Synthesis and Relative Diatropicity of a Remarkably Aromatic Thia[13]annulene

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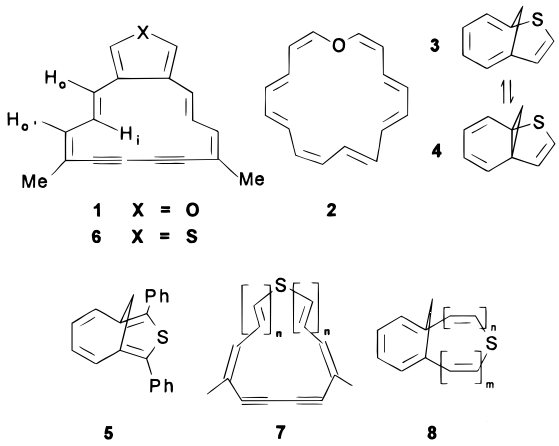
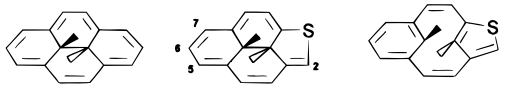
Abstract: 2,4-Bis(bromomethyl)-3-methylthiophene was synthesised as an intermediate to prepare the strained thiophenobenzophanediene **11**, which readily thermally valence isomerizes to **the novel thia[13]annulene 10**. This thia-annulene is notably diatropic and shows about 40% of the ring current of the parent bridged [14]annulene **9**, which is substantially more than an analogous oxaannulene, **18**, and substantially less than the azaannulene **19**.

Introduction

Aromaticity continues to be a topical subject, despite the many difficulties involved in defining its measurement.[1] Aromaticity of the five-membered heteroatom containing ring systems has of course received much coverage, and recently the relationship of "classical" and "magnetic" concepts of aromaticity in such systems has been discussed by Schleyer.[2] He concludes that by all accounts, the aromaticity order of pyrrole > thiophene > furan is firmly established. Larger heteroannulenes have also received considerable study,[3] in part because of an interest in their aromaticity relative to that of benzene. In general, aza[$4n + 2$]annulenes of the pyridine type are strongly diatropic, whereas the other hetero-types, e.g. furan or thiophene analogues, are much more variable. Further, estimation of the degree of aromaticity in the latter species is difficult, especially for the weakly diatropic examples. For example, in **1**, a measure of the aromaticity is taken as the difference in chemical shift between the inner (H_i) and outer (H_o) protons.[4] However, such protons are subject to quite severe anisotropic effects from the neighboring acetylenic groups, and as well, as the authors suggest, the molecules are probably conformationally mobile. Unfortunately, removal of the yne groups, as in **2**, leaves the molecules quite floppy, nonplanar, and often non-aromatic.[5] Few thiaannulenes have been prepared: the methanothia[9]annulene, **3**, appears to exist[6] as the norcaradiene isomer **4**. In Kato's[7] annulene **5**, the annulene form is stable, but diatropicity conclusions based on coupling constant data suggested the compound had little aromaticity. Sondheimer's[8] thia[13]annulene **6**, and Ojima's series **7** (n = 2−4)[9] and **8** (n = 2−4, $m = n + 1$)[10] appear to be diatropic, though not strongly. In these cases, despite their elegant syntheses, it is difficult to calibrate the aromaticity because of anisotropy effects, conformational mobility, or just plain lack of a good comparison parent annulene, particularly one with the same geometry. Some of these problems can be overcome by use of dimethyldihydropyrene, **9**, as the parent comparison annulene and the probe for aromaticity. Specifically, its skeleton is held rigidly planar by the bridge and thus is not floppy, and as well its internal methyl protons are sensitive and excellent ring current probes that are not subject to large anisotropic effects by external groups because of the distance involved and the fact that they are three σ bonds distant from the π-system.[11,12] Since molecular model calculations (see below) indicated very little geometry difference between **9** and **10**, we decided that the thia[13]annulene **10** would be a good target to realistically



1 X = O; **6** X = S; **2**; **3** ⇌ **4**; **5**; **7**; **8**



9; **10**; **11**

[⊗] Abstract published in *Advance ACS Abstracts,* January 1, 1996.

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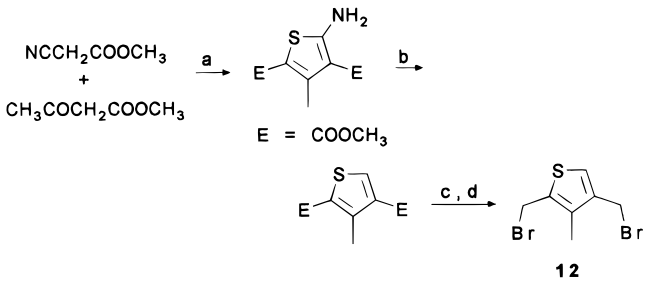
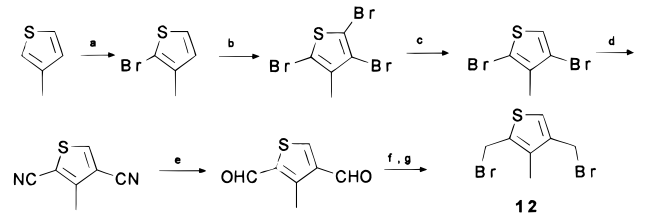
Scheme 1[a]



[a] (a) S/Et_2NH/t-BuOH, 60%, see ref 15. (b) $NaNO_2/H_2SO_4$/EtOH, 77%. (c) DIBAH, 60%. (d) $PBr_3/CHCl_3$, 80%.

Scheme 2[a]



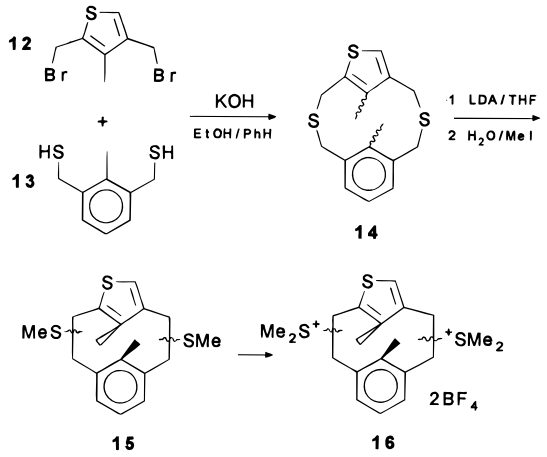
[a] (a) NBS/AcOH (ref 16). (b) $2Br_2/CHCl_3$, 90%. (c) Zn-AcOH/THF/H_2O, 80%. (d) CuCN/NMP, 55%. (e) DIBAH/PhH, 84%. (f) $NaBH_4$/MeOH; 93%. (g) $PBr_3/CHCl_3$, 80%.

estimate the diatropicity of a thiaannulene relative to its annulene parent, **9**. This paper describes the results of that study.

Syntheses

Many substituted and annelated dihydropyrenes have been synthesized through their valence isomers, the metacyclophanedienes.[11, 12] We thus anticipated that **10** would be accessible from its valence isomer **11** via the *cis*-stilbene to dihydrophenanthrene rearrangement, either photochemically or thermally, in the same way that **9** can be obtained from metacyclophane-1,9-diene.[13] In conversion of **11** to **10**, a new sp^3-sp^3 bond is formed and strain is substantially reduced, while the resonance energy of a benzene and a thiophene are lost; in the case of **9** the resonance energy of two *benzene* rings is lost, thus we thought that **11** to **10** should be favorable. AM1 calculations[14] of H_f for **10** and **11** gave values of 101.2 and 113.4 kcal/mol, supporting the idea that conversion of **11** to **10** should be favorable. The starting point for the synthesis of **11** would be the bis(bromomethyl)thiophene **12**. This was synthesized in overall yield of about 25% using two different routes shown in Schemes 1 and 2. The former, four steps starting from acyclic materials, was discovered last and is shorter than the seven steps starting from commercial 3-methylthiophene, shown in Scheme 2.

Coupling of the bis-thiol[13] **13** with dibromide **12**, gave the thiacyclophane **14** in 71% yield,[17] as a 70:30 mixture of *anti:syn* isomers. Unfortunately, we were unable to separate these isomers easily by chromatography, though for characterization purposes, the *anti* isomer was obtained pure by fractional crystallization *ten times* from toluene−ethanol, mp 228−230 °C. As required, the internal methyl protons were shielded at δ 1.88 and 1.21 by the opposite thiophene and benzene rings, respectively. In the *syn* isomer these appear at δ 2.36 and 2.33, normal aromatic methyl positions. In this isomer, however, the thiophene proton at δ 6.32 is now shielded by the facing benzene ring by 0.7 ppm, from its position at δ 7.03 in the *anti* isomer.



Since Wittig rearrangement[18] usually converts *syn*-[3,3]dithiametacyclophanes to *anti*-[2,2]ring contracted products, for synthetic purposes, the *anti/syn* mixture of **14** was subjected to Wittig rearrangement using LDA in THF. However, before quenching the intermediate thiolates with methyl iodide, water was added, such that any thiophene ring protons that had been deprotonated by the strong base present in the rearrangement step were reprotonated, and then alkylation of the thiolates with methyl iodide proceeded cleanly to give a 75% yield of only the mixed *anti* isomers **15**. The ^{1}H NMR spectrum clearly indicated the *anti* structure, since the internal methyl protons were strongly shielded at δ 1.57 (methylbenzene) and 0.71 (methylthiophene), while the S-methyl protons were at δ 2.25 and 2.11. The ^{13}C NMR spectrum showed several peaks for the S-Me carbons, indicating several isomers with different orientation of the S-Me (though all *anti cyclophanes*) to be present. This mixture gave a correct elemental analysis and correct molecular ion in the mass spectrum. The mixture of isomers was converted to its bis(dimethylsulfonium) fluoroborate,[13] **16,** and this was then reacted with potassium *tert*-butoxide in THF at 80 °C in the dark. The thia[13]annulene **10** was isolated directly in 30% yield, presumably by way of the Hofmann elimination product, its valence isomer **11** which spontaneously thermally converts to **10**. Isolation of **10** was difficult because it was fairly light sensitive, so workup and chromatographic purification were carried out in the dark. It was obtained as orange-red plates, mp 70−71 °C dec, mass spectrum M^+ at *m/z* 238, with loss of one and then two methyl groups; in the solid state the compound was reasonably stable, and a satisfactory C/H analysis could be obtained.

Diatropicity Discussion

The ^{1}H NMR spectrum of **10** shows the internal methyl protons strongly shielded at δ −1.16 and −1.32 and the external protons deshielded at δ 6.84−7.34, leaving leaves no doubt that **10** is a diatropic annulene that contains a fairly strong ring current. An unambiguous estimate of the ring current in **10** relative to the annulene parent **9** can easily be made: In **9**, the chemical shift of the internal methyl protons is δ −4.25, while that of the protons in **17**, a model in which no ring current flows, is δ +0.97. Thus the ring current shielding of the internal methyl protons is 5.22 ppm;[11] in **10** this shielding is 2.21 ppm, using an average chemical shift of δ −1.24 for the methyl protons. **The relative ring current (which we equate to aromaticity) of 10 to 9 is thus (2.21/5.22) × 100% = 42%.** This ignores any direct through space or through bond effect of the sulfur atom on the chemical shift of the methyl protons. However, these should be small since first the sulfur atom is four and five bonds distant, and thus any charge effect through

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(14) Performed using HyperChem, Version 2.

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(16) Kellog, R. M.; Schaap, A. P.; Harper, E. T.; Wynberg, H. *J. Org. Chem.* **1968**, *33*, 2902−2909.

(17) The reverse coupling, using the bis-thiol of **12** and the bis-bromide of **13**, gave only 55% yield of the same *anti/syn* ratio. The thiol was not very stable.

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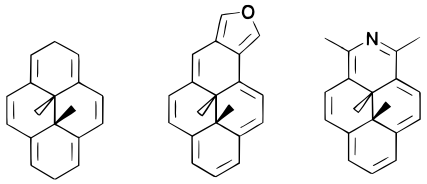
the bonds should be minimal, and the through space distances[19] from the protons to the sulfur atom are quite large at 3.93 and 4.34 Å on average for the two methyl groups. The difference in chemical shift between the two methyl groups of **10** is 0.16 ppm, which perhaps reflects this difference in distance, but is small relative to the chemical shift difference caused by the ring current change. Calculations also indicate a very small change in geometry between **10** and **9**. The dihedral angles that the methyl groups make with the ring plane change only by 2−4°, and with the exception of the five-membered ring, the ring angle changes are also minimal. The methyl protons thus do not much change their location with respect to the center of the induced ring current magnetic field, and thus the observed chemical shifts should reasonably well represent the strengths of the two fields. A second estimate of the relative ring currents can be made from the distant proton H-6, which is not subject to steric effects[11] and is far from the sulfur atom itself. In **10**, H-6 appears at δ 6.85, while in **9** it is at δ 8.14; the model shift is δ 6.13 and thus the relative aromaticity is 36%, in reasonable agreement with the other estimate, especially since the carbons and protons in **10** bear small charges, while those of **9** do not. As well, the areas of the two annulenes **9** and **10** are close but not identical; thus the comparisons made here are only approximate and represent a lower boundary value, *however, it is clear that the thiaannulene **10** has about 40% of the diatropicity* of the parent annulene **9.** This is substantial, and can leave the reader in no doubt that a thiaannulene can have substantial aromaticity. While not accepted by all, diatropicity has become one of the main experimental measurements of aromaticity,[20] and since Haddon[21] has demonstrated that **9**, like benzene, has 100% of the theoretically possible ring current, comparisons to



17 **18** **19**

9 are in our opinion reasonable best estimates for relative aromaticities. Thus in such a comparison, the furan-like oxaannulene **18**[22] and the pyridine-like aza-annulene **19**[23] have about 13% and 95% of the maximum ring currents, respectively. This leads to a preliminary experimental aromaticity order for furan, thiophene, and pyridine *like annulenes*, and places an *experimental* numerical value, albeit approximate one, on such an order. ^{13}C NMR data also support the increasing ring currents in **18** < **10** < **9**: the ^{13}C shifts for the internal methyl carbons are δ 19.9 and 19.5, 17.4 and 16.0, and 14.0, respectively, and for the internal bridge carbons they are δ 40.3 and 40.4, and 36.6, and 30.0, respectively, clearly showing the increased shielding on going from **18** to **10** to **9**.

Increasing aromaticity from **18** to **10** to **9** should also mean increased bond delocalization, or less bond alternation. Coupling constants for the adjacent bonds $^3J_{6,7}$ and $^3J_{5,6}$ in **10** are 9.0 and 6.38 Hz, respectively. In the less aromatic, more bond fixed furan **18**, the corresponding values are 9.76 and 5.66 Hz, while in the fully delocalized **9** they are equal at 7.31 Hz. Since vicinal coupling constants relate simply to bond orders,[24] there is thus some homogeneity between the ring current order of aromaticity and the bond-order values.

Conclusions

An undeniably diatropic thiaannulene, **10**, has been prepared, and ring current estimates give it approximately 40% of the ring current of the [14]annulene parent, **9**. It is thus relatively more aromatic than the oxaannulene **18**, and less aromatic than the azaannulene **19**. Coupling constants support the lesser degree of bond alternation in **10** than in **18**.

Experimental Section

Melting points were determined on a Reichert 7905 melting point apparatus integrated to a chrome−alumel thermocouple. Infrared spectra, major peaks only, calibrated with polystyrene, were recorded on a Bruker IFS25 FT-IR spectrometer as KBr disks unless otherwise stated. Ultraviolet−visible spectra were recorded on a Cary 5 spectrometer in cyclohexane. Proton NMR spectra were recorded at 90 MHz on a Perkin-Elmer R-32 or at 250 MHz on a Bruker WM 250 using $CDCl_3$ as solvent and either TMS as internal standard or the $CHCl_3$ peak at 7.24 ppm. Carbon NMR spectra were recorded at 62.9 MHz in $CDCl_3$, using the solvent peak at 77.0 ppm for calibration. Mass spectra were recorded on a Finnigan 3300 gas chromatography mass spectrometer using methane gas for chemical ionization (CI) or electron impact (EI) at 70 eV. Elemental analyses were carried out by Canadian Microanalytical Services Ltd., Vancouver, BC. All evaporations were carried out under reduced pressure on a rotary evaporator, and all organic extracts were washed with water and dried over anhydrous $MgSO_4$. SiGel refers to Merck Silica Gel, 70−230 mesh. PE refers to distilled petroleum ether, bp 30−60 °C.

2,4-Dimethyl 2-Amino-3-methylthiophene-2,4-dicarboxylate. Diethylamine (37 g, 0.5 mol) was added to a stirred mixture of methyl cyanoacetate (50 g, 0.5 mol), methyl acetoacetate (58 g, 0.5 mol), and sulfur (16 g, 0.5 mol) in *t*-BuOH (250 mL) at 40 °C under nitrogen. The resulting dark-red reaction mixture was heated at 70−75 °C for 2 days. Then the solution *(caution: foul smelling)* was concentrated in vacuo, filtered through a short column of SiGel (250 g), and chromatographed over SiGel (1 kg), using 1:1 $CHCl_3$−PE as eluant, to give a foul-smelling yellowish brown solid which upon recrystallization from $CHCl_3$/hexane gave pure product as colorless crystals (69 g, 60%): mp 126−127 °C; ^{1}H NMR (250 MHz) δ 6.59 (broad s, 2H), 3.80, 3.75 and 2.64 (s, 3H each); ^{13}C NMR δ 166.4, 166.3, 163.2, 148.2, 108.3, 108.0, 51.4, 51.0, 16.0; IR 3400, 3300, 1718, 1655, 1605, 1530, 1442, 1291, 1228, 1090, 1053, 1003 cm^{-1}; EI MS *m/z* 229 (M^+). Anal. Calcd for $C_9H_{11}NO_4S$: C, 47.15; H, 4.84; N, 6.11. Found: C, 46.99; H, 4.77; N, 6.04.

2,4-Dimethyl 3-Methylthiophene-2,4-dicarboxylate. An ice-cold solution of sodium nitrite (8.0 g, 0.12 mol) in water (10 mL) was added dropwise, via a syringe whose tip was kept below the surface (*this is essential to ensure the proper mixing of the reactants without raising the internal temperature of the reaction mixture*) of a solution of the above aminothiophene (25.0 g, 0.109 mol) and concentrated H_2SO_4 (25 mL) in anhydrous EtOH (175 mL), with vigorous stirring, at −2 °C (*internal temperature*, ice−NH_4Cl mixture). The solution was stirred at −2 °C for 30 min, gently warmed to 40 °C, and heated at 40−50 °C for 1 hour. After the evolution of gas had ceased, the reaction mixture was cooled to 25 °C, neutralized with $NaHCO_3$, and then extracted with ether (5 × 100 mL). The combined ether extracts were washed with water, 10% aqueous $NaHCO_3$, and saturated NaCl and then were dried and evaporated to yield a dark-red solid. The

(19) Calculated using PCMODEL 386, V4.0 from Serena Software, Box 3076, Bloomington, IN 47402-3076. This is an MM2+Pi calculation, and in our experience gives good values for geometries of annulenes and cyclophanes.

(20) See for example: Garratt, P. J. In *Aromaticity*; Wiley-Interscience: New York, 1986; p 292. Aihara, J. *Pure Appl. Chem.* **1982**, *54*, 1115−1128. Zhou, Z. *Int. Rev. Phys. Chem.* **1992**, *11*, 243−261.

(21) Haddon, R. C. *Tetrahedron* **1972**, *28*, 3635−3655.

(22) Mitchell, R. H.; Zhou, P. *Tetrahedron Lett.* **1991**, *32*, 6319−6322. While **18** could be considered as a [14]annulene fused to a furan, rather than an oxa[17]annulene, the contribution to the ring current from the [14]-annulene will be rather small because of the disfavored structure with a delocalized bond fused to both the [14]annulene and furan structures.

(23) Boekelheide, V.; Pepperidine, W. *J. Am. Chem. Soc.* **1970**, *92*, 3684−3688.

(24) Cremer, D.; Günther, H. *Justus Liebigs Ann. Chem.* **1972**, *763*, 87−108.

crude product was chromatographed over SiGel, using 3:7 ether−PE to give the diester as shiny white needles (18.0 g, 77%). A small portion was further purified by sublimation at 100 °C/0.1 mm: mp 102−104 °C; ^{1}H NMR (250 MHz) δ 8.17 (s, 1H), 3.85, 3.83, and 2.77 (s, 3H each); ^{13}C NMR δ 162.9, 162.5, 147.0, 137.6, 133.3, 128.3, 51.9, 51.6, 14.5; IR 3111, 1731, 1705, 1530, 1429, 1379, 1266, 1228, 1053, 1015, 764 cm^{-1}; EI MS *m/z* 214 (M^+). Anal. Calcd for $C_9H_{10}O_4S$: C, 50.46; H, 4.71. Found: C, 50.46; H 4.59.

2,4-Bis(hydroxymethyl)-3-methylthiophene. DIBAH (14 mL, 1.6 M solution in hexane, 22 mmol) was added dropwise to a mechanically stirred solution of the above diester (2.14g, 10 mmol) in dry ether (100 mL) at 0 °C under argon. After the solution was stirred at 25 °C for 4 h, it was quenched cautiously with MeOH (10 mL). The reaction mixture was evaporated to dryness, and the residue was sohxlet extracted with ether. Evaporation of the extract and recrystallization of the residue from heptane yielded the diol (0.95 g, 60%) as colorless needles: mp 95−97 °C; ^{1}H NMR (250 MHz, CD_3CN) δ 7.09 (s, 1H), 4.61 and 4.45 (s, 2H each), 2.60 (broad s, 2H, OH), 2.10 (s, 3H); ^{13}C NMR (CD_3CN) δ 143.6, 139.9, 133.5, 121.2, 59.9, 57.9, 11.9 (CH_3) ; IR 3274, 1454, 1404, 1316, 1191, 1090, 1010, 1003, 864, 777 cm^{-1}; CI MS *m/z* 159 (MH^+). Anal. Calcd for $C_7H_{10}O_2S$: C, 53.14; H, 6.37. Found: C, 53.11; H, 6.32.

2,4-Bis(bromomethyl)-3-methylthiophene (12). PBr_3 (1.2 mL, 13 mmol, excess) was added dropwise to a stirred solution of the above diol (1.8 g, 11.4 mmol) in dry $CHCl_3$ (50 mL, refluxed over P_4O_{10} and distilled to remove EtOH) containing 2 drops of pyridine at 0 °C. The mixture was allowed to warm to 25 °C and stirred for 4 h. It was then quenched with the addition of ice−water (10 mL), and the organic layer was separated, washed with water, 10% aqueous $NaHCO^3$, and saturated NaBr, and then dried. The solvent was evaporated to leave a brown gummy residue, which on *immediate* recrystallization from hexane gave the dibromide as an unstable, colorless microcrystalline solid (2.6 g, 80%): mp 112−115 °C dec, which decomposed on standing within 3 days; ^{1}H NMR (250 MHz) δ 7.25 (s, 1H), 4.64 and 4.40 (s, 2H each), 2.22 (s, 3H); ^{13}C NMR δ 137.8, 136.5, 134.9, 125.1, 26.7, 25.5, 11.9; CI MS *m/z* 287, 285, 283 (1:2:1, MH^+). Anal. Calcd for $C_7H_8Br_2S$: C, 29.60; H, 2.84. Found: C, 30.02; H, 2.87.

2,4,5-Tribromo-3-methylthiophene. Bromine (320 g, 2.0 mol) was added dropwise to a well stirred solution of 2-bromo-3-methylthiophene[16] (178 g, 1.0 mol) in $CHCl_3$ (50 mL), which was cooled to about 5 °C, over 10 h. The mixture was then refluxed for 10 h, and after cooling to 25 °C, KOH (100 g) in 95% EtOH (500 mL) was added cautiously (*HIGHLY EXOTHERMIC!*) to the mixture which was then refluxed for an additional 4 h. The mixture was then poured in to ice water (3 L) and $CHCl_3$ (500 mL), and the dark brown organic layer was washed, dried, and evaporated to give a dark-brown solid. This was extracted with hot heptane (600 mL). The heptane extracts were filtered through a short column of neutral alumina (50 g) and the solvent was evaporated from the filtrate to give the pure product (302 g, 90%) as colorless needles: mp 29−31 °C (lit.[25,26] mp 27−28.5, 33 °C); ^{1}H NMR (90 MHz) δ 2.15 (s); EI MS *m/z* 339, 337, 335, 333 (1:3:3:1, M^+).

2,4-Dibromo-3-methylthiophene. Zinc dust (9.70 g, 0.149 mol) was added to a vigorously stirred mixture of glacial AcOH (26 mL), water (70 mL), and THF (10 mL), the mixture was brought to a gentle reflux, and then the heat was removed. 2,4,5-Tribromo-3-methylthiophene (50.0 g, 0.149 mol) in THF (5 mL) was then added dropwise at such a rate that the reaction mixture kept refluxing. After the addition was complete (∼30 min), the mixture was refluxed for 10 h, and then cooled to 25 °C and extracted with $CHCl_3$ (250 mL). The organic layer was washed with water, 10% aqueous $NaHCO_3$, and saturated aqueous NaCl and then dried and evaporated. Distillation of the crude product at 0.3 mm gave 2,4-dibromo-3-methylthiophene (30 g, 80%) as a clear liquid: bp 62−64 °C/0.3 mm (lit.[27] bp 80 °C/10 mm); ^{1}H NMR (90 MHz) δ 7.20 (s, 1H), 2.18 (s, 3H); EI MS *m/z* 259, 257, 255 (1:2:1, M^+).

2,4-Dicyano-3-methylthiophene. CuCN (17.5 g, 0.19 mol) was added, in small portions with vigorous stirring, to a warm (∼60 °C) solution of 2,4-dibromo-3-methylthiophene (42.0 g, 0.16 mol) in *N*-methylpyrrolidinone (100 mL) and the whole mixture was heated to 140−160 °C. After 3 h, it was cooled to about ∼80 °C, CuCN (17.5 g, 0.19 mol) was added in small portions, and the mixture was again heated to 140−160 °C for an additional 4 h. It was then cooled to ∼60 °C and poured into a 50:50 v/v mixture of ammonia and water (600 mL), stirred well for 3 h, and filtered. The residue was washed with CH_2Cl_2 (400 mL) and the filtrate extracted with CH_2Cl_2 (5 × 100 mL). The CH_2Cl_2 extracts were combined and the solvent was evaporated. The residue obtained was taken up in ether (500 mL) and washed well with water and dried. Removal of the ether gave the crude product as a dark-brown solid, which upon sublimation (80 °C/0.1 mm) gave the product as colorless needles (13 g, 54%): mp 134 °C (sublimes); ^{1}H NMR (90 MHz) δ 8.05 (s, 1H), 2.55 (s, 3H); ^{13}C NMR δ 150.4, 139.5, 113.6, 112.9, 112.1, 108.0, 14.6; IR 3086, 2208, 1643, 1442, 1391, 1101, 877, 839 cm^{-1}; EI MS *m/z* 148 (M^+). Anal. Calcd for $C_7H_4N_2S$: C, 56.74; H, 2.72; N, 18.91. Found: C, 56.41; H, 2.83, N, 18.28.

2,4-Bis(formyl)-3-methylthiophene. DIBAH (70 mL, 1 M solution in hexane, 70 mmol) was added dropwise over 1 h to a mechanically stirred solution of the above dicyanide (5.0 g, 33.7 mmol) in dry benzene (70 mL) under argon. The solution was stirred for an additional hour and then quenched with the sequential addition of MeOH (10 mL), a 50:50 v/v mixture of MeOH−water (20 mL), and 10% HCl (25 mL). The mixture was then extracted with ether (4 × 75 mL). The ether extracts were washed well with water, dried, and evaporated to give crude product as an orange-yellow solid. This was sublimed (90 °C/0.1 mm) to give the pure dialdehyde (4.36 g, 84%) as colorless needles: mp 106−108 °C; ^{1}H NMR (250 MHz) δ 10.10, 9.97 (s, 1H each), 8.37 (s, 1H), 2.78 (s, 3H); ^{13}C NMR δ 185.4, 182.3, 146.2, 144.9, 141.8, 140.3, 13.2; IR 3073, 1693, 1643, 1530, 1404, 1350, 1241, 1090, 814, 701, 676 cm^{-1}. CI MS *m/z* 155 (MH^+). Anal. Calcd for $C_7H_6O_2S$: C, 54.53; H, 3.92. Found: C, 54.06; H, 3.74.

2,4-Bis(hydroxymethyl)-3-methylthiophene by Reduction of the Dialdehyde. $NaBH_4$ (380 mg, 10 mmol) was added to a solution of the above dialdehyde (2.0 g, 13 mmol) in MeOH (80 mL). The mixture was stirred at 25°C for 3 h, and then concentrated HCl (4−5 drops) was added to quench the reaction and the solvent was evaporated. The solid residue was extracted with ether (100 mL) and the ether was evaporated to yield the crude product which was recrystallized from heptane to give the diol (1.9 g, 93%), identical to the previous sample.

9,17-Dimethyl-2,11-dithia[3]metacyclo[3](2,4)thiophenophane (14). A solution of the dibromide **12** (2.00 g, 7.0 mmol) and the dithiol **13**[13] (1.30 g, 7.0 mmol) in argon purged benzene (500 mL) was added to a mechanically well stirred solution of KOH (0.93 g, 85%, 14 mmol) in argon purged 95% EtOH (1000 mL) slowly over 24 h. Then the solvents evaporated and the solid residue was extracted with CH_2Cl_2 (200 mL) and water (100 mL). The CH_2Cl_2 extract was washed, dried, and evaporated to yield the crude cyclophane **14** (1.90 g, 89%), essentially pure by NMR. Chromatography on SiGel using 1:1 CH_2Cl_2−PE as eluant returned 1.50 g (71%) of the pure thiacyclophane **14** as a mixture of *syn* and *anti* isomers. These could not be separated by column chromatography, but a small portion of pure *anti*-**14** could be obtained by repeated (*ten!*) fractional recrystallization from toluene/EtOH. The initial ratio of the *anti/syn* isomers was determined to be 70:30 by ^{1}H NMR.

anti-Thiacyclophane 14: mp 228−230 °C dec; ^{1}H NMR (250 MHz) δ 7.28−6.98 (m, 3H, H-5,6,7) 7.03 (s, 1H, H-14), 3.98−3.36 (m, 8H), 1.88 (s, 3H, Ph-9′-CH_3), 1.21 (s, 3H, 17′-CH_3); ^{13}C NMR δ 138.1, 137.1 (×2), 137.0, 135.6, 134.0, 130.6, 129.6, 125.1, 123.2, 33.1, 31.2, 28.7, 27.2, 15.7, 12.1; IR 1467, 1404, 739 cm^{-1}. CI MS *m/z* 307 (MH^+). Anal. Calcd for $C_{16}H_{18}S_3$: C, 62.70; H, 5.92. Found: C, 62.44; H, 5.81.

***syn*-Thiacyclophane 14** (by subtraction of the peaks due to *anti*-**14**): ^{1}H NMR (250 MHz) δ 7.13−6.85 (m, 3H, H-5,6,7), 6.32 (s, 1H, H-14), 4.25−3.60 (m, 8H), 2.36, 2.33 (s, 3H each); ^{13}C NMR δ 136.9, 136.6, 135.9, 135.1, 134.2, 132.5, 130.1, 128.7, 125.3, 124.4, 36.9, 34.9, 31.6, 31.1, 16.8, 13.6.

Wittig Rearrangement of the Thiacyclophane 14. LDA (0.5 mL, 2.5 M solution in cyclohexane, Aldrich, 1.2 mmol, excess) was injected

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by a syringe into a stirred solution of mixed isomers of the thiacyclophane **14** (100 mg, 0.32 mmol) in dry THF (10 mL) under argon at −10 °C. The color of the solution changed from colorless to dark-brown. The solution was allowed to warm to 25 °C over 30 min, and then water (100 μL) was added. The color of the reaction mixture bleached to pale yellow, and then CH_3I (1 mL, large excess) was added and stirring was continued for 3 h. The solvent was then evaporated, and the residue was extracted with CH_2Cl_2. The extracts were dried and evaporated to yield the crude product. This was chromatographed on SiGel, using 7:3 PE−CH_2Cl_2 as eluant, to give **15** as a mixture of many isomers (80 mg, 73%); ^{1}H NMR (250 MHz) δ 7.72−6.84 (m, 4H), 4.41−2.03 (m, 6H), 2.25, 2.11 (s, 3H each), 1.57, 0.71 (s, 3H each, internal-CH_3); ^{13}C NMR δ (major peaks) 144.5, 143.8, 140.2, 137.4, 136.3, 136.2, 128.7, 125.1, 124.1, 121.6, 51.9, 51.7, 42.6, 38.2, 17.9, 15.9, 15.3, 12.7; CI MS *m/z* 334 (M^+). Anal. Calcd for $C_{18}H_{22}S_3$: C, 64.62; H, 6.63. Found: C, 64.50; H, 6.50.

Bis-Sulfonium Salt 16. Dimethoxycarbonium fluoroborate[28] (Borsch reagent, 345 mg, ∼80% oil, 1 mmol, excess) was added, as a suspension in dry CH_2Cl_2 (5 mL), to a stirred solution of the cyclophane **15** (80 mg, 0.24 mmol) in CH_2Cl_2 (10 mL) under argon at −30 °C (dry ice−acetone). After the addition, the cooling bath was removed and the solution allowed to warm to 25 °C over 3 h. Ethyl acetate (10 mL) was added and the stirring was continued for another 24 h. An off-white crystalline precipitate formed and was fitered under suction, washed with dry ethyl acetate (10 mL), and dried overnight under vacuo. The salt **16** (152 mg, ∼100%) was quite unstable hence it was used directly in the next step. It decomposed at ∼60−65 °C.

trans-9b,9c-Dimethyl-9b,9c-dihydrophenyleno[1,9-bc]thiophene (10). *t*-BuOK (100 mg, 95%, 0.78 mmol) was added to a stirred suspension of the bis-salt **16** (152 mg, 0.24 mmol) in dry THF (10 mL) under argon. The reaction flask was protected from light by means of aluminum foil. The reaction mixture was heated to a gentle reflux for 30 min, cooled to 25 °C, and quenched with degassed, saturated aqueous NH_4Cl (5 mL). The organic layer was separated, washed with degassed, saturated aqueous NaCl (5 mL) and evaporated to leave a dark-brown residue. The residue was chromatographed rapidly on SiGel, deactivated with 10% water, eluting with pentane under argon, under as dark conditions as possible to give the thia[13]annulene as a reddish orange solid (17 mg, 30%). Recrystallization from degassed methanol gave orange-red plates: mp 70−71 °C dec; ^{1}H NMR (250 MHz, CD_2Cl_2) δ 7.34 (s, 1H, H-2), 7.26 (d, 1H, $J_{3,4}$ = 9.3 Hz, H-3), 7.22 (d, 1H, H-4), 7.22 (d, 1H, H-7), 7.05 (d, 1H, $J_{5,6}$ = 6.38 Hz, H-5), 6.95 (d, 1H, $J_{8,9}$ = 6.05 Hz, H-9), 6.86 (d, 1H, H-8), 6.84 (dd, 1H, $J_{6,7}$ = 9.0 Hz, H-6), −1.16 and −1.32 (s, 3H each); ^{13}C NMR (CD_2Cl_2) δ 138.0, 137.6, 136.7, 126.2, 125.1, 124.0, 121.1, 120.2, 119.6, 118.5, 114.2, 36.6, 30.1, 17.4, 16.0 ; UV λ_{max} nm (log ϵ_{max}) 545 (2.27), 505 (2.52), 470 (2.67), 443 (2.68), 356 (3.44), 343 sh (3.55), 320 (3.63). EI MS *m/z* 238 (M^+), 223, 208. Anal. Calcd for $C_{16}H_{14}S$: C, 80.63; H, 5.92. Found: C, 80.23; H, 5.90.

2,4-Bis(mercaptomethyl)-3-methylthiophene. Thiourea (1.53 g, 20.2 mmol) was added to a stirred solution of the dibromide **12** (2.84 g, 10 mmol) in a 1:1 v/v mixture of dry THF and EtOH (50 mL). The mixture was refluxed for 2 h under argon and cooled to 25 °C, and then the crystalline thiouronium salt obtained was filtered. After drying the thiouronium salt overnight under vacuum, it was added to an argon purged solution of KOH (5.2 g, 85%, 40 mmol) in water (25 mL). The mixture was then refluxed for 3 h under argon, cooled to ∼5 °C, acidified with 20% aqueous H_2SO_4, and extracted with ether. The extracts were dried and evaporated to give the crude dithiol. This was recrystallized from $CHCl_3$ under argon to yield the pure dithiol as off-white crystals (1.71 g, 90%), mp ∼18 °C, which were stable under nitrogen but polymerized rapidly upon exposure to air: ^{1}H NMR (250 MHz) δ 6.96 (s, 1H), 3.83 and 3.61 (d, 2H each, J = 7 Hz), 2.16 (s, 3H), 1.88 and 1.66 (t, 1H each, J = 7 Hz, SH); ^{13}C NMR δ 140.7, 138.4, 132.3, 119.7, 22.8, 21.7, 11.9; CI MS *m/z* 191 (MH^+). Anal. Calcd for $C_7H_{10}S_3$: C, 44.17; H, 5.30. Found: C, 43.83; H, 5.03. When this thiol was coupled with 1,3-bis(bromomethyl)toluene,[13] as described for **14** above, only 55% of **14** was isolated.

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