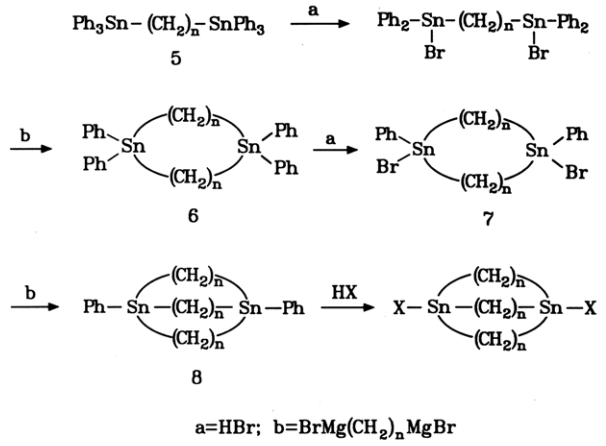
(2) Newcomb, M.; Madonik, A. M.; Blanda, M. T.; Judice, J. K. *Organometallics* **1987**, *6*, 145-150.

(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.

(4) Newcomb, M.; Horner, J. H.; Blanda, M. T.; Squattrito, P. J. *J. Am. Chem. Soc.*, in press.

0022-3263/89/1954-4626$01.50/0

Scheme I



In this paper we report details of the preparation of bicyclic hosts suitable for binding chloride and bromide anions. The binding of chloride ion by bicyclic hosts **2a–e** in organic media and the binding of bromide ion by hosts **3c–e** in organic media were studied by ^{119}Sn NMR spectroscopy. Bu_3SnCl, Bu_3SnBr, and macrocycle **4** were employed as model compounds for comparisons. All of the binding results are consistent with the inclusion of guest halide ions within the cavities of the bicyclic hosts, and size-selective binding of both guest anions was observed.

Preparation of Hosts. The synthetic route to the hosts is shown in Scheme I.[5,6] The reaction of triphenyltin chloride with a di-Grignard reagent gave an α,ω-bis(triphenylstannyl)alkane (**5**). Selective cleavage of one phenyl group from each tin atom by reaction with HCl or HBr was possible. Macrocyclic skeletons **6** were then produced in a subsequent reaction with a di-Grignard reagent. Repeating the sequence of selective cleavage and reaction with a di-Grignard reagent gave macrobicyclic skeletons **8**. Cleavage of the final phenyl group from each tin atom in **8** gave the Lewis acidic hosts **2** or **3**, depending upon the acid employed. Model compounds for complexation studies were produced by similar methods.

In the macrocyclization and macrobicyclization steps, oligomerization and polymerization reactions are possible. Although very high dilution reactions would be expected to lead to optimum yields of the desired products, there is a practical limitation on the dilution when one wishes to obtain gram quantities of products. We have found it convenient to add dilute THF solutions of the di-Grignard and the tin halide simultaneously to THF in a reaction vessel over the period of a few hours. Typically, our yields of desired products in the macrocyclization and macrobicyclization steps were 30–40% after purification by preparative reverse-phase chromatography and crystallization.

The selective cleavage of only one phenyl group from a polyphenyl-substituted tin atom is a key element in our syntheses. The resulting tin halides can only be purified by recrystallization, and the cleavage reaction must result in high conversions to monohalo tins with very little multiple phenyl cleavage. In order to accomplish this, we used standardized solutions of HCl or HBr in CH_2Cl_2. Approximately 90% of the required amount of acid solution was added to CH_2Cl_2 solutions of the substrates at −78 °C, and the solutions were allowed to warm to room temperature slowly. ^{13}C NMR spectra of the resulting mixtures were then obtained, and the relative amounts of trialkyl(aryl)tin halide and tetraalkyl(aryl)tin groups were determined by comparison of the characteristic α-carbon signals for each. The amount of acid necessary to complete the cleavage reaction was then calculated from the NMR results, and the cleavage reaction procedure was repeated. Typically, 70–90% yields of the halide products were obtained.

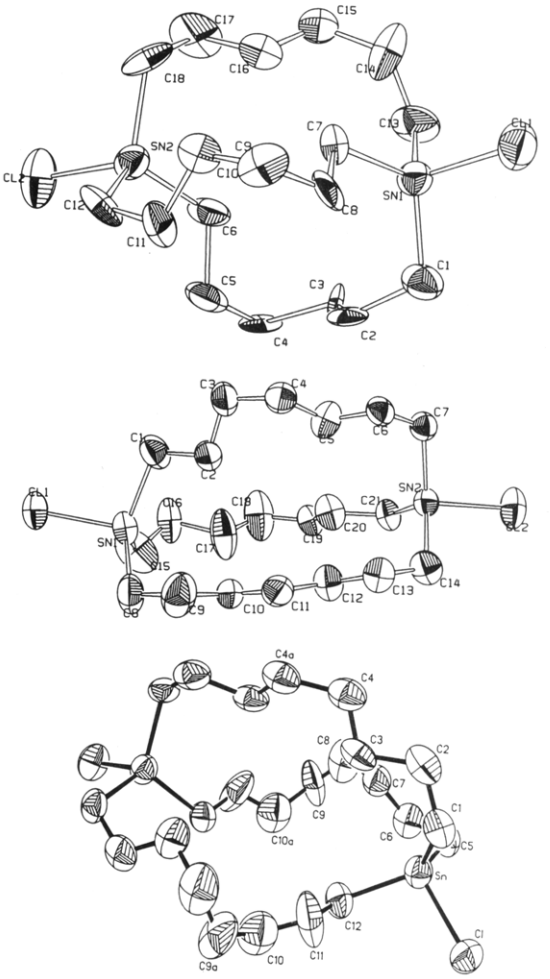
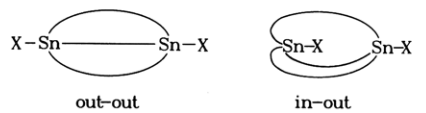


Figure 1. ORTEP drawings of hosts **2a** (top), **2b** (middle), and **2c** (bottom).

Structures of Hosts in Solution. The ^{119}Sn NMR chemical shifts for the free hosts in halogenated solvents were in the range δ 150–160 for chloride hosts **2** and δ 130–140 for bromide hosts **3**. For the short chain (C-6, C-7, C-8) chloride hosts **2a–c**, only one ^{119}Sn NMR signal was observed; conformational changes obviously were fast, and the hosts have structures with both chlorides outside of the macrobicyclic core. For **2a–c**, these "out–out" structures also exist in the solid state;[7] ORTEP drawings of these hosts are shown in Figure 1.



The ^{119}Sn NMR spectra of the C-10 chloride host **2d** and the C-12 host **2e** in halogenated solvents were more complex. These spectra contained one large signal and two smaller signals of equal intensity (see Figure 2). Appar-

(5) Azuma, Y.; Newcomb, M. *Organometallics* **1984**, *3*, 9–14.
(6) Newcomb, M.; Blanda, M. T.; Azuma, Y.; Delord, T. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1159–1160.

(7) X-ray results for **2a** and **2c** have been reported.[4] Results for **2b** and **3d** (Horner, J. H.; Squattrito, P. J.; Blanda, M. T., unpublished) will be submitted for publication.

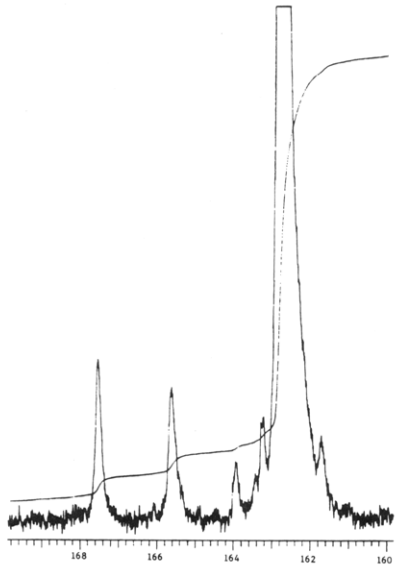


Figure 2. ^{119}Sn NMR spectrum of host **2d** in $CDCl_3$. The signals integrate in the ratio of 1:1:24.

ently, when the linking chains in the chloride hosts are longer than eight methylene units, the hosts can exist as a second low-energy stereoisomer, an in–out isomer which, in the absence of halide ion, exchanges only slowly on the NMR time scale with the out–out isomer. Because the tin atoms of the in–out isomer are not identical, the set of equally intense minor signals was readily assigned to this species. The minor signals were shown not to arise from chemical impurities by the addition of a small amount of chloride ion to the host solutions; the chloride ion catalyzed the isomerization between the out–out and in–out isomers as discussed below, and the ^{119}Sn spectra collapsed to a single signal.[8]

Although the exchange between the out–out and in–out isomers in **2d** and **2e** was slow on the NMR time scale in the absence of added chloride, the mixtures appeared to be in equilibrium as indicated from studies with added chloride. The two low-energy structures permit two modes of exchange of chloride from the host–chloride complex, dissociation of chloride from an out position to give the in–out isomer and dissociation of chloride from the cavity to give the out–out isomer, and these two processes occur at different rates. The relative populations of the in–out and out–out host isomers resulting from simulations of spectra of host–chloride mixtures for **2d** were similar to those measured directly for the free hosts.

For the bromide hosts **3**, the larger bromide apparently precluded the in–out isomer for the C-10 host **3d**. A single ^{119}Sn NMR signal was observed for this host as well as for the C-8 host **3c**. The out–out isomer for **3c** and **3d** was suggested as the predominant isomer from inspection of models. Host **3d** was also obtained as the out–out isomer in the solid state as determined by X-ray crystallography[7] (Figure 3).

The complex ^{119}Sn NMR spectrum of the C-12 bromide host **3e** suggested that at least two minor isomers were present in solution in the absence of added halide. One minor signal in the spectrum was broadened by an exchange process (as shown by variable temperature studies) that apparently equilibrated this signal with the major signal from **3e** or another minor signal coincident with the major signal, but a second minor signal in the spectrum

(8) This behavior is reminiscent of that of the protonated bicyclic amines; cf. Simmons, H. E.; Park, C. H. *J. Am. Chem. Soc.* **1968**, *90*, 2429–2431, 2431–2432.

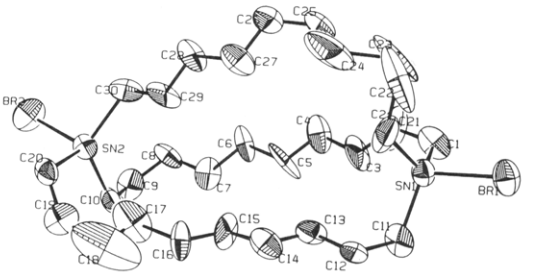


Figure 3. ORTEP drawing of host **3d**.

exhibited no line broadening due to exchange. As with the chloride hosts, addition of free bromide to the mixture resulted in a collapse of the ^{119}Sn NMR spectrum to one signal. One of the minor isomers of **3e** probably had the in–out structure. We are reluctant to assign an in–in structure to the other minor species because models suggest that this isomer is too strained to exist. It is possible that the second minor isomer was a variation of either the out–out or in–out structure that differed from the parent in the linking chain conformations, although the slow exchange on the NMR time scale indicates an unusually high activation energy for such conformational isomerism.

Depending on the polarity of the solvent and concentrations, simple trialkyltin halides can aggregate in solution by the formation of a Lewis acid–base interaction between the halide of one molecule and the tin of another.[9] However, there is no evidence that tributyltin chloride aggregates appreciably in $CDCl_3$, and our bicyclic hosts did not aggregate to any appreciable extent in the halogenated solvents we used. In forming a stannate complex with a donor, a trialkyltin halide expands from a tetrahedral structure to a trigonal-bipyramidal structure with the halide and donor at the apical positions.[10] This means that the binding sites of our smaller hosts with the out–out structure were directed into the host cavities and intermolecular association would not be possible. Intermolecular association would be possible for the in–out isomers of the larger hosts, but the similarity in the ^{119}Sn NMR chemical shifts for the in–out and out–out isomers showed that aggregates were not present because these chemical shifts are especially sensitive to the coordination of the tin atom.[2,3] In fact, as indicated by the ^{119}Sn chemical shifts, even self-association between the internal halide of the in–out isomer and the distant tin atom of the same host was not appreciable.

Preliminary Binding Studies. When tetrahexylammonium chloride was added to $CDCl_3$ solutions of tributyltin chloride at 20 °C, the ^{119}Sn NMR chemical of the single sharp line moved steadily upfield from δ 153 and asymptotically approached ca. δ –60 as the ratio of chloride to tin species increased. The signal at δ 153 in the absence of chloride arises from free Bu_3SnCl, and that at δ –60 is due to the stannate $(Bu_3SnCl_2)^-$. A similar trend was observed when tetrahexylammonium bromide was added to $CDCl_3$ solutions of tributyltin bromide; however, due to the small binding constant of Bu_3SnBr, the limiting chemical shift was not approached as rapidly. Free Bu_3SnBr resonated at δ 140.6, and the stannate $(Bu_3SnBr_2)^-$ was estimated to resonate at ca. δ –70.

(9) Davies, A. G.; Milledge, H. J.; Puxley, D. C.; Smith, P. J. *J. Chem. Soc. A* **1970**, 2862–2866. Smith, P. J.; Tupciauskas, A. P. *Annu. Rep. NMR Spectrosc.* **1978**, *8*, 291–370. Petrosyan, V. S. *Prog. NMR Spectroc.* **1977**, *11*, 115–148. Nadvornik, M.; Holecek, J.; Handlir, K.; Lycka, A. *J. Organomet. Chem.* **1984**, *275*, 43–51.

(10) Hanison, P. G.; Molloy, K.; Phillips, R. C.; Smith, P. J.; Crowe, A. J. *J. Organomet. Chem.* **1978**, *160*, 421–434. Nicholson, J. W. *Coord. Chem. Rev.* **1982**, *47*, 263–282.

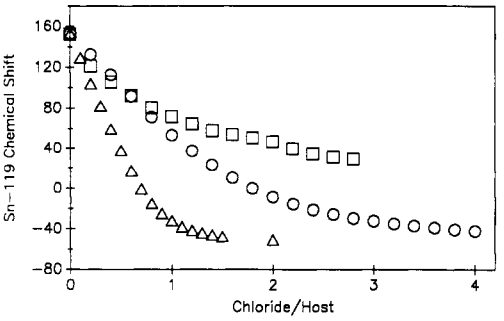


Figure 4. Titration plots of Bu_3SnCl in $CDCl_3$ (△), host **2d** in CH_2Cl_2 (□), and macrocycle **4** in $CDCl_3$ (○).

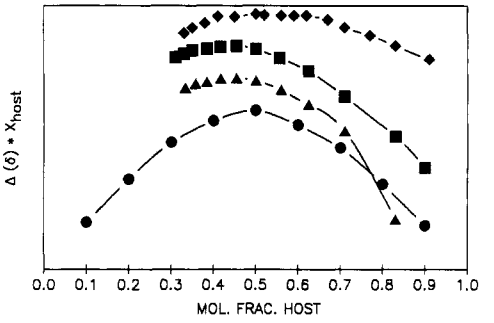


Figure 5. Job plots for Bu_3SnCl (●), **2e** (▲), **3d** (■), and **3e** (◆). The *Y* axes have been normalized.

Upfield chemical shifts in the ^{119}Sn NMR spectra of the C-7 through C-12 chloride hosts (**2b–e**) were observed in the presence of tetrahexylammonium chloride showing that these hosts bound chloride in solution. However, the ^{119}Sn NMR spectrum of the C-6 chloride host (**2a**) was unchanged even in the presence of a large excess of chloride at high concentration; this small host is not a Lewis acid for chloride although it has been shown to bind the smaller fluoride ion strongly.[3b] The three representatives in the bromide series of hosts (**3c–d**) bound bromide as evidenced by the upfield ^{119}Sn NMR shifts observed when tetrahexylammonium bromide was added to solutions of these species.

Stoichiometries of Host–Guest Complexes. Three methods were employed to determine the stoichiometries of the complexes formed between the hosts and halide ions. When the binding constants were large and exchange was fast, simple titration plots of the ^{119}Sn chemical shifts versus the ratio of guest to host indicated the stoichiometry of the complex. Job's method of continuous variation, adapted for NMR studies, could also be used over a broad range of binding constants when the dynamic exchange between free host and complex was fast on the NMR time scale. For the cases where exchange between free host and complex was slow on the NMR time scale, the stoichiometry of the complex was apparent from its ^{119}Sn chemical shift. For all of the bicyclic hosts except **2a** and **3c**, the host–guest stoichiometries were found to be 1:1; host **2a** does not bind chloride and host **3c** bound bromide too weakly to permit a direct determination of the stoichiometry of the complex.

The C-10 and C-12 chloride hosts (**2d,e**) and the chloride binding models Bu_3SnCl and macrocycle **4** exchanged chloride rapidly on the NMR time scale and bound chloride relatively strongly. The stoichiometries of the chloride complexes of these species were apparent from simple titration plots of δ_{obs} versus the chloride/host ratio (see Figure 4). Bu_3SnCl bound one chloride anion with the result that the ^{119}Sn NMR chemical shifts approached ca. δ −60 at high concentrations of chloride. The limiting value of δ_{obs} for hosts **2d** and **2e** in the presence of excess chloride, however, was only ca. δ 30. This represents about half of the upfield shift expected for a complex where each tin atom bound one chloride and is consistent with a 1:1 host–guest stoichiometry for the predominant complex. Unlike the case with the bicyclic hosts, the limiting chemical shift for the model macrocycle **4** in the presence of excess chloride was ca. δ −50, close to that observed for Bu_3SnCl. Thus, for the poorly organized macrocycle, a 1:2 host–guest stoichiometry was obtained. Previously, we found that macrocyclic hosts **1** also complexed chloride with 1:2 host–guest stoichiometry.[2]

Job's method of continuous variation can also be applied to NMR results when the species are in rapid exchange.[11] In principle, this method for determining complex stoichiometry has an advantage over titration curves in that the binding constants need not be large; thus, the ^{119}Sn NMR chemical shifts at high concentrations of halide did not need to approach a limiting value from which one could deduce the ratio of halide to tin in the complex. One should note that, in practice, complexes with large formation constants result in sharp breaks in the Job plot whereas those with small formation constants give much smoother curves, the maxima of which can be difficult to determine.

Job plots[11] of $\Delta\delta X_H$ versus X_H for the C-12 chloride host (**2e**) complexing chloride and the C-10 and C-12 bromide hosts (**3d,e**) complexing bromide are shown in Figure 5. Also shown in the figure is the data for Bu_3SnCl binding chloride. Because the *Y* axes in these plots have been normalized in Figure 5, the values of $\Delta\delta$, which are related to the formation constants of the complex, are not apparent. Both of the bromide hosts bound bromide weakly resulting in small $\Delta\delta$ values and smooth curves in the Job plots. The maximum in the curve for Bu_3SnCl is at X_H = 0.5 as expected for a 1:1 complex. The maxima in the

(11) In the method of continuous variation,[12] one mixes equal concentration solutions of two species, A and B, in varying ratios and measures a property characteristic of the complex formed. Because the total concentration, [A] + [B], is constant in all solutions, the concentration of an AB complex will reach a maximum value when [A] = [B] and the concentration of an A_2B complex will reach a maximum value when [A] = 2[B], etc. A plot of concentration of complex as a function of the mole fraction of A in solution is constructed; the maximum amount of complex is found at the point corresponding to the mole-fraction of A in the complex. With rapidly exchanging free host and complex studied by ^{119}Sn NMR spectroscopy, we are interested in the number of halide ions bound by the host in the complex. Self-association of the hosts is not important, so the only tin-containing species present are the host (H) and the complex (C). The following derivation applies where C_i is the concentration of species i, $C_{H(0)}$ is the initial concentration of host, δ_i is the chemical shift of species i, and δ_{obs} is the observed chemical shift.

$$C_H = C_{H(0)} - C_C$$

$$\delta_{obs} = (\delta_H C_H + \delta_C C_C)/C_{H(0)}$$

$$\delta_{obs} = (\delta_H C_{H(0)} - \delta_H C_C + \delta_C C_C)/C_{H(0)}$$

$$\delta_{obs} = C_C(\delta_C - \delta_H)/C_{H(0)} + \delta_H C_{H(0)}/C_{H(0)}$$

$$\delta_{obs} - \delta_H = C_C(\delta_C - \delta_H)/C_{H(0)}$$

$$C_C = (\delta_{obs} - \delta_H)C_{H(0)}/(\delta_C - \delta_H)$$

Because $(\delta_C - \delta_H)$ is a constant, the concentration of the complex is proportional to $\Delta\delta$ (the observed chemical shift minus the chemical shift of the free host) times the initial concentration of host. An appropriate Job plot for our situation would be $\Delta\delta$ times the initial concentration of host as a function of the mole fraction of host (X_H). However, because of the constraint of the method of continuous variation that the sum of the host and guest concentrations are equal in all measurements, $C_{H(0)}$ in the final expression above can be replaced by the X_H in the host–guest mixture. Thus, we used plots of $\Delta\delta X_H$ as a function of the X_H.

(12) Connors, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; Wiley-Interscience: New York, 1987; pp 24–28.

curves for host **2e** binding chloride and host **3d** binding bromide occurred at the experimental points for $X_H = 0.45$, and each is greater than the corresponding experimental value at $X_H = 0.50$ by less than 2%; for both of these hosts, 1:1 complexes are indicated.

The data for the C-12 bromide host **3e** binding bromide was difficult to interpret. The total $\Delta\delta$ observed in the study was only 3.1 ppm, and the maximum in the Job plot was highly dependent on the value chosen for δ_0 for the free host. As noted above, the ^{119}Sn NMR spectrum of **3e** in the absence of added bromide contained a major signal and two (downfield) minor signals. When the δ_0 value for the Job plot was taken to be the chemical shift of the major signal, the plot had a maximum at the experimental point for $X_H = 0.42$. However, when the δ_0 value was taken to be weighted average of all of the signals in the spectrum of the free host, the maximum of the plot occurred at $X_H = 0.50$, consistent with a 1:1 complex. We believe the latter approach is more reasonable because the free host appeared to be an equilibrium mixture of isomers; the latter plot is shown in Figure 5.

The stoichiometries of the complexes were obvious when the free host and complex exchanged slowly on the NMR time scale because of the large chemical shift difference between stannane and stannate tin atoms. As noted, the stannate $(Bu_3SnCl_2)^-$ resonates about 210 ppm upfield from stannane Bu_3SnCl. $CDCl_3$ solutions of the C-8 chloride host **2c** and tetrahexylammonium chloride at low temperatures contained signals from the free host at δ 150 and the complex at δ 30. The upfield shift for the complex is only about half of that expected if both tin atoms were "stannate" tins (i.e. a 1:2 complex), and it was apparent that this chemical shift resulted from either a rapid exchange of one chloride between the two tin atoms of the host in a "stannane–stannate" structure or from a "bis-hemistannate" structure in which the guest chloride was shared by both tin atoms.[13] In either case, the complex between **2c** and chloride would have 1:1 stoichiometry. At low temperatures, the C-7 and C-10 chloride hosts (**2b** and **2d**) also exchange with their chloride complexes slowly; for each, the signal for the complex at ca. δ 30 shows that it has a 1:1 stoichiometry.

The stoichiometry for the C-8 bromide host **3c** binding bromide could not be determined directly. This host binds bromide only weakly, and the chemical shift changes observed when bromide was added were too small to permit a Job plot analysis. Further, the free host and complex were in fast exchange on the NMR time scale which prevented a direct measurement of the chemical shift of the complex. Based on the results with the other bicyclic hosts, it is reasonable to assume that the complex between **3c** and bromide has 1:1 stoichiometry.

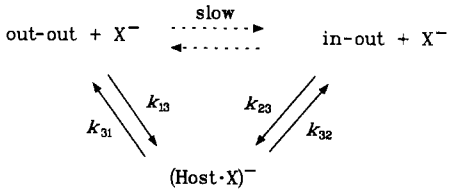
Rate and Equilibrium Constants for Anion Binding. For each of the chloride bicyclic hosts **2b–e** in the presence of added chloride salt, it was possible to observe temperature-dependent dynamic phenomena in ^{119}Sn NMR studies. Similarly, the C-12 bromide host **3e** in the presence of added bromide salt displayed temperature-dependent dynamic behavior in NMR studies. The dynamic processes mixed the signals of the free hosts at ca. δ 150 with those of their 1:1 complexes with halide at ca. δ 30. Simulation of the spectra provided rate constants for the formation and dissociation of the complexes. Equilibrium constants for formation of the complexes were calculated from the rate constants, by integration of the distinct signals in spectra in the low-exchange limit or by

(13) Subsequent low-temperature NMR studies[4] have shown that the "stannane–stannate" structure exists for this complex.

Scheme II

$$\text{Host} + X^- \underset{k_d}{\overset{k_f}{\rightleftharpoons}} (\text{Host}\cdot X)^-$$

Scheme III



estimating the populations of free host and complex in spectra in the fast-exchange limit. All equilibrium constants were fit to the simple model in eq 1 and are expressed by eq 2.

$$\text{host} + \text{guest} \rightleftarrows \text{complex} \quad (1)$$

$$K_{eq} = [\text{complex}]/[\text{host}][\text{guest}] \quad (2)$$

In the simulations of ^{119}Sn NMR spectra of the smaller chloride hosts **2b** and **2c**, a simple two-site exchange model was used (Scheme II). The chemical shifts for the free host and the complex were known from the lower temperature spectra. We have found that another dynamic process can be observed for the **2c**–chloride complex at temperatures even lower than those studied here; it is the "chloride jump" from one tin atom to the other within the complex.[4] This "chloride jump" is the major contributor to T_2 for the complex at very low temperatures, but it is not important for the exchange process between free host and complex in the temperature range of interest for this study and can be assumed to result in a fixed contribution to the T_2 of the complex, which is now dominated by the free host–complex exchange. Similar "halide jumps" might occur within other complexes, but these also should be fast, and their effects on T_2 of the complex should be unimportant in comparison to that of the bulk exchange processes.

For the larger chloride hosts **2d** and **2e**, two isomers exist for the free host, the predominant out–out isomer and the minor in–out isomer. In the simulations of spectra of **2d**, we used a three-site exchange model (Scheme III). A multisite model was required because the rate constants for binding and dissociation for the in–out isomer–complex were appreciably faster than those for the out–out isomer–complex. In principle, because the in–out isomer should have two distinct tin signals, a four-site exchange model should be applied in the simulations. However, because the rate constants for exchange of both positions in the in–out isomer with the complex must be identical and because the chemical shifts for the two tin atoms of the free in–out isomer differed at most by only a few ppm from one another and from the signal for the out–out isomer whereas they differed by about 120 ppm from the signal for the complex, a three-site model was adequate; the assignment of the chemical shifts for the in–out isomer was relatively unimportant. In fact, as is apparent in the results discussed below, weighing errors that resulted in errors in the estimates for free halide in the solutions clearly were the major sources of deviations in our kinetic determinations.

For the model compounds Bu_3SnCl and Bu_3SnBr, exchange with halide was fast on the NMR time scale at all temperatures we studied, and it was not possible to obtain rate constants for binding. Equilibrium constants for binding were obtained by the use of the double-reciprocal

Table I. Equilibrium Constants for Complexation of Halides by Tributyltin Halides[a]

tin species	halide	solvent	temp, °C	K_{eq}, M^{-1}
Bu_3SnCl	chloride	$CDCl_3$	−50	270
			−20	80
			20	17
			50	7
		CH_2Cl_2[b]	20	500
Bu_3SnBr	bromide	$CDCl_3$	20	3.3

[a] From spectra of solutions of tributyltin halide plus tetrahexylammonium halide; equilibrium constants were solved by the Hildebrand–Benesi method. [b] The solvent contained 10% benzene-d_6.

(Hildebrand–Benesi) method. This method was also used to determine reliable equilibrium constants at 20 °C for most of the hosts **2** and **3** binding halides.

The double-reciprocal method can be applied in NMR studies when the species are in fast exchange.[14] Because we were measuring the chemical shift of the tin-containing species, it was necessary to work at reasonably high concentrations of hosts, and the initial concentration of guest halide was often a poor approximation for the concentration of free halide. Therefore, a computer program was written that solved the double-reciprocal function for K_{eq} by a least-squares fit, used the value for K_{eq} to recalculate the concentration of halide at each point, iterated to give a new value for K_{eq}, etc. Even with a poor initial estimate for K_{eq}, the program converged within 5–10 iterations.

One of the initial input variables for the double-reciprocal program[14] was the value for δ_H. When the binding constants were small, slight changes in the value chosen for δ_H resulted in dramatic changes in the value of K_{eq}. Given the fact that some of the hosts existed as two isomers, the estimation of δ_H often was not trivial. In order to minimize errors resulting from the selection of δ_H, we took the following approach. The double-reciprocal method solved for δ_C as well as K_{eq}, and the value for δ_C also varied dramatically with small changes in δ_H when the binding constant was small. We used the calculated value for δ_C as a check on the selected value for δ_H; specifically for binding by bicyclic hosts, we required the input value of δ_H to be such that the calculated value for δ_C fell within the range 20–30 ppm.

Details of the measurements of rate and equilibrium constants for the various species studied are given below. Rate constants for dissociation and formation of complexes and equilibrium constants for binding are given in the tables that follow. We have included error limits for the rate constants when more than one solution was studied at a given temperature. The error limits on the rate constants for formation of the complex are larger than those for dissociation due to the fact that the simulations yield first-order (and pseudo-first-order) rate constants for exchange. Dissociation of the complex is a first-order process, but formation of the complex is a second-order process, and the pseudo-first-order rate constants for formation must be converted to second order rate constants by division by the concentration of free halide in the solutions.

(14) In the NMR adaptation of the Hildebrand–Benesi method,[15] the appropriate function is

$$(\delta_{obs} - \delta_H)^{-1} = (\delta_C - \delta_H)^{-1} + (K_{eq}(\delta_C - \delta_H))^{-1}[G]^{-1}$$

where δ_{obs} is the observed chemical shift, δ_H is the chemical shift of the free host, δ_C is the chemical shift of the complex, [G] is the concentration of the free halide, and K_{eq} is the formation constant for the complex. One may plot $(\delta_{obs} - \delta_H)^{-1}$ versus $[G]^{-1}$ to obtain $(\delta_C - \delta_H)^{-1}$ as the intercept and $(K_{eq}(\delta_C - \delta_H))^{-1}$ as the slope. From these values both δ_C and K_{eq} can be calculated.

(15) Reference 12, pp 189–200.

Table II. Rate of Equilibrium Constants for the 2b–Chloride Complex in $CDCl_3$[a]

temp, °C	k_d, s^{-1}	k_f, M^{-1} s^{-1}	K_{eq},[b] M^{-1}
−60	6.5×10^2	4.9×10^2	0.76
−50	1.6×10^3	8.1×10^2	0.52
−40	4.4×10^3	1.6×10^3	0.37
20	2.1×10^5	6.1×10^4	0.29
35	4.0×10^5	8.1×10^4	0.20
50	7.8×10^5	1.0×10^5	0.13

[a] Spectra of a $CDCl_3$ solution containing 15 equiv of tetrahexylammonium chloride per host were obtained. The spectra were simulated with a two-site model; the rate constants are believed to be accurate to about ±10%. [b] Equilibrium constants were measured directly from spectra by integration of distinct signals at −60, −50, and −40 °C and by the position of the single line in the 35 and 50 °C spectra. The value at 20 °C is from the Hildebrand–Benesi method.

This division introduced a substantial error because we did not have a direct method for measuring free halide concentrations, and we were required to calculate the values from the amounts of each material initially weighed, the percentage of complex present in the solutions, and the volumes of the solutions.

Bu_3SnCl. Solutions of Bu_3SnCl and tetrahexylammonium chloride in $CDCl_3$ were studied at 50, 20, −20, and −50 °C. Fast exchange was observed in all cases. Given that the signals for the complexed and uncomplexed species were separated by 210 ppm (30 000 Hz in a 9.4 T field), the exchange rate exceeded 1×10^7 s^{-1} at −50 °C. The Hildebrand–Benesi method gave K_{eq} values that are given in Table I. The value for K_{eq} increased dramatically as the temperature was lowered. A series or solutions of Bu_3SnCl and tetrahexylammonium chloride in CH_2Cl_2 also were studied at 20 °C by the above method.

Bu_3SnBr. Solutions of Bu_3SnBr and tetrahexylammonium bromide in $CDCl_3$ were studied at 20 °C. Fast exchange was observed. The value for K_{eq} determined by the Hildebrand–Benesi method was 3.3 M^{-1}. At 20 °C, K_{eq} for Bu_3SnBr binding bromide is about 20% of that for Bu_3SnCl binding chloride; this reflects the reduced Lewis acidity of trialkyltin bromides in comparison to trialkyltin chlorides.

Host 2a. The ^{119}Sn NMR spectrum of **2a** in $CDCl_3$ (0.08 M) at 30 °C contained a sharp peak at δ 148.5. Spectra at 30 and −50 °C were unaltered in the presence of 0.41 M tetrahexylammonium chloride. With the assumptions that the spectrum would be in the fast exchange limit at 30 °C and that the complex could resonate at ca. δ 30, the binding constant was less than 0.003 M^{-1}. With the assumption that the spectrum would be in the slow exchange limit at −50 °C, the binding constant was less than 0.01 M^{-1}.

Host 2b. A titration experiment was conducted in which aliquots of a 0.89 M solution of tetrahexylammonium chloride in $CDCl_3$ were added to a 0.1 M $CDCl_3$ solution of the C-7 host **2b** at 20 °C. Spectra were in the fast exchange limit at this temperature, and the signal originally at δ 148.3 shifted upfield only slightly with each addition. Ultimately, the signal was shifted 10 ppm in the presence of a 15-fold excess of chloride. The Hildebrand–Benesi treatment for solutions containing 1, 5, 10, and 15 equiv of chloride per host gave $K_{eq} = 0.29$ M^{-1} at 20 °C.

Variable-temperature studies (60 to −50 °C) were performed on a $CDCl_3$ solution that was 0.033 M in **2b** and 0.5 M in chloride. The system was clearly in the fast exchange limit above 0 °C. Coalescence occurred between 0 and −20 °C, but the actual coalescence temperature could not be observed due to the small amount of complex

Table III. Rate and Equilibrium Constants for the 2c–Chloride Complex[a]

temp, °C	solvent	spectra[b]	k_d, s^{-1}	k_f, M^{-1} s^{-1}	K_{eq}, M^{-1}
−50	$CDCl_3$	4	$(2.0 \pm 0.8) \times 10^2$	$(9 \pm 4) \times 10^3$	45
−40		4	$(3.6 \pm 0.4) \times 10^2$	$(2 \pm 1) \times 10^4$	56
−30		4	$(8.4 \pm 0.5) \times 10^2$	$(3.7 \pm 0.8) \times 10^4$	44
−20		3	$(2.0 \pm 0.3) \times 10^3$	$(7 \pm 2) \times 10^4$	35
−10		1	4×10^3	1×10^5	25
−10	$CDCl_2CDCl_2$	4	$(1.8 \pm 0.4) \times 10^3$	$(2.5 \pm 0.5) \times 10^4$	14 ± 1
30		4	$(2.5 \pm 0.3) \times 10^4$	$(2 \pm 1) \times 10^5$	7.0 ± 1.0
50		5	$(1.0 \pm 0.1) \times 10^5$	$(5.1 \pm 0.6) \times 10^5$	4.9 ± 0.5
70		5	$(2.4 \pm 0.3) \times 10^5$	$(8.4 \pm 0.8) \times 10^5$	3.4 ± 0.5
90		5	$(5.7 \pm 0.3) \times 10^5$	$(1.3 \pm 0.1) \times 10^6$	2.6 ± 0.2

[a] Results from line shape analyses using a two-site model. Errors, when given, are one standard deviation. [b] Number of spectra recorded; the spectra run in $CDCl_2CDCl_2$ contained 0.5–6.0 equiv of tetrahexylammonium chloride per host, while those run in $CDCl_3$ contained 1 equiv of chloride per host.

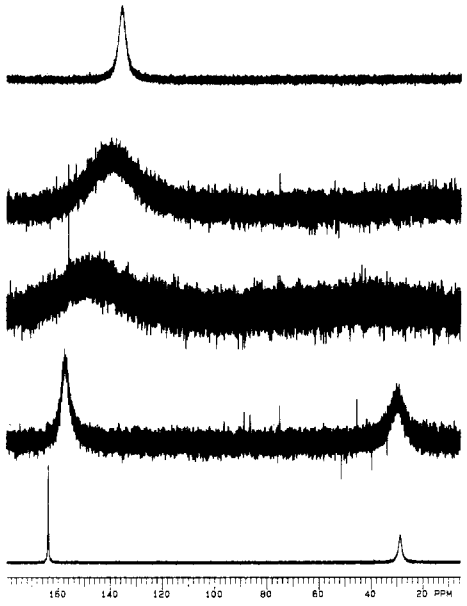


Figure 6. ^{119}Sn NMR spectra of host **2c** in the presence of chloride. From the top, the temperatures are 90, 50, 30, −10, and −50 °C.

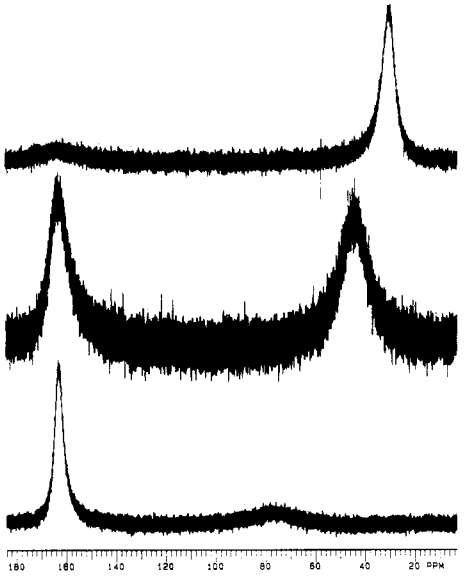


Figure 7. ^{119}Sn NMR spectra of host **2d** at −50 °C in the presence of 1.0 (top), 0.5 (middle), and 0.2 (bottom) equiv of chloride.

present. At and below −30 °C, signals for the free host (δ 155) and the complex (δ 30) were observed. Simulations of spectra in the fast exchange and slow exchange regions were possible; the resulting values are given in Table II. The chemical shift of the free host observed over the range −60 to 20 °C was temperature dependent ($\Delta\delta$ = 0.16 ppm/°C); the values for δ of the free host used in the simulations at high temperatures were extrapolated from those measured directly at low temperature.

Host 2c. The binding of the C-8 bicycle **2c** with chloride was studied over a 140 °C temperature range using $CDCl_3$ and $CDCl_2CDCl_2$ solutions. At 90 °C, a single tin resonance was observed. Cooling caused the line to broaden until coalescence was reached between 30 and 50 °C. At 30 °C two very broad signals were observed near δ 155 and 30. Ultimately, relative sharp lines were obtained at −50 °C. Representative spectra are shown in Figure 6. Simulations of the spectra over the entire temperature range studied were possible; the results are given in Table III.

Host 2d. Studies of the C-10 bicycle were conducted over the temperature range 50 to −50 °C with $CDCl_3$ solutions. In the absence of added chloride, two isomers of the host were observed; the major (out–out) isomer gave a single peak, and the minor (in–out) isomer gave two equal intensity peaks (see Figure 2). The chemical shift from the out–out isomer varied steadily with temperature from δ 163 at −50 °C to δ 152 at 20 °C. The two lines from the in–out isomer were several ppm downfield from the major signal in the spectra, and these lines shifted upfield as the temperature was increased in a manner that paralleled that of the major signal.

Binding studies were conducted with solutions that contained 0.2, 0.5, and 1.0 equiv of chloride per host. A single resonance was observed at high temperatures. This peak broadened on cooling, and coalescence was reached near −20 °C. Spectra recorded at lower temperatures contained two signals; however, the upfield peak varied in chemical shift as a function of the concentration of chloride (Figure 7). This behavior indicated a second dynamic phenomenon that was still fast on the NMR time scale at −50 °C. The upfield signal resulted from time averaging of the signals of the complex and the in–out isomer of the free host, and it shifted further upfield at higher concentrations of chloride due to the increased concentration of the complex at the expense of this minor isomer.

The spectra were simulated with the three-site model of Scheme III. The δ value for the complex was estimated to be 21 ppm based on a −50 °C spectrum of a mixture that contained 4 equiv of chloride per host and by analogy to the chemical shifts observed for other host **2**–chloride complexes; we believe this value is unlikely to be in error by more than a few ppm. At temperatures below coalescence, the values for k_{31} and k_{32} could be determined directly from the three-site model because integration of the two lines gave the ratio (site 1):(site 2 + site 3) and the chemical shift of the upfield signal gave the ratio (site 2):(site 3). At temperatures above coalescence, however,

Table IV. Rate and Equilibrium Constants for the 2d–Chloride Complex in $CDCl_3$[a]

temp, °C	k_{31},[b] s^{-1}	k_{32},[c] s^{-1}	k_{13},[d] M^{-1} s^{-1}	K_{eq},[e] M^{-1}	host ratio[f]
-50	$(5.2 \pm 2.1) \times 10^3$	$(2.4 \pm 0.7) \times 10^5$	$(5 \pm 2) \times 10^5$	95 ± 25	6.4 ± 0.2
-40	$(9.3 \pm 2.4) \times 10^3$	ca. 3×10^5	$(7 \pm 1) \times 10^5$	85 ± 15	5.3 ± 1.1
-30	$(2.1 \pm 0.4) \times 10^4$	$(2–5) \times 10^5$	$(8 \pm 2) \times 10^5$	40 ± 20	5.0 ± 0.5
-20	$(6.0 \pm 0.6) \times 10^4$	$>1 \times 10^5$	$(1.0 \pm 0.7) \times 10^6$	26 ± 20	
0	$(1.6 \pm 0.4) \times 10^5$		$(2.6 \pm 0.6) \times 10^6$	22 ± 15	
20	$(3.9 \pm 1.2) \times 10^5$		$(3.5 \pm 0.5) \times 10^6$	8 ± 2	
50	$(1.1 \pm 0.1) \times 10^6$		$(7.5 \pm 0.8) \times 10^6$	5.6 ± 0.5	

[a] Results from line shape analyses using a three-site model below 0 °C and a two-site model for higher temperatures for spectra of $CDCl_3$ solutions containing 0.2, 0.5, and 1.0 equiv of tetrahexylammonium chloride per host; errors are one standard deviation. [b] Rate constant for dissociation from the cavity of the complex to give the out–out isomer. [c] Rate constant for dissociation from the end of the complex to give the in–out isomer. [d] Rate constant for complexation of chloride by the out–out isomer. [e] Equilibrium constant for binding chloride in the cavity. [f] Ratio of out–out isomer to in–out isomer of free host.

only the ratio of free to complexed species could be measured from the chemical shift of the one signal. Because the relative populations of the two isomers of free host varied little between -50 and -20 °C, we assumed that they would not vary greatly at higher temperatures; thus, the in–out isomer population was taken to be 20% that of the out–out isomer for the high temperature simulations. Changes in the value for the ratio of the out–out to in–out isomers of free host at the higher temperatures had only a minor effect on the calculated rate constants for binding of the out–out isomer.

Table IV contains the results from the simulations. Variations in the kinetic values obtained from different solutions at a given temperature reached a factor of 2.2 in some simulations. These differences probably resulted from errors in the estimate of free chloride in each solution. As would be expected, the variations were smaller at higher temperatures where the equilibrium constants are smaller; because the amounts of free chloride were greater at the higher temperatures, a constant error in total chloride introduced as a weighing error resulted in a smaller percentage error. We were able to determine that the initial assignment of δ for the complex was not the origin of the variations in the kinetic values by changing this δ value in the simulations.

Host 2e. A series of solutions of the C-12 host **2e** and tetrahexylammonium chloride in $CDCl_3$ were studied at 20 °C. Fast exchange was observed. Treatment of the data by the Hildebrand–Benesi method gave a binding constant of 6 M^{-1}.

Studies with the C-12 host in CH_2Cl_2 were conducted over the temperature range 20 to -60 °C. At temperatures below -60 °C, crystals formed in the samples. Spectra of samples containing 0.2, 0.5, and 1.0 equiv of chloride per host were obtained. A single peak was observed at high temperatures. Coalescence was reached at -40 °C, and the spectra at -60 °C were in slow exchange although the signals at this temperature were very broad. As with host **2d**, the chemical shift of the upfield signal from the complex was found to be dependent on chloride concentration, indicating a second dynamic process and the presence of two isomers of the host. For example, the upfield signal at -60 °C in the sample containing 0.5 equiv of chloride was at δ 38 whereas that from the sample containing 1.0 equiv of chloride was at δ 28. Another series of studies was performed with one solution of **2e** and tetrahexylammonium chloride in $CDCl_3$ at 20, -20, and -50 °C.

The three-site exchange model was used to simulate the spectrum at -60 °C containing 0.5 equiv of chloride in CH_2Cl_2, and this model could have been applied for all of the simulations. However, because the population of the in–out isomer was definitely less than 20% that of the out–out isomer and probably only 10% that of the out–out isomer as judged from ^{119}Sn and ^{13}C NMR spectra of the free host at 20 °C and from the -60 °C spectra in the presence of chloride, we ignored the minor isomer and applied the two-site model for all other simulations. The δ value for the complex used in the simulations was again 21 ppm. The results are given in Table V.

Table V. Rate and Equilibrium Constants for the 2e–Chloride Complex[a]

temp, °C	solvent	k_{31},[b] s^{-1}	k_{13},[b] M^{-1} s^{-1}	K_{eq},[c] M^{-1}
-60	CH_2Cl_2[d]	$(2.7 \pm 1.3) \times 10^4$	*e*	large
-40		$(7.8 \pm 0.3) \times 10^4$	*e*	large
-20		$(2.0 \pm 0.2) \times 10^5$	$(2.2 \pm 0.2) \times 10^7$	115 ± 20
0		$(4.7 \pm 0.4) \times 10^5$	$(2.6 \pm 0.1) \times 10^7$	56 ± 2
20		$(9.7 \pm 1.5) \times 10^5$	$(3.4 \pm 0.2) \times 10^7$	34 ± 6
-50	$CDCl_3$	$(5–10) \times 10^4$	*f*	
-20		3×10^5	2×10^6	7
20		2.5×10^6	1.0×10^7	4

[a] Results from line shape analyses using a two-site model. Spectra of two or three solutions in CH_2Cl_2 were studied with tetrahexylammonium chloride to host ratios of 0.2 to 1.0; errors are one standard deviation. Spectra of one solution in $CDCl_3$ with a chloride to host ratio of 0.5. [b] Rate constants for dissociation and association of chloride equilibrating the complex with the out–out isomer. [c] Equilibrium constant for binding chloride within the cavity. [d] The solvent contained 10% benzene-d_6. [e] The concentration of free chloride at these temperates was too small to permit calculations of k_{13}. [f] This spectrum was near coalescence, and a wide range of kinetic values and populations in the simulations gave comparable fits.

Host 3c. Due to very weak binding of bromide by the C-8 host, a Job plot analysis was not possible. Five solutions of **3c** and tetrahexylammonium bromide in $CDCl_3$ were prepared; the bromide to host ratios ranged from 40:1 to 100:1. ^{119}Sn NMR spectra recorded at 20 °C were in fast exchange. Qualitatively, the weak binding was evidenced by the fact that the upfield shift seen in the sample containing a 100-fold excess of bromide (at 0.4 M concentration) was only 7 ppm, representing about 6% complexation. Analysis of the results by the Hildebrand–Benesi method gave a binding constant at 20 °C of 0.3 M^{-1}.

In the analysis of the binding constant for **3c**, the selection of δ_H was critical. As discussed above, we chose values that resulted in the correct calculated δ_C for a 1:1 complex of host and bromide;[14] for **3c** such stoichiometry is assumed. Because of the small binding constants, the amounts of free host were substantially greater than the amounts of complex in each solution, and we must caution that the results thus lie in the region of high uncertainty as defined by Deranleau.[16] Nevertheless, our knowledge of δ_C, which is equivalent to knowing ϵ in an absorbance study, reduces the unknowns in the Hildebrand–Benesi method to one and substantially increases the reliability of our measurements.

(16) Deranleau, D. A. *J. Am. Chem. Soc.* **1969**, *91*, 4044–4049.

Table VI. Rate and Equilibrium Constants for the 3e–Bromide Complex in $CDCl_3$[a]

temp, °C	k_d,[b] s^{-1}	k_f,[c] M^{-1} s^{-1}	K_{eq},[d] M^{-1}
−50	2.9×10^5	7.3×10^5	2.5
25	4.3×10^6	3.1×10^6	0.72
50	7.1×10^6	4.1×10^6	0.58

[a] Simulations using a two-site model of spectra of a solution in $CDCl_3$ containing 16 equiv of tetrahexylammonium bromide to host. [b] Rate constant for dissociation of bromide from the cavity to give the out–out isomer; the estimated accuracy is ±10%. [c] Rate constant for binding within the cavity from the out–out isomer; the estimated accuracy is ±25%. [d] Equilibrium constant for binding chloride within the cavity.

Host 3d. NMR spectra of eight solutions of the C-10 host **3d** and tetrahexylammonium bromide in $CDCl_3$ were obtained at 20 °C. The bromide to host ratio varied from 2:1 to 32:1. All spectra were in fast exchange. Analysis of the results by the Hildebrand–Benesi method gave a binding constant at 20 °C of 1.4 M^{-1}.

Host 3e. NMR spectra of five solutions of the C-12 host **3e** and bromide in $CDCl_3$ were obtained at 20 °C. The bromide to host ratio ranged from 2:1 to 16:1. Analysis of the results by the Hildebrand–Benesi method gave a binding constant at 20 °C of 0.7 M^{-1}. Temperature-dependent dynamic behavior was apparent in spectra of solutions of **3e** and bromide. Spectra recorded at −50, 25, and 50 °C contained a broad signal that was simulated with the two-site model using a value of δ 28 for the complex. The results are given in Table VI.

Size-Selective Binding of Halides. Arrhenius functions for the dissociation of halide from the cavity of the complexes and binding of halide by the out–out isomers were solved from the kinetic values and are collected in Table VII, which also contains the rate constants at 20 °C calculated from these functions. The limited data for **2e** in $CDCl_3$ and the high uncertainty in the kinetic values at −20 °C resulted in an Arrhenius function that is only very approximate. Table VIII contains the equilibrium constants at 20 °C for binding guest halide within the cavity of the various hosts. The values of K_{eq} in Table VIII result from direct determinations at 20 °C by the Hildebrand–Benesi method using several solutions of host and guest or from division of the calculated rate constants at 20 °C given in Table VII.

The binding constants in Table VIII show size-selective binding between halides and the macrobicyclic hosts with the maximum binding of chloride occurring with the C-8 host **2c** and the maximum binding of bromide occurring with the C-10 host **3d**. It would appear that the fit of the anion into the bicyclic hosts' cavity is an important factor in the overall stability of the complex. This conclusion might sound trivial given the vast amount of data available correlating cation binding strengths with the cavity size of cation binding agents like crown ethers and cryptands; however, at the outset of our studies, it was not apparent that we would find this type of behavior because the crystal diameters of chloride and bromide are quite similar (3.6 and 3.9 Å, respectively).[17]

Because the guest anions are encrypted within the cavities of the hosts, there is a substantial decrease in the binding constant when the cavity becomes too small to accommodate the guest. In the case of the C-6 host **2a**, the cavity is so small that the compound is not a Lewis acid for any donor we have studied thus far except the small fluoride ion.[3b] The effect of an oversized cavity is much smaller, however, and only slight decreases in binding are seen for the hosts that provide cavities larger than that of the best fit.

The effect of the bicyclic hosts' structures on the kinetics of the binding process were quite dramatic. The tributyltin chloride complex with chloride dissociates in $CDCl_3$ with a rate constant greater than 1×10^7 s^{-1} at −60 °C, representing a free energy of activation of less than 5.5 kcal/mol. Chloride dissociation from within the cavity of a bicyclic host is substantially slower with free energies of activation at comparable temperatures as high as 10.5 kcal/mol. It is likely that dissociation from within the complex is slowed by an entropic effect involving organization of the linking chains in a manner that permits the exit of the halide guest. Such an effect is suggested by the behavior of the C-10 host **2d** in $CDCl_3$. For this system, the in–out isomer is 0.8 kcal/mol less stable than the out–out isomer at −50 °C, but, at this temperature, dissociation of chloride from the end of the complex to give the in–out isomer ($\Delta G^{\ddagger}$ = 7.4 kcal/mol) is about 500 times faster than dissociation of chloride from the cavity to give the more stable out–out isomer ($\Delta G^{\ddagger}$ = 9.1 kcal/mol).

Inspection of the kinetic values in Table VII reveals a monotonic increase in the rate constants for formation of the complexes with chloride in solvent $CDCl_3$. This trend results mainly from decreases in the activation energies as the chains become longer, and entropic demands, as reflected in the log A values, are relatively constant. No such smooth change in the rate constants for dissociation is apparent. Indeed, the selectivity for binding chloride in $CDCl_3$ is dominated by the erratic changes in the rate constants for dissociation which appear to be almost equally dependent on the activation energies and the entropic terms.

The fact that the binding constants for the oversized hosts are reduced only slightly from the maximum value suggests that there is not a dramatic difference in the mode of halide binding between the best fit host and the larger analogs. This feature, coupled with the observation that the best fit bicyclic hosts do not bind halide more strongly than the simple trialkyltin halides, suggests that the halide in the cavity of the hosts is held only by one tin atom and not bound simultaneously by the two Lewis acidic tin atoms. Such binding has been demonstrated experimentally for the C-8 host **2c** binding chloride.[4] Specifically, in the solid state, the **2c**–chloride complex is unsymmetrical with the guest bound to only one tin atom, and very low temperature ^{119}Sn NMR spectra of the **2c**–chloride complex show significant line broadening due to the dynamic exchange process that equilibrates the pentacoordinate "stannate" tin atom that binds the guest chloride with the tetracoordinate "stannane" tin atom. If this model of binding, with the guest jumping across the cavity from one tin to the other, holds for all of the larger hosts, then one might expect to see slight cooperativity between the acidic sites in that some stabilization could be expected as the distance between the tin atoms is decreased.

Conclusion

Size-selective binding of halides in organic media has been demonstrated with the Lewis acidic, tin-containing macrobicycles, but with labile halide groups attached to the tin atoms, hosts **2** and **3** will have limited utility. However, the series of studies in this work demonstrate that anion binding can be controlled in a rational manner by preorganized hosts. Replacement of the labile halides with groups that bind more strongly to tin but are still electron withdrawing should result in species that retain

(17) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry A Comprehensive Text*, 3rd ed.; Wiley-Interscience: New York, 1972; p 52.

Table VII. Activation Parameters and Rate Constants at 20 °C for Complexations of Chloride[a]

		dissociation			association		
host	solvent	log (A/s^{-1})	E_a[b]	$10^{-4}k_d$,[c] s^{-1}	log (A/M^{-1} s^{-1})	E_a[b]	$10^{-4}k_f$,[c] M^{-1} s^{-1}
2b	$CDCl_3$	11.9 ± 0.1	8.8 ± 0.1	21	9.9 ± 0.3	7.1 ± 0.3	4.0
2c	$CDCl_3$	11.0 ± 0.4	8.9 ± 0.5	2.3	10.9 ± 0.3	7.1 ± 0.3	40
2c	$CDCl_2CDCl_2$	12.4 ± 0.2	11.0 ± 0.3	1.5	9.1 ± 0.4	5.0 ± 0.6	23
2d	$CDCl_3$	11.5 ± 0.3	8.0 ± 0.3	34	9.5 ± 0.2	3.9 ± 0.3	390
2e[d]	$CDCl_3$	(12.2)	(7.8)	240	(11.4)	(5.9)	1000
2e	CH_2Cl_2[e]	10.2 ± 0.2	5.6 ± 0.3	100	8.7 ± 0.3	1.6 ± 0.3	3200
3e[f]	$CDCl_3$	10.0 ± 0.1	4.6 ± 0.1	370	8.3 ± 0.1	2.5 ± 0.1	270

[a] Arrhenius functions for binding chloride within the cavity of the hosts; errors are one standard deviation. [b] In kilocalories/mole. [c] At 20 °C. [d] Approximate values, see text. [e] The solvent contained 10% benzene-d_6. [f] For complexation of bromide.

Table VIII. Equilibrium Constants for Complexation at 20 °C

host	guest	solvent	K_{eq}, M^{-1}	method[a]
Bu_3SnCl	Cl^-	$CDCl_3$	17	HB
		CH_2Cl_2[b]	500	HB
2a		$CDCl_3$	<0.003	*c*
2b		$CDCl_3$	0.3 (0.2)	HB (*K*)
2c		$CDCl_3$	17	*K*
2c		$CDCl_2CDCl_2$	15	*K*
2d		$CDCl_3$	11	*K*
2e		$CDCl_3$	6 (4)	HB (*K*)
		CH_2Cl_2[b]	32	*K*
Bu_3SnBr	Br^-	$CDCl_3$	3.3	HB
3c		$CDCl_3$	0.3	HB
3d		$CDCl_3$	1.4	HB
3e		$CDCl_3$	0.7 (0.7)	HB (*K*)

[a] Obtained from the Hildebrand–Benesi (HB) method with 4–8 solutions of host and guest or from the kinetic (*K*) values listed in Table VII. [b] The solvent contained 10% benzene-d_6. [c] Limiting value obtained from one solution; see text for details.

the selective binding characteristics and can be employed as Lewis acidic hosts with a variety of anionic and basic guests. One should also expect to find more selective binding in series of hosts that contain more than two acidic sites.

Experimental Section

General. ^{13}C and ^{119}Sn NMR spectra were obtained on Varian XL-200 and XL-400 spectrometers equipped with variable temperature probes; gated decoupling was used for the ^{119}Sn NMR spectra. ^{13}C NMR chemical shifts are reported in ppm downfield from internal Me_4Si. ^{119}Sn NMR chemical shifts are reported in ppm downfield from internal Me_4Sn. Chromatographic purifications were accomplished at medium pressure on reverse-phase C-18 bonded silica (Lichroprep RP-18, 42-63 μ, EM Reagents) using THF/methanol mixtures for elution. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Tetrahydrofuran used for synthetic reactions was distilled from potassium benzophenone under nitrogen before use. 1,12-Dibromododecane (Aldrich) was distilled before use; other organic dibromides (Aldrich) were used as received. Tributyltin chloride (Alfa), triphenyltin chloride (Aldrich), and anhydrous HCl and HBr (Matheson) were used as obtained. Tetrahexylammonium bromide and chloride (Aldrich) were dried in a high vacuum at room temperature for at least 24 h before use. Tributyltin bromide was prepared from the reaction of tributyl(phenyl)tin with HBr in CH_2Cl_2 by the method described below for the hosts and was purified by vacuum distillation (bp 95–100 °C, 0.5 Torr; lit.[18] bp 163 °C, 12 Torr). All Grignard reactions were performed under nitrogen or argon atmospheres; canula transfers were used. Analyses were performed by Galbraith Laboratories.

Compounds 5 and 6 were prepared by the method of Azuma and Newcomb[5] and were typically obtained in 75% and 35% yields, respectively, after purification by reverse-phase chromatography and recrystallization. 1,7-Bis(triphenylstannyl)heptane (mp 90–92 °C from hexanes) and 1,1,9,9-tetraphenyl-1,9-distannacyclohexadecane (mp 95–97 °C from methanol–THF) are new.

Compounds 7 were prepared by the following general method. A solution of the appropriate compound **6** (0.01–0.02 M) in CH_2Cl_2 was cooled to −78 °C. A standardized solution of HCl or HBr in CH_2Cl_2 (0.1–0.6 M) containing ca. 1.8–1.9 equiv of acid was added over 0.5–1 h to the reaction vessel. The mixture was allowed to warm to room temperature over 4–5 h with stirring. An aliquot of the reaction mixture was removed and concentrated at reduced pressure. The residue was dissolved in $CDCl_3$, and a ^{13}C NMR spectrum was recorded. The signals for the α-carbon adjacent to a diphenyltin (δ 10–11) and the α-carbon adjacent to a phenylhalotin (δ 17–19) were used to determine the extent of the cleavage reaction. The entire reaction sequence was repeated using the calculated amount of acid required to complete the cleavage reaction. If necessary, the sequence was repeated a third time. The solvent was removed at reduced pressure. Products **7** were used as thus obtained or were recrystallized. The purity of all products was judged to be <95% based on the absence of any extraneous signals in their ^{13}C NMR spectra.

1,8-Dibromo-1,8-diphenyl-1,8-distannacyclotetradecane (7a): ^{13}C NMR ($CDCl_3$) δ 140.2, 136.0, 128.6, 128.4, 33.0, 24.8, 18.0.

1,9-Dibromo-1,9-diphenyl-1,9-distannacyclohexadecane (7b): ^{13}C NMR ($CDCl_3$) δ 139.1, 136.6, 130.7, 129.0, 33.7, 28.7, 26.1, 17.9.

1,10-Dibromo-1,10-diphenyl-1,10-distannacyclooctadecane (7c) was recrystallized from hexane: mp 90–92 °C; ^{13}C NMR ($CDCl_3$) δ 139.39, 135.33, 129.54, 128.55, 33.18, 28.42, 25.71, 18.01; ^{119}Sn NMR ($CDCl_3$) δ 61.8.

1,12-Dibromo-1,12-diphenyl-1,12-distannacyclodocosane (7d) was recrystallized from hexane: mp 50–54 °C; ^{13}C NMR ($CDCl_3$) δ 140.14, 135.44, 129.56, 128.61, 33.34, 29.20, 28.77, 28.51, 18.21; ^{119}Sn NMR ($CDCl_3$) δ 62.5.

1,12-Dichloro-1,12-diphenyl-1,12-distannacyclodocosane was recrystallized from hexane: mp 78–80 °C; ^{13}C NMR ($CDCl_3$) δ 140.86, 135.40, 129.71, 128.72, 33.55, 29.28, 28.88, 25.51, 18.37; ^{119}Sn NMR (CH_2Cl_2/benzene-d_6) δ 78.95.

1,14-Dibromo-1,14-diphenyl-1,14-distannacyclohexacosane (7e) was recrystallized from hexane: mp 55–59 °C; ^{13}C NMR ($CDCl_3$) δ 140.13, 135.34, 129.53, 128.57, 33.46, 29.46, 29.34, 28.89, 25.88, 18.33.

Bicycles 8 were prepared by the following general method. A solution of the appropriate di-Grignard reagent in THF (ca. 500 mL, 0.02 M) and a solution of compound **7** in THF (ca. 500 mL, 0.02 M) were added simultaneously to a flask initially containing 500 mL of THF over a period of 2.5–5 h at room temperature. After stirring for 12–24 h, the reaction was terminated, and 60–70% of the solvent was removed at reduced pressure. The resulting solution was washed with saturated ammonium chloride solution and saturated sodium chloride solution, and the organic phase was dried ($MgSO_4$). Solvent was removed at reduced pressure, and the resulting residue was purified by reverse-phase chromatography. Crude products thus obtained were recrystallized from methanol–THF.

1,8-Diphenyl-1,8-distannabicyclo[6.6.6]eicosane (8a) was purified by reverse-phase chromatography using 35/65 THF–methanol as the eluant: 20%; mp 124–126 °C; ^{13}C NMR ($CDCl_3$) δ 141.1, 136.4, 128.4, 128.2, 33.1, 25.3, 10.5; ^{119}Sn NMR ($CDCl_3$) δ −44.1. The structure of **8a** was confirmed by the X-ray crystal structure of the chloro derivative **2a**.[7]

(18) Jones, W. J.; Evans, P. P.; Gulwell, T.; Griffiths, D. C. *J. Chem. Soc.* **1935**, 39–47.

1,9-Diphenyl-1,9-distannabicyclo[7.7.7]tricosane (8b) was purified by reverse-phase chromatography using 40/60 THF–methanol as the eluant: 42%; mp 96–97 °C; ^{13}C NMR ($CDCl_3$) δ 141.2, 137.3, 128.9, 128.7, 33.6, 28.5, 26.4, 10.9; ^{119}Sn NMR ($CDCl_3$) δ −44.0. The structure of **8b** was confirmed by the X-ray crystal structure of the chloro derivative **2b**.[7]

1,10-Diphenyl-1,10-distannabicyclo[8.8.8]hexacosane (8c) was purified by reverse-phase chromatography using 40/60 THF–methanol as the eluant: 30–40%; mp 92–94 °C; ^{13}C NMR ($CDCl_3$) δ 141.3, 136.2, 128.3, 128.2, 33.5, 28.1, 26.2, 10.3; ^{119}Sn NMR ($CDCl_3$) δ −44.4. Anal. Calcd for $C_{36}H_{58}Sn_2$: C, 59.37; H, 8.02. Found: C, 59.41; H, 8.08. The structure of **8c** was confirmed by X-ray crystallography.[6]

1,12-Diphenyl-1,12-distannabicyclo[10.10.10]dotriacontane (8d) was purified by reverse-phase chromatography using 60/40 THF–methanol and then 50/50 THF–methanol as the eluant: 30–40%; mp 56–58 °C; ^{13}C NMR ($CDCl_3$) δ 142.45, 136.16, 127.82 (two carbons), 33.58, 29.09, 28.75, 26.52, 10.45; ^{119}Sn NMR ($CDCl_3$) δ −44.0. Anal. Calcd for $C_{42}H_{70}Sn_2$: C, 62.09; H, 8.68. Found: C, 62.25; H, 8.68. The structure of **8d** was confirmed by X-ray crystallography.[7]

1,14-Diphenyl-1,14-distannabicyclo[12.12.12]octatriacontane (8e) was purified by reverse-phase chromatography using 60/40 THF–methanol and then 50/50 THF–methanol as the eluant: 30–40%; mp 53–54 °C; ^{13}C NMR ($CDCl_3$) δ 142.59, 136.31, 127.93 (two carbons), 33.82, 29.49, 29.38, 28.97, 26.44, 10.42; ^{119}Sn NMR ($CDCl_3$) δ −44.2. Anal. Calcd for $C_{48}H_{82}Sn_2$: C, 64.30; H, 9.21. Found: C, 63.92; H, 8.85.

Hosts 2 and 3 were prepared from compounds **8** and HCl or HBr by a method similar to that described above for the preparation of compounds **7**. All of the crude products were recrystallized from hexane or chloroform/hexane.

1,8-Dichloro-1,8-distannabicyclo[6.6.6]eicosane (2a) was obtained in 85% yield: mp 116–119 °C; ^{13}C NMR ($CDCl_3$) δ 31.6, 24.8, 19.9; ^{119}Sn NMR ($CDCl_3$) δ 148.5.

1,9-Dichloro-1,9-distannabicyclo[7.7.7]tricosane (2b) was obtained in 75% yield: mp 138–139 °C; ^{13}C NMR ($CDCl_3$) δ 34.4, 29.1, 26.3, 20.3; ^{119}Sn NMR ($CDCl_3$) δ 148.3.

1,10-Dichloro-1,10-distannabicyclo[8.8.8]hexacosane (2c) was obtained in 84% yield: mp 101–105 °C; ^{13}C NMR ($CDCl_3$) δ 32.74, 28.08, 25.21, 18.87; ^{119}Sn NMR ($CDCl_3$) δ 152.4.

1,12-Dichloro-1,12-distannabicyclo[10.10.10]dotriacontane (2d) was obtained in 90% yield: mp 35–37 °C; ^{13}C NMR ($CDCl_3$) δ 33.40, 29.03, 28.77, 25.60, 19.08 for the major isomer; ^{119}Sn NMR ($CDCl_3$) δ 152.38 (87), 156.8 (6.5), 163.4 (6.5).

1,14-Dichloro-1,14-distannabicyclo[12.12.12]octatriacontane (2e) was obtained in 85% yield: mp 69–71 °C; ^{13}C NMR ($CDCl_3$) δ 33.62, 29.40, 29.35, 28.98, 25.70, 19.08 for the major isomer; ^{119}Sn NMR ($CDCl_3$) δ 151.79 (85), 155.25 (15).

1,10-Dibromo-1,10-distannabicyclo[8.8.8]hexacosane (3c) was obtained in 68% yield: mp 92–93 °C; ^{13}C NMR ($CDCl_3$) δ 32.59, 27.98, 25.45, 18.69; ^{119}Sn NMR ($CDCl_3$) δ 131.87.

1,12-Dibromo-1,12-distannabicyclo[10.10.10]dotriacontane (3d) was obtained in 70% yield: mp 44–46 °C; ^{13}C NMR ($CDCl_3$) δ 33.1, 28.8, 28.6, 25.9, 18.6; ^{119}Sn NMR ($CDCl_3$) δ 132.68.

1,14-Dibromo-1,14-distannabicyclo[12.12.12]octatriacontane (3e) was obtained in 78% yield: mp 35–40 °C; ^{13}C NMR ($CDCl_3$) δ 33.4, 29.3, 29.1, 28.9, 26.0, 18.3 for the major isomer; ^{119}Sn NMR ($CDCl_3$) δ 132.8 (80), 138.5 (15), 142.0 (5).

1,12-Dibutyl-1,12-dichloro-1,12-distannacyclododecane (4). To a solution of **7d** in THF (0.07 M) was added a solution of BuMgBr in THF at room temperature. The reaction mixture was worked up by the method described above for the preparation of compounds **8**. 1,12-Dibutyl-1,12-diphenyl-1,12-distannacyclododecane was isolated in 92% yield: oil; ^{13}C NMR ($CDCl_3$) δ 142.05, 136.42, 134.10, 127.2., 29.54, 29.10, 29.04, 27.37, 26.65, 13.69, 9.83. This intermediate was then treated with HCl by the method described above for the preparation of compounds **7** to give product **4** in 62% yield after recrystallization from hexane: mp 76–77 °C; ^{13}C NMR ($CDCl_3$) δ 33.56, 29.32, 28.30, 27.83, 26.82, 25.57, 18.17, 17.73, 13.63; ^{119}Sn NMR ($CDCl_3$) δ 152.8.

Titration Experiments. A solution of host (0.05–0.2 M) was prepared. Aliquots of a solution of tetrahexylammonium halide (0.5–1.0 M) were added, and ^{119}Sn NMR spectra were recorded after each addition. The concentration of host and guest halide for each solution were calculated for use in Hildebrand–Benesi analyses.

Job Plots. Equimolar solutions (0.1–0.4 M) of host and tetrahexyammonium halide were prepared and mixed in various amounts. ^{119}Sn NMR spectra of the mixtures were recorded, and the chemical shifts were analyzed by the method for NMR results.[11]

NMR Simulations. ^{119}Sn NMR spectra of solutions of hosts and tetrahexylammonium halide that exhibited dynamic phenomena were simulated. Two-site simulations were carried out with standard lineshape equations.[19] Three-site simulations were accomplished by the Kubo–Sack method.[20] All calculations were performed on a PC using programs written in-house. The total contribution to T_2 excluding exchange was taken to be 0.03 s; this is the experimental value determined for host **2c** in the absence of halide. Typically, changes in rate constants of 5–10% from those of the best fit resulted in noticeable spectral changes. Thus, the maximum estimated error in the kinetic values resulting from errors in the simulations would be substantially smaller than the differences in the kinetic values found for different solutions of a given host with halide, and we assumed that no measurable error was introduced in the simulation.

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Registry No. **2a**, 111495-45-5; **2b**, 122145-63-5; **2c**, 111469-26-2; **2d**, 111469-27-3; **2e**, 111495-46-6; **3c**, 122145-64-6; **3d**, 122145-65-7; **3e**, 122171-18-0; **4**, 122145-74-8; **5b**, 122145-66-8; **6a**, 87518-36-3; **6b**, 122145-67-9; **6c**, 87531-98-4; **6d**, 87518-37-4; **6e**, 8718-38-5; **7a**, 122145-68-0; **7b**, 122145-69-1; **7c**, 122145-70-4; **7d**, 122145-71-5; **7e**, 122145-72-6; **8a**, 111469-24-0; **8b**, 122145-73-7; **8c**, 94193-74-5; **8d**, 111469-25-1; **8e**, 111495-44-4; $BrMg(CH_2)_6MgBr$, 17036-36-1; $BrMg(CH_2)_7MgBr$, 59321-71-0; $BrMg(CH_2)_8MgBr$, 45037-87-4; $BrMg(CH_2)_{12}MgBr$, 59434-46-7; Bu_3SnCl, 1461-22-9; Bu_3SnBr, 1461-23-0; Ph_3SnCl, 639-58-7; 1,12-dichloro-1,12-diphenyl-1,12-distannacyclododecane, 111469-22-8; 1,12-dibutyl-1,12-diphenyl-1,12-distannacyclododecane, 122145-75-9.

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