Diastereoselective Self-Assembly of a Pentacoordinate Siliconate Tetraanionic Molecular Square. A Mechanistic Investigation

Joshua J. Pak,[†] John Greaves, Dianne J. McCord, and K. J. Shea*

Department of Chemistry, University of California, Irvine, California 92717-2025

Received April 3, 2002

Condensation of (±)-5,5′,6,6′-tetrahydroxy-1,1′-spirobis(indane) (**1**) and phenyltriethoxysilane with triethylamine in refluxing THF results in formation of a tetraanionic molecular square incorporating four pentavalent siliconates. The macrocyclization is stereoselective. Of the four possible macrocyclic tetramers, a single isomer, *meso*-**2** (C_{2h}), is produced in high yield from racemic **1**. Reaction intermediates leading to formation of macrocycle **2** were identified by electrospray time-of-flight mass spectrometry (ES-TOF-MS). The reaction proceeds by a path that deviates from conventional step-growth polymerization. The condensations produce linear dimers, trimers, and tetramers. The configurational flexibility of the pentacovalent siliconate and the angular connector, bisspirocatechol **1**, predispose specific oligomers toward macrocyclization. At the linear tetramer stage, there are a total of six possible stereoisomers. Calculations reveal little difference in energy between the paths that lead to them. The *RSSR* and *SSRR* diastereomers undergo macrocyclization, and the product, *meso*-**2** (C_{2h}), precipitates from solution. Crossover experiments establish the reversibility of the reaction, even after formation and precipitation of cyclic tetramer. The high reaction yields are accounted for by a *self-correcting* mechanism to produce what is found to be (computationally) the most stable (and most likely least soluble) diastereomer.

Introduction

In recent years, the area of self-assembly has become a central focus in supramolecular chemistry. Indeed, self-assembly has become one of the more important tools for the synthesis of molecular, supramolecular, and nanoscale structures.[2] Macrocycles are one of the more frequently encountered structural motifs in supramolecular assemblies. Examples include many rigid *cationic* molecular squares and rectangles comprised of building blocks with ca. 90° angles.[3] Macrocyclic polyions have expanded the range of organizational forces for supramolecular assembly. The origin of the selectivity in many cyclic self-assembly systems is often attributed to structural information that is an intrinsic property of the basic subunits. There have been several studies probing the details of the assembly process.[4,5]

We recently reported the first example of a *tetraanionic* molecular square, a polyanionic counterpart of cationic systems.[6,7] The macrocycle **2** is comprised of four anionic pentacoordinate siliconate groups with four triethylammonium cations as counterions. We report observations that provide insight to the origin of the diastereoselective formation of tetraanion **2**. The analysis includes electrospray ionization time-of-flight mass spectrometry (ESI-TOF-MS) and semiempirical computational studies of the reaction intermediates and products.

Results and Discussion

A molecular square containing four pentacovalent siliconate atoms is formed by the condensation of the *racemic* spirocatechol **1** with phenyltriethoxysilane in refluxing THF containing a 3-fold excess of triethylamine (eq 1). The reaction was complete after approximately 48 h to afford a white precipitate in >80% yield. When a slight excess (10−30%) of phenyltriethoxysilane was used, an even higher yield of the cyclic

---

[†] Current address: Chemistry Department, Idaho State University, Pocatello, ID 83209.

(1) (a) Lehn, J.-M., Chair E. D., Atwood, J. L., Davis, J. E. D., MacNicol, D. D., Vögtle, F., Eds. *Comprehensive Supramolecular Chemistry*; Pergamon: Oxford, U.K., 1987−1996; Vols. 1−11. (b) Fujita, M. *Acc. Chem. Res.* **1999**, *32*, 53.

(2) (a) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853. (b) Fujita, M.; Kwon, Y. J.; Ashizu, S.; Ogura, K. *J. Am. Chem. Soc.* **1994**, *116*, 1151. (c) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348. (d) MacGillivray, L. R.; Atwood, J. L. **1999**, *38*, 1018. (e) Caulder, D. L.; Raymond, K. N. **1999**, *32*, 975.

(3) Gutsche, C. D. *Calixarenes*; Monographs in Supramolecular Chemistry 1; Royal Society of Chemistry: London, 1992.

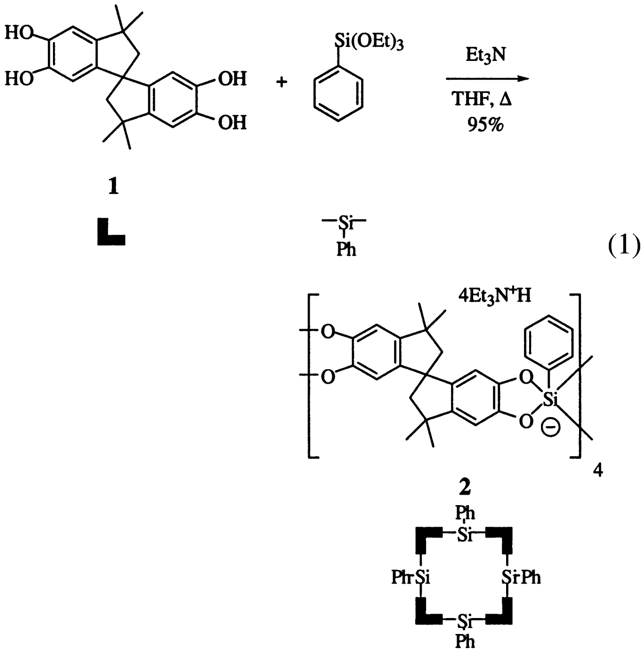
(4) Hoegberg, A. G. S.; Weber, M, *Acta Chem. Scand., Ser. B* **1983**, 55−9.

(5) (a) Levin, M. D.; Stang, P. J. *J. Am. Chem. Soc.* **2000**, *122*, 7428. (b) Ashton, P. R.; Heiss, A. M.; Pasini, D.; Raymo, F. M.; Shipway, A. N.; Stoddart, J. F.; Spencer, N. *Eur. J. Org. Chem.* **1999**, *995*, 5. (c) Sun, S.-S.; Lees, A. J. *J. Am. Chem. Soc.* **2000**, *122*, 8956. (d) Suissa, M. R.; Romming, C.; Dale, J. *Chem. Eur. J.* **1999**, *5*, 3055. (e) Ercolani, G. *J. Phys. Chem. B* **1998**, *102*, 5699.

(6) Small, J. H.; McCord, D. J. Greaves, J.; Shea, K. J. *J. Am. Chem. Soc.* **1995**, *117*, 11588.

(7) McCord, D. J.; Small, J. H.; Greaves, J.; Van, Q. N.; Shaka, A. J.; Fleischer, E. B.; Shea, K. J. *J. Am. Chem. Soc.* **1998**, *120*, 9763.

10.1021/om020263x CCC: $22.00
Publication on Web 07/10/2002



(1)

tetramer (>95%) was observed. The salt was filtered and washed with excess THF to provide a fine white powder.

We initially anticipated that the use of an angular biscatechol subunit would result in condensation polymers with structural motifs that could include helices and macrocycles. Quite unexpectedly, the resulting powder exhibited spectral and analytical properties characteristic of a pure substance instead of mixtures of diastereomeric oligomers. The sharp resonances in the ^{1}H and ^{13}C NMR (DMSO) and absence of catechol end groups indicated a single cyclic structure. Electrospray mass spectrometry provided conclusive evidence for formation of the macrocyclic tetramer structure. Spectra were obtained in both positive and negative ion modes. The positive ion spectra revealed two odd-electron peaks at 1768 Da ($[M + 4H]^+$) and 1870 Da ($[M + Et_3NH + 3H]^+$). The negative ion spectra also gave a peak at 1767 Da corresponding to $[M + 3H]^-$. The isotopic distributions were consistent with the molecular formula $C_{120}H_{103}O_{16}Si_4$, in agreement with a cyclic array of four spirocatechol-siliconate repeat units with four triethylammonium counterions. The ^{13}C NMR spectra revealed 29 resonances for the core macrocycle, and the ^{29}Si NMR spectra showed two resonances at −86.3 and −86.9 ppm. These data are consistent with a cyclic tetramer with C_{2h} symmetry.[6,7] Of the four possible diastereomeric products (Figure 1), the data were consistent with the diastereomer *meso*-**2** (C_{2h}). The exclusive formation of *meso*-**2** (C_{2h}) is a striking example of stereoselective self-assembly.

The condensation polymerization of silanes and catechol falls into a class of step-growth polymerization reactions between two bifunctional monomers (AA + BB system). The polymerization occurs by a series of condensation steps to form first monomer, then dimer, trimer, tetramer, and so forth (Figure 2). Step-growth polymerization requires a high degree of conversion to obtain high-molecular-weight polymer. According to Carother's equation ($X_n = 1/(1 - P)$), assuming a stoichiometric amount of monomers at 75% conversion, the number average molecular weight (X_n) reaches the tetramer stage.[8] An even higher degree of conversion is necessary to achieve $DP_n = 4$ when one of the monomers is used in excess.

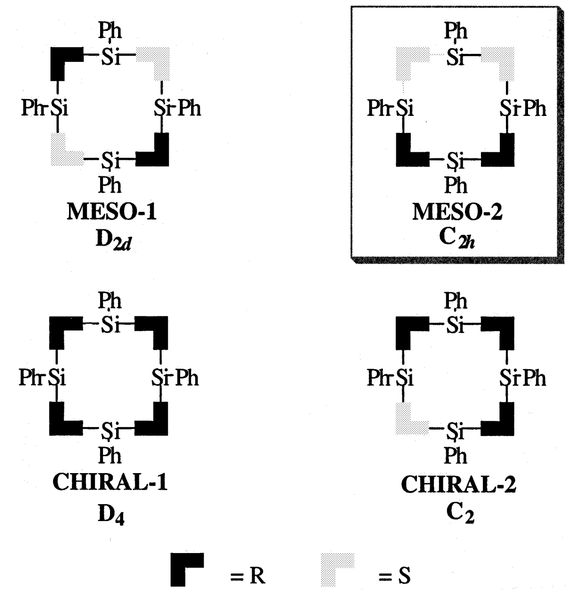


Figure 1. Schemetic representation of the diastereomeric tetraspirosiliconates. The enantiomers of spirocatechol **1** are represented by dark and light shading.

In the condensation of **1** with phenyltriethoxysilane, little if any linear oligomer could be found. The highly diastereoselective cyclotetramerization competes effectively with the linear condensation polymerization.[9] What is the origin of the selectivity? A mechanistic framework, first suggested by Hoegberg,[10] incorporates three key features. First, it is assumed that the reaction follows a traditional step-growth pathway generating a mixture of linear oligomeric intermediates (i.e. monomer, dimer, trimer, etc.). The use of (±)-spirobiscatechol **1** can result in an oligomer population that is comprised of a mixture of diastereomers. The formation of *meso*-**2** (C_{2h}) can *only* occur from two of the six possible linear tetramers. The high yield and diestereoselectivity can arise by a kinetically controlled stereoselective oligomerization to provide the two "correct" linear tetramers (*RRSS*, *SRRS*, or *RSSR*) that undergo subsequent macrocyclization.[11]

In the absence of a stereoselective oligomerization, the intermediates must be able to equilibrate, providing a *self-correcting* mechanism for recycling "incorrect" diastereomeric oligomers in the reaction pool: that is, thermodynamic control.

Mass Spectroscopic Analysis. To shed light on the mechanistic pathway, we first examined the evolution of reaction intermediates using electrospray ionization time-of-flight mass spectrometry (ESI-TOF-MS). This method provides a relatively soft ionization for the

---

(8) Odian, G. *Principle of Polymerization*; Wiley: New York, 1991.

(9) Ercolani, G.; Mandolini, L.; Mencarelli, P.; Roelens, S. *J. Am. Chem. Soc.* **1993**, *115*, 3901.

(10) (a) Hoegberg, A. G.; Sverker, J. *Am. Chem. Soc.* **1980**, *102*, 6046−6050. (b) Hoegberg, A. G. Sverker, J. *J. Org. Chem.* **1980**, *45*, 4498−4500.

(11) Tunstad, L. M.; Tucker, J. A.; Dalcanale, E.; Weiser, J.; Bryant, J. A.; Sherman, J. C.; Helgeson, R. C.; Knobler, C. B.; Cram, D. J. *J. Org. Chem.* **1989**, *54*, 1305.

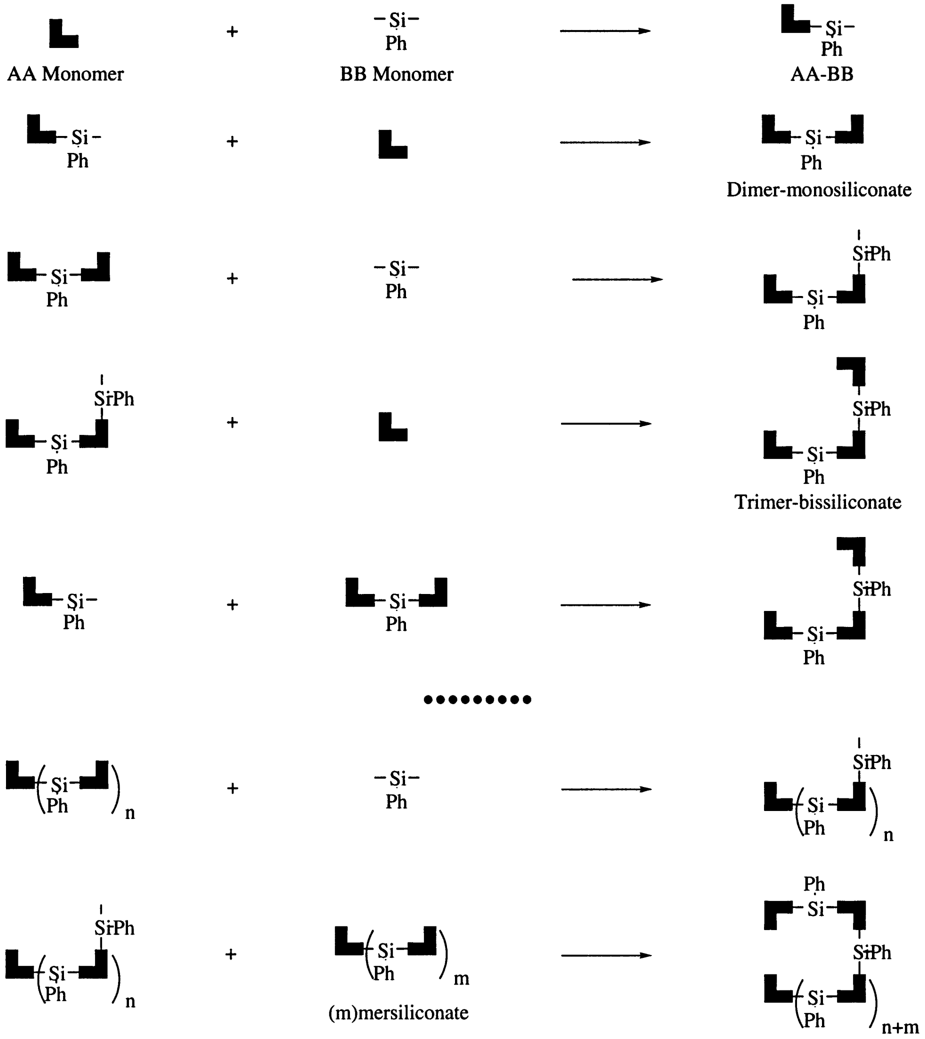


Figure 2. Progression of a step-growth polymerization of (±)-spirocatechol **1** and phenyltriethoxysilane.

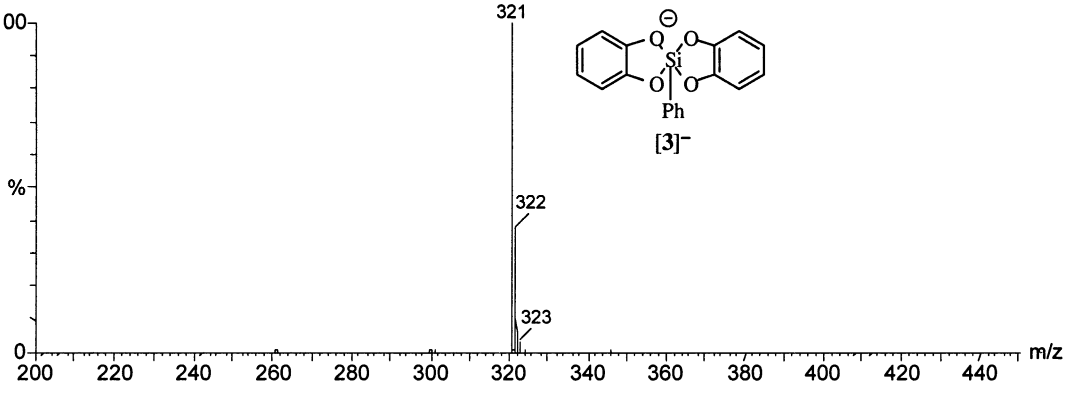


Figure 3. ESI-TOF-MS spectra of the model siliconate **3** in the negative ion mode.

analysis of multiply charged siliconate species without extensive fragmentation.

Since few examples of mass spectrometry of siliconates have been reported,[6,7,12] the applicability of this method for the analysis was first established with a model compound, phenylbiscatechol siliconate **3**. Acetonitrile solutions of the triethylammonium salt of **3** were analyzed by ESI-TOF-MS in the negative ion mode. Only one major peak corresponding to [**3**]$^-$ was observed at 321 Da (Figure 3). There were no significant peaks corresponding to fragmentation of the molecular ion.

The conditions developed for compound **3** were used to study the condensation between (±)-spirocatechol **1** and phenyltriethoxysilane. The reaction was periodically sampled over 48 h and revealed at least four distinct siliconate intermediates. The species included dimer-monosiliconate **4**, trimer-monosiliconate **5**, trimer-bissiliconate **6** and acyclic tetramer-trissiliconate **7** at 781 Da ([**4**]$^-$), 1121 Da ([**5**]$^-$), 1223 Da ([**6** + H]$^-$),

---

[12] (a) Narula, S. P.; Shankar, R.; Meenu. *Phosphorus, Sulfur Silicon Relat. Elem.* **1996**, *113*, 237. (b) Ho, Y.; Squires, R. R. *Org. Mass Spectrom.* **1993**, *28*, 1658.

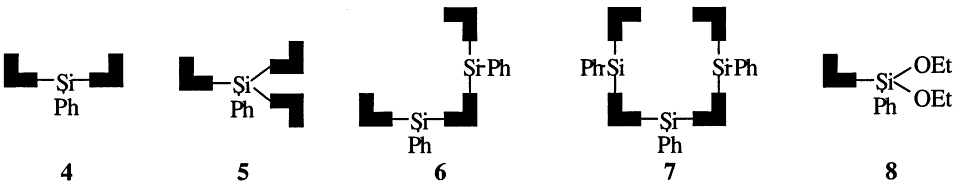


Figure 4. Macrocyclization reaction intermediates (**4**–**7**) of square **2**.

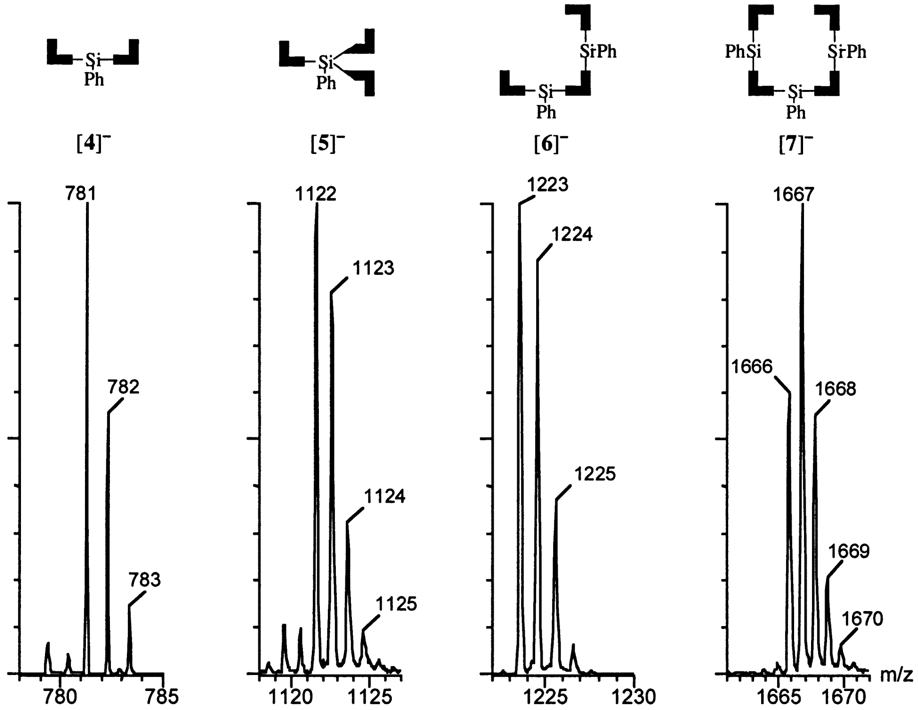


Figure 5. ESI-TOF-MS spectra in the negative ion mode of reaction intermediates of the macrocyclization.

and 1665 Da ([**7** + 2H]$^-$), respectively (Figures 4 and 5). Interestingly, species resulting from a single condensation, i.e., compound **8**, at 489 Da were not observed. In addition to the singly charged ions with mass corresponding to dianionic and trianionic intermediates **6** and **7**, doubly and triply changed species at 612 Da ([**6**]$^{2-}$)and 833 Da ([**7** + H]$^{2-}$) were also present in the mass spectra. Since their intensities were found to vary as a function of both ionization energy and sample preparation, quantification of the relative ratios of the intermediates over time was precluded. The data permit assignment of structure to the intermediates that lead to the final cyclic product, but the technique does not distinguish between stereoisomers of the intermediates.

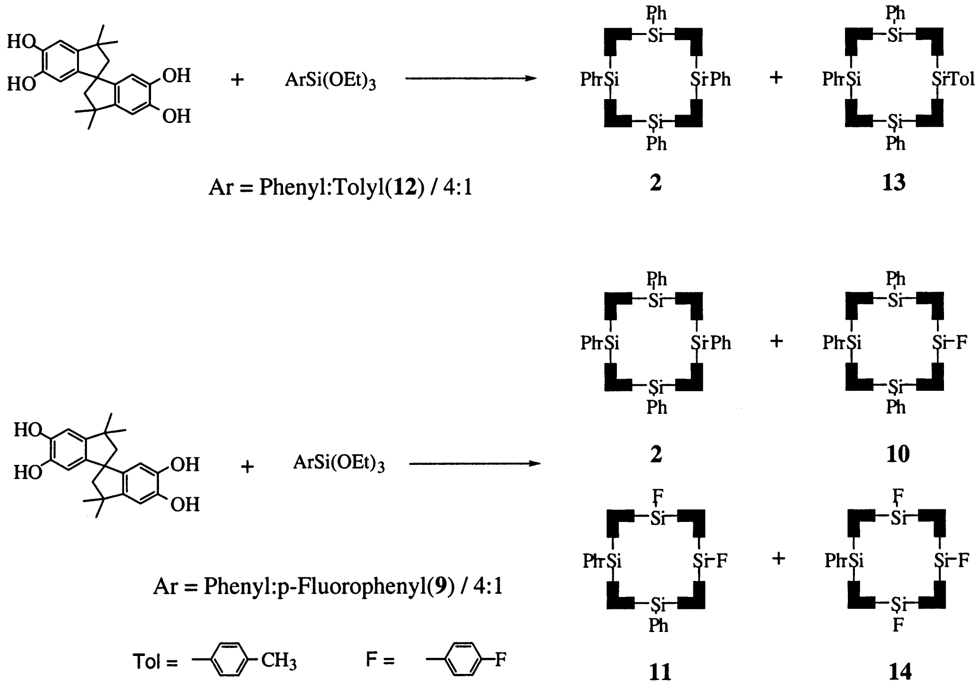
Mechanism of the Stereoselective Macrocyclization. Possible explanations for the selectivity include a *path selective* oligomerization, i.e., stereoselective trimerization and tetramerization followed by cyclization, to produce *meso*-**2** (C_{2h}) or cyclization from an equilibrating pool of oligomers to produce *meso*-**2** (C_{2h}) followed by precipitation.

There are a total of six diastereomeric *linear* tetramers. Only two of the six have the correct sequence to form *meso*-**2** (C_{2h}) upon macrocyclization (*RSSR* and *SSRR*). In addition, only two out of a possible three linear trimers have a sequence that can lead to “productive” tetramers. The requirements for a diastereoselective condensation pathway arise at a very early stage in the oligomerization. Efforts to obtain direct experimental evidence (i.e. chromatographic separation) for the diastereomeric composition of oligomers has so far been unsuccessful. However, computational studies (vide infra) do not provide compelling support for a *path selective* diastereoselective oligomerization.

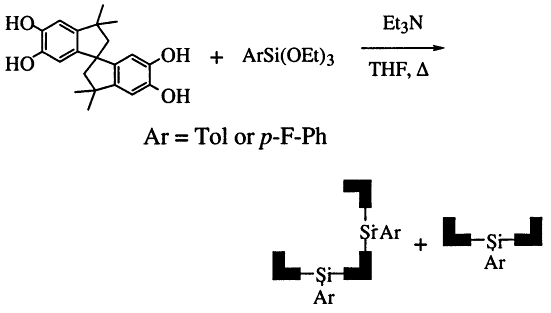
A more plausible scenario involves equilibration of diastereomeric oligomers.[9,10] In this context it is important to note that the condensation results in formation of a precipitate approximately 12 h into the reaction. The amount of precipitate steadily increases over the next 36 h. Within the detection limit of NMR, the precipitate was found to be comprised only of *meso*-**2** (C_{2h}). It is quite likely, therefore, that precipitation removes product from solution, displacing the reaction equilibrium in favor of the cyclic tetramer.[11]

To establish the reversibility of the oligomerization process, we introduced several functional phenyltriethoxysilanes into the macrocyclization reaction. Tolyl- and (*p*-fluorophenyl)triethoxysilane derivatives (**9** and **12**, respectively) were synthesized by reaction of the corresponding aryl Grignard reagents with tetraethoxysilane. When these monomers were used in place of phenyltriethoxysilane, the reaction did not produce precipitates. Instead, the solution separated into a viscous gellike material and a clear liquid phase after 2 days of refluxing. Mass spectrometry of the gel phase revealed the presence of dimer-monosiliconate and trimer-bissiliconate condensation products but no evidence of cyclic tetramer (eq 2). Since EtOH is not

Scheme 1. Partial Derivatization of Molecular Squares



removed from the reaction, this may represent the reaction equilibrium.



(2)

It was possible, however, to incorporate substoichiometric quantities of functional phenylsilanes (less than 0.25 equiv of total silane) into the molecular squares. These reactions produced a precipitate which was shown by mass spectrometry to contain a mixture of nonfunctionalized and partially functionalized cyclic tetramers. For example, reaction of a 4:1 mixture of phenyl- and tolyltriethoxysilane **12** gave a white solid in nearly quantitative yield (Scheme 1). The ESI-TOF-MS spectra (Figure 7) revealed the solid was comprised of a mixture of macrocycle **2** and mono-tolyl containing cyclic tetramer **13** in a 5:1 ratio. Similarly, when a 4:1 mixture of phenyl- and (*p*-fluorophenyl)triethoxysilane was used, the solids contained macrocycles with zero to three fluorobenzenes (**2**, **10**, **11**, and **14**) (Figure 6). Interestingly, the monofluoro derivative was the predominant species in the mixture, in contrast to the tolyl system (Scheme 2). Although the incorporation of substituted tolyl- and *p*-fluorophenylsilane could be verified by ^{1}H and ^{13}C NMR spectroscopy, quantifying the amount of functional groups incorporated by this technique was difficult, due to the complexity of the spectra.

The formation of only *linear oligomers* in the condensation of pure tolyl- and (*p*-fluorophenyl)triethoxysilane with spirocatechol **1** is significant. The lack of cyclic tetramer may be attributed to the greater solubility of the fully substituted derivatives. In the absence of a mechanism to funnel off product, the oligomerization proceeds via a more traditional condensation polymerization with formation of a distribution of low-molecular-weight diastereomeric oligomers. It has also been noted that precipitates do not form when phenyltriethoxysilane and spirocatechol **1** are condensed in the presence of tri-*n*-butylamine. The solubility of the cyclic tetramer therefore is influenced by both para substitution and the nature of the countercation. Apparently only partial incorporation of functional phenyl rings can occur to a point without significant disruption of the crystal lattice.

The redistribution of oligomers and product was established by the crossover experiments shown in Scheme 2. Tetrasiliconate *meso*-**2** (C_{2h}) was treated with (*p*-fluorophenyl)triethoxysilane (**9**) (4.0−6.7 equiv) under three different reaction conditions. The conditions (cases 1−3) were chosen to approximate those found at various stages in the polycondensation reaction and to establish the relationship between the solubility of macrocycle **2** and the facility with which it equilibrates among the linear intermediates. The siliconate **2** was refluxed in THF with 2 equiv of triethyamine and 6.7 equiv of (*p*-fluorophenyl)triethoxysilane (**9**) for 48 h (case 1). The reaction mixture remained heterogeneous throughout. Since the solubility of *meso*-**2** (C_{2h}) in THF or 1 M EtOH in THF is very low ($\sim 4.1 \times 10^{-4}$ M), these conditions most closely resemble those used for the synthesis of macrocycle **2**. The resultant solid was filtered and subjected to ESI-TOF-MS analysis. The mass spectra indicated the presence of small amounts of macrocycles containing one or two *p*-fluorophenyl moieties (**10** and **11**) in addition to unreacted starting macrocycle **2**. This observation requires that equilibration can occur under the reaction conditions even after formation and precipitation of macrocyclic product.

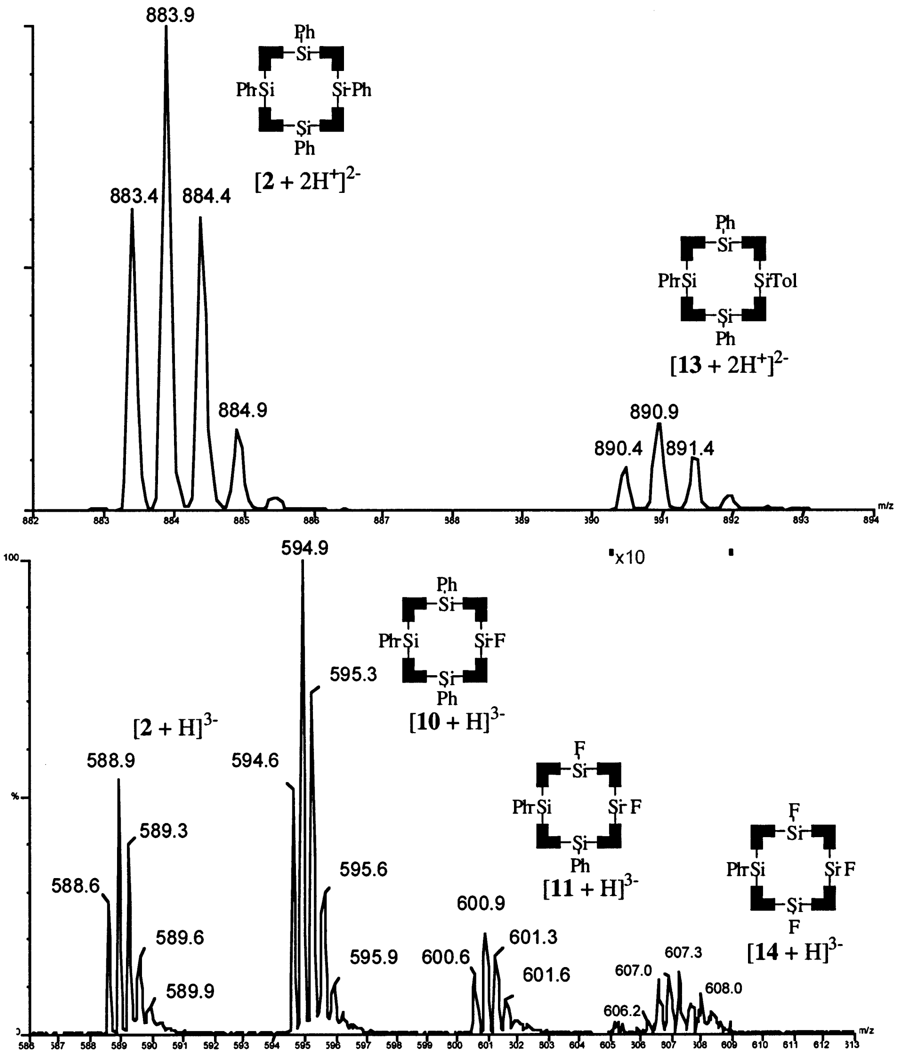


Figure 6. ESI-TOF-MS spectra in the negative ion mode of tolyl- and (*p*-fluorophenyl)siliconate derivatives.

Table 1. Calculated Energies of Anionic Siliconate Compounds.

compd	designation	energy (kcal/mol)
4	*RR*	−438.11
	RS	−438.03
6a	*RRR*	−674.00
6b	*RSR*	−671.85
6c	*RRS*	−675.41
chiral-**2** (D_4)	cyclic *RRRR*	−879.31
meso-**2** (D_{2d})	cyclic *RSRS*	−883.81
chiral-**2** (D_4)	cyclic *RRRS*	−895.91
meso-**2** (C_{2h})	cyclic *RRSS*	−898.75

Two additional reactions were explored where the macrocycle **2** has greater solubility. These experiments led ultimately to homogeneous solutions. One solvent system contained a 1:3 mixture of CH_3CN/THF (case 2). The second consisted of a 1:3 mixture of EtOH and THF (and **3**). In case 2, CH_3CN was added to increase the solubility of macrocycle **2**. This resulted in the reaction turning homogeneous whithin 4 h. In case 3, EtOH was used to study its effect on the condensation equilibrium. Under these conditions, the reaction became homogeneous within 30 min of refluxing. Both reactions were refluxed for 48 h and then cooled. The solutions were concentrated to afford pale yellow solids, which were then subjected to ESI-TOF-MS analysis.

For case 2, mass spectrometric analysis indicated increased amounts of fluoro-substituted cyclic tetramer along with starting material. Some degradation of cyclic tetramer to acyclic linear oligomers was also noted under the reaction conditions. Interestingly, under the reaction conditions using EtOH/THF (case 3), only trace amounts of starting material **2** and fluoro-substituted macrocycle were observed. The reaction mixture consisted of predominantly biscatechol monoarylsiliconate dimers **4a** and **4b**.

These studies establish facile equilibration between *meso*-**2** (C_{2h}) and acyclic intermediates. Despite the low solubility of *meso*-**2** (C_{2h}) in THF, small amounts of *p*-fluorophenyl-substituted macrocycles were produced. The ratio of functionalized macrocyclic products **10** and **11** relative to unreacted starting material *meso*-**2** (C_{2h}) was 3.5:1.5:100 (Figure 7). However, in CH_3CN/THF, where the cyclic tetraanion **2** has greater solubility (case 2), there was an accelerated equilibration between macrocycle **2** and acyclic intermediates, as evidenced by the increase in functionalized macrocycles found in the same reaction period. The ratio of macrocycles **10** and **11** relative to *meso*-**2** (C_{2h}) was found to be 73:20:100. In refluxing EtOH/THF (case 3), the macrocycle was not stable and degraded, producing mostly acyclic intermediates **4a** and **4b**.

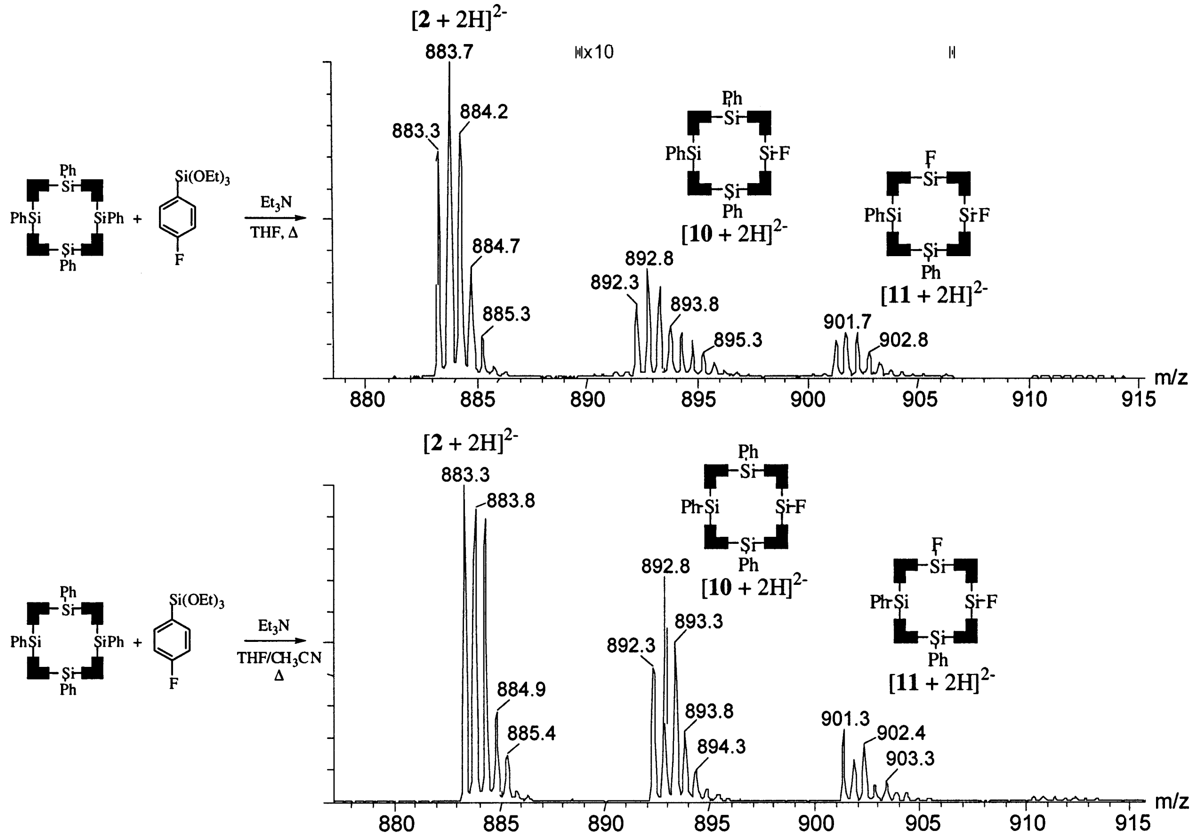
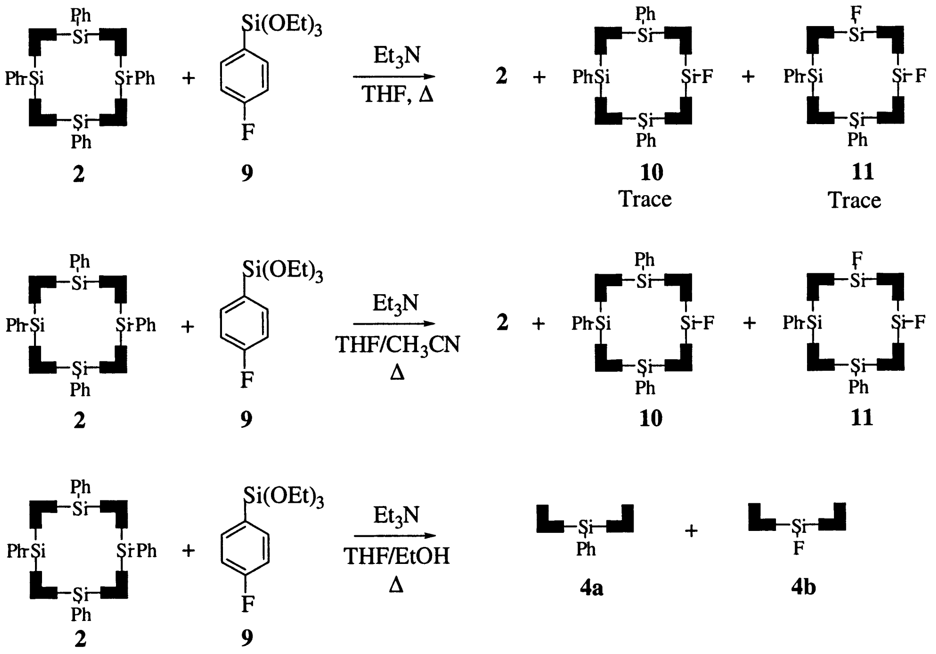


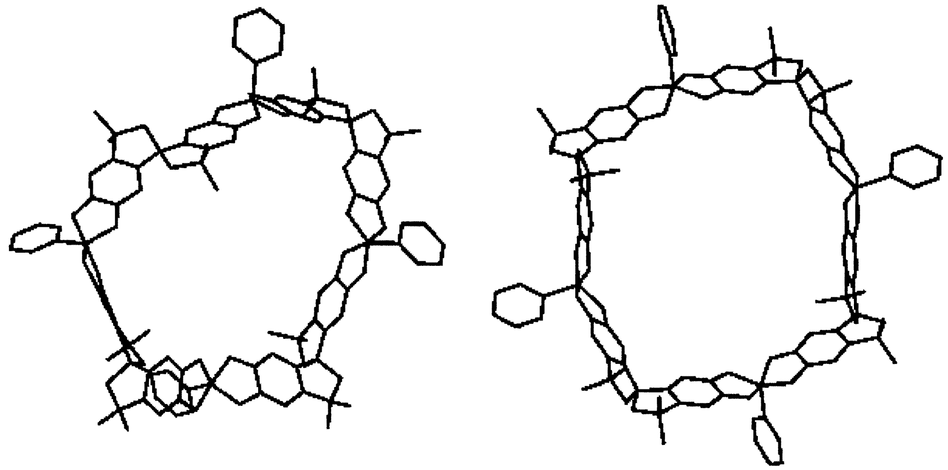
Figure 7. ESI-TOF-MS spectra in the negative ion mode of (*p*-fluorophenyl)siliconate derivatives.

Scheme 2. Substitution Reactions of the Tetraanionic Macrocycle 2 with (*p*-Fluorophenyl)triethoxysiloxane



Computational Studies. The minimum energies of the four possible diastereomeric products and their reaction precursors were estimated using PM3 (Spartan 5.0) (Table 1). Calculations were performed in the absence of any counterions.

It was anticipated that there would be little diastereoselectivity in dimer formation. Indeed, no difference was observed in the calculated energies of *SR*- and *RR*-**4** (Table 1). Of the three possible diastereomeric trimers (**6a**–**c**), only the *RRS* (**6c**) can lead to *meso*-**2** (C_{2h}). The *RRS* oligomer would then required to populate only *RRSS* and *SRRS* tetramers to achieve the correct sequence for macrocycle formation. At the trimer stage, there was little calculated energy difference between the *RRR* (**6a**) and *RRS* (**6c**) diastereomers.. In light of the similar energies, there is little basis for a diastereoselective formation of the *RRS* oligomer. With the finding that equilibration of oligomers occurs under the reaction



chiral-1 *meso*-**2**

Figure 8. Calculated frameworks of *chiral*-**2** (C_2) and *meso*-**2** (C_{2h}) macrocyclic tetrasiliconate. The hydrogen atoms have been omitted for clarity. The distorted square in chiral-**2** (C_2) arises primarily from deformations at the pentacoordinate silicon.

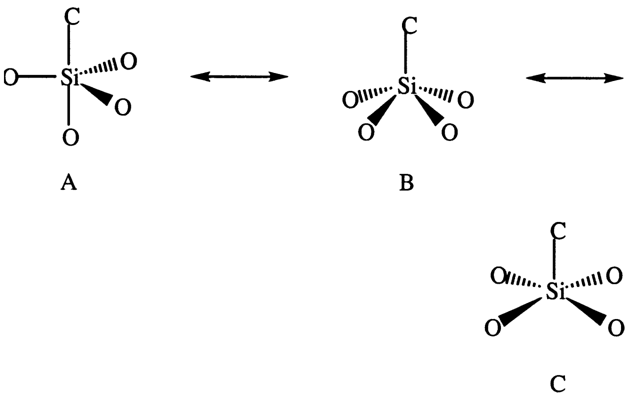


Figure 9. Spectrum of geometries of pentacoordinate siliconate.

conditions, there only remains a question as to why *meso*-**2** (C_{2h}) is formed in the reaction. Examination of Table 1 reveals that *meso*-**2** (C_{2h}) has the lowest calculated energy of the four possible diastereomers.

This isomer was estimated to be approximately 3−10 kcal/mol lower in energy than the other diastereomers. The macrocycle *chiral*-**2** (D_4) exhibited the next lowest energy ($\Delta E = -895.91$ kcal/mol) followed by *meso*-**2** (D_{2d}) and *chiral*-**2** (D_4) with energies of $\Delta E = -883.81$ and −879.31 kcal/mol, respectively.

An analysis of the calculated geometry of the siliconate centers of the four diastereomers provides some insight to the origins of their relative stability. The crystal structure of the unconstrained biscatechol siliconate **3** shows a slightly distorted-trigonal-bipyramidal geometry B at silicon with Si−O−C bond angles ranging between 105 and 107°[13] (Figure 9). Deviations of siliconate geometry from trigonal bipyramidal (A) or square pyramidal (C) result in an increase in energy of the system.[14] Examination of the O−Si−C bond angles in the calculated structures of all four siliconate centers of the diastereomeric macrocycles reveal that *meso*-**2** (C_{2h}) most closely approximates the “ideal” siliconate geometry with bond angles (98−111°) that deviate only minimally from the biscatechol siliconate model compound **3**. On the other hand, the O−Si−C bond angles in *chiral*-**1**, the highest energy isomer, contains siliconate centers with O−Si−C bond angles that range from 90 to 124°. These relatively large deviations from the model compound suggest that siliconate centers are the most compliant and reflect the distortions imposed by enforcing cyclization of linear tetramers that do not lead to *meso*-**2** (C_{2h}).

Thus, it appears that the *meso*-**2** (C_{2h}) diastereomer, containing a cyclic array of *RRSS* spirocatechols, produces a relatively strain-free macrocycle. The other diastereomers have increasingly greater distortions at the siliconate centers, reflecting the greater strain in these macrocycles.

Consideration of the preceding allows for the following conclusions. The self-assembly involves an equilibrating mixture of diastereomeric oligomers of more or less equal energy. The reversibility is aided by accumulation of ethanol during the reaction. This equilibration allows a continuous supply of the “correct” sequence of linear tetramer for macrocyclization. At the tetramer stage, the formation of *meso*-**2** (C_{2h}) is preordained by what may be a kinetic bias for cyclization of *RSSR* and *SSRR* linear tetramers to form the most stable cyclic structure. Following formation of this diastereomer, it is removed from the reaction mixture by its low solubility. If the precipitation pathway is removed, the equilibrium will shift toward the formation of linear dimer and trimers.

Summary

ESI-TOF-MS analysis has been used to identify reaction intermediates in the condensation of phenyltriethoxysilane with (±)-spirobiscatechol **1** to form the macrocycle *meso*-**2** (C_{2h}). This technique was able to establish that the oligomerization reaction is reversible. The reversibility plays a crucial role in the reaction. The reaction believed to proceed through an equilibrating mixture of acyclic oligomers **4**−**7**. Equilibration was supported by the observation that aryl silicon groups

---

[13] Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371.

[14] (a) Holmes, R. R.; Day, R. O.; Chandrasekhar, V.; Harland, J. J.; Holmes, J. M. *Inorg. Chem.* **1985**, *24*, 2009. (b) Holmes, R. R. *Chem. Rev.* **1996**, 96, 927.

in macrocycle **2** can be replaced under the reaction conditions. Macrocyclization proceeds from two of the possible six linear tetramers to the lowest energy macrocyclic tetramer, *meso*-**2** (C_{2h}). Under the reaction conditions, *meso*-**2** (C_{2h}) is siphoned from the reaction equilibrium due to its low solubility in THF. The angular motif of (±)-spirobiscatechol **1** and the linear connectivity of the siliconate contribute to the near-quantitative formation of the rectangular macrocycle. Computational studies of possible diastereomeric tetramers showed that *meso*-**2** (C_{2h}) exhibited the lowest energy, favoring the succession of events leading to high diastereoselectivity.

Experimental Section

General Methods. Routine proton, carbon-13, and silicon-29 NMR spectra were obtained using 500 and 400 MHz spectrometers and were recorded in DMSO-d_6 or $CDCl_3$ at room temperature unless otherwise specified. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane, using the residual DMSO as an internal standard for ^{1}H (500 or 400 MHz) and ^{13}C (125 MHz) NMR spectra (^{1}H, δ 7.27; ^{13}C, δ 77.0). ^{29}Si (99 MHz) NMR spectra were referenced to tetramethylsilane as an external standard (^{29}Si, δ 0.00). Coupling constants are expressed in hertz.

Infrared spectra were recorded on FTIR as pressed pellets (KBr). CIMS were obtained on a high-resolution mass spectrometer. LSIMS (mNBA matrix) were obtained using a high-resolution mass spectrometer in the positive ion mode using a Cs ion gun. Electrospray ionization mass spectra were obtained on a orthogonal time-of-flight mass spectrometer equipped with a Z-spray source and operated in negative ion mode. Samples were dissolved in acetonitrile and were introduced via a syringe pump at 500 μL/min.

Samples were analyzed at two different cone voltages, 40 and 80 V, to aid in the interpretation of the spectra obtained. At 40 V multiply charged species (2− and 3−) predominated, and these could be collisionally dissociated under the higher energy (80 V) conditions to a majority singly charged anion. Because of the presence of pentavalent silicone in these compounds, the interpretation of the spectra is frequently complicated by the presence of counterions; therefore, the reduction to a singly charged species would be highly advantageous.

Triethylamine was distilled from calcium hydride under an atmosphere of nitrogen prior to use. Tetrahydrofuran was dried by passing through a column of alumina under an atmosphere of argon prior to use. Silanes were dried and distilled from calcium hydride under an atmosphere of nitrogen prior to use unless otherwise noted. All other chemicals were of reagent quality and were used as received form the manufacturers.

General Cyclization Procedure A. To a refluxing solution of 5,5′,6,6′-tetrahydroxy-1,1′-spirobis(indane) (**1**) (1.0 equiv) and aryltriethoxysilane (1.0−1.3 equiv) in anhydrous THF was added dry triethylamine (ca. 4 equiv). The reaction mixture was stirred and refluxed under a nitrogen atmosphere for 2 to 5 days until a white precipitate had formed. The mixture was cooled to room temperature and the precipitate was collected by filtration and washed with THF. Residual solvent was removed under vacuum. The resultant solid was dissolved in acetonitrile and analyzed by using ES-TOF-MS.

Tetranuclear Macrocyclic Siliconate (2). To a refluxing solution of 5,5′,6,6′-tetrahydroxy-1,1′-spirobis(indane) (1.50 g, 4.40 mmol) and phenyltriethoxysilane (1.11 g, 4.44 mmol) in anhydrous THF (11 mL) was rapidly added dropwise dry triethylamine (1.34 g, 13.2 mmol). The mixture was stirred and kept under reflux under a nitrogen atmosphere for 4 days, with the formation of a white precipitate occurring within 48 h. The mixture was cooled to room temperature, and the precipitate was collected by filtration and rinsed with THF. Residual solvent was removed in vacuo to give 1.73 g (80%) of pure product. (Use of excess phenyltriethoxysilane (10−30%) resulted in a higher yield of product (95%)). ^{1}H NMR (500 MHz): δ 8.75 (br s, 4H), 7.47 (m, 8H), 7.09 (m, 12H), 6.36 (s, 4H), 6.34 (s, 4H), 5.84 (s, 4H), 5.82 (s, 4H), 2.95 (q, 24H, J = 7.28), 2.12 (d, 4H, J = 12.63), 2.03 (d, 4H, J = 12.66), 1.95 (d, 4H, J = 12.44), 1.94 (d, 4H, J = 12.76), 1.24 (s, 12H), 1.21 (s, 12H), 1.19 (s, 12H), 1.17 (s, 12H), 1.04 (t, 36H, J = 7.29). ^{13}C NMR (125 MHz): δ 149.4, 149.3, 142.5, 142.3, 140.1, 139.4, 139.2, 138.1, 134.8, 134.6, 127.5, 127.4, 126.7, 104.5, 104.3, 102.5, 59.8, 59.6, 57.1, 45.7, 42.4, 42.3, 32.0, 31.6, 31.1, 30.7, 8.5. ^{29}Si NMR (99 MHz, DMSO-d_6): δ −86.3, −86.9. FTIR (KBr): 3442, 2951, 2861, 1637, 1485, 1361, 1279, 1224, 1116, 865, 833, 742, 705, 601 cm^{-1}. Anal. Calcd for $C_{132}H_{164}N_4O_{16}Si_4$: C, 72.89; H, 7.60; N, 2.58; Si, 5.16. Found: C, 72.68; H, 7.94; N, 2.13; Si, 5.24.

(*p*-Fluorophenyl)triethoxysilane (9). In a 250 mL three-neck round-bottom flask equipped with a reflux condenser, effective stirring, an atmosphere of nitrogen, and an equilibrating addition funnel were placed magnesium turnings (0.98 g, 40.5 mmol), tetraethoxysilane (16.4 g, 81.1 mmol), and 15 mL of dry THF with a fleck of iodine. The reaction mixture was stirred and brought up to gentle reflux. 4-Iodofluorobenzene (5.0 g, 22.5 mmol) dissolved in 10 mL of dry THF was added via an addition funnel over a 2 h period with maintaining gentle reflux. After the addition, the reaction mixture was stirred under reflux for an additional 12 h. The mixture was cooled, and 100 mL of dry hexanes was used to precipitate the salts. The solid was removed by filtration, and the filtrate was concentrated under reduced pressure. The resulting cloudy oil was dissolved in 100 mL of dry hexanes, and the salt was filtered. After removal of volatile solvent, the resulting oil was distilled under vacuum, affording a light yellow oil in 68% (3.7 g) yield. ^{1}H NMR (400 MHz): δ 7.58 (d, 2H, J = 7.0), 7.18 (d, 2H, J = 7.0), 3.86 (q, 6H, J = 7.2), 1.24 (t, 9H, J = 7.2). ^{13}C NMR (100 MHz): δ 164.5, 136.9, 126.7, 115.0, 58.7, 18.2. FTIR (neat): 1167, 1295, 1390, 1438, 1502, 1587, 1906, 2877, 2919, 2973 cm^{-1}. HRMS: calcd for $C_{12}H_{19}FO_3Si$ 258.1087, found 258.1095.

4-(Triethoxysilyl)toluene (12). In a 500 mL three-neck round-bottom flask equipped with a reflux condenser, effective stirring, an atmosphere of nitrogen, and an equilibrating addition funnel were placed magnesium turnings (3.70 g, 0.150 mol), tetraethoxysilane (62.6 g, 0.300 mol), and 50 mL of dry THF with a fleck of iodine. The reaction mixture was stirred and brought up to gentle reflux. 4-Bromotoluene (14.7 g, 0.0858 mol) dissolved in 40 mL of dry THF was added via an addition funnel over a 2 h period while maintaining gentle reflux. After the addition, the reaction mixture was stirred under reflux for an additional 12 h. The mixture was cooled, and 200 mL of dry hexanes was used to precipitate the salts. The solid was removed by filtration, and the filtrate was concentrated under reduced pressure. The resulting cloudy oil was dissolved in 200 mL of dry hexanes, and the salt was filtered. After removal of volatile solvent, the resulting oil was distilled under vacuum, affording a light yellow oil in 74% (16.1 g) yield. ^{1}H NMR (400 MHz): δ 7.58 (d, 2H, J = 7.0), 7.18 (d, 2H, J = 7.0), 3.93 (q, 6H, J = 6.9), 2.38 (s, 3H), 1.25 (t, 9H, J = 7.0). ^{13}C NMR (100 MHz): δ 140.3, 134.8, 128.6, 127.2, 58.6, 21.6, 18.2. ^{19}F NMR (99 MHz): −110.6. FTIR (neat): 1167, 1295, 1390, 1443, 1604, 2360, 2926, 2975 cm^{-1}. HRMS: calcd for $C_{13}H_{22}O_3Si$ 254.1363, found 254.1338.

Preparation of Tolyl-Functionalized Macrocycle 13. To a refluxing solution of 5,5′,6,6′-tetrahydroxy-1,1′-spirobis(indane) (500 mg, 1.47 mmol), phenyltriethoxysilane (565 mg, 2.35 mmol), and 4-triethoxysilytoluene (**12**) (150 mg, 0.59 mmol) in anhydrous THF (4.0 mL) was rapidly added dropwise dry triethylamine (445 mg, 4.4 mmol). The mixture was stirred and kept under reflux under a nitrogen atmosphere for 2 days.

The mixture was cooled to room temperature, and the precipitate was collected by filtration and rinsed with THF (100 mL). Residual solvent was removed in vacuo to give 528 mg of solid. ES-TOF-MS (in CH_3CN): 883.9 ([**2** + 2H]$^{2-}$, 100), 890.9 ([**13** + 2H]$^{2-}$, 20).

Preparation of Fluoro-Functionalized Macrocycles 10, 11, and 14. To a refluxing solution of 5,5′,6,6′-tetrahydroxy-1,1′-spirobis(indane) (500 mg, 1.17 mmol), phenyltriethoxysilane (565 mg, 2.35 mmol), (*p*-fluorophenyl)triethoxysilane (**9**), and phenyltriethoxysilane (143 mg, 0.59 mmol) in anhydrous THF (4.0 mL) was rapidly added dropwise dry triethylamine (445 mg, 4.4 mmol). The mixture was stirred and kept under reflux under a nitrogen atmosphere for 2 days. The mixture was cooled to room temperature, and the precipitate was collected by filtration and rinsed with THF (100 mL). Residual solvent was removed in vacuo to give 542 mg of solid. ES-TOF-MS (in CH_3CN): 588.9 ([**2** + H]$^{3-}$, 55), 594.9 ([**10** + H]$^{3-}$, 100), 600.9 ([**11** + H]$^{3-}$, 20), 607.3 ([**14** + H]$^{3-}$, 1.3).

Reversibility Experiment (Case 1). To a refluxing THF solution (4.0 mL) of tetrasiliconate macrocycle **2** (200 mg, 0.092 mmol) and (*p*-fluorophenyl)triethoxysilane (150 mg, 0.62 mmol) was added dry triethylamine (0.30 mL, 2.0 mmol). The reaction mixture was stirred and refluxed under a nitrogen atmosphere for 2 days. The reaction remained heterogeneous the entire time. The mixture was cooled to room temperature, and the precipitate was collected by filtration and washed with THF. Residual solvent was removed under vacuum. ES-TOF-MS (in CH_3CN): 883.7 ([**2** + 2H]$^{2-}$, 100), 892.8 ([**10** + 2H]$^{2-}$, 3.50), 901.7 ([**11** + 2H]$^{2-}$, 1.5).

Reversibility Experiment (Case 2). To a refluxing THF (3.0 mL)/CH_3CN (1.0 mL) solution of the tetrasiliconate macrocycle **2** (100 mg, 0.046 mmol) and (*p*-fluorophenyl)triethoxysilane (45 mg, 0.18 mmol) was added dry triethylamine (0.04 mL, 0.28 mmol). The reaction mixture was stirred and refluxed under a nitrogen atmosphere for 2 days. The reaction became heterogeneous within 4 h. The mixture was cooled to room temperature, and volatiles were removed under vacuum, giving a pale yellow solid. The solid was collected and washed with THF. Residual solvent was removed under vacuum. ES-TOF-MS (in CH_3CN): 883.8 ([**2** + 2H]$^{2-}$, 100), 892.8 ([**10** + 2H]$^{2-}$, 73), 901.8 ([**11** + 2H]$^{2-}$, 20).

Reversibility Experiment (Case 3). To a refluxing THF (3.0 mL)/EtOH (1.0 mL) solution of tetrasiliconate macrocycle **2** (100 mg, 0.046 mmol) and (*p*-fluorophenyl)triethoxysilane (45 mg, 0.18 mmol) was added dry triethylamine (0.04 mL, 0.28 mmol). The reaction mixture was stirred and refluxed under a nitrogen atmosphere for 2 days. The reaction became heterogeneous within 30 min. The mixture was cooled to room temperature, and the volatiles were removed under vacuum, giving a pale yellow solid. The solid was collected and washed with THF. Residual solvent was removed under vacuum. ES-TOF-MS (in CH_3CN): 781.3 ([**4a**] $^{-}$, 65), 799.3 ([**4b**]$^{-}$, 100).

Acknowledgment. Financial support from the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. J.J.P. gratefully appreciates helpful discussion and assistance on computational work from Dr. Fleischer and Dr. Hi Yoo.

OM020263X