in- and *out*-Cyclophanes Bearing Non-Hydrogen Bridgehead Substituents

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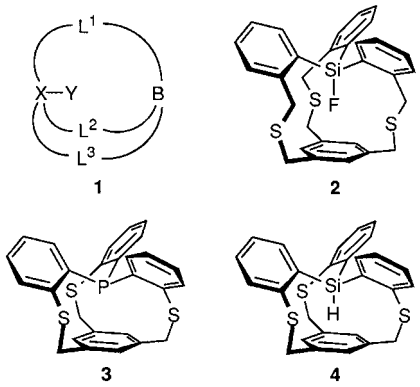
The syntheses of several cyclophanes containing a triaryl(element) "top" poised above a trisubstituted benzene "base" were carried out to install a non-hydrogen atom as a substituent on a bridgehead with an inwardly directed geometry. Most significantly, the tribenzo 6-fluoro-6-sila-2,10,19-trithia-[5^{6,14}][11]metacyclophane **2** was prepared by condensation of tris[2-(bromomethyl)phenyl]fluorosilane and 1,3,5-tris(mercaptomethyl)benzene in 0.4% yield. The X-ray structure of **2** shows that the cyclophane adopts an *in*-configuration; i.e., the fluorine atom is on the interior of the macrocycle and only 2.8 Å from the center of the basal aromatic ring. Compound **2** is one of only a very few molecules to contain a non-hydrogen *in*-atom, and the *in*-fluorosilane of **2** is the largest *in*-functional group to have been installed in any molecule. Similar attempts to prepare an *in*-phosphine oxide were unsuccessful, although the corresponding *in*-phosphines were prepared, and an attempt to prepare an *in*-methylsilane led instead to the corresponding *out*-isomer.

in/*out*-Stereoisomerism is often observed in medium- and large-ring bicyclic organic structures. For the *in*-isomers, schematically represented by **1**, there must be sufficient space to accommodate the inwardly directed functionalities X−Y. Not surprisingly then, a comprehensive review of *in*/*out*-stereoisomerism[1] noted that the vast majority of inside functional groups are methines (X−Y = C−H), amines (N−lp), and ammonium ions (N$^+$−H), and the only compounds containing *in*-functionalities with Y larger than a hydrogen atom or lone pair are the *in*,*out*-isomers of Whitlock's enormous, macrocyclic bis(phosphine oxides),[2] where the linking arms (L) between the phosphine oxide bridgeheads are 14−16 atoms long and steric congestion is not an issue. We now report the syntheses of *in*-cyclophane **2**, in which an *in*-fluorosilane (X−Y = Si−F) is pressed into the face of a benzene ring, and several related cyclophanes with *in*- and *out*-configurations at their bridgeheads.[3]



1 **2** **3** **4**

Results and Discussion

Initial Computational Studies. We reported the syntheses of *in*-phosphine **3** and *in*-silane **4** several years ago,[4,5] but all attempts to place a larger apical functionality in that framework failed. Therefore, before beginning any additional experimental work, an extensive series of AM1 calculations[6] was performed to identify the best candidates for successful preparation of an *in*-cyclophane with a "heavy atom" bridgehead substituent. The results have been grouped in Table 1 according to the length of the three linking arms between the triaryl(element) "top" and the trisubstituted benzene "base". (Only the semiempirical calculations were available to guide our work; the ab initio calculations in Table 1 were performed *after* the experimental studies and will be discussed later.) For the cyclophanes with 2-atom links, the calculations indicate that *in*-geometries are favored for the phosphine **3** and silane **4**. However, the X-ray structure of **4** shows significant distortions of the basal ring due to pressure from the *in*-hydrogen,[5] so it is not surprising that the *in*-phosphine oxide **5** and *in*-fluorosilane **6** are calculated to be much more strained than the corresponding *out*-isomers.

With the addition of one or two methylene groups to each of the linking bridges in these cyclophanes, the inclusion of a non-hydrogen *in*-atom becomes much more favorable. The *in*-phosphine oxide **9** is strongly preferred over its *out*-isomer, the *in*-phosphine oxide **13** and *in*-fluorosilane **2** are more modestly preferred, and the *in*- and *out*-methylsilanes **15** are essentially equal in energy. Therefore, these four were chosen as the prime synthetic targets. The outcome of the syntheses, of course, will depend entirely on kinetic factors, because the key reactions to be used—nucleophilic substitutions of alkyl halides by thiolates—are essentially irreversible. However, the product geometry is not determined until the

(1) Alder, R. W.; East, S. P. *Chem. Rev.* **1996**, *96*, 2097−2111.

(2) (a) Friedrichsen, B. P.; Whitlock, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 9132−9134. (b) Friedrichsen, B. P.; Powell, D. R.; Whitlock, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 8931−8941.

(3) A communication describing a part of this work has been published: Dell, S.; Vogelaar, N. J.; Ho, D. M.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 6421−6422. An extremely detailed discussion of the syntheses of the cyclophanes may be found in: Dell, S., Ph.D. Dissertation, Princeton University, 1998.

(4) Pascal, R. A., Jr.; West, A. P., Jr.; Van Engen, D. *J. Am. Chem. Soc.* **1990**, *112*, 6406−6407.

(5) L'Esperance, R. P.; West, A. P., Jr.; Van Engen, D.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 2672−2676.

(6) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902−3909.

10.1021/jo990727+ CCC: $18.00
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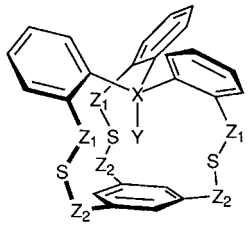
Table 1. Computational Data for Various *in*- and *out*-Cyclophanes



central atoms	computational level[a]	config.[b]	ΔH_f (AM1, kcal/mol) or E (HF, au[c])	difference[d] (*in* − *out*, kcal/mol)	exptl. geom.
		Cyclophanes with 2-Atom Links (Z_1 = —, Z_2 = CH_2)			
X = P, Y = lp[e] (**3**)	AM1	in	165.65	−5.41	*in*
	AM1	out	171.06		
X = Si, Y = H (**4**)	AM1	in	116.28	−0.01	*in*
	AM1	out	116.29		
X = P, Y = O (**5**)	AM1	in	104.64	16.78	
	AM1	out	87.86		
X = Si, Y = F (**6**)	AM1	in	55.57	27.88	
	AM1	out	27.69		
		Cyclophanes with 3-Atom Links (Z_1 = CH_2, Z_2 = CH_2)			
X = P, Y = lp (**7**)	AM1	*in*	140.56	−6.32	*in*
	AM1	*out*	146.88		
X = Si, Y = H (**8**)	AM1	*in*	86.07	−7.33	
	AM1	*out*	93.40		
X = P, Y = O (**9**)	AM1	*in*	55.91	−5.50	
	AM1	*out*	61.41		
X = Si, Y = F (**2**)	AM1	*in*	3.55	−0.55	*in*
	AM1	*out*	4.10		
	HF/STO-3G	*in*	−2701.155 30	−17.65	
	HF/STO-3G	*out*	−2701.127 17		
	HF/3-21G(*)	*in*	−2718.913 97	−14.28	
	HF/3-21G(*)	*out*	−2718.891 21		
X = Si, Y = Me (**10**)	AM1	*in*	91.32	8.20	
	AM1	*out*	83.12		
		Cyclophanes with 4-Atom Links (Z_1 = CH_2, Z_2 = CH_2CH_2)			
X = P, Y = lp (**11**)	AM1	*in*	124.50	−1.26	*in*
	AM1	*out*	125.76		
X = Si, Y = H (**12**)	AM1	*in*	69.93	−1.01	
	AM1	*out*	70.94		
X = P, Y = O (**13**)	AM1	*in*	38.00	−0.94	
	AM1	*out*	38.94		
X = Si, Y = F (**14**)	AM1	*in*	−16.88	1.73	
	AM1	*out*	−18.61		
X = Si, Y = Me (**15**)	AM1	*in*	61.70	−0.03	*out*-C_1
	AM1	*out*	61.73		
	AM1	*out* (C_1)	63.82		
	HF/STO-3G	*in*	−2757.994 30	−9.51	
	HF/STO-3G	*out*	−2757.976 88		
	HF/STO-3G	*out* (C_1)	−2757.979 15		
	HF/3-21G(*)	*in*	−2775.776 16	−6.05	
	HF/3-21G(*)	*out*	−2775.762 51		
	HF/3-21G(*)	*out* (C_1)	−2775.766 52		

[a] See the Experimental Section for computational details. [b] Except as noted, all structures possess C_3 symmetry. [c] One au = 627.503 kcal/mol. [d] Negative values favor the *in*-isomer. [e] lp = lone pair electrons.

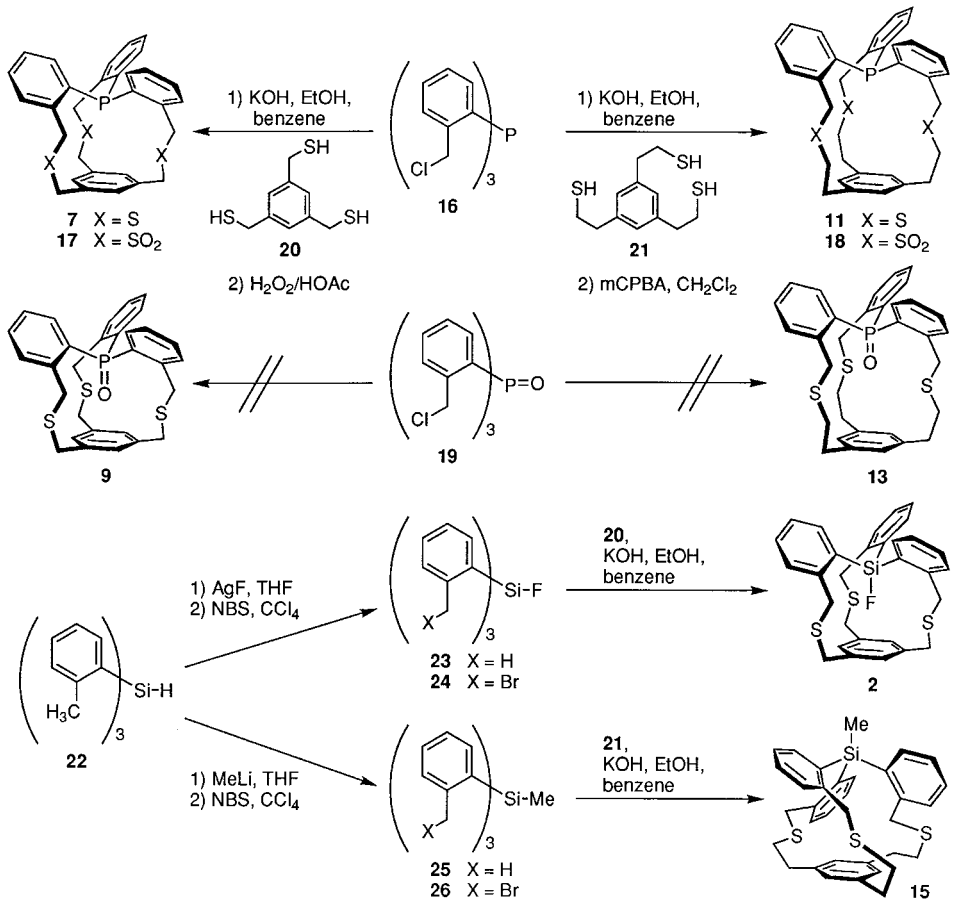
last cyclization step, so the geometries of the competing transition states for this step likely resemble those of the *in*- and *out*-products, and the relative energies in Table 1 should be reasonable guides of what products to expect.

Phosphaphanes. According to the AM1 calculations, the phosphine oxide **9** has the strongest preference for an *in*-configuration of any of the cyclophanes containing a non-hydrogen bridgehead substituent. Two methods for the synthesis of such a molecule were examined.

In the first approach, tris[2-(chloromethyl)phenyl]-phosphine[7] (**16**) and 1,3,5-tris(mercaptomethyl)benzene[8] (**20**) were condensed, under conditions of high dilution (1.1 mM for each component) in 2:1 benzene−ethanol with KOH as the base, to give the *in*-phosphine **7** in 59% yield (Scheme 1). However, the phosphine proved very resistant to oxidation, and even prolonged treatment with hydrogen peroxide in acetic acid at reflux returned only the trisulfone **17** in 98% yield. The *in*-geometry of the highly crystalline **17** was unambiguously established by X-ray analysis, and its molecular structure is illustrated in Figure 1. No unusual distortions are observed in the cyclophane, which has approximate C_3 symmetry, and the molecule seems relatively unstrained. Most importantly, the phosphorus atom is 4.201(2) Å above the mean plane of the basal aromatic ring, so there is ample room for inclusion of an oxygen atom, but the steric impediment to oxygenation must be too great.

(7) Letsinger, R. L.; Nazy, J. R.; Hussey, A. S. *J. Org. Chem.* **1958**, *23*, 1806−1807.
(8) Nakazaki, M.; Yamamoto, K.; Miura, Y. *J. Org. Chem.* **1978**, *43*, 1041−1044.

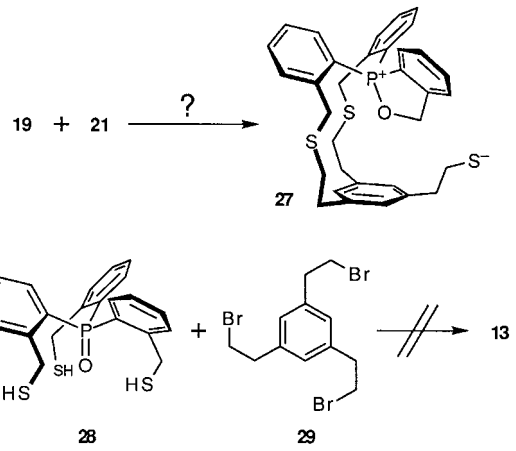
Scheme 1



It may be necessary to insert the oxygen before the macrocyclization; thus, in a second approach, the direct synthesis of **9** was attempted by condensation of tris[2-(chloromethyl)phenyl]phosphine oxide[7] (**19**) and trithiol **20**. Unfortunately, no cyclophanes, either *in* or *out*, were isolated from any of several such reactions. The product mixtures were quite complex, and even mass spectral analysis of the crude organic extracts failed to show any significant ions corresponding to the desired cyclophane **9**. A possible explanation for the failure of this condensation is that the oxygen significantly increases the steric hindrance to the *in*-cyclization, whereas the *out*-isomer may simply be too strained to form in detectable amounts.

We therefore decided to attempt the synthesis of the larger phosphine oxide **13** (Scheme 1), for which there is additional space in the central cavity and presumably also a bit more flexibility in the structure to permit easy oxidation of the phosphine. In this case, condensation of **16** and 1,3,5-tris(mercaptoethyl)benzene[9] (**21**) gave the *in*-phosphine **11** in 51% yield, but unfortunately, peracid oxidation of **11** gave only the trisulfone **18** in 99% yield. Once again, the phosphine was untouched. X-ray analysis established the *in*-geometry of **18** (Figure 1); the phosphorus atom is 5.402(2) Å from the basal aromatic ring.

The direct synthesis of **13** from phosphine oxide **19** and trithiol **21** was also unsuccessful in several attempts, forcing us to consider reasons for the failure of the macrocyclization other than simple steric hindrance. One possibility is that the phosphine oxide might react intramolecularly with a chloromethyl group, leading to intermediate heterocycles (e.g., **27**) with poor geometries



for ring opening to give the desired cyclophane. For this reason we synthesized tris[2-(mercaptomethyl)phenyl]-phosphine oxide (**28**, data not shown) and condensed it with 1,3,5-tris(bromoethyl)benzene[10] (**29**), a reaction in which the nucleophiles and electrophiles are reversed from the previous attempts, but once again no cyclophanes were isolated. This and several other failed reactions, in which **19** was allowed to react with a variety of tripodal nucleophiles, led us to abandon all attempts

(9) Ricci, A.; Danieli, R.; Rossini, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1691−1693.

(10) Cochrane, W. P.; Pauson, P. L.; Stevens, T. S. *J. Chem. Soc. (C)* **1968**, 630−632.

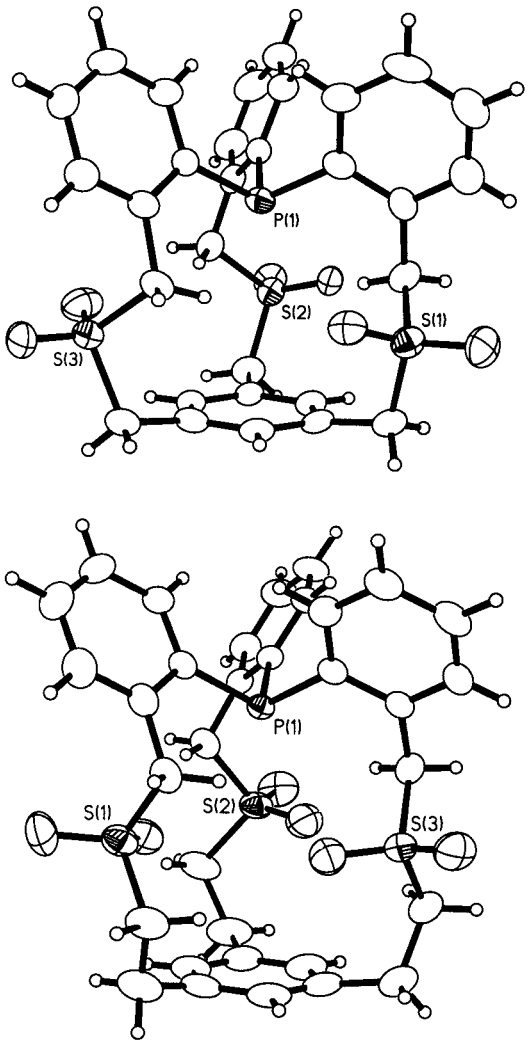


Figure 1. Molecular structures of *in*-cyclophanes **17** (above) and **18** (below). Only one of the two very similar, crystallographically independent molecules of **18** is shown. Thermal ellipsoids have been drawn at the 50% probability level.

to prepare *in*-phosphine oxides, and we turned to the synthesis of cyclophanes containing bridgehead silicon atoms.

An *in*-Fluorosilaphane. Fluorosilanes are larger than phosphine oxides (typical bond distances: C_3Si-F, 1.64 Å; $C_3P{=}O$, 1.49 Å), and thus the preference for the *in*-configuration of fluorosilaphane **2** is calculated to be substantially less than for **9** (Table 1). Still, **2** remained the best alternative to the phosphine oxides. For the synthesis of **2** (Scheme 1), tri(*o*-tolyl)silane[11] (**22**) was fluorinated at silicon with AgF, and then it was brominated with NBS to yield tris[2-(bromomethyl)phenyl]-fluorosilane (**24**). Finally, condensation of **24** with trithiol **20**, under conditions of high dilution (1.9 mM) in 2:1 benzene−ethanol in the presence of KOH, gave the desired **2**, but in a disappointing 0.4% yield. Even so, the isolation of **2** was achieved only by its direct crystallization from an otherwise intractable chromatographic fraction.

The X-ray structure of **2** (Figure 2) unambiguously establishes the inside location of the fluorine atom.

(11) Benkeser, R. A.; Riel, F. J. *J. Am. Chem. Soc.* **1951**, *73*, 3472−3474.

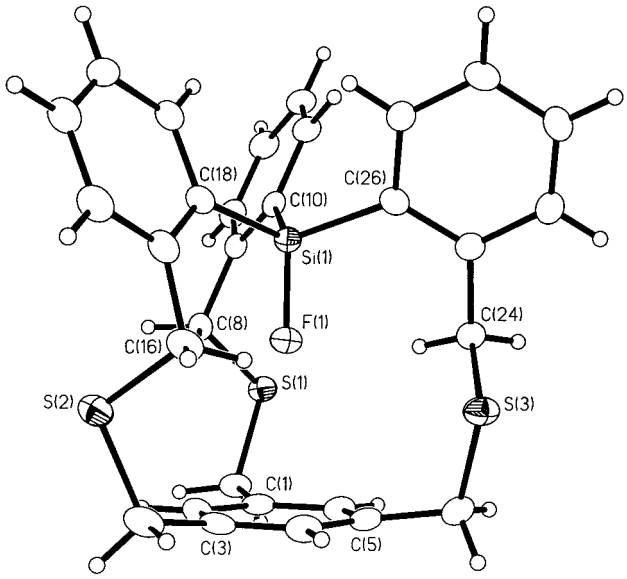


Figure 2. Molecular structure of *in*-cyclophane **2**. Thermal ellipsoids have been drawn at the 50% probability level.

Cyclophane **2** has approximate C_3 symmetry, and the distance from the fluorine to the mean plane of the basal aromatic ring is 2.813(2) Å. In our preliminary communication,[3] we reported a 298 K determination of the structure of **2**. However, two factors led us to redetermine the structure at low temperature (110 K), and it is this structure which is illustrated in Figure 2. First of all, both the ^{1}H NMR and mass spectra of the "bulk" **2** suggest that a small amount (∼15%) of the *in*-hydroxo cyclophane is present, and thus the possibility of occupational disorder in the X-ray sample added some uncertainty to the critical "inside" bond distances. To address this question, a piece of the crystal used for the room temperature X-ray measurements was cut off and analyzed by mass spectrometry; this material proved to contain only **2** with no hydroxo contaminant. Second, some time after our initial publication, a superior diffractometer with very low temperature capability became available, and so a 110 K determination of the structure of **2** was carried out using the remainder of the original crystal. Happily, the two determinations are extremely similar, but the precision of the 110 K structure is somewhat better.

A comparison of the structure of **2** with that of the related *in*-phosphaphane **17** is illustrated in Figure 3. The ideal C−X−C bond angles for phosphines and silanes, and for sulfones and thioethers, are not the same, so differences in the overlaid geometries are not necessarily the effect of strain in the molecules. However, the extra distortion in the basal ring of **2** and the elevated position of the silicon of **2** relative to the phosphorus of **17** *suggest* that there is some strain introduced by the contact between the fluorine atom and the basal ring of **2**.

The Si−F bond distance of 1.595(2) Å [1.591(3) Å in the 298 K determination[3]] is unusually short for a tri(alkyl/aryl)fluorosilane (other fluorosilanes can have shorter bonds[12]). The only tetracoordinate triarylfluo-

(12) The presence of additional fluorine atoms (or other heteroatoms) significantly shortens the Si−F bond. For example, the average Si−F bond distance for C_2XSi-F, where X = O or F, is 1.60 Å, and among these, Si−F distances of 1.57 Å are not uncommon.

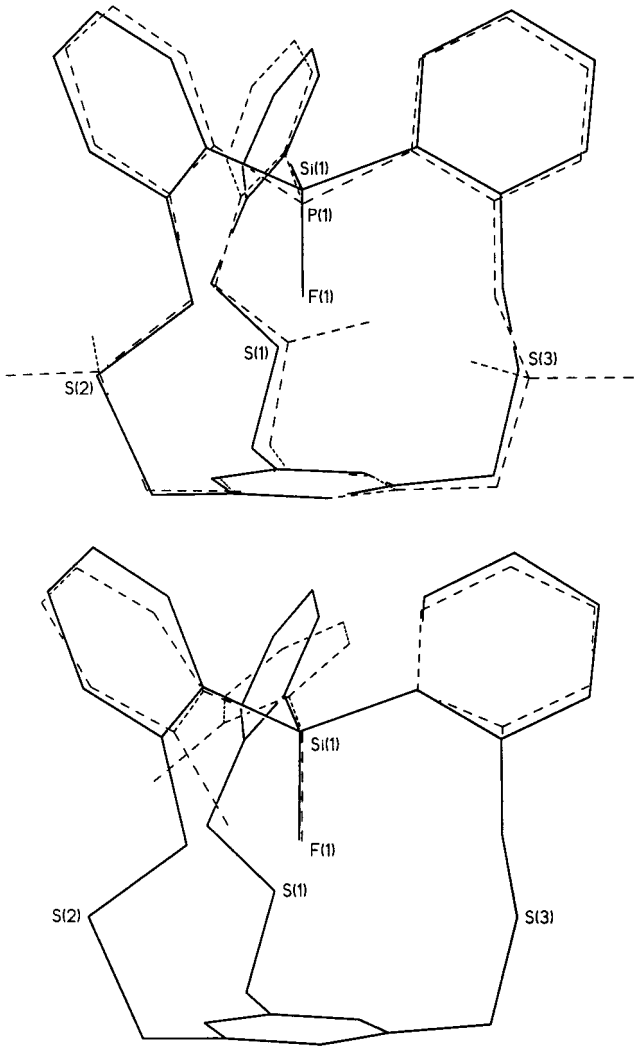


Figure 3. Comparison of the X-ray structure of cyclophane **2** with those of the related molecules **17** and **23**. Above: overlay plot of **2** (solid lines) and **17** (dashed lines). Below: overlay plot of **2** (solid lines) and **23** (dashed lines).

rosilane in the Cambridge Structural Database[13] is tris-{2-[(dimethylamino)methyl]phenyl}fluorosilane,[14] in which the Si−F distance is 1.627 Å, and the mean Si−F distance for all tetracoordinate tri(alkyl/aryl)fluorosilanes in the database is 1.64 Å, with none less than 1.604 Å. Given the paucity of structural data for triarylfluorosilanes, we decided to determine the structure of the precursor tri(*o*-tolyl)fluorosilane (**23**). This molecule adopts a conformation similar to that of the "top" of cyclophane **2** (see Figure 3), and **23** proved to have an Si−F bond distance of 1.601(1) Å (298 K). Thus, although the Si−F bond in **2** is the shortest so far observed for any tri(alkyl/aryl)-fluorosilane, it is only 0.01 Å shorter than that observed in a very good nonmacrocyclic model compound, so the amount of steric compression of the Si−F bond in **2** is modest.

The fluorine atom in **2** is a uniquely encapsulated functional group. It has close nonbonded contacts to three methylene hydrogens [H(8a), H(16a), H(24a); average 2.25 Å], the three corresponding methylene carbons [C(8), C(16), C(24); average 2.98 Å], and the six basal ring carbons [C(1)−C(6); average 3.14 Å]. However, the ^{1}H NMR spectrum of **2** is not particularly unusual, and its ^{19}F NMR resonance (δ −155.3) is not far from that of the precursor **23** (δ −160.6).[16] One expects to observe compressional frequency enhancement of the Si−F stretching band in the IR spectrum of **2**, a phenomenon we have observed previously in cyclophanes with *in*-C−H and *in*-Si−H bonds,[5,15] but the Si−F stretch falls in a complex region of the IR (800−1000 cm^{-1}), making a definite assignment of this band impossible.

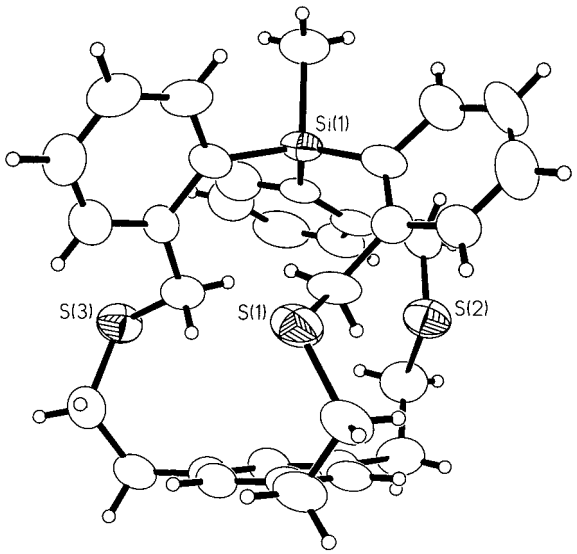


Figure 4. Molecular structure of *out*-cyclophane **15**. Thermal ellipsoids have been drawn at the 50% probability level.

An *out*-Methylsilaphane. Can an even larger *in*-functional group be placed in a similar cyclophane? AM1 calculations (Table 1) suggested that the methylsilaphane **15** would stand an even chance of adopting an *in*-geometry. Accordingly, tri(*o*-tolyl)(methyl)silane[17] (**25**) was treated with NBS and light to give the tribromide **26**, and this was condensed with trithiol **21** to yield the methylsilaphane **15** in 22% yield (Scheme 1). The ^{1}H NMR spectrum of **15** is strikingly different from others in this study: **15** shows six distinct methylene resonances, whereas the thioethers **2**, **7**, and **11** have relatively simple spectra in which there is averaging of the diastereotopic methylene proton resonances. This indicates than **15** has a less mobile structure than the others, and its relatively "normal" methyl resonance at δ 0.73 further suggests that **15** adopts an *out*-configuration. This geometry was confirmed by X-ray analysis, and the molecular structure of **15** is shown in Figure 4. Notably, the structure is not even approximately C_3-symmetric, but is instead a C_1 structure in which one of the three aryl groups on the silane is more nearly parallel to the basal ring than the other two. This *out*-cyclophane provides an interesting contrast to the *in*-isomers in this

(13) Allen, F. H.; Kennard, O.; Taylor, R. *Acc. Chem. Res.* **1983**, *16*, 146−153.

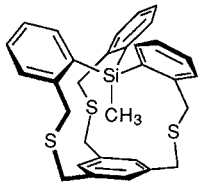
(14) Breliere, C.; Carre, F.; Corriu, R. J. P.; Royo, G.; Wong Chi Man, M. *Organometallics* **1994**, *13*, 307−314.

(15) (a) Pascal, R. A., Jr.; Grossman, R. B.; Van Engen, D. *J. Am. Chem. Soc.* **1987**, *109*, 6878−6880. (b) Pascal, R. A., Jr.; Winans, C. G.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 3007−3010.

(16) Incorrect ^{19}F chemical shifts were given in the initial communication;[3] these were corrected very shortly thereafter: Dell, S.; Vogelaar, N. J.; Ho, D. M.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 7663.

(17) Howell, J. A. S.; Palin, M. G.; Yates, P. C.; McArdle, P.; Cunningham, D.; Goldschmidt, Z.; Gottlieb, H. E.; Hezroni-Langerman, D. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1769−1775.

study, but it denies an opportunity for some interesting NMR and IR experiments. Furthermore, the calculated strain present in a smaller *in*-methylsilaphane such as **10** (see Table 1) would seem to preclude its synthesis by any direct macrocyclization reaction, and indeed, Damrauer's recent synthesis of an even smaller methylsilaphane leads to the *out*-isomer **30**.[18]



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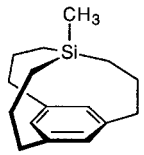

30

Ab Initio Computational Studies. The unusual C_1-symmetric structure of compound **15** led us to reevaluate our initial calculations concerning this molecule. By using the X-ray geometry as a starting point for geometry optimization, it was found that the observed C_1 conformation is a separate potential minimum in AM1 calculations, but that it is about 2 kcal/mol higher in energy than either the *in* or *out* C_3-symmetric conformations (Table 1). Although the observed C_1 structure might simply be the result of crystal packing forces, we chose to examine the problem with low-level ab initio calculations. These gave surprising results. At the HF/STO-3G level,[19] C_1-*out*-**15** is found to be 1.4 kcal/mol more stable than C_3-*out*-**15**, in accord with the X-ray structure, *but* it is fully 9.5 kcal/mol less stable than C_3-*in*-**15**. This pattern was repeated at the HF/3-21G(*) level, where C_1-*out*-**15** is 2.5 kcal/mol lower in energy than C_3-*out*-**15**, but 6.0 kcal/mol higher than C_3-*in*-**15**. The strong preference for the *in*-isomer in these ab initio calculations is in sharp contrast to the AM1 calculations, which found the *in*- and *out*-isomers to be essentially equal in stability. We then turned to compound **2**, where AM1 calculations yield only a slight advantage (0.6 kcal/mol) for the *in*-isomer. Once again the ab initio methods strongly preferred the *in*-isomers. At the HF/STO-3G level, C_3-*in*-**2** was favored by 17.6 kcal/mol over C_3-*out*-**2** and, at the HF/3-21G(*) level, by 14.3 kcal/mol.

These discrepancies between the semiempirical and ab initio methods are very large for molecules that have no really unusual bonding, merely unusual shapes. The fact that only the (apparently) less stable, *out*-isomer of **15** is experimentally observed is also a bit disconcerting, even though, as we have noted above, the syntheses of these cyclophanes are under kinetic control. So far, however, we have been unable to provide an unambiguous experimental test of the relative stability of any pair of *in*- and *out*-isomers. Only one member of any pair has been formed in our macrocyclizations, and attempts to invert the silicon of **2** by treatment with fluoride ion have so far been unsuccessful. More significantly, attempted thermal isomerizations[20] of the *in*-phosphines **7** and **11** have not yielded detectable amounts of the corresponding *out*-isomers.[21] It would be desirable to calculate the relative stabilities of these molecules by using high-level ab initio or density functional methods, but such calculations are presently out of reach.

Conclusion. The tightly encapsulated fluorine in compound **2** is, for the present, a unique *in*-functional group. It is clear from the 100-fold difference in the yields of the syntheses of the phosphine **7** and the fluorosilane **2** that the presence of the *in*-atom strongly inhibits macrocyclization. Not only is the *in*-atom a steric impediment to the approach of the sulfur nucleophile, but it may also bias the conformations of partly cyclized intermediates to give unfavorable geometries for final ring closure. However, this does not explain the failure to observe *out*-cyclophanes in attempts to prepare the *in*-phophine oxide **13**. The easy synthesis of the *out*-methylsilane **15** (22% yield) shows that *out*-**13** cannot not be too strained to form in a direct condensation of **19** and **21**, yet it was not observed, and for this we have no good explanation. For the future, we suspect that compounds with other, relatively simple, non-hydrogen *in*-functional groups may be prepared but that the placement of more complex *in*-functionalities containing multiple "heavy atoms" in small cyclophanes will require an entirely different synthetic approach.

Experimental Section

Phosphaphane 7. 1,3,5-Tris(mercaptomethyl)benzene[8] (**20**, 0.37 g, 1.7 mmol) and tris[(2-chloromethyl)phenyl]phosphine[7] (**16**, 0.71 g, 1.7 mmol) were mixed in 2:1 benzene−ethanol (1.5 L), and the solution was heated to reflux. An argon-saturated solution of KOH (0.46 g, 8.2 mmol) in ethanol (70 mL) was added over 6 h. After 20 h, the solution was cooled, and the solvent was evaported under reduced pressure to leave a white precipitate. The precipitate was extracted twice with hot chloroform. The extracts were combined, the solvent was evaporated, and the resulting light yellow oil was chromatographed on silica gel (solvent, 2:1 hexanes−toluene) to yield **7** as a white solid (0.517 g, 1.01 mmol, 59%); mp 288−291 °C. ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 6 H), 3.75 (d, J = 4 Hz, 6 H), 6.57 (ddd, J = 8, 4, 1 Hz, 3 H), 7.07 (ddd, J = 8, 8, 1 Hz, 3 H), 7.26 (s, 3 H), 7.28 (ddd, J = 8, 8, 1 Hz, 3 H), 7.44 (ddd, J = 8, 5, 1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 31.4 (d, J_{PC} = 32 Hz), 36.6, 127.5, 129.4, 129.6, 129.9 (d, J_{PC} = 4 Hz), 134.4, 134.6 (d, J_{PC} = 13 Hz), 139.2 (d, J_{PC} = 2 Hz), 142.8 (d, J_{PC} = 27 Hz); MS, *m*/*z* 514 (M^+, 86), 71 (100); exact mass 514.1029, calcd for $C_{30}H_{27}PS_3$ 514.1013.

Phosphaphane Trisulfone 17. A mixture of compound **7** (50 mg, 0.097 mmol), acetic acid (6 mL), and 30% hydrogen peroxide (3 mL) was heated at reflux for 20 h. An additonal 2 mL of hydrogen peroxide was added, and heating was continued for another 20 h. The solvent was evaporated to leave the highly insoluble **17** (58 mg, 0.095 mmol, 98%); mp >400 °C. ^{1}H NMR (DMSO-d_6) δ 4.69 (br s, 6 H), 4.82 (s, 6 H), 7.40 (m, 12 H), 7.77 (s, 3 H); MS, *m*/*z* 610 (M^+, 27), 546 (M − SO_2, 12), 482 (M − 2SO_2, 6), 418 (M − 3SO_2, 100); exact mass 610.0705,

(18) Kwochka, W. R.; Damrauer, R.; Schmidt, M. W.; Gordon, M. S. *Organometallics* **1994**, *13*, 3728−3732.

(19) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986; pp 63−100.

(20) Baechler, R. D.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 3090−3093.

(21) However, the *in*-phosphine **11** *can* be inverted under these conditions. Prior to submission of this paper, it was found that heating **11** with sulfur in benzene in a sealed tube smoothly yields the *out*-phosphine sulfide. The reaction is first order in **11** with a half-life of 36 h at 145 °C, and it is independent of sulfur concentration. In addition, the desulfurization of the *out*-sulfide with Si_2Cl_6 at room temperature, a process known to proceed with retention of configuration at phosphorus, yields exclusively the *in*-phosphine. These and additional experiments and computational results indicate that the preference for the *in*-phosphine **11** over its out isomer is much greater than the 1.3 kcal/mol given by the AM1 calculations, and they indirectly lend support to the larger *in*/*out* energy differences found in the ab initio calculations for **2** and **15** (Chen, Y.; Pascal, R. A., Jr., unpublished results).

calcd for $C_{30}H_{27}O_6PS_3$ 610.0707. Single crystals, suitable for X-ray analysis, were obtained from DMSO−MeOH.

Phosphaphane 11. 1,3,5-Tris(mercaptoethyl)benzene[9] (**21**, 0.19 g, 0.71 mmol) and compound **16** (0.29 g, 0.71 mmol) were mixed in 2:1 benzene−ethanol (750 mL), and the solution was heated to reflux. An argon-saturated solution of KOH (0.19 g, 3.4 mmol) in ethanol (45 mL) was added over 2.5 h. After 39 h, the solution was cooled, and the solvent was evaporated under reduced pressure to leave a white residue. The residue was extracted twice with hot chloroform. The combined extracts were concentrated, and the resulting yellow oil was chromatographed on silica gel (solvent, 1:1 hexanes−toluene) to yield **11** as a white solid (201 mg, 0.36 mmol, 51%); mp 226−229 °C. ^{1}H NMR ($CDCl_3$) δ 2.88 [overlapping t (6 H) and t (6 H)], 3.66 (s, 6 H), 6.55 (dd, J = 7, 3, 3 H), 7.02 (dd, J = 7, 7 Hz 3 H), 7.23 (s, 3 H), 7.26 (dd, J = 7, 7 Hz, 3 H), 7.54 (dd, J = 7, 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 33.4, 36.07 (J_{PC} = 28 Hz), 36.63, 127.3 (J_{PC} = 10 Hz), 128.1 (J_{PC} = 14 Hz), 129.2, 129.3, 133.6, 135.6 (J_{PC} = 16 Hz), 140.6, 142.1 (J_{PC} = 26 Hz); MS, m/z 556 (M^+, 100); exact mass 556.1494, calcd for $C_{33}H_{33}PS_3$ 556.1482.

Phosphaphane Trisulfone 18. *m*-Chloroperbenzoic acid (50−60% by wt) was purified as follows: it was dissolved in CH_2Cl_2, washed with phosphate buffer (10 mL) at pH 7.5, dried over Na_2SO_4 and concentrated to dryness. To an ice-chilled, stirred solution of cyclophane **11** (36.9 mg, 0.066 mmol) in CH_2Cl_2 (10 mL), a solution of *m*-CPBA in CH_2Cl_2 (10 mL) was added dropwise. The ice bath was removed, and the reaction stirred for 1 day under argon. The CH_2Cl_2 mixture was washed with a solution of sodium thiosulfate followed by saturated Na_2CO_3, and it was dried over Na_2SO_4. The solvent was evaporated to give **18** as a beige solid (42.7 mg, 0.065 mmol, 99%); mp >400 °C. ^{1}H NMR ($CDCl_3$) δ 3.22 (t, J = 5 Hz, 6 H), 3.57 (t, J = 5 Hz, 6 H), 4.29 (s, 6 H), 6.55 (ddd, J = 7, 4, 1 Hz, 3 H), 7.15 (s, 3 H), 7.21 (dd, J = 7, 7 Hz, 3 H), 7.38 (dd, J = 7, 7 Hz, 3 H), 7.61 (dd, J = 7, 7 Hz, 3 H); MS, m/z 652 (M^+, 100); exact mass 652.1190, calcd for $C_{33}H_{33}O_6PS_3$ 652.1177. Single crystals, suitable for X-ray analysis, were obtained from CH_2Cl_2−MeOH.

Tri(*o*-tolyl)fluorosilane (23). Tri(*o*-tolyl)silane[11] (**22**, 4.11 g, 13.6 mmol), silver fluoride (5.15 g, 40.6 mmol), and THF (100 mL) were heated at reflux for 4 days under argon. After cooling, the reaction mixture was filtered through neutral alumina, and concentration of the filtrate yielded a yellow-green oil. Chromatography on silica gel (solvent, hexanes) gave **23** as a colorless oil which solidified upon drying under vacuum (3.04 g, 9.50 mmol, 70%); mp 83−84 °C. Crystals from the solid mass proved suitable for X-ray analysis. ^{1}H NMR ($CDCl_3$) δ 2.36 (d, J_{HF} = 2 Hz, 9 H), 7.12 (dd, J = 7, 7 Hz, 3 H), 7.24 (m, 6 H), 7.36 (ddd, J = 7, 7, 1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 23.2 (d, J_{FC} = 2 Hz), 125.3, 130.3, 131.1, 132.2, (d, J_{FC} = 16 Hz), 136.3, (d, J_{FC} = 4 Hz), 145.0; ^{19}F NMR (CD_2Cl_2, $CFCl_3$ reference) δ −160.6; MS, m/z 320 (M^+, 17), 228 (M − C_7H_8, 100), 213 (M − C_7H_8 − CH_3, 57); exact mass 320.1391, calcd for $C_{21}H_{21}FSi$, 320.1397.

Tris[2-(bromomethyl)phenyl]fluorosilane (24). A solution of compound **23** (2.9 g, 9.1 mmol) and NBS (5.32 g, 29.9 mmol) in CCl_4 (50 mL) at reflux was illuminated with a tungsten lamp for 2 days. After the mixture cooled, the succinimide was filtered away, and the filtrate was concentrated to leave a yellow oil. The oil was chromatographed on silica gel (solvent, 12:1 hexanes−toluene) to give **24** as a white solid (1.73 g, 3.1 mmol, 34%); mp 127−129 °C. ^{1}H NMR ($CDCl_3$) δ 4.54 (s, 6 H), 7.27 (dd, J = 7, 7 Hz, 3 H), 7.33 (dd, J = 7, 1.5 Hz, 3 H), 7.51 (ddd, J = 7, 7, 1.5 Hz, 3 H), 7.58 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 33.7 (d, J_{FC} = 3 Hz), 128.0, 131.2 (d, J_{FC} = 15 Hz), 131.7, 132.3, 136.9 (d, J_{FC} = 3 Hz), 144.4; MS, m/z 556 (M^+ [$^{79}Br_2{}^{81}Br$], 2), 477 (M − Br, 47), 178 (100); exact mass 557.8682, calcd for $C_{21}H_{18}F^{79}Br^{81}Br_2Si$ 557.8671.

Fluorosilaphane 2. A solution of 1,3,5-tris(mercaptomethyl)benzene (**20**, 0.625 g, 2.89 mmol) and compound **24** (1.61 g, 2.89 mmol) in 2:1 benzene−ethanol (1.5 L) was heated to reflux. An argon-saturated solution of KOH (0.535 g, 9.54 mmol) in ethanol (100 mL) was added over 8 h. After 12 h of heating, the solution was cooled, and the solvent was evaporated to leave a white precipitate. The precipitate was extracted twice with hot chloroform. The extracts were combined, the solvent was evaporated, and the residue was chromatographed on silica gel (solvent, 4:1 toluene−hexanes) to yield a pale yellow oil. Further purification by preparative TLC (solvent, 1:1 toluene−hexanes) gave a colorless oil (29 mg). This material exhibited a single component by TLC (solvent, benzene; R_f 0.37), the mass spectrum showed the correct molecular ion for **2**, but the ^{1}H NMR spectrum clearly indicated that a mixture was present. This could not be further fractionated by chromatography, but direct crystallization from $CHCl_3$−EtOH yielded 6 mg of **2** (0.011 mmol, 0.4%) as crystals suitable for spectroscopic and crystallographic analysis. ^{1}H NMR (CD_2Cl_2) δ 3.71 (s, 6 H), 3.77 (s, 6 H), 7.14 (m, 6 H), 7.16 (s, 3 H), 7.36 (m, 6 H); ^{19}F NMR (CD_2Cl_2) δ −155.3; MS, m/z 530 (M^+, 19), 178 (100); exact mass 530.1018, calcd for $C_{30}H_{27}FS_3Si$ 530.1028.

Tri(*o*-tolyl)(methyl)silane (25). Tri(*o*-tolyl)silane[11] (0.670 g, 2.2 mmol), methyllithium (3.1 mL, 1.4 M in hexanes, 4.4 mmol), and THF (15 mL) were heated to reflux overnight under argon. The reaction mixture was cooled in an ice bath, and 1 M HCl was added to quench the reaction. Ether was added, the layers were separated, and the aqueous layer was extracted with ether. The combined organics were dried over Na_2SO_4 and concentrated under reduced pressure to leave a reddish-brown semisolid. Chromatography on silica gel (solvent, hexanes) gave compound **25** as a colorless oil that solidified upon drying under vacuum (0.627 g, 1.98 mmol, 89%); mp 83−84 °C [lit.[17] 87−88 °C]. ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 3 H), 2.28 (s, 9 H), 7.12 (dd, J = 7, 7 Hz, 3 H), 7.23 (m 6 H), 7.34 (ddd, J = 7, 7, 1 Hz, 3 H).

Tris[*o*-(bromomethyl)phenyl](methyl)silane (26). A solution of compound **25** (0.61 g, 1.9 mmol) and NBS (1.10 g, 6.3 mmol) in CCl_4 (15 mL) was illuminated with a tungsten lamp for 1 day. After the solution cooled, the succinimide was filtered off, and the filtrate was concentrated to leave a yellow oil. Chromatography on silica gel (solvent, 16:1 hexanes−toluene) gave **26** as a white semisolid (685 mg, 1.3 mmol, 65%). ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3 H), 4.39 (s, 6 H), 7.24 (d, J = 4 Hz, 6 H), 7.4 (m, 3H), 7.59 (d, J = 8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 1.5, 34.7, 128.3, 131.1, 132.1, 134.6, 136.7, 144.3; MS m/z 537 (M^+ [$^{79}Br_2{}^{81}Br$], 6), 457 (M − HBr, 23), 179 (100).

Methylsilaphane 15. Compounds **21** (0.27 g, 1.1 mmol) and **26** (0.58 g, 1.1 mmol) were mixed in 2:1 benzene−ethanol (1.125 L), and the solution was heated to reflux. An argon-saturated solution of KOH (0.28 g, 5.0 mmol) in ethanol (75) mL was added over 6 h. After 21 h, the solution was cooled, and the solvent was evaporated under reduced pressure to leave a white precipitate. The precipitate was extracted twice with hot chloroform. The combined extracts were concentrated, and the resulting mixture was chromatographed on silica gel (solvent, toluene) to yield a pale yellow solid. A compound exhibiting R_f = 0.38 on silica gel TLC (solvent, 5:1 toluene−hexanes) was isolated, and it was further purified by preparative TLC (solvent, 5:1 toluene−hexanes) to give cyclophane **15** as a white solid (131 mg, 0.23 mmol, 22%); mp 193° (dec). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73 (s, 3 H), 2.43 (m, 3 H), 2.85 (m, 9 H), 2.98 (d, J = 14 Hz, 3 H), 3.30 (d, J = 14 Hz, 3 H), 6.92 (s, 3 H), 7.20 (ddd, J = 7, 7, 1.5 Hz, 3 H), 7.33 (m, 6 H), 7.53 (d, 7 Hz, 3 H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 4.9 (Si−CH_3), 35.2, 37.3, 38.4, 126.4, 128.2, 129.0, 129.7, 136.1, 136.6, 140.9, 145.0; MS, m/z 568 (M^+, 19), 149 (100); exact mass 568.1754, calcd for $C_{34}H_{36}S_3Si$ 568.1749. Single crystals, suitable for X-ray analysis, were obtained from $CHCl_3$−MeOH.

General X-ray Crystallographic Procedures. X-ray data were collected by using graphite monochromated Mo Kα radiation (0.710 73 Å) on either a Siemens P4 diffractometer (compounds **15**, **17**, and **18**) or a Nonius KappaCCD diffractometer (compounds **2** and **23**). Processing of the diffraction data was accomplished by using Siemens XSCANS[22] for the former structures, and by using DENZO-SMN[23] for the latter.

(22) *XSCANS*, Release 2.10b; Siemens Analytical X-ray Instruments: Madison, WI, 1994.

(23) Otwinowski, Z.; Minor, W. *Methods Enzymol.* **1997**, *276*, 307−326.

Table 2. Crystallographic Data for Compounds 2, 15, 17, 18, and 23

	15	**17**	**18**	**2**	**23**
chemical formula	$C_{34}H_{36}S_3Si$	$C_{30}H_{27}O_6PS_3 \cdot C_2H_6SO \cdot 0.33CH_4O$	$C_{33}H_{33}O_6PS_3 \cdot 1.25CH_2Cl_2$	$C_{30}H_{27}FS_3Si$	$C_{21}H_{21}FSi$
formula weight	568.90	699.47	758.90	530.79	320.47
crystal size (mm)	0.50 × 0.40 × 0.18	0.35 × 0.15 × 0.05	0.50 × 0.30 × 0.18	0.25 × 0.05 × 0.05	0.38 × 0.15 × 0.05
space group	$P2_12_12_1$ (No. 19)	$R\bar{3}$ (No. 148)	$C2/c$ (No. 15)	$P2_1/c$ (No. 14)	$P2_1/c$ (No. 14)
a, Å	9.1208 (15)	40.1915 (19)	42.327 (3)	10.3293 (4)	16.6635 (7)
b, Å	9.1691 (14)	40.1915 (19)	15.109 (2)	17.0485 (6)	7.8104 (3)
c, Å	35.880 (6)	10.3636 (7)	30.136 (3)	15.3155 (5)	14.4375 (4)
α, deg	90	90	90	90	90
β, deg	90	90	133.514 (7)	109.324 (2)	101.079 (3)
γ, deg	90	120	90	90	90
V, Å^3	3000.7 (8)	14498 (2)	13977 (2)	2545.1 (2)	1844.0 (1)
Z	4	18	16	4	4
ρ_{calcd}, g/cm^3	1.259	1.442	1.443	1.385	1.154
μ, mm^{-1}	0.309	0.394	0.49	0.365	0.134
T, K	298 (2)	298 (2)	230 (2)	110 (2)	298 (2)
θ_{max}, deg	25.0	25.0	25.0	27.5	27.5
reflections					
total	6053	5936	12473	32769	32945
unique	5271	5509	12297	5843	4221
observed [$I > 2\sigma(I)$]	2385	2728	6830	3901	2641
$R(F)$ (obs. data)[a]	0.068	0.051	0.050	0.048	0.051
$wR(F^2)$ (obs. data)[a]	0.143	0.099	0.115	0.095	0.118
S (obs. data)[a]	1.10	1.04	1.06	1.06	1.09
$R(F)$ (all data)[a]	0.150	0.111	0.092	0.093	0.095
$wR(F^2)$ (all data)[a]	0.170	0.111	0.128	0.113	0.142
S (all data)[a]	0.85	0.79	0.83	1.02	1.02

[a] $R(F) = \sum||F_o| - |F_c||/\sum|F_o|$; $wR(F^2) = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$; S = goodness-of-fit on $F^2 = [\sum w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p is the number of parameters refined.

All structures were solved by direct methods using Siemens SHELXTL,[24] and all were refined by full-matrix least-squares on F^2 using SHELXTL or SHELXTL-93.[25] All non-hydrogen atoms were refined anisotropically, and hydrogens were included with a riding model. In the case of structures **17** and **18**, the SQUEEZE/BYPASS procedure[26] implemented in PLATON-96[27] was employed to account for disordered solvent electron density. Specific crystal, reflection, and refinement data are contained in Table 2, and full details are provided in the Supporting Information.

Computational Methods. Semiempirical and ab initio molecular orbital calculations were performed by using the SPARTAN program package (versions 4 and 5), Wavefunction, Inc., Irvine, CA), and its built-in default thresholds for wave function and gradient convergence were employed. Frequency calculations were performed on the AM1-optimized equilibrium geometries to verify that these were true potential minima.

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Supporting Information Available: Crystal structure reports for compounds **2**, **15**, **17**, **18**, and **23**, including full experimental details, tables, and figures; Cartesian coordinates for the computed geometries of the isomers of compounds **2**−**15**; and ^{1}H NMR spectra and selected ^{13}C NMR spectra of compounds **2**, **7**, **11**, **15**, and **23**−**26**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO990727+

(24) Sheldrick, G. M. *SHELXTL* Version 5; Siemens Analytical X-ray Instruments: Madison, WI, 1996.

(25) Sheldrick, G. M. *SHELXL-93. Program for the Refinement of Crystal Structures*; University of Gottingen, 1993.

(26) Van der Sluis, P.; Spek, A. L. *Acta Crystallogr., Sect. A* **1990**, *46*, 194−201.

(27) Spek, A. L. *Acta Crystallogr., Sect. A* **1990**, *46*, C34.