cis-1,3,6,8,10b,10c-Hexamethyl-10b,10c-dihydropyrene-2,7-dione: The Use of a Tether to Control the Stereochemistry[‡]

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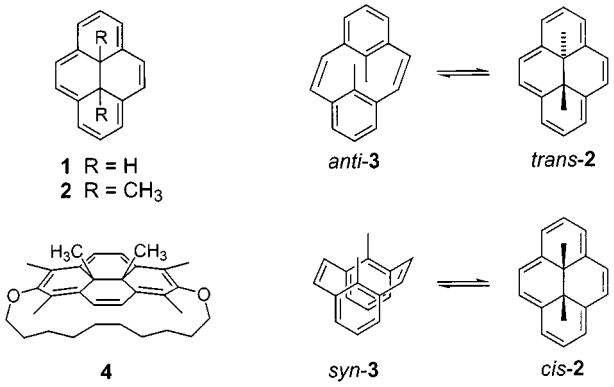
The title compound was prepared as part of an effort to accomplish the first synthesis of a *cis*-10b,10c-dimethyl-10b,10c-dihydropyrene according to our "tethered metacyclophane" strategy. The 11-step synthesis starting from 2,4,6-trimethylphenol had an overall yield of 4.1%. An X-ray crystal structure determination revealed a bowl-shaped structure and an almost fully eclipsed central ethano unit; AM1 calculations predict the heat of formation of this compound to be 9.7 kcal mol^{-1} higher than that of its *trans* isomer.

The 10b,10c-dihydropyrene skeleton has attracted a great deal of theoretical and experimental interest due to the aromatic character of its 14 π-electron periphery.[1] Since the parent system **1** is prone to the loss of hydrogen to give pyrene,[2] most of the work in this area has been conducted on analogues that bear substituents at the internal (10b and 10c) positions. By far the most prominent of these are the 10b,10c-dimethyl-10b,10c-dihydropyrenes (DMDHPs) **2**.

DMDHPs are normally prepared by the valence isomerization of the corresponding [2.2]metacyclophanedienes **3** (Scheme 1), which exhibit *syn*/*anti* conformational isomerism. Since the valence isomerization is stereospecific, the *anti*-[2.2]metacyclophanedienes become *trans*-DMDHPs and the *syn*-[2.2]metacyclophanedienes are transformed into *cis*-DMDHPs. The "cyclophane route"[3] that is generally used for the synthesis of the [2.2]metacyclophanedienes leads predominantly to the formation of *anti* conformers and hence *trans*-DMDHPs. As a result, *cis*-DMDHPs are not easily accessible compounds and they are not well studied experimentally.

We recently demonstrated how the presence of a third bridge (a tether) during the synthesis of the [2.2]metacyclophanediene system could ensure the formation and maintenance of only the *syn* conformation and thus lead exclusively to the *cis* isomer of the DMDHP.[4] *cis*-Dimethyldihydropyrenophane **4** was prepared by this strategy and its X-ray crystal structure was determined, thus providing the first experimentally derived structural data for the *cis*-DMDHP skeleton.



Scheme 1. The [2.2]metacyclophanediene−10b,10c-dihydropyrene equilibrium

The ultimate goal of this work is to develop a general strategy for the synthesis of *cis*-DMDHPs **6** (Scheme 2). In order to accomplish this, ways of efficiently excising the tethers from *cis*-dimethyldihydropyrenophanes **5** or their valence isomeric *syn*-[2.2]metacyclophanedienes **7** must be developed. In order to do this, the tether will have to contain functionality that is robust enough to survive the synthetic pathway, but nevertheless be susceptible to some sort of cleavage reaction that will not affect the *cis*-DMDHP system. Thus the oxygen atoms in **4** were included not only for the sake of synthetic simplicity, but (more importantly) also to allow removal of the tether once it has served its purpose of controlling the stereochemistry. The full "tethered metacyclophane" strategy is outlined in Scheme 2 and we now report the results of our initial attempts at its implementation in whole.

For the synthesis of **4**, the twelve-atom tether was chosen specifically to be short enough to control the conformation,[5] but long enough to avoid the imposition of any strain on the *cis*-DMDHP moiety. Such strain would be

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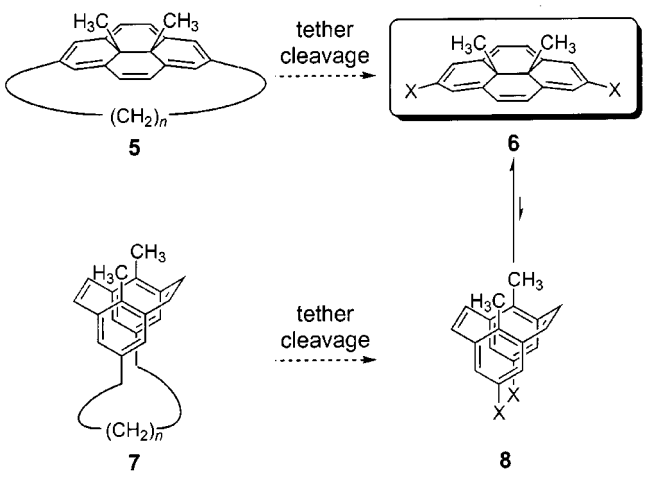
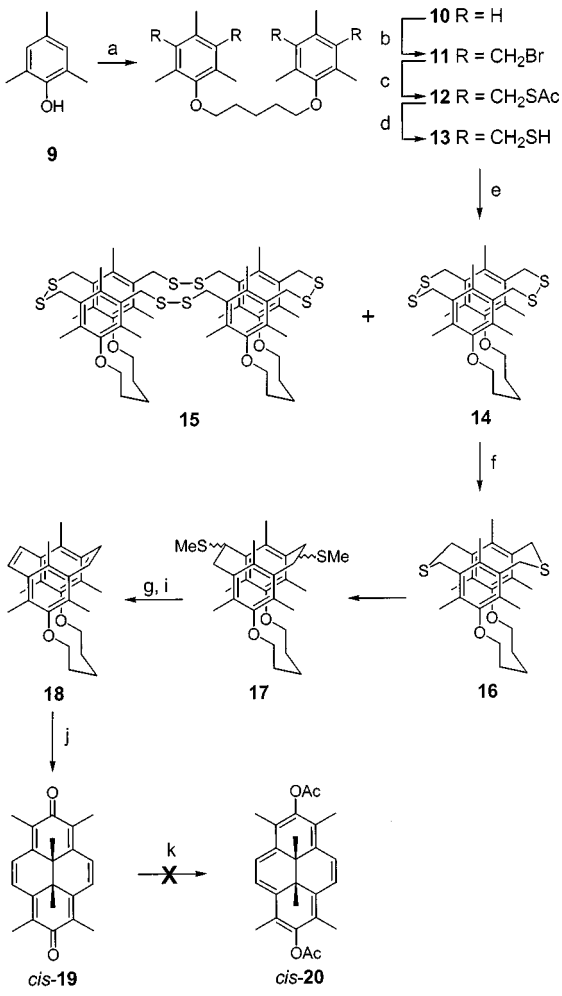


Scheme 2. The "tethered metacyclophane" strategy for the synthesis of *cis*-10b,10c-dimethyl-10b,10c-dihydropyrenes

expected to shift the equilibrium between dihydropyrenophane and tethered metacyclophanediene (*cf.* **5** and **7**) away from the desired dihydropyrenophane. For this work, the position of this equilibrium was not important because the tether was destined to be removed. This being the case, the possibility of employing a significantly shorter tether presented itself. In addition to the benefit of a degree of atom economy, it was expected that a shorter tether would allow for a more efficient intramolecular cyclophane formation than in the route leading to **4**. A seven atom tether was eventually chosen.

The synthesis (Scheme 3) commenced with the *O*-alkylation of 2,4,6-trimethylphenol (**9**) with 1,5-dibromopentane to give diether **10** (81%), which was bromomethylated to give tetrabromide **11** (58%). The analogous bromomethylation during the synthesis of **4** was poor (8%), thus necessitating the use of a five-step sequence (from **9**) for the preparation of synthetically useful amounts of the desired tetrabromide. Although the reason is not obvious, **10** is less susceptible to ether cleavage under acid conditions than its counterpart with five extra carbon atoms in the tether. In any event, it was gratifying that tetrabromide **11** could be prepared in >20 g amounts in two steps from **9**.

For the formation of the cyclophane unit, the use of Na_2S/Al_2O_3 [6] was not investigated because of the poor results obtained with the homologue of **11** with a twelve atom tether.[4] Instead **11** was treated with potassium thioacetate to form the tetrakis(thioacetate) **12** (96%) and this was hydrolyzed under basic conditions to afford tetrathiol **13** (93%). Twofold intramolecular oxidative thiol coupling gave rise to the desired tetrathiacyclophane **14**[7] (61%) along with a small amount of what is tentatively assigned as the dimer **15** (4%).[8] The 61% yield of **14** is significantly better than the 31% yield obtained for its homologue with a twelve atom tether.[4] It would appear as though the decision to work with a shorter tether was well founded. Even more pleasing was that the subsequent desulfurization of **14** with HMPT to give **16** proceeded with a very good yield of 84%, in contrast to the unimpressive 21% yield obtained for the

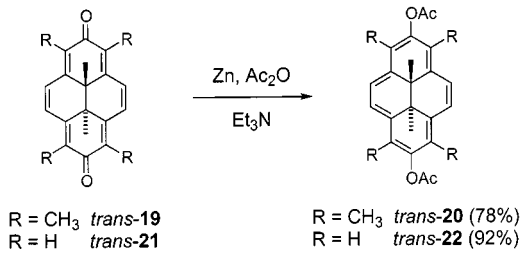


Scheme 3. The synthesis of *cis*-**19** and its attempted conversion into *cis*-**20**; reagents and conditions: a) 1,5-dibromopentane, K_2CO_3, DMF, 80 °C, 19 h, 81%; b) 1,3,5-trioxane, 35% HBr/HOAc, reflux, 1 h, 58%; c) KSAc, CH_3CN, reflux, 23 h, 96%; d) KOH, DMF, 60 °C, 7 h, 93%; e) I_2, pyridine, 1:1 CH_2Cl_2/95% ethanol, room temp., 8 days, 61%; f) HMPT, benzene, reflux, 5 days, 84%; g) $(MeO)_2CHBF_4$, CH_2Cl_2, room temp., 12−17 h; h) *t*BuOK, THF, room temp., 23 h, 78% over two steps; i) *t*BuOK, 1:1 THF/*t*BuOH, room temp., 2 h, 30% over two steps; j) $(NH_4)_2Ce(NO_3)_6$, CH_3CN, room temp., 15 min, 81%; *k*) Zn, Ac_2O, Et_3N, room temp., 9 h

analogous reaction in the synthesis of **4**.[4] Ring contraction of **16** by our preferred *S*-methylation/Stevens rearrangement protocol proceeded normally to afford isomer mixture **17** (78%). *S*-Methylation of **17**, followed by treatment with base, then afforded cyclophanediene **18** (30%). Despite the disappointing yield for the last step, more than a gram of **18** was prepared in a single run.

The stage was now set for attempts to cleave the tether. The intention was to oxidatively cleave the aryl alkyl ethers to give *cis*-**19** and then convert this quinone into *cis*-DMDHP *cis*-**20**. Precedents for both the oxidative cleavage and the reductive acylation (Scheme 4) steps were provided by Boekelheide et al. from their seminal reports on the synthesis of *trans*-DMDHPs, in which *trans*-**21** was converted into *trans*-**22**,[9] and also by Renfroe et al.,[10] who later described the synthesis of *trans*-**20** from *trans*-**19**. Oxidation of **18** with ceric ammonium nitrate (CAN) afforded qui-

none *cis*-**19** in 81% yield. However, contrary to the behavior of its *trans* isomer, all attempts to reductively acylate *cis*-**19** resulted in complete consumption of the starting material and the formation of only intractable material. No traces of the desired *cis*-DMDHP *cis*-**20** were ever detected. The overall yield of *cis*-**19** over 11 steps from **9** was 4.1%, the majority of the losses having occurred during the conversion of **17** to **18**.



Scheme 4. Precedent for the proposed reductive acylation

The reason for the failure of the reductive acylation of *cis*-**19** is not immediately obvious considering the high yields with which *trans*-**19** and *trans*-**21** underwent the same reaction. That *cis*-**19** is amenable to reduction was ascertained from cyclic voltammetry in acetonitrile containing Bu_4NPF_6, in which two reversible one-electron reductions at formal potentials of −1.17 and −1.33 V versus SCE were observed.[11] By comparison, the corresponding potentials for benzoquinone are at −0.54 and −1.4 V.[12] It may therefore be that strain in the product *cis*-**19** is an important factor. The structures of *cis*-**19** and *trans*-**19** were calculated at the AM1 level of theory (MOPAC) and the calculated heat of formation of the *cis* isomer was found to be 9.70 kcal mol^{-1} higher than that of its *trans* counterpart. It is conceivable that, as a result of this, *cis*-**19** is unable to withstand the conditions of the reductive acylation. Milder methods for the reductive acylation of *cis*-**19** may ultimately prove to be successful, but the instability problem does not bode well for the general use of the current tether cleavage approach for the synthesis of *cis*-DMDHPs. To circumvent this problem, a different type of tether and an alternative method for its cleavage will have to be employed. This will form the basis of future work in this area.

Despite the disappointment with the reductive acylation, the successful tether removal from **18** to give *cis*-**19** is at least a partial proof of principle of our strategy. Furthermore, the unusual quinone *cis*-**19** is an interesting compound in its own right. A single crystal X-ray structure determination *cis*-**19** was performed (Figure 1) and a number of interesting structural features were evident. As in the case of dihydropyrenophane *cis*-**4**, all of the features of interest originate from the central ethano unit, which is almost perfectly eclipsed. The torsion angles of the three pairs of aligned bonds on C(15) and C(16) are all less than 1°. For example, the C(21)−C(15)−C(16)−C(22) torsion angle is just 0.3(2)°, which compares to a value of 6.8° for the analogous angle in *cis*-**4**. The fuller eclipsing of the

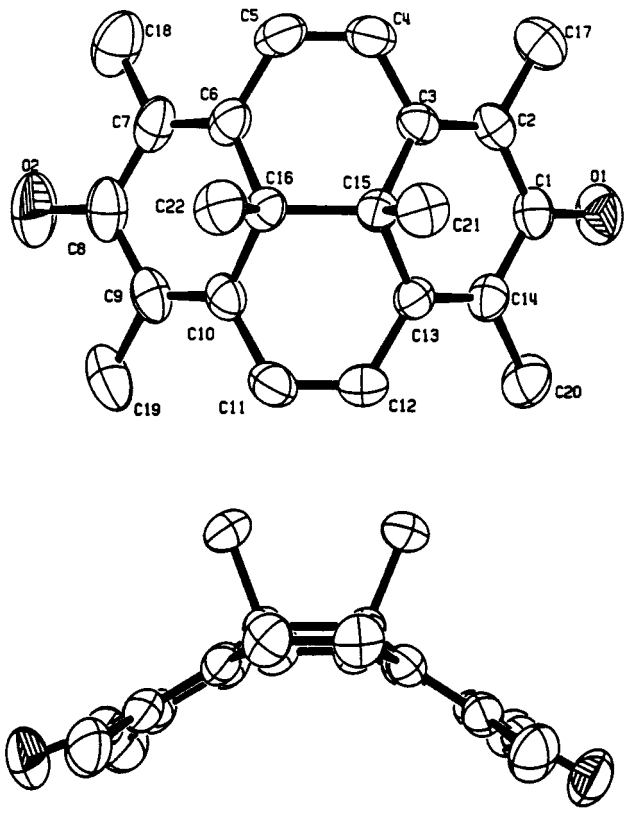


Figure 1. Top and side views of *cis*-**19** in the crystal; the crystallographic numbering differs from systematic numbering; selected distances (Å) and angles (°): C(1)−O(1)1.232(2), C(1)−C(2) 1.473(3), C(2)−C(3) 1.345(3), C(3)−C(4) 1.456(3), C(3)−C(15) 1.517(3), C(4)−C(5) 1.325(3), C(15)−C(16) 1.623(3), C(21)−C(22) 2.777(3); C(2)−C(1)−C(14) 118.4(2), C(1)−C(2)−C(3) 120.5(2), C(2)−C(3)−C(4) 122.1(2), C(2)−C(3)−C(15) 122.4(2), C(3)−C(4)−C(5) 120.0(2), C(3)−C(15)−C(21) 103.1(1), C(3)−C(15)−C(16) 112.7(1), C(3)−C(15)−C(13) 112.3(1), C(21)−C(15)−C(16)−C(22) 0.3(2)

ethano group in *cis*-**19** is reflected in a more symmetrical sp^2-hybridized framework around it.

The geometric constraints of the ethano group impose a nonplanar conformation on the sp^2 skeleton, which results in the adoption of a bowl shape with the internal methyl groups protruding from the convex face. The largest deviation from planarity is a consequence of torsions about the single bonds at the junction of the saturated and unsaturated parts of the molecule, for example C(3)−C(4). The torsion angles about these bonds deviate from 180° (a coplanar arrangement of the adjoined double bonds) by 35.5−37.3 ° (average: 36.3°). The remaining torsion angles around the perimeter are all within 5° of 0° or 180°, except for those around C(7)−C(8) and C(8)−C(9), which deviate by 11.9(2)° and 12.2(2)°, respectively. This can be seen as a 10.4° bend of the C(7)−C(8)−C(9) plane of atoms (left hand side of Figure 1) with respect to the adjacent C(6)−C(7)−C(9)−C(10) plane of atoms *away* from the center of the bowl. The same effect is discernable at the other end of the molecule, but its magnitude is much smaller. The analogous torsion angles are 0.8 and 3.6°, and the analogous inter-plane angle is 2.1°.

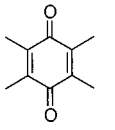
In our recent work on the [n](2,7)pyrenophanes, the nonplanarity of the polycyclic aromatic system was quantified by measuring the angles formed between various planes of atoms.[13] Although an analogous full treatment of *cis*-**19** can be performed, the presence of the saturated ethano unit in *cis*-**19** makes it less meaningful. However, the angle between the planes of atoms C(2)−C(3)−C(13)−C(14) and C(6)−C(7)−C(9)−C(10) provides a yardstick for comparing the bend in these related systems. The value of 62.3° for *cis*-**19** is less than that found for the analogous angle in 1,7-dioxa[7](2,7)pyrenophane (73.1°),[13a] but slightly greater than those in 1,8-dioxa[8](2,7)pyrenophane (57.3°)[13b] and [8](2,7)pyrenophane (52.0°).[13c]

The distortions in the eclipsed ethano unit are similar to those observed for *cis*-**4**. The C(15)−C(16) bond [1.623(3) Å] is elongated significantly and C(15)−C(21) [1.567(3) Å] and C(16)−C(21) [1.565(3) Å] are slightly elongated. The central atoms C(15) and C(16) each have two compressed bond angles around them (103.1−104.2°) and four slightly enlarged angles (111.3−112.8°). The remaining bond lengths and angles in the molecule are within normal ranges.[14]

The internal methyl groups lie well within van der Waals contact, the distance between C(21) and C(22) being 2.777(3) Å. As in the case of *cis*-**4**, the hydrogen atoms on C(21) and C(22) were located from the first difference map, which points to the presence of an unusually high barrier to rotation.[15] This notion was supported by the results of a variable temperature NMR experiment. The peak height ratio of the external to internal methyl signals in CD_2Cl_2 solution at room temperature was 2.8:1 and this increased steadily to 4.9:1 as the temperature was decreased to −90 °C. At this temperature, the signal for the internal proton was considerably broader than that of the external protons.

The AM1 calculated structure is in quite good agreement with the X-ray crystal structure. A perfectly eclipsed ethano unit is predicted. As in the case of the [n](2,7)pyrenophanes, the calculations predict a more bent sp^2 framework than is observed.[16] The large torsion angles in the periphery are calculated to average 39.3°, which is 3.0° greater than the observed average value. As expected, the AM1 calculations on *trans*-**19** predict a more planar sp^2 skeleton. The largest torsion angles in the periphery are associated with the same single bonds as those in *cis*-**19** and have an average of 12.6°.

The spectroscopic data for *cis*-**19** and those available for *trans*-**19** were compared with one another and with those of comparison compounds *trans*-**21**, duroquinone **23** and 1,4-benzoquinone **24** (Table 1). The ^1H NMR spectroscopic data for *cis*-**19** do not differ dramatically from those of its *trans* isomer or the comparison compounds.[17] The IR absorptions of *cis*-**19** in the carbonyl region are observed at lower frequencies than those of *trans*-**19**. As might be expected for the less planar π system, the longest wavelength absorption maximum (327 nm) of *cis*-**19** in its UV/Vis spectrum is at a shorter wavelength than that of *trans*-**19** (348 nm).



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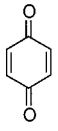

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In conclusion, the ultimate goal of generating *cis*-**20** was not achieved because of the unexpected failure of the reductive acylation of *cis*-**19**. However, the demonstration of the high yielding removal of the tether from **18** with the concomitant closure of the key central bond constitutes a partial success. Future work in this area will be aimed at the use of different tethers and different methods for their cleavage.

Table 1. Selected spectroscopic and physical data for *cis*-**19**, *trans*-**19** and some comparison compounds

	cis-**19**	*trans*-**19**	*trans*-**21**	**23**	**24**
δ(CH_3 internal)	1.83	2.02	1.92		
δ(CH_3 external)	1.89	1.95		2.02	
δ(H vinyl)	6.74	6.55	6.42 6.15		6.78
IR [$\tilde{\nu}$, cm^{-1}]	1630 1610	1640 1625	[a]	1639	1666
UV/Vis (solvent)	(CH_3CN)	(CH_3OH)	(C_6H_{12})		
(λ_{max} (nm), log ε)	267 (4.27) 306 (4.17) 327 (4.23)	225 (4.36) 286 (4.73) 295 (4.77) 348 (4.18)	268 (4.69) 277 (4.63) 312 (4.18) 325 (4.28) 342 (4.11)		
Mp (°C)	235−236	284−285	252		
Ref.	this work	[10]	[9a]	this work	this work

[a] Not reported.

Experimental Section

General: Solvents for reactions performed under nitrogen were dried and distilled according to standard procedures. All other chemicals were reagent grade and used as received. Chromatographic separations were performed on Merck silica gel 60 (230−400 mesh). TLC plates were visualized using a 254 nm UV lamp. Melting points were obtained on a Thomas Hoover 7427-H10 Melting Point Apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded a General Electric GE-300 NM instrument operating at 300.1 and 75.47 MHz, respectively, using $CDCl_3$ solutions. ^{1}H chemical shifts are relative to internal tetramethylsilane. ^{13}C chemical shifts are relative to the solvent resonance (δ = 77.0). Mass spectra were recorded on a V. G. Micromass 7070HS instrument operating at 70 eV. Infrared spectra (nujol) were recorded on a Mattson Polaris FT instrument. Ultraviolet-visible spectra were recorded on a Cary 5E spectrometer. Combustion analyses were performed by the Microanalytical Services Laboratory, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

1,5-Bis(2,4,6-trimethylphenoxy)pentane (10): 2,4,6-Trimethylphenol **9** (20.4 g, 150 mmol) and 1,5-dibromopentane (17.0 g, 74.0 mmol) were added to a room temperature suspension of K_2CO_3 (31.1 g, 225 mmol) in DMF (100 mL). The mixture was stirred at 80 °C for 19 h, cooled to room temperature, diluted with water (600 mL) and extracted with diethyl ether (400 mL). The organic layer was washed with an aqueous 10% HCl solution, water, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography of the residue (hexanes/ethyl acetate, 15:1) afforded **10** (20.5 g, 81%) as a colorless solid. A small portion of this product was recrystallized from hexane/dichloromethane to give colorless prisms: m.p. 44−45 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72−1.84 (m, 2 H), 1.87−1.97 (m, 4 H), 2.27 (s, 6 H), 2.28 (s, 12 H), 3.81 (t, *J* = 6.4 Hz, 4 H), 6.86 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.2, 20.7, 22.9, 30.3, 72.1, 129.4, 130.5, 132.9, 153.7. MS (EI, 70 eV): *m*/*z* (%) = 340 (2) [M^+], 205 (57), 149 (46), 136 (82), 119 (53), 91 (78), 69 (100). $C_{23}H_{32}O_2$ (340.5): calcd. C 81.13, H 9.47; found C 81.20, H 9.45.

1,5-Bis[3,5-bis(bromomethyl)-2,4,6-trimethylphenoxy]pentane (11): 1,3,5-Trioxane (21.1 g, 234 mmol) was added to a room temperature solution of **10** (20.0 g, 58.7 mmol) in 35% HBr/HOAc (187 mL). The mixture was heated at reflux for 1 h, cooled to room temperature, and poured into 95% ethanol (1 L). The precipitate was collected by suction filtration, washed with water, washed with 95% ethanol and then dried under high vacuum to afford **11** (24.2 g, 58%) as a colorless solid. A small portion of this product was recrystallized from hexane/dichloromethane to give colorless crystals: m.p. 202−203 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.74−1.84 (m, 2 H), 1.88−1.99 (m, 4 H), 2.37 (s, 12 H), 2.43 (s, 6 H), 3.73 (t, *J* = 6.1 Hz, 4 H), 4.59 (s, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 14.7, 22.9, 30.1, 72.8, 131.5, 132.6, 133.5, 154.2. MS (EI, 70 eV): *m*/*z* (%) M^+ not observed, 635/633/631/629 (0.5/1.5/1.5/0.3) [M^+ − Br], 553/551/549 (1.2/1.9/0.9), 473/471 (1.0/2.2), 471/469 (2.2/3.1), 393 (20), 391 (40), 389 (22), 313 (21), 311 (27), 243 (30), 241 (30), 163 (47), 69 (100). $C_{27}H_{36}Br_4O_2$ (712.2): calcd. C 45.53, H 5.10; found C 45.98, H 5.27.

1,5-Bis[3,5-bis(acetylthiomethyl)-2,4,6-trimethylphenoxy]pentane (12): Tetrabromide **11** (23.9 g, 32.5 mmol) was added under a nitrogen atmosphere to a room temperature suspension of potassium thioacetate (23.0 g, 201 mmol) in acetonitrile (200 mL). The mixture was heated at reflux for 23 h, cooled to room temperature and poured into cold water (1 L). The precipitate was collected by suction filtration, washed with water and dried under high vacuum to yield **12** (22.4 g, 96%) as a light brown solid. A small portion of this product was recrystallized from dichloromethane/95% ethanol for analysis: m.p. 87−88 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70−1.80 (m, 2 H), 1.85−1.95 (m, 4 H), 2.25 (s, 6 H), 2.26 (s, 12 H), 2.37 (s, 12 H), 3.68 (t, *J* = 6.7 Hz, 4 H), 4.20 (s, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 15.7, 22.9, 29.5, 30.1, 30.3, 72.7, 130.0, 131.7, 132.0, 154.1, 196.0. MS (EI, 70 eV): *m*/*z* (%) M^+ not observed, 456 (6), 381 (17), 312 (13), 237 (23), 203 (20), 193 (14), 179 (17), 161 (49), 103 (56), 43 (100). $C_{35}H_{48}O_6S_4$ (693.0): calcd. C 60.66, H 6.98; found C 60.32, H 6.83.

1,5-Bis[3,5-bis(thiomethyl)-2,4,6-trimethylphenoxy]pentane (13): A solution of KOH (14.4 g, 254 mmol) in water (30 mL) was added under a nitrogen atmosphere to a room temperature solution of **12** (22.0 g, 31.7 mmol) in DMF (200 mL). The mixture was stirred at 60 °C for 7 h and cooled in an ice bath. An aqueous 10% HCl solution (200 mL) was added slowly to the cold mixture. The precipitate was collected by suction filtration, washed with water and dried under high vacuum to afford **13** (15.5 g, 93%) as a light brown solid. A small portion of this product was recrystallized from dichloromethane/95% ethanol to give colorless crystals: m.p. 135−137 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (t, *J* = 6.5 Hz, 4 H), 1.74−1.84 (m, 2 H), 1.88−1.98 (m, 4 H), 2.35 (s, 12 H), 2.42 (s, 6 H), 3.72 (t, *J* = 6.3 Hz, 4 H), 3.79 (d, *J* = 6.5 Hz, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 15.0, 22.9, 23.8, 30.1, 72.7, 128.2, 129.4, 136.7, 154.2. MS (EI, 70 eV): *m*/*z* (%) = 524 (3) [M^+], 457 (2), 339 (6), 297 (100), 195 (56), 163 (26), 161 (24), 149 (26), 69 (73). $C_{27}H_{40}O_2S_4$ (524.9): calcd. C 61.79, H 7.68; found C 61.52, H 7.73.

9,11,13,19,21,23-Hexamethyl-1,7-dioxa-15,16,25,26-tetrathia[7.4.4]-(1,3,5)cyclophane (14): Solutions of iodine (14.5 g, 57.2 mmol) in 95% ethanol (600 mL) and tetrathiol **13** (15.0 g, 28.6 mmol) in dichloromethane (600 mL) were added simultaneously by syringe pump over 8 days under a nitrogen atmosphere to a vigorously mechanically stirred room temperature mixture of pyridine (50 mL), 95% ethanol (500 mL) and dichloromethane (500 mL). The mixture was stirred for a further 3 h after completion of the addition and the solvents were removed under reduced pressure. The residue was taken up in dichloromethane (600 mL) and the resulting solution was washed with aqueous 10% HCl solution, water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography (hexanes/dichloromethane, 4:1) to afford **14** (9.15 g, 61%) and **15** (0.54 g, 4%).

14: Colorless prisms, m.p. (heptane/dichloromethane) >280 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68−1.95 (m, 6 H), 2.23 (s, 6 H), 2.31 (s, 3 H), 2.39 (s, 6 H), 2.42 (s, 3 H), 3.41 (d, *J* = 15.5 Hz, 2 H), 3.44 (d, *J* = 14.4 Hz, 2 H), 3.82−3.78 (m, 2 H), 4.13 (d, *J* = 15.4 Hz, 2 H), 4.28 (d, *J* = 14.8 Hz, 2 H), 4.32−4.38 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 15.2, 15.7, 18.7, 23.5, 27.2, 29.9, 35.6, 38.5, 71.6, 74.8, 129.7, 130.1, 130.6, 130.7, 133.9, 135.4, 152.4, 155.3. MS (EI, 70 eV): *m*/*z* (%) = 521 (49), 520 (26) [M^+], 456 (21), 423 (12), 392 (25), 233 (39), 228 (35), 196 (21), 163 (37), 133 (21), 119 (25), 41 (100). $C_{27}H_{36}O_2S_4$ (520.8): calcd. C 62.27, H 6.97; found C 62.34, H 6.94.

15: Colorless prisms, m.p. (heptane/dichloromethane) >280 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68−1.82 (m, 12 H), 2.20−2.52 (several s, 36 H), 3.37−4.34 (several m, 24 H). MS (EI, 70 eV): *m*/*z* (%) M^+ not observed, 520 (69, M^+/2), 456 (19), 455 (21), 423 (15), 392 (24), 377 (18), 233 (28), 228 (31), 163 (34), 133 (21), 119 (25), 41 (100). $C_{54}H_{72}O_4S_8$ (1041.6): calcd. C 62.27, H 6.97; found C 62.82, H 7.43.

9,11,13,18,20,22-Hexamethyl-1,7-dioxa-15,24-dithia[7.3.3]-(1,3,5)cyclophane (16): Tetrathiacyclophane **14** (9.15 g, 17.6 mmol) was added in ten approximately equal portions at ca. 5−10 h intervals under a nitrogen atmosphere to a solution of HMPT (22.9 g, 141 mmol) at reflux in benzene (500 mL). After the final addition, the reaction was held at reflux for a further 24 h, cooled to room temperature and concentrated under reduced pressure. The residue was suspended in 95% ethanol and then suction filtered. The collected solids were washed with 95% ethanol, dried under high vacuum and subjected to flash chromatography (hexanes/dichloromethane) to afford **16** (6.73 g, 84%) as colorless prisms: m.p. >300 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34−1.42 (m, 2 H), 1.68−1.78 (m, 4 H), 2.23 (s, 12 H), 2.45 (s, 6 H), 3.65 (d, *J* = 15.6 Hz, 4 H), 3.89 (m, 4 H), 4.45 (d, *J* = 15.4 Hz, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 18.4, 19.4, 26.5, 32.9, 72.8, 127.8, 128.8, 134.4, 155.0. MS (EI, 70 eV): *m*/*z* (%) = 456 (100) [M$^+$], 423 (28), 233 (26), 193 (40), 192 (46), 191 (57), 163 (74), 69 (84). $C_{27}H_{36}O_2S_2$ (456.7): calcd. C 71.01, H 7.95; found C 70.63, H 7.67.

Mixture of Stereoisomers of 9,11,13,17,19,21-Hexamethyl-14,22-bis(methylthio)-1,7-dioxa[7.2.2](1,3,5)cyclophane and 9,11,13,17,19,21-Hexamethyl-14,23-bis(methylthio)-1,7-dioxa[7.2.2](1,3,5)-cyclophane (17): $(MeO)_2CHBF_4$ (23.8 g, 147 mmol) was added at −40 °C under a nitrogen atmosphere to a solution of **16** (6.70 g, 14.7 mmol) in dichloromethane (300 mL). The cooling was removed and the mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was slurried with ethyl acetate (50 mL). The solids were collected by suction filtration, washed with ethyl acetate and dried under high vacuum to afford the bis(methylsulfonium tetrafluoroborate) salt of **16**. This salt was added to a mixture of potassium *tert*-butoxide (9.90 g, 88.2 mmol) in dry THF (200 mL) at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 23 h and then diethyl ether and aqueous 10% HCl solution were added. The organic layer was washed with water, dried over $MgSO_4$ and dried under high vacuum. Flash chromatography (dichloromethane) of the residue afforded **17** (5.59 g, 78% from **16**) as a pale yellow solid: m.p. 78−158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25−1.95 (m, 6 H), 2.03−2.53 (several s, 24 H), 1.95−5.23 (several m, 10 H). MS (EI, 70 eV): *m*/*z* (%) = 484 (84) [M$^+$], 469 (100), 437 (11), 421 (42), 191 (19), 163 (21). $C_{29}H_{40}O_2S_2$ (484.8): calcd. C 71.85, H 8.32; found C 71.76, H 8.26.

9,11,13,17,19,21-Hexamethyl-1,7-dioxa[7.2.2](1,3,5)cyclophane-14,22-diene (18): $(MeO)_2CHBF_4$ (6.81 g, 42.1 mmol) was added at 0 °C under a nitrogen atmosphere to a solution of **17** (5.10 g, 10.5 mmol) in dichloromethane (100 mL). The mixture was stirred at room temperature for 17 h. The solvent was removed under reduced pressure and the residue was slurried with ethyl acetate (50 mL).). The solids were collected by suction filtration, washed with diethyl ether and dried under high vacuum to afford the bis(methylsulfonium tetrafluroborate) salt of **17**. This salt was added to a mixture of potassium *tert*-butoxide (5.22 g, 46.5 mmol) at −20 °C in THF/*tert*-butyl alcohol (100 mL, 1:1) under a nitrogen atmosphere. The cooling was removed and the mixture was stirred at room temperature for 2 h and then diethyl ether and aqueous 10% HCl solution were added. The organic layer was washed with water, dried over $MgSO_4$ and dried under high vacuum. Flash chromatography (hexanes/dichloromethane, 1:1) of the residue afforded **18** (1.08 g, 30% from **17**) as light brown solid. A small portion of this product was recrystallized from heptane/dichloromethane to give light-brown prisms: m.p. 195−197 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16−1.24 (m, 2 H), 1.60−1.69 (m, 4 H), 1.98 (s, 12 H), 2.18 (s, 6 H), 3.85−3.90 (m, 4 H), 7.08 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 19.0, 24.4, 27.3, 72.0, 124.9, 133.0, 133.9, 138.5, 151.2. MS (EI, 70 eV): *m*/*z* (%) = 388 (43) [M$^+$], 373 (44), 358 (20), 287 (48), 275 (34), 259 (100), 247 (46), 232 (34), 229 (26), 215 (28), 202 (35). $C_{27}H_{32}O_2$ (388.5): calcd. C 83.46, H 8.30; found C 83.25, H 8.05.

***cis*-1,3,6,8,10b,10c-Hexamethyl-10b,10c-dihydropyrene-2,7-dione (19):** A solution of ceric ammonium nitrate (0.526 g, 0.960 mmol) in water (2 mL) was added to a warm solution of **18** (0.117 g, 0.301 mmol) in acetonitrile. The mixture was stirred at room temperature for 15 min, quenched with water and concentrated under reduced pressure. The residue was taken up in diethyl ether and water, and the organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography (dichloromethane) to afford **19** (0.078 g, 81%) as orange needles: m.p. 235−236 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.83 (s, 6 H), 1.89 (s, 12 H), 6.74 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.2, 36.9, 42.6, 128.9, 130.7, 152.0, 185.4. MS (EI, 70 eV): *m*/*z* (%) = 318 (42) [M$^+$], 303 (30), 290 (11), 288 (28), 275 (47), 260 (58), 247 (100), 232 (57), 217 (35), 215 (35), 202 (46). IR (nujol): $\tilde{\nu}$ = 1630, 1610, 1468, 1377, 1362, 1267, 1047, 1005 cm^{-1}. UV/Vis (CH_3CN): λ_{max} (log ε) = 267 (4.27), 306 (sh, 4.17), 327 (4.23). $C_{22}H_{22}O_2$ (318.4): calcd. C 82.99, H 6.96; found C 82.54, H 6.96.

Crystal Data for *cis*-19: Yellow irregular crystal (0.45 × 0.40 × 0.20 mm) from heptane/dichloromethane, $C_{22}H_{22}O_2$, *M* = 318.41, orthorhombic, *Pbca* (#61), *Z* = 8, *a* = 13.920(2), *b* = 25.070(2), *c* = 9.556(3) Å, *V* = 3334.9(9) Å^3, D_c = 1.268 g cm^{-3}, *F*(000) = 1360, μ (Mo-K_α) = 0.79 cm^{-1}. Data collection at 26 ± 1 °C with a Rigaku AFC6S diffractometer equipped with graphite monochromated Mo-K_α radiation (λ = 0.71069 Å), ω−2θ scan type with ω scan width = 0.84 + 0.35tanθ, ω scan speed 4.0° min^{-1} [up to 10 rescans for weak reflections with $I < 10.0\sigma(I)$], 4346 reflections measured, Lorentz-polarization and secondary extinction (coeff. = 1.93187 × 10^{-7}) corrections, giving 2096 with $I < 2.00\sigma(I)$. Solution and refinement by direct methods using the teXsan package of the Molecular Structure Corporation;[18] all non-hydrogen atoms were refined anisotropically; full-matrix least-squares refinement with 284 variable parameters led to *R* = 0.050, R_w = 0.038, GOF = 3.30.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-162877. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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