JOC*Article*

Synthesis and Characterization of Cationic Iodonium Macrocycles

Ukkiramapandian Radhakrishnan and Peter J. Stang*

Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City, Utah 84112

stang@chemistry.utah.edu

A synthetic strategy for the high-yield preparation of iodonium containing macrocycles such as rhomboids, a square, and a pentagon is described, with the long-term objective of preparing iodonium compounds for potential molecular electronics applications. Two cationic rhomboid shaped molecules were prepared for the first time (55−70%) by the treatment of compounds **11** and **12a** or **12b** with Me_3SiOTf. The reaction of dication **8** with **6** in the presence of Me_3SiOTf gave an iodonium containing molecular square in 70% yield. In addition, a pentagon-shaped macromolecule was prepared in 60% yield. These iodonium-containing charged macromolecules were characterized by multinuclear NMR, mass spectrometry, and physical means.

Introduction

One of the most exciting and rewarding challenges chemists face today is to devise a wholly synthetic macromolecular system for potential applications in nanotechnology.[1] Since the discovery of crown ethers by Pederson, the interest in the synthesis of *neutral* macrocycles such as cyclodextrins, crown ethers, and cryptands, which can act as molecular or cationic receptors has continually increased.[2] In recent years, the synthesis and investigation on the properties of *cationic* macromolecules have attracted attention as well.[3,4] To date, there are two major category of charged macromolecular systems those containing nitrogen−carbon bonds (**1**)[3] and nitrogen−metal bonds (**2**)[4] that have been explored for their potential application in molecular electronics[4,5] and host−guest chemistry.[6,7] Stoddart et al. have utilized cationic cyclobis(paraquat-*p*-phenylene) **1** as a basic entity in a number of electrochemically switchable molecular and supramolecular systems such as catenanes and rotaxanes (Chart 1).[3,8] The catenanes

CHART 1
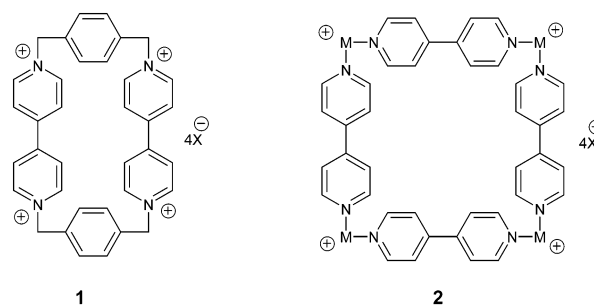
and rotaxanes are important structural units for the construction of artificial nanomolecular machines.[9]

Most of the work in this area has been guided and governed by the synthetic availability, stability, fatigue resistance, and toxicity of a given molecular architecture to be used as a basis for complex design. It is well-known that polyvalent iodonium compounds are widely available and meet all of these basic requirements.[10] Furthermore, the Martin−Arduengo formalism predicts the likely formation of macrocyclic tetraiodonium salts **3** and **4** using 8-I-2 monocationic iodonium salts that have experimentally proven T-shaped geometry with a 90° bond angle (Chart 2).[11,12] Despite the importance of charged

(1) *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J., Durr, H., Eds.; VCH: Weinheim, Germany, 1991. (b) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89.

(2) (a) Pederson, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495. (b) Pederson, C. J. *Aldrichim. Acta*, **1971**, *4*, 1. (c) *Synthetic Multidentate Macrocyclic Compounds*; Izatt, R. M., Christensen, J. J., Eds.; Academic Press: New York, 1978.

(3) (a) Pease, A. R.; Jeppensen, J. O.; Stoddart, J. F.; Luo, Y.; Collier, C. P.; Heath, J. R. *Acc. Chem. Res.* **2001**, *34*, 611. (b) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725.

(4) (a) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853. (b) Olenyuk, B.; Whiteford, J. A.; Fechtenkotter, A.; Stang, P. J. *Nature* **1999**, *398*, 796. (c) Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502. (d) Fujita, M. *Chem. Soc. Rev.* **1998**, *27*, 417. (e) Fujita, M.; Ogura, K. *Coord. Chem. Rev.* **1996**, *148*, 249.

(5) (a) Sauvage, J.-P. *Acc. Chem. Res.* **1998**, *31*, 611. (b) *Nanosystems, Molecular Machinery, Manufacturing and Computation*; Drexler, K., Ed.; Wiley: New York, 1992. (c) *Molecular Electronic Devices*; Carter, F. E., Ed.; Marcel Dekker: New York, 1987.

(6) (a) *Host−Guest Complex Chemistry/Macrocycles*; Vögtle, F., Webber, E., Eds.; Springer-Verlag: Berlin, 1985. (b) *Inclusion Phenomena and Molecular Recognition*; Atwood, J. L., Ed.; Plenum: New York, 1990.

(7) (a) Bradley, D. *Science* **1993**, *259*, 890. (b) Amato, I. *Science* **1993**, *260*, 753. (c) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1304.

(8) (a) Bissell, R. A.; Cordova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133. (b) Balzani, V.; Gomez-Lopez, M.; Stoddart, J. F., *Acc. Chem. Res.* **1998**, *31*, 405.
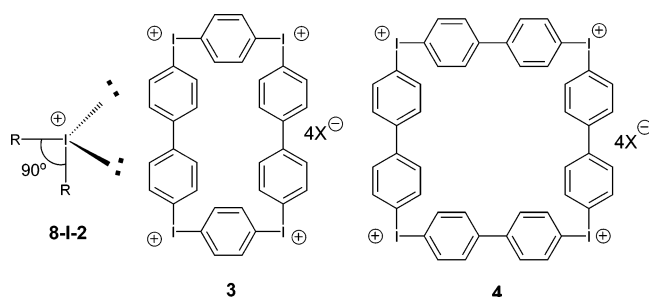
(9) (a) Collier, J. P.; Matterstei, G.; Wong, E. W.; Luo, Y.; Beverly, K.; Sampaio, J.; Raymo, F. M.; Stoddart, J. F. *Science* **2000**, *289*, 1172. (b) *Molecular Catenanes, Rotaxanes and Knots*; Sauvage, J.-P., Buchecker, D., Eds.; Wiley-VCH: Weinheim, 1999. (c) Schill, G. *Catenanes, Rotaxanes and Knots*; Academic Press: New York, 1971.

(10) (a) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123; **2002**, *102*, 2523. (b) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, 1997. (c) Wirth, T.; Hirt, U. H. *Synthesis* **1999**, 1271.
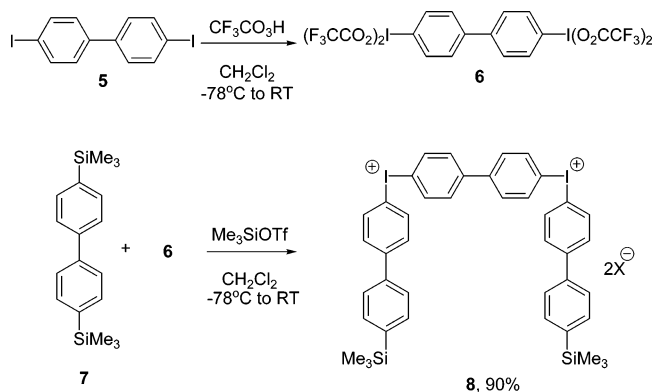
(11) Stang, P. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 274. (b) Stang, P. J.; Arif, A. M.; Crittell, C. M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 281.

(12) Perkins, C. W.; Martin, J. C.; Arduengo, A. J.; III; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753.

CHART 2

8-I-2   **3**   **4**

SCHEME 1

5   **6**

7   **8**, 90%

SCHEME 2

9   **10**, 80%

11, 60%

SCHEME 3

11

(12a) R = Me
(12b) R = H

(13a) 71%
(13b) 55%

macromolecules and a significant amount of information available on the properties of iodonium compounds, surprisingly only one example on the practical synthesis of a charged iodonium containing macromolecule has been described to date.[13] Presented here is a versatile method for the construction of *cationic* macromolecules such as rhomboids, a square, and a pentagon in high yield using T-shaped iodonium compounds as the shape-defining corner units. The structures of these macrocycles were confirmed by physical means and multinuclear NMR and mass spectrometry.

Results and Discussion

Synthesis of Building Units. An efficient method for the synthesis of unsymmetrical diaryliodonium compounds involves the known reaction of [bis(trifluro-acetoxy)iodo]arenes or [hydroxy(sulfonyloxy)iodo] arenes with trimethylsilyl-substituted aromatic compounds in the presence of Lewis acids.[14] Syntheses of angular and linear building blocks for the stepwise construction of iodonium-containing macrocycles were carried out via these methods.
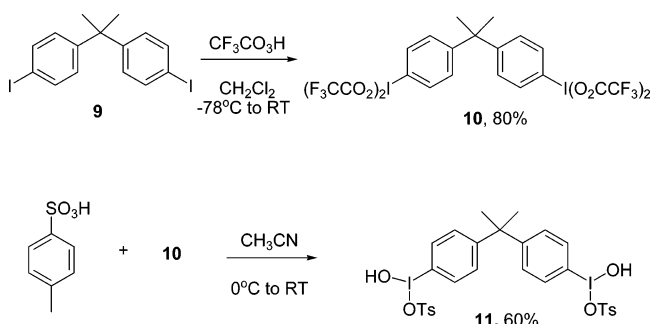
Compound **8** was prepared as outlined in Scheme 1. Oxidation of commercially available 4,4′-diiodobiphenyl **5** with CF_3CO_3H [prepared from $(CF_3CO)_2O$ and 80% H_2O_2] gave **6** in 77% yield.[15] Reaction of **6** with 2 equiv of **7** and Me_3SiOTf gave bisiodonium triflate salt **8** in 90% isolated yield. Dication **8** is an off-white stable compound, soluble in methanol but insoluble in $CHCl_3$, CH_2Cl_2, and hexanes.

Angular building block **11** was prepared as a stable white solid by the oxidation of compound **9** with CF_3-CO_3H, followed by hydrolysis with toluenesulfonic acid (Scheme 2).

Cationic Molecular Rhomboids. The simplest and smallest iodonium-containing rhomboid shaped macromolecule can be prepared by the reaction of one ~109° iodonium angular building block with another angular trimethylsilyl derivative. Compound **11** corresponds well with the geometrical requirement for the angular iodonium building block. The counterpart, trimethylsilyl derivative **12a** (R = Me), was prepared from the corresponding iodo compound by lithiation, followed by quenching with chlorotrimethylsilane.[16] The reaction of compounds **11** and **12a** in CH_2Cl_2, in the presence of Me_3SiOTf, gave a pale yellow solid after evaporation of the solvent. When this solid was dissolved in methanol, the addition of diethyl ether resulted in the precipitation of rhomboid **13a** (70% isolated yield) as a stable, microcrystalline solid (Scheme 3). We have also studied the reactions of compounds **11** and **12a** in the presence of other Lewis acids such as $BF_3 \cdot Et_2O$ and CF_3CO_2H and found that the yields of rhomboids were lower.

Similarly, addition of Me_3SiOTf to a mixture of **11** and **12b** (R = H) in CH_2Cl_2 at −78 °C and stirring at room temperature for 3−4 h resulted in the formation of unsymmetrical rhomboid **13b** in 55% yield (Scheme 3). Both of these macrocycles are very stable at room temperature and soluble in methanol but insoluble in chloroform, methylene chloride, and nitromethane.

Cationic Molecular Square. The synthesis of a square can be achieved by the coupling of two linear iodonium compounds with two linear trimethylsilyl derivatives either in one step or multiple steps. Initially, we attempted to construct a square-shaped macromol-

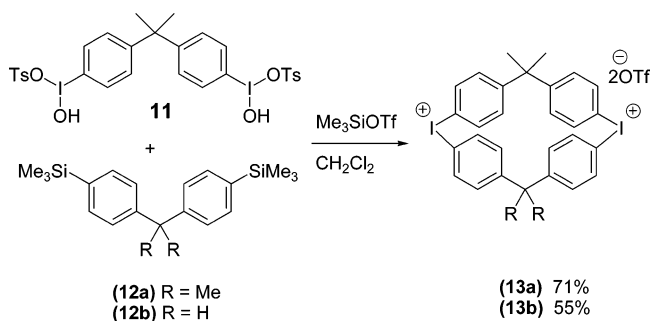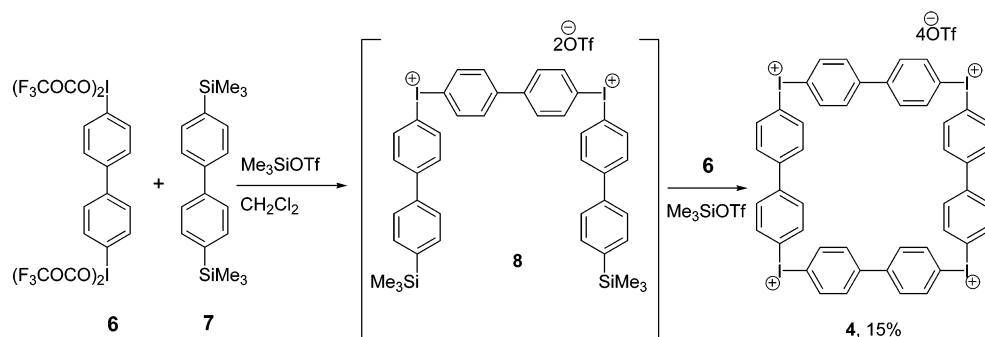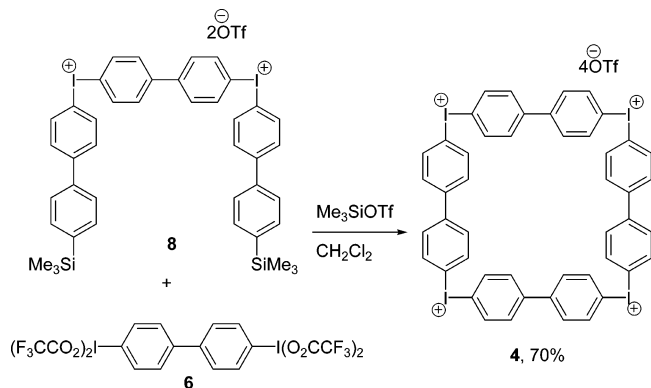(13) Stang, P. J.; Zhdankin, V. V. *J. Am. Chem. Soc.* **1993**, *115*, 9808.
(14) (a) Gallop, P. M.; Paz, M. A.; Fluckiger, R.; Stang, P. J.; Zhdankin, V. V.; Tykwinski, R. R. *J. Am. Chem. Soc.* **1993**, *115*, 11702. (b) Kuehl, C. J.; Bolz, J. T.; Zhdankin, V. V. *Synthesis* **1994**, 312.
(15) Yagupolskii, L. M.; Maletina, I. I.; Kondratenko, N. V.; Orda, V. V. *Synthesis* **1978**, 835.

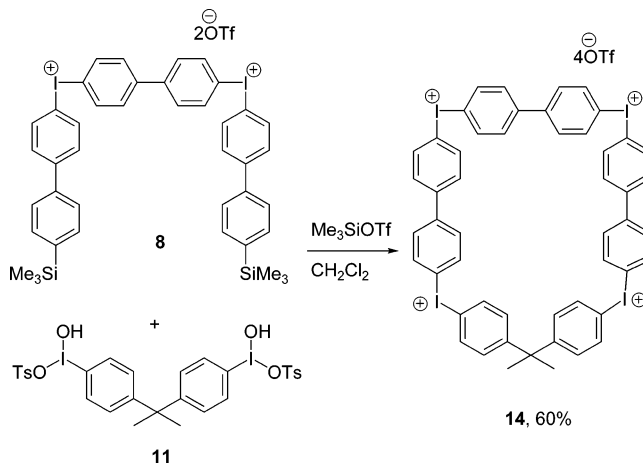(16) Habich, D.; Effenberger, F. *Synthesis* **1979**, 841.

SCHEME 4

SCHEME 5

SCHEME 6

ecule in a single step. The reaction of linear compound **6** with **7** in the presence of Me₃SiOTf gave molecular square **4** as a minor product (15%) with oligomers as major products. We hypothesized that the reaction sequence involves the formation of **8** as an intermediate, which in turn reacted with one more iodonium compound to give macrocycle **4** (Scheme 4).

In contrast, stepwise formation of **4** via treatment of **8** with iodonium trifluoroacetate **6** in the presence of Me₃-SiOTf resulted in the formation of **4** in 70% yield (Scheme 5).

Cationic Molecular Pentagon. It was envisaged that a pentagon-shaped molecule might be prepared via the coupling of dication **8** with the angular diiodonium species **11**. As expected, the reaction of **11** with dication **8** and Me₃SiOTf in CH₂Cl₂ at −78 °C gave pentagon **14** in 60% yield (Scheme 6).

Template-Assisted Synthesis. Template-assisted synthesis is one of the more efficient methods for the selective preparation of macrocycles and molecular receptors.[17] The template effect not only speeds up the reaction rates, but it also leads to much higher yields of products.[17] A recent report described the template-assisted synthesis of tetracationic macromolecules using dimethoxybenzene (DMB) as a neutral guest.[18] The DMB formed a weak complex with the dication and acts as a good template for the cyclization reaction. Hence, we investigated the possibility of using a neutral guest (DMB) as a template to improve the yield of the final cyclization reaction. The reaction of **8** with **6** and Me₃SiOTf in the presence of DMB gave **4** in 70% isolated yield (Scheme 7), indicating

(17) *Templated Organic Synthesis*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 2000.
(18) Philp, D.; Stoddart, J. F. *Synlett* **1991**, 445.

that there is no template effect and the neutral guest, DMB, does not enhance this reaction.

NMR Spectroscopic Analysis. The new macrocycles were characterized by NMR (¹H, ¹³C, ¹⁹F), mass spectrometry, and elemental analysis. In all macrocycles (**4**, **13a**, **13b**, and **14**), the protons attached to the carbons ortho to the iodines were observed downfield compared to the meta protons. The ortho and meta hydrogens were magnetically coupled to each other with a coupling constant of 8.4−9.0 Hz. The ¹H NMR showed two multiplets at 8.06 ppm (ortho) and 7.41 ppm (meta) for rhomboid **13a** and two multiplets at 8.05 ppm (ortho) and 7.56 ppm (meta) for the aromatic protons of square (**4**), indicative of highly symmetrical structures.

The ¹H NMR of the unsymmetrical rhomboid **13b** consists of two multiplets for the ortho and meta protons of the aromatic structural units. In the case of pentagon **14**, the ¹H NMR showed two multiplets for the ortho and meta protons of the linear biphenyl units at 8.14 and 7.64 ppm; it also contained two doublets at 7.95 and 7.19 ppm for the ortho and meta protons of the angular diphenyl units. The hydrogens of the methyl group in **14** were observed at 1.56 ppm as a singlet. The presence of the counterion (CF₃SO₃⁻) in all of these compounds was confirmed by the signal at −78 ppm in ¹⁹F NMR. The ¹³C{H} NMR data for these macrocycles were consistent with the structural formulations.

Mass Spectroscopic Analysis. The molecular composition of these macrocycles was established by mass spectrometry. Fast atom bombardment (FAB) and electrospray ionization (ESI) mass spectrometry provided charge state information and isotopic resolution for

SCHEME 7
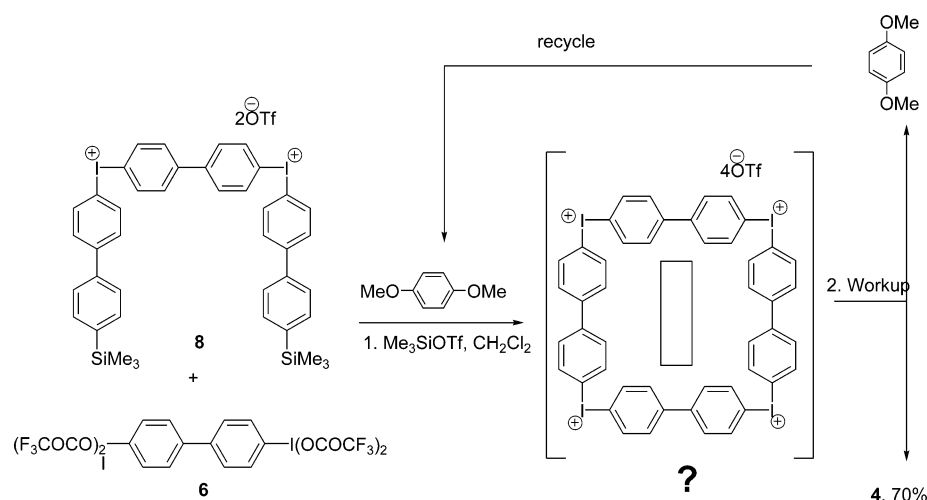
molecular ions corresponding to the macrocycles. The peak at $m/z = 790$ was isotopically resolved (m/z spacing of 1) allowing direct charge state assignment as $+1$ charge state. The calculated molecular weight of an intact macromolecule minus one triflate is 791.04 and the experimental molecular weight is 790.9, in excellent agreement.

FAB analysis of **13b** gave a peak at $m/z = 763$ due to the loss of one triflate (M-OTf)$^+$ as well as a peak at 615 for $(M - 2OTf + H^+)^+$ in agreement with the composition of macrocycle **13b**. The FAB mass spectrum of **4** has a peak at $m/z = 1564$ that corresponds to the molecular ion of the cationic portion $(M - OTf)^+$ of **4**. Likewise, the peak at 707 corresponds to the doubly charged cation $(M - 2OTf)^{2+}$ of **4**. Electrospray ionization mass spectrometry (ESI/MS) was used to identify the composition of pentagon **14**. In the mass spectrum of **14**, the $+1$ species resulting from the loss of one triflate with a mass-to-charge ratio $m/z = 1605$ and a peak at $m/z = 728.03$ attributable to the loss of two triflates were observed.

Molecular Modeling. As suitable X-ray quality crystals could not be obtained, the square-shaped macrocycle was structurally minimized.[19] Figure 1 displays the minimized CPK space-filling model of macrocycle **4**. The calculated distance between diagonal iodine atoms is 1.5
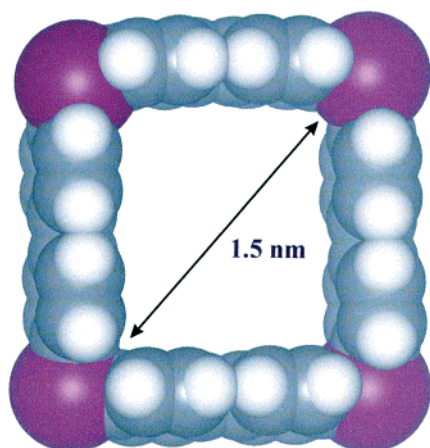
nm, while the distance between the two parallel biphenyl rings is about 1.1 nm.

Conclusion

In summary, we have described an efficient method for the synthesis of iodonium-containing macrocycles such as rhomboids, a square, and a pentagon in high yield. Syntheses of these macromolecules were carried out by the reaction of [bis(trifluoroacetoxy)iodo]arenes or [hydroxy(sulfonyloxy)iodo] with trimethylsilyl-substituted aromatic compounds in the presence of Me$_3$SiOTf. In addition, an attempt was made to improve the yield of square using dimethoxybenzene (DMB) as a template and found that DMB does not increase the yield of square. The structures of these macrocycles were established using elemental analysis, NMR and mass spectrometry. These iodonium-containing macromolecules may find potential application in nanotechnology.

Experimental Section

All experiments were performed under an inert atmosphere of nitrogen using standard Schlenk technique. The solvents used in the reactions were reagent or HPLC grade and purified in the following manner: methylene chloride was distilled from calcium hydride, diethyl ether was distilled from sodium/benzophenone, and CH$_3$CN was distilled from calcium hydride. Trifluoroacetates **6**, **10**,[15] and Me$_3$SiOTf[20] were prepared using a modified literature procedure. The trimethylsilyl derivatives (**7**, **12a**, and **12b**) were prepared from the corresponding iodides using BuLi/TMSCl.[16]

Preparation of 8. In a Schlenk flask (25 mL) equipped with a magnetic stir bar were placed **6** (0.426 g, 0.5 mmol), **7** (0.294 g, 1 mmol), and CH$_2$Cl$_2$ (15 mL) under a N$_2$ atmosphere. To this mixture was added Me$_3$SiOTf (0.6 mL) at −78 °C, and the mixture was allowed to warm to room temperature. After 4 h, the solvent was evaporated and the residue was dissolved in a methanol/CH$_2$Cl$_2$ (2:1) mixture to remove any oligomers. The solvent was evaporated again, and the residue was washed with ether to yield **8** (0.52 g, 90%): ^{1}H NMR (DMSO-d_6/CDCl$_3$, 300 MHz) δ 8.05 (d, 4H, $J = 8.2$ Hz), 8.00 (d, 4H, $J = 8.3$ Hz), 7.6−7.45 (m, 16H), 0.21 (s, 18H); ^{19}F NMR (DMSO-d_6/CDCl$_3$) −78.13; FAB/MS m/z 1005 (M − OTf), 428 (M − 2OTf). Anal.

FIGURE 1.

(19) Hyperchem 5.1, Hypercube, Inc., 1997.
(20) Demuth, M.; Mikhail, G. *Synthesis* **1982**, 827.

Calcd for $C_{44}H_{42}S_2Si_2I_2O_6F_6$: C, 45.76; H, 3.67. Found: C, 45.43; H, 3.55.

Preparation of 11. To a stirred solution of trifluroacetate **10** (2.05 g, 2.3 mmol) in CH_3CN was added $TsOH \cdot H_2O$ (0.513 g, 2.7 mmol) at 0 °C. The mixture was warmed to room temperature and stirred until the formation of a white crystalline precipitate. The product was filtered, washed with dry CH_2Cl_2 (10 mL), and dried in vacuo to give **11** (1.12 g, 60%): ^{1}H NMR (DMSO-d_6/CDCl$_3$, 300 MHz) δ 8.15 (d, 4H, J = 8.4 Hz), 7.51 (d, 4H, J = 8.7 Hz), 7.42 (d, 4H, J = 8.4 Hz), 7.16 (d, 4H, J = 8.7 Hz), 2.24 (s, 6H), 1.83 (s, 6H); ^{13}C NMR (CD$_3$OD, 75 MHz) δ 157.1, 143.1, 141.9, 137.2, 131.4, 129.9, 126.9, 119.8, 48.1, 45.3, 30.5, 21.3; ESI/MS m/z 481.1 (M − 2OTs), 447.9 [M − (2OTs + 2OH)].

Preparation of 13a. To a mixture of **11** (0.21 g, 0.25 mmol) and **12a** (0.085 g, 0.25 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added Me$_3$SiOTf (0.6 mL). The reaction mixture was allowed to warm to room temperature. After 4 h, the solvent was evaporated and the residue was dissolved in a methanol/ CH_2Cl_2 (2:1) mixture to remove any oligomers. The solvent was evaporated, and the residue was washed with ether to yield **13a**: yield (70%, 0.16 g); ^{1}H NMR (CD$_3$OD, 300 MHz) δ 8.06 (d, 8H, J = 9.0 Hz), 7.41 (d, 8H, J = 8.7 Hz), 1.63 (s, 12H); ^{13}C NMR (CD$_3$OD, 75 MHz) δ 153.0 (C$_i$-I), 134.2 (C$_o$-I), 129.6 (C$_m$-I), 111.5 (C$_p$-I), 120.8 (q, J = 319 Hz), 42.9 (C$_i$-Me), 29.1 (Me); ^{19}F NMR (CD$_3$OD) −78.13; FAB/MS m/z 790 (M − OTf), 642 (M − 2OTf + H$^+$). Anal. Calcd for $C_{32}H_{28}F_6I_2O_6S_2$: C, 40.87; H, 3.00; S, 6.82. Found: C, 41.04; H, 3.24; S, 6.44.

Preparation of Macrocycle 13b. To a mixture of **11** (0.205 g, 0.25 mmol) and **12b** (0.078 g, 0.25 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added Me$_3$SiOTf (0.6 mL). The reaction mixture was allowed to warm to room temperature and stirred for 4 h. Workup was done as above: yield (55%, 0.125 g); ^{1}H NMR (CD$_3$OD, 300 MHz) δ 8.04 (m, 8H), 7.31 (d, 8H, J = 8.4 Hz), 4.04 (s, 2H), 1.63 (s, 6H); ^{13}C NMR (CD$_3$OD, 75 MHz) δ 155.2, 146.1, 137.8, 136.2, 135.7, 133.1, 131.1, 129.2, 128.1 (q) 44.2 (−CH$_2$−), 41.0 (C$_i$-Me), 29.8 (Me); ^{19}F NMR (CD$_3$OD) −78.13;

FAB/MS m/z 763 (M − OTf), 615.1 (M − OTf + H$^+$). Anal. Calcd for $C_{30}H_{24}F_6I_2O_6S_2$: C, 39.49; H, 2.65; S, 7.03. Found: C, 39.51; H, 3.04; S, 6.73.

Preparation of Macrocycle 4. In a Schlenk flask (25 mL) equipped with a magnetic stir bar were placed **6** (0.212 g, 0.25 mmol), **8** (0.25 g, 0.25 mmol), and CH_2Cl_2 (10 mL) under an N$_2$ atmosphere. To this mixture was added Me$_3$SiOTf (0.6 mL) at −78 °C, and the solution was allowed to warm to room temperature and stirred for 4 h. Workup was done as above: yield (0.275 g, 71%); ^{1}H NMR (CD$_3$OD, 300 MHz) δ 8.29 (d, 16H, J = 8.7 Hz), 7.77 (d, 16H, J = 8.7 Hz); ^{13}C NMR (DMSO-d_6/CDCl$_3$, 75 MHz) δ 141.6 (C$_i$-I), 135.9 (C$_o$-I), 130.2 (C$_m$-I), 116.2 (C$_p$-I), 120.8 (q, J = 319 Hz); ^{19}F NMR (CD$_3$OD) −78.13; FAB/MS m/z 1564 (M − OTf), 1415 (M − 2OTf + H$^+$), 707 (M − 2OTf). Anal. Calcd for $C_{52}H_{32}F_{12}I_4O_{12}S_4$: C, 36.47; H, 1.88; S, 7.49. Found: C, 36.09; H, 2.19; S, 7.29.

Preparation of Macrocycle 14. To a mixture of **8** (0.25 g, 0.25 mmol) and **11** (0.205 g, 0.25 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added Me$_3$SiOTf (0.6 mL). The reaction mixture was allowed to warm to room temperature and stirred for 4 h. Workup was done as above: yield (60%, 0.26 g); ^{1}H NMR (DMSO-d_6/CDCl$_3$, 300 MHz) δ 8.14 (m, 12H), 7.95 (d, 4H, J = 8.7 Hz), 7.64 (m, 12H), 7.19 (d, 4H, J = 8.4 Hz) 1.56 (s, 6H); ^{13}C NMR (CD$_3$OD, 75 MHz) δ 155.9, 144.3, 137.3, 137.2, 136.5, 131.9, 131.6 (all Ar), 129.1 (q, J = 319 Hz) 116.1 (C$_i$-Ar), 113.4 (C$_i$-Ar), 44.9 (C$_i$-Me), 30.4 (Me); ^{19}F NMR (CD$_3$OD) −78.13; ESI/MS m/z 1605 (M − OTf), 728.03 (M − 2OTf). Anal. Calcd for $C_{55}H_{38}F_{12}I_4O_{12}S_4$: C, 37.65; H, 2.18; S, 7.31. Found: C, 37.55; H, 2.51; S, 7.39.

Supporting Information Available: Proton and mass spectra for compounds **4**, **13a**, **13b**, and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO030246X