Syntheses and Reactions of the First Dithia[3.1.3.1]metacyclophanes, [2.1.2.1]Metacyclophanes, and [2.1.2.1]Metacyclophanedienes[1]

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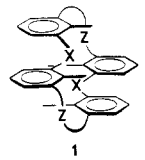
Two new cyclophane series, the dithia[3.1.3.1]metacyclophanes **5** and the [2.1.2.1]metacyclophanedienes **6**, are synthesized and their chemistry is described. On the basis of this chemistry, such cyclophanes appear not to adopt the syn or anti conformations found in the [2.2]metacyclophanes, but a geometry in which the X,Y groups are distant in space.

Introduction

Cyclophanes have attracted considerable attention over the last two decades because of their interesting stereochemistry and potential interring electronic interactions.[2] Most attention however has been given to the lower members of the series, with very little information available at the start of this work on higher cyclophanes.[3] Specifically we were interested in [3.1.3.1]- and [2.1.2.1]-metacyclophanes, which have exceptionally interesting stereochemistry in that either the stepped conformation of the *syn*- and *anti*-[2.2]metacyclophanes, e.g., **1**, could be adopted, or a more open crown type structure, e.g., **2**.



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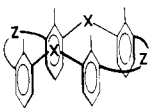

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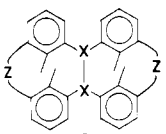

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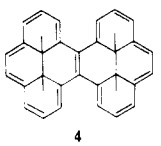

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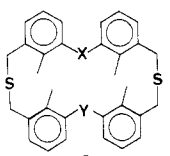

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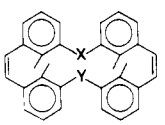
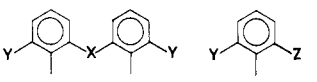


6

In the event that a stepped structure was adopted, closure of a bond between X–X of **1** would lead to the edge fused metacyclophanes **3**, potential precursors to the interesting[5] [14]annuleno[14]annulene **4**. In either case determination of the conformational preferences of such cyclophanes, particularly as the hybridization of the bridges is changed, would yield knowledge useful in future targeting of synthetic schemes designed to yield more highly fused ring systems.

Results and Discussion

Dithia[3.3]cyclophanes have been extremely fruitful precursors to both [2.2]cyclophanes and cyclophanedienes.[6] We therefore chose **5** to access the [2.1.2.1]cyclophanes **6**, and thought that interesting X,Y groups in **5** and **6** would be combinations of C=O and CH_2 for three reasons. Firstly, this made the precursors **7** synthetically accessible.



7 **8**

Secondly, variation of the X,Y bridge as sp^3 or sp^2 units might change the geometry adopted by **5** or **6**, and thirdly, such groups provided several options to examine the chemistry of bridge formation in the products **6**. Thus the initial synthetic objective chosen was **5** (X = CO, Y = CH_2) requiring the dibromide **7A** (X = CO, Y = CH_2Br) and the dithiol **7B** (X = CH_2, Y = CH_2SH).

Reaction of commercial 2,6-dichlorotoluene **8A** (Y = Z = Cl) with 1.1 equiv of CuCN yielded 2-chloro-6-cyanotoluene **8B** (Y = Cl, Z = CN) more easily than previous routes.[8] Reduction of this nitrile with Dibal in benzene then yielded aldehyde **8C** (Y = Cl, Z = CHO), which on further reduction with $NaBH_4$ in THF gave alcohol **8D** (Y = Cl, Z = CH_2OH) in overall 39% yield from **8A** (Y = Z = Cl). This alcohol was also obtained from the mono-Grignard reagent **8E** (Y = Cl, Z = MgCl) with paraformaldehyde. Treatment of alcohol **8D** (Y = Cl, Z = CH_2OH) with PBr_3 gave bromide **8F** (Y = Cl, Z = CH_2Br), which with methoxide ion gave ether **8G** (Y = Cl, Z = CH_2OCH_3). This could also be obtained from alcohol **8D** with NaH followed by methyl iodide. Formation of the Grignard reagent **8H** (Y = MgCl, Z = CH_2OCH_3) was exceptionally difficult. Iodine-activated magnesium,[9] or Rieke[20] magnesium prepared from potassium and $MgBr_2$, or magnesium generated from $MgCl_2$ and sodium naphthalenide[11] all failed to react. Use of 2 equiv of magnesium with *1 equiv* of 1,2-dibromoethane as an entrainment reagent[12] did however give the Grignard **8H** (Y = MgCl, Z = CH_2OCH_3), which on reaction with ethyl formate gave 60% of the alcohol **7C** (X = CHOH, Y = CH_2OCH_3), mp 113–114 °C. This alcohol could also be obtained by reaction of Grignard **8H** (Y = MgCl, Z = CH_2OCH_3) with aldehyde **8I** (Y = CHO, Z = CH_2OCH_3), itself obtained by conversion of **8G** (Y = Cl, Z = CH_2OCH_3) into nitrile **8J** (Y = CN, Z = CH_2OCH_3) as previously with CuCN, and

(1) Taken from the doctoral thesis of Yee-Hing Lai, University of Victoria, Sept, 1980.
(2) (a) Keehn, P.; Rosenfeld, S. "Cyclophanes"; Academic Press: New York, 1983. (b) Vögtle, F. "Cyclophanes"; Springer-Verlag: Heidelberg, 1983.
(3) For a comprehensive review of cyclophane conformations, see: Mitchell, R. H. In "Cyclophanes"; Keehn, P., Rosenfeld, S., Eds.; Academic Press: New York, 1983; Chapter 4.
(4) Mitchell, R. H.; Lai, Y. H. *Tetrahedron Lett.* **1980**, *21*, 2633.
(5) (a) For a review, see: Mitchell, R. H. *Isr. J. Chem.* **1980**, *20*, 594. (b) Mitchell, R. H.; Williams, R. V.; Mahadevan, R.; Lai, Y-H.; Dingle, T. W. *J. Am. Chem. Soc.* **1982**, *104*, 2571.
(6) For a review, see: Mitchell, R. H. *Heterocycles* **1978**, *11*, 563.
(7) All compounds prepared were satisfactorily characterized by ^1H NMR, mass spectroscopy, IR (where appropriate), and elemental analysis (new) and were obtained pure by TLC unless otherwise stated.
(8) Lindsay, W. S.; Stokes, P.; Humber, L. G.; Boekelheide, V. *J. Am. Chem. Soc.* **1961**, *83*, 943.
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(10) Rieke, R. D.; Bales, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 1775.
(11) Arnold, R. T.; Kulenovic, S. T. *Synth. Commun.* **1977**, *7*, 223.
(12) Pearson, D. E.; Cowan, D.; Beckler, J. D. *J. Org. Chem.* **1959**, *24*, 504.

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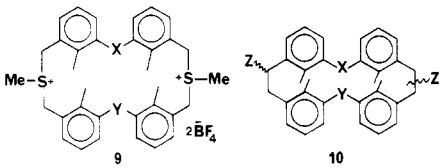
reduction of this with Dibal in benzene.

Jones oxidation[13] of the alcohol **7C** (X = CHOH, Y = CH_2OCH_3) gave ketone diether **7D** (X = CO, Y = CH_2OCH_3), mp 65–66 °C, which with refluxing 48% HBr–concentrated H_2SO_4 (2:1) gave the desired ketone dibromide **7A** (X = CO, Y = CH_2Br), mp 162–163 °C. Direct reduction of alcohol **7E** (X = CHOH, Y = CH_2OCH_3) with $NaBH_4$ in CF_3COOH[14] at 0 °C gave an excellent yield of the diarylmethane **7C** (X = CH_2, Y = CH_2OCH_3), mp 53.5–55 °C, which on similar treatment with HBr–H_2SO_4 gave dibromide **7F** (X = CH_2, Y = CH_2Br), mp 115–116 °C. This was converted to the dithiol **7B** (X = CH_2, Y = CH_2SH), mp 66.5–67.5 °C in 97% yield by the thiourea method.[15] High dilution coupling[16] of dithiol **7B** (X = CH_2, Y = CH_2SH) and dibromide **7A** (X = CO, Y = CH_2Br) gave after chromatography 70–80% yields of the desired dithiacyclophane **5A** (X = CO, Y = CH_2), mp 297–299 °C dec. Its molecular weight of 522 was indicated by a very intense MH^+ peak in its chemical-ionization (CI) mass spectrum and thus confirmed its structure as a dimer. Is ^1H NMR spectrum, which showed the Ar_2CH_2 protons as a singlet at δ 3.95 and the bridging $-CH_2S-$protons also as a singlet at δ 3.74, together with two singlet methyl proton signals at δ 1.97 (>C=O unit) and δ 1.85 (>CH_2 unit), indicated that **5A** was a single conformationally mobile stereoisomer. Variable temperature studies later confirmed this and are discussed in detail in the subsequent paper of this issue. Further, no stereoisomers were observed on thin-layer chromatography of **5A** under conditions where they are readily observed in other systems.[16,17] Conversion of **5A** (X = CO, Y = CH_2) into the cyclophanediene **6A** (X = CO, Y = CH_2) was thus investigated next. Wittig rearrangement[16] of **5A** (X = CO, Y = CH_2) using lithium diisopropylamide (LDA) in THF followed by addition of methyl iodide gave a nonseparable mixture of products, however conversion of **5A** to its bis(methyl sulfonium) salt, **9**, using the Borsch



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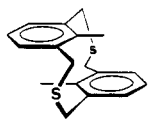
reagent[18] $(CH_3O)_2C^+HBF_4^-$, followed by a Stevens rearrangement of **9** (*t*-BuOK/THF) gave a 50% yield of **10A** (X = CO, Y = CH_2, Z = SCH_3) as a mixture of stereoisomers. The characteristic[16] $-SCH_3$ protons appeared at δ 1.90 and a correct MH^+ peak at *m/e* 551 was observed in its CI mass spectrum. The final elimination to give **6A** (X = CO, Y = CH_2) could be achieved by two methods: remethylation of **10A** (X = CO, Y = CH_2, Z = SCH_3) with $(CH_3O)_2C^+HBF_4^-$ gave 89% of **10B** (X = CO, Y = CH_2, Z = $S^+(CH_3)_2BF_4^-$) which on further treatment with *t*-BuOK/THF gave the diene **6A** (X = CO, Y = CH_2) in 30–55% yield. Alternatively oxidation of **10A** (X = CO, Y = CH_2, Z = SCH_3) with bromine in aqueous potassium bicarbonate[19] gave a quantitative yield of the disulfoxide **10C** (X = CO, Y = CH_2, Z = $SOCH_3$), which on refluxing for 12 h in *N*-methyl-2-pyrrolidinone gave 50–75% yields of **6A** (X = CO, Y = CH_2). In cyclophane chemistry[6] thermal elimination of PhSOH has been more commonly used[20] than MeSOH elimination, though the latter has been occasionally used.[21] In the above example it appears preferable to the base-catalyzed Me_2S elimination. As obtained the diene **5A** (X = CO, Y = CH_2) was found by TLC and by NMR to be a mixture of stereoisomers in a 75:25 ratio. Only small quantities of each stereoisomer could be obtained pure by chromatography. The major isomer, mp 291–293 °C, showed two distinct sets of two singlets each for the methyl protons: one set at δ 2.37 and 2.28, the other at δ 1.18 and 1.09. One signal within each set was assigned to the methyls of the "benzophenone unit", the other to the "diarylmethane unit". Since in the case of the parent thiacyclophanes **11** and **12**, the internal



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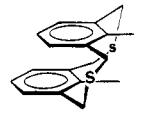
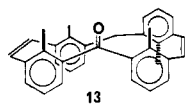


12

methyl protons of the anti isomers **11** appear at δ 1.30 and those of *syn*-**12** appear at δ 2.54, we assumed that in this isomer of **6A** (X = CO, Y = CH_2), we likewise had one set of *anti*-methyls and one set of *syn*-methyls and assigned this isomer the syn,anti structure **13**. The minor isomer,



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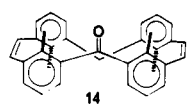


14

mp 286–288 °C, gave a similar mass spectrum to **13** with a strong MH^+ peak in its CI mass spectrum. In its ^1H NMR spectrum, however, all the methyl protons occurred as a singlet at δ 1.24 (the region of "*anti*-methyls") and thus the anti structure **14** was tentatively assigned. We assumed in this case there was an accidental chemical shift degeneracy between the methyls of the two halves of the molecule. To further support these initial assignments, for the major isomer **13**, two clear sets of aryl hydrogens were observed, one set of 6 H in the syn aryl ring region at δ 6.68–6.13 and one set in the anti aryl region[3] at δ 7.47–6.98.

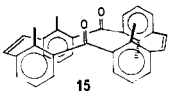
The minor isomer **14** however only showed one set of aryl hydrogens at δ 7.64–7.06, in the anti aryl region. Both isomers showed AB multiplets for the olefinic protons, the major isomer showing J_{AB} = 11.5 Hz, that of the minor isomer not being clear (only the inner lines were clear); the major isomer showed the $-CH_2-$ group as an AB at δ_A 4.09 and δ_B at 3.51 (J_{AB} = 15 Hz) and the minor isomer as a singlet at δ 4.27. Moreover the more symmetrical isomer **14** would be expected by analogy to have a higher melting point than **13**. Thus collectively we had no reason to doubt our original stereochemical assignments. However, after studying the chemistry of **13** we were forced to review these assignments (see below).

Molecular models of **13** and **14** indicated that there should be no steric reason why *in these conformations*, formation of the central bridge should be inhibited, and indeed attack on the carbonyl by an external basic nu-

(13) Bowers, A.; Halsall, T. G.; Jones, E. R. H.; Lemin, A. J. *J. Chem. Soc.* **1953**, 2548.
(14) Gribble, G. W.; Leese, R. M. *Synthesis* **1977**, 172.
(15) Speziale, A. J. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, p 401.
(16) Mitchell, R. H.; Boekelheide, V. *J. Am. Chem. Soc.* **1974**, *96*, 1547. Mitchell, R. H.; Otsubo, T.; Boekelheide, V. *Tetrahedron Lett.* **1975**, 219.
(17) (a) Mitchell, R. H.; Williams, R. V.; Dingle, T. W. *J. Am. Chem. Soc.* **1982**, *104*, 2560. (b) Mitchell, R. H.; Yan, J. S. H.; Dingle, T. W. *Ibid.* **1982**, *104*, 2551.
(18) Borch, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5303; *J. Org. Chem.* **1969**, *34*, 627. See also: Meerwein, H.; Bodenbenner, K.; Borner, P.; Kunert, F.; Wunderlich, K. *Liebigs Ann. Chem.* **1960**, *632*, 38.
(19) Drabowicz, J.; Midura, W.; Mikokajczyk, M. *Synthesis* **1979**, 39.
(20) Otsubo, T.; Boekelheide, V. *Tetrahedron Lett.* **1975**, 3881; *J. Org. Chem.* **1977**, *42*, 1085.
(21) Otsubo, T., Gray, R.; Boekelheide, V. *J. Am. Chem. Soc.* **1978**, *100*, 2449. Kamp, D.; Boekelheide, V. *J. Org. Chem.* **1978**, *43*, 3475. Potter, S. E.; Sutherland, I. O. *J. Chem. Soc., Chem. Commun.* **1973**, 520.

cleophile (rather than attack by the proximal methylene bridge, for example, after anion formation) looked unlikely! Irradiation of **6A** (X = CO, Y = CH_2) (a mixture of **13** and **14**) in CCl_4 with a medium-pressure mercury lamp/Pyrex apparatus merely returned unchanged starting material, as did reflux of the mixture with KH in THF, in complete contrast to the reaction of benzophenone with diphenylmethane, in which formation of 1,1,2,2-tetraphenylethanol under photolytic (radical) or basic (anionic) conditions is well documented.[22] LDA in refluxing THF gave a brown color, but only unchanged **6A** was recovered after workup. *n*-Butyllithium generated a transient red color and gave the alcohol **6E** (X = C(OH)(*n*-Bu), Y = CH_2) as the major product. Even the much less nucleophilic *tert*-butyllithium at −78 °C gave the alcohol **6F** (X = C(OH)(*t*-Bu), Y = CH_2) as a main product. None of the minor products could be identified as **3** (X–X = >C(OH)CH<, Z=CH=CH). Such results with bases as bulky at *t*-BuLi suggested that the C=O group was indeed accessible and was not shielded from external attack by the methyls, as molecular models of **13** or **14** had indicated. These results were later confirmed by the examples to be described below.

The next target we chose to examine was **6B** (X = Y = CO). Thus in the same way as for **7F** (X = CH_2, Y = CH_2Br), the dibromide **7A** (X = CO, Y = CH_2Br) was converted to dithiol **7G** (X = CO, Y = CH_2SH), mp 77–78 °C, although in reduced yield (57%). Coupling of **7A** (X = CO, Y = CH_2Br) with **7G** (X = CO, Y = CH_2SH) gave 67% of dithiacyclophane **5B** (X = Y = CO), mp 326–331 °C dec. Its dimeric structure was confirmed by a MH^+ peak at *m/e* 537 in its mass spectrum. Since the compound is extremely insoluble in most organic solvents, its ^1H NMR spectrum was obtained only with difficulty, but two singlets could be seen at δ 1.88 ($-CH_3$) and δ 3.67 ($-CH_2S-$) which suggested a conformationally mobile phane. Methylation of **5B** (X = Y = CO) with $(CH_3O)_2C^+HBF_4^-$ and Stevens rearrangement (*t*-BuOK/THF) as described above gave 36% of cyclophane **10D** (X = Y = CO, Z = SCH_3) as a mixture of stereoisomers. Oxidation[19] gave 97% of mixed sulfoxides **10E** (X = Y = CO, Z = $SOCH_3$), which on pyrolysis in *N*-methyl-2-pyrrolidinone at 150–160 °C for 14 h gave 60% yield of diene **6B** (X = Y = CO), again as a mixture of two isomers. However, only one TLC spot was obtained in this case, and separation of these isomers by chromatography proved to be more difficult than for **6A** (X = CH_2, Y = CO). Only a small sample of the major isomer (75% of mixture) was obtained pure, mp 318–320 °C, and this isomer showed, like **13**, two sets of methyl protons, a singlet at δ 2.41 ("syn region") and a singlet at δ 1.14 ("anti region") in its ^1H NMR spectrum, as well as a strong MH^+ peak at *m/e* 469 in its CI mass spectrum and was thus assigned, analogous to **13**, the syn,anti structure **15**. The minor isomer showed



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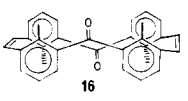
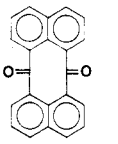


16

only a singlet at δ 1.30 ("anti region") for the methyl protons, and analogous to **14** was assigned the anti,anti structure **16** (as for **13** and **14** these were later to be revised).

We wished to ascertain whether the two carbonyl groups of **15** or **16** were close enough to allow bond formation. Benzophenone is readily coupled to tetraphenylethylene by using an active titanium species;[23] however reductive coupling of the mixture of diketones **6B** (X = Y = CO) (**15**, **16**) by using either of $TiCl_3$–$LiAlH_4$[24] or $TiCl_4$–Zn[25] gave complex mixtures of products in which no **3** (X–X = C=C, Z = CH=CH) could be found.

Cyclization of 2,2′-diacylbiphenyls to give phenanthrenes[26] and of the diketone **17** to give the strained ace



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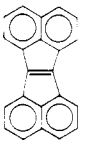
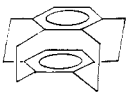


18

bridged naphthalene[27] **18** readily occurred with hydrazine, however reaction of the mixed isomers of **6B** (X = Y = CO) under acidic[26] or basic[27] conditions returned only starting material. The tetrabridged cyclophane **19** has been pre-



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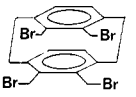

20

pared[28] by intramolecular coupling of the tetrabromide **20** with activated zinc dust,[29] however reaction of dibromide **6C** (X = Y = CHBr) under a variety of conditions again only returned the starting material. Dibromide **6c**, mp 247–249 °C, was obtained by reduction of ketone **6B** (X = Y = CO) with $NaBH_4$ in wet THF to give 84% of alcohol of **6D** (X = Y = CHOH), which with PBr_3 in benzene gave 97% of bromide **6C** (X = Y = CHBr).

Thus in these examples too, the carbonyl or bromide groups appear to be resistant to coupling, indicative perhaps of them not being close in space and of an incorrect stereochemistry assignment to **15** and **16**.

Since the thiacyclophanes **5A** (X = CO, Y = CH_2) and **5B** (X = Y = CO) were both believed to be conformationally mobile at room temperature (based on their simple ^1H NMR spectra, see above) we thought it worthwhile to see if the central bond could be joined in these systems in which the outer bridges are the longer C–S–C rather than C–C units.

Thus reduction of **5B** (X = Y = CO) with $NaBH_4$ in THF gave the dialcohol **5C** (X = Y = CHOH), which with PBr_3 in benzene gave dibromide **5D** (X = Y = CHBr), mp 350 °C. However, reflux of **5D** with activated zinc dust[29] in acetonitrile returned starting material, whereas when dimethyl sulfoxide was used as solvent, ketone **5B** (X = Y = CO) was formed.[30]

Conclusions

We have achieved the synthesis of the first [3.1.3.1]-metacyclophanes **5A** (X = CO, Y = CH_2) and **5B** (X = Y = CO) and have shown that these can be successfully transformed into the [2.1.2.1]metacyclophanes **6A** (X = CO, Y = CH_2) and **6B** (X = Y = CO). The initial stereochemistries assigned to the latter were **13** and **14** and **15** and **16**, respectively. However after extensive investigation of bond formation between X and Y in **5** and **6**,

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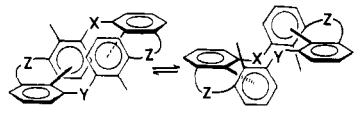
we conclude that X and Y are distant from each other in space.

We thus undertook a detailed variable temperature NMR study of these and derived cyclophanes, the results of which indicate that these cyclophanes are fluxional and have the stereochemistry shown as **21**. The results that lead to these conclusions are described in detail in the accompanying succeeding paper.[31]



21

Experimental Section

All melting points were determined on a Kofler hot stage and are uncorrected. ^{1}H NMR spectra were determined in $CDCl_3$ (unless otherise stated) on a Perkin-Elmer R12B (60 MHz) or R32 (90 MHz) spectrometer. ^{13}C NMR spectra were recorded on a Nicolet-TT-14 spectrometer operating at 15.1 MHz. All chemical shifts are reported in ppm downfield from tetramethylsilane used as internal standard. IR spectra were recorded on a Pye-Unicam SP1000 or Perkin-Elmer 283 infrared spectrometer. Mass spectra were determined on a Hitachi Perkin-Elmer RMU-17 or Finnigan 3300 mass spectrometer at 70 eV using electron-impact (EI) or methane-chemical ionization (CI). Relative intensities are given in parentheses. Only the molecular ion containing ^{35}Cl, or ^{79}Br is given for compounds containing these halogens. Correct isotope patterns were obtained in all cases. Microanalyses were performed either by this department or by Canadian Microanalytical Services (Vancouver, B.C.). All evaporations were carried out under reduced pressure on a rotary evaporator at about 40 °C, and all organic layers were washed with water (unless otherwise stated) and dried with anhydrous magnesium or sodium sulfate.

3-Chloro-2-methylbenzonitrile 8B (Y = Cl, Z = CN). Copper(I) cyanide (100.0 g, 1.116 mol) was added to a solution of 2,6-dichlorotoluene (101.0 g, 0.627 mol) in *N*-methyl-2-pyrrolidinone (315 mL). The mixture was then heated with stirring to about 170 °C and maintained at this temperature for 48 h. The reaction mixture was then cooled and poured into well stirred aqueous ammonia (concentrated "880": H_2O, 1:1, 1.5 L) and the total was then well extracted with dichloromethane (3 × 1 L). The organic layers were washed, dried, and evaporated to about 100 mL. Pentane (50 mL) was added and the mixture was chromatographed over silica gel with pentane as eluant. Unchanged **8A** (Y = Z = Cl), 1.98 g, (2%) was eluted first, followed by product **8B** (Y = Cl, Z = CN): 44.71 g (47%); bp 124–125 °C (28 torr);[32] ^{1}H NMR (60 MHz) δ 7.66–7.02 (m, 3 H, Ar H), 2.56 (s, 3 H, Ar CH_3); IR (neat) 2240 (C≡N), 1570, 1466, 1445, 1386, 1145, 1022, 830, 790, 702 cm^{-1}.

3-Chloro-2-methylbenzaldehyde 8C (Y = Cl, Z = CHO). Diisobutylaluminum hydride (0.16 mol) in hexane (145 mL) was added dropwise with good stirring under N_2 to a solution of the nitrile **8B** (Y = Cl, Z = CN) (19.70 g, 0.13 mol) in dry benzene (150 mL) at 20 °C. After 3 h, the viscous yellow solution was decomposed by using ice bath cooling by addition of firstly methanol (35 mL), then methanol/H_2O (1:1, 50 mL), and finally concentrated HCl/H_2O (1:2, 175 mL) so that the resultant solution was slightly acidic. The mixture was then extracted with ether, and the organic extracts were washed, dried, and evaporated to a pale yellow liquid. This upon distillation yielded 17.65 g (88%) of the aldehyde **8C** as a colorless liquid, bp 123–125 °C (28 torr), which solidified on standing: mp 30.5–31.5 °C; ^{1}H NMR (60 MHz) δ 10.28 (s, 1 H, CHO), 7.82–7.16 (m, 3 H, Ar H), 2.71 (s, 3 H, Ar CH_3); IR (neat) 1700 (C=O), 1598, 1455, 1246, 1185, 790, 720, 705 cm^{-1}; MS (EI) M$^+$·, *m/e* 154 (80), 153 (100), 125 (65).

Anal. Calcd for C_8H_7ClO: C, 62.14; H, 4.53. Found: C, 61.92; H, 4.56.

3-Chloro-2-methylbenzyl Alcohol 8D (Y = Cl, Z = CH_2OH). Method a. By reduction of aldehyde **8C** (Y = Cl, Z = CHO). A solution of aldehyde **8C** (23.18 g, 150 mmol) in THF (170 mL) was added dropwise to a stirred slurry of $NaBH_4$ (1.82 g, 48.2 mmol) in THF (50 mL) at 20 °C. After 3.5 h, the reaction mixture was made acidic with concentrated HCl/H_2O (1:1). The aqueous layer was saturated with NaCl and extracted with ether (2 × 200 mL). The organic layers were combined, dried, and evaporated. The residue was recrystallized from benzene to yield 21.73 g (93%) of colorless crystals of alcohol **8D**: mp 86–87 °C; ^{1}H NMR (60 MHz) δ 7.40–6.92 (m, 3 H, Ar H), 4.63 (s, 2 H, CH_2O), 2.35 (s, 3 H, Ar CH_3) and 1.82 (s, 1 H, OH); IR (KBr) 3220 (b, OH), 1460, 1186, 1158, 1025, 798, 732, 656 cm^{-1}. MS (EI) M$^+$·, *m/e* 156 (41), 138 (100), 105 (50), 71 (75). Anal. Calcd for C_8H_9ClO: C, 61.35; H, 5.79. Found: C, 61.19; H, 5.82.

Method b. Through the Grignard reagent **8E** (Y = MgCl, Z = Cl). A solution of dichloride **8A** (Y = Z = Cl) (10.0 g, 62 mmol) in dry THF (20 mL) was added to Mg turnings (33.21 g, 1.37 mol) under N_2. 1,2-Dibromoethane (0.5 mL) was added to initiate the reaction and then more dichloride **8A** (190 g, 1.18 mol) in dry THF (380 mL) was added dropwise to maintain gentle reflux. Reflux was continued until the bulk of the magnesium was consumed, and then powdered paraformaldehyde (41.0 g, 1.37 mol, dried over P_2O_5) was added in three batches at 15-min intervals to the cooled Grignard reagent. After the reaction was refluxed for 12 h, it was recooled, ice water added, and then dilute H_2SO_4 until acidic. The mixture was then extracted with ether. The organic layers were combined, washed, dried, and evaporated to give a yellow residue which after washing with pentane gave 163 g (84%) of alcohol **8D**, identical with the sample prepared by method a above.

2-(Bromomethyl)-6-chlorotoluene 8F (Y = Cl, Z = CH_2Br). A solution of PBr_3 (5.2 mL, 54 mmol) in dry benzene (50 mL) was added slowly to a vigorously stirred solution of alcohol **8D** (Y = Cl, Z = CH_2OH) (12.52 g, 80 mmol) in dry benzene (200 mL) containing 5 drops of pyridine. After stirring for 2 h, the mixture was washed with H_2O, aqueous $NaHCO_3$, and H_2O, dried, and evaporated. The resulting pale yellow liquid was distilled to give the highly lachrymatory bromide **8F**: 16.54 g (94%) as a colorless oil; bp 143–144 °C (28 torr); ^{1}H NMR (60 MHz) δ 7.40–6.84 (m, 3 H, Ar H) 4.42 (s, 2 H, CH_2Br), 2.41 (s, 3 H, Ar CH_3); IR (neat) 1460, 1218, 1186, 1016, 790, 719, 633 cm^{-1}; MS (EI) M$^+$·, *m/e* 218 (6), 139 (100), 103 (34). Anal. Calcd for C_8H_8BrCl: C, 43.77; H, 3.67. Found: C, 43.72; H, 3.66.

2-Chloro-6-(methoxymethyl)toluene 8G (Y = Cl, Z = CH_2OCH_3). Method a. From bromide **8F** (Y = Cl, Z = CH_2Br). The bromide **8F** (14.27 g, 65 mmol) was added to a solution of sodium methoxide (prepared by dissolving Na (1.8 g, 78 mmol) in methanol (70 mL)) under N_2 and was refluxed for 2.5 h. After the reaction had cooled, most of the methanol was removed and water and ether were added. The organic layer was washed, dried, and evaporated to leave a yellow liquid, which upon distillation yielded 9.88 g (89%) of ether **8G** as a colorless liquid: bp 123–124 °C (28 torr); ^{1}H NMR (60 MHz) δ 7.40–6.84 (m, 3 H, Ar H), 4.37 (s, 2 H, CH_2O), 3.34 (s, 3 H, OCH_3), 2.33 (s, 3 H, Ar CH_3); IR (neat), 1460, 1385, 1200, 1180, 1150, 1100, 1020, 780, 720 cm^{-1}; MS (EI) M$^+$·, *m/e* 170 (11), 138 (100), 103 (51).

Anal. Calcd for $C_9H_{11}ClO$: C, 63.35; H, 6.50. Found: C, 63.49; H, 6.52.

Method b. From alcohol **8D** (Y = Cl, Z = CH_2OH). A solution of alcohol **8D** (52.2 g, 0.33 mol) in dry THF (200 mL) was added dropwise to a suspension of NaH (19.20 g, 50% solid in mineral oil, washed several times with pentane) in dry THF (50 mL) and the mixture was stirred until evolution of H_2 ceased. Methyl iodide (25 mL, 0.4 mol) was then added dropwise, and the mixture was stirred at 20 °C for 5 h. Water and ether were then added, and the organic layer was then washed, dried, and evaporated to give 50.4 g (91%) of **8D**, identical with that prepared by method a.

3-(Methoxymethyl)-2-methylbenzonitrile 8J (Y = CN, Z = CH_2OCH_3). Copper(I) cyanide (81.4 g, 0.91 mol) was gradually added to a well stirred solution of ether **8G** (Y = Cl, Z = CH_2OCH_3) (155 g, 0.91 mol) in *N*-methyl-2-pyrrolidinone (450 mL), which was then heated under reflux for 12 h. A further portion of CuCN (81.4 g, 0.91 mol) was then added, and the mixture was again heated under reflux for a further 12 h. After cooling to about 100 °C, the reaction mixture was then poured into concentrated ammonia/ice (1:1, ~2 L). Both the resulting solution and the precipitate (partly product) were extracted well with dichloromethane (~1.5 L total) and then the organic extracts

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(32) No literature[8] data given.

were evaporated. The residual dark oil was dissolved in ether (300 mL), washed several times, and then stirred vigorously with water (300 mL) for about 12 h (to remove most *N*-methyl-2-pyrrolidinone). The ethereal layer was then dried and evaporated. The residual brown oil on distillation yielded 110.6 g (76%) of nitrile **8J**, as a colorless liquid: bp 150–154 °C (28 torr); ^{1}H NMR (60 MHz) δ 7.70–7.05 (m, 3 H, Ar H), 4.41 (s, 2 H, CH_2), 3.38 (s, 3 H, OCH_3), 2.39 (s, 3 H, Ar CH_3); IR (neat) 2230 (C≡N), 1460, 1385, 1202, 1138, 1105, 795 cm^{-1}; MS (EI) M$^+$·, *m/e* 161 (9), 146 (17), 129 (100), 116 (14), 103 (19). Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.47; H, 6.91; N, 8.49.

3-(Methoxymethyl)-2-methylbenzaldehyde 8I (Y = CHO, Z = CH_2OCH_3). Diisobutylaluminum hydride (66 mmol) in hexane (65 mL) was added dropwise to a well stirred solution of nitrile **8J** (Y = CN, Z = CH_2OCH_3) (8.86 g, 55 mmol) in dry benzene (60 mL) under N_2. After stirring for 12 h, the mixture was decomposed with ice bath cooling with methanol (15 mL), then methanol/H_2O (1:1, 30 mL), and finally concentrated HCl/H_2O (1:2) until slightly acidic. The mixture was then extracted with ether, and the combined organic extracts were dried and evaporated to give a yellow liquid which on distillation gave 7.58 g (84%) of aldehyde **8I**, as a colorless liquid: bp 148–150 °C (28 torr); ^{1}H NMR (60 MHz) δ 10.31 (s, 1 H, CHO), 7.85–7.13 (m, 3 H, Ar H), 4.45 (s, 2 H, CH_2O), 3.48 (s, 3 H, OCH_3), 2.60 (s, 3 H, Ar CH_3); IR (neat) 1700 (C=O), 1600, 1590, 1460, 1380, 1240, 1110, 795 cm^{-1}; MS (EI) M$^+$·, *m/e* 164 (11), 163 (100), 135 (59), 132 (89), 131 (28), 103 (35). Anal. Calcd for $C_{10}H_{12}O$: C, 74.06; H, 6.22. Found: C, 74.29; H, 6.30.

Bis(3-(methoxymethyl)-2-methylphenyl)methanol 7C (X = CHOH, Y = CH_2OCH_3). Method a. From aldehyde **8I** (Y = CHO, Z = CH_2OCH_3). A solution of the chloride **8G** (Y = Cl, Z = CH_2OCH_3) (35.65 g, 0.21 mol) and 1,2-dibromoethane (17 mL, 0.20 mol) in dry THF (250 mL) was added dropwise under N_2 under reflux conditions to a stirred suspension of Mg turnings (10.1 g, 0.42 mol) in dry THF (25 mL) to which 1,2-dibromoethane (1 mL) had been previously added. After the addition, the mixture was further refluxed for 6–8 h. The Grignard reagent **8H** (Y = MgCl, Z = CH_2OCH_3) so obtained was then cooled to about 20 °C and aldehyde **8I** (Y = CHO, Z = CH_2OCH_3) (31.20 g, 0.19 mol) in dry THF (100 mL) was then added dropwise over 45 min. The mixture was then stirred for a further 1 h at 20 °C and then 1 h at reflux. After the mixture had cooled, dilute HCl was added until the reaction mixture was acidic. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were then washed with saturated $NaHCO_3$ solution, dried, and evaporated to give a pale yellow solid which after washing with pentane yielded 43.9 g (77%) of the alcohol **7C**. A portion was recrystallized from cyclohexane as colorless crystals: mp 113–114 °C; ^{1}H NMR (60 MHz) δ 7.53–7.00 (m, 6 H, Ar H), 6.14 (s, 1 H, C*H*OH), 4.40 (s, 4 H, CH_2O), 3.33 (s, 6 H, OCH_3), 2.18 (s, 6 H, Ar CH_3):, 2.07 (s, 1 H, CHO*H*); IR (KBr) 3400 (b, OH) 1450, 1390, 1195, 1110, 1095, 800, 775 cm^{-1}; MS (EI) M$^+$·, *m/e* 300 (50), 236 (88), 221 (34), 206 (24), 205 (55), 163 (100).

Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.77; H, 8.31.

Method b. From ethyl formate. Ethyl formate (8.1 mL, 0.10 mol) was added to the Grignard reagent **8H** (0.21 mol, prepared exactly as described above in method a) and the mixture was stirred at 20 °C for 1 h and then at reflux for 1 h. After the mixture had cooled, dilute HCl and ether were added. The organic layer was washed, dried, and evaporated to a residue which after washing with pentane yielded 18.8 g (60%) of alcohol **7C**, identical with the sample prepared by method a.

Bis(3-(methoxymethyl)-2-methylphenyl) Ketone 7D (X = CO, Y = CH_2OCH_3). Jones reagent[13] (prepared by dissolving CrO_3 (2.67 g) and concentrated H_2SO_4 (2.3 mL) in water (10 mL)) was added dropwise to a solution of alcohol **7C** (X = CHOH, Y = CH_2OCH_3) (5.41 g, 18 mmol) in acetone (75 mL) until an orange-brown coloration persisted. After 10 min, H_2O (75 mL) and ether (200 mL) were added. The organic layer was washed, dried, and evaporated to yield crude ketone which was filtered through a short column of silica gel (3.5 × 30 cm) with dichloromethane as eluant to give 5.09 g (95%) of ketone **16P**, which on recrystallization from benzene gave colorless crystals: mp 65–66 °C; ^{1}H NMR (90 MHz) δ 7.78–7.18 (m, 6 H, Ar H), 4.60 (s, 4 H, CH_2O), 3.49 (s, 6 H, OCH_3), 2.42 (s, 6 H, Ar CH_3); IR (KBr) 1680 (C=O), 1460, 1390, 1312, 1272, 1254, 1210, 1132, 1108, 958, 803, 770, 751, 641 cm^{-1}; MS (EI) M$^+$·, *m/e* 298 (5), 261 (86), 234 (62), 221 (100), 219 (33), 163 (19). Anal. Calcd for $C_{19}H_{22}O_3$: C; 76.48; H, 7.43. Found: C, 76.31; H, 7.39.

Bis(3-(bromomethyl)-2-methylphenyl) Ketone 7A (X = CO, Y = CH_2Br). The ether **7D** (X = CO, Y = CH_2OCH_3) (1.64 g, 5.5 mmol) was added to a mixture of concentrated HBr (48%, 40 mL) and concentrated H_2SO_4 (20 mL) and was heated under reflux for 12 h. After the mixture had cooled, benzene (100 mL) and water (50 mL) were added and the mixture was stirred until all the solids dissolved. The benzene layer was then washed, dried, and evaporated. The residual dark solid was preadsorbed onto silica gel (5 g) and chromatographed over a column of silica gel (3.5 cm × 40 cm) with pentane–dichloromethane (1:1) as eluant to yield 1.62 g (74%) of bromide ketone **7A**, which on recrystallization from cyclohexane gave colorless crystals: mp 162–163 °C; ^{1}H NMR (90 MHz) δ 7.70–7.20 (m, 6 H, Ar H), 4.65 (s, 4 H, CH_2Br), 2.49 (s, 6 H, Ar CH_3); IR (KBr) 1660 (C=O), 1455, 1382, 1304, 1252, 1210, 1130, 955, 808, 800, 756, 728, 710 cm^{-1}; MS (EI) M$^+$·, *m/e* 394 (5), 379 (10), 315 (100), 300 (10), 236 (20), 221 (20), 211 (12). Anal. Calcd for $C_{17}H_{16}Br_2O$: C, 51.55; H, 4.07. Found: C, 51.43; H, 3.97.

Bis(3-(methoxymethyl)-2-methylphenyl)methane 7E (X = CH_2, Y = CH_2OCH_3). A mixture of the alcohol **7C** (X = CHOH, Y = CH_2OCH_3) (4.51 g, 15 mmol) and powdered $NaBH_4$ (5.68 g, 150 mmol) was added in portions with vigorous stirring over 60 min to CF_3COOH (100 mL) at 0 °C under N_2 [**caution**: effervescence]. After a further 15 min, aqueous $NaHCO_3$ solution was cautiously added, and the reaction was extracted with dichloromethane. The organic layer was washed, dried, and evaporated to give 4.02 g (94%) of ether **7E**, a portion of which on recrystallization from cyclohexane–pentane gave colorless crystals: mp 53.5–55 °C; ^{1}H NMR (90 MHz) δ 7.50–6.93 (m, 6 H, Ar H), 4.59 (s, 4 H, CH_2O), 4.06 (s, 2 H, Ar_2CH_2), 3.47 (s, 6 H, OCH_3), 2.26 (s, 6 H, Ar CH_3); IR (KBr) 1460, 1388, 1200, 1130, 1100, 960, 807, 791 cm^{-1}; MS (EI) M$^+$·, *m/e* 284 (28), 220 (61), 219 (42), 207 (39), 206 (38), 205 (100), 193 (36), 192 (35). Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.11; H, 8.49.

Bis(3-(bromomethyl)-2-methyphenyl)methane 7F (X = CH_2, Y = CH_2Br). The ether **7E** (X = CH_2, Y = CH_2OCH_3) (4.41 g, 15.5 mmol) was added to concentrated HBr (48%, 26 mL) and concentrated H_2SO_4 (6 mL) and was heated under reflux for 12 h. After the mixture had cooled, H_2O (100 mL) and benzene (150 mL) were added and the mixture was stirred until all the solids dissolved. The benzene layer was then washed, dried, and evaporated and the resulting brown solid was preadsorbed into silica gel (50 g) and chromatographed on a column of silica gel (3 × 45 cm) with pentane–dichloromethane (3:1) as eluant to give after recrystallization from cyclohexane 5.41 g (91%) of dibromide **7F**: mp 115–116 °C; ^{1}H NMR (90 MHz) δ 7.52–6.89 (m, 6 H, Ar H), 4.46 (s, 4 H, CH_2Br), 4.03 (s, 2 H, Ar_2CH_2), 2.30 (s, 6 H, Ar CH_3); IR (KBr) 1460, 1440, 1245, 1208, 800, 790, 740, 725, 712, 681 cm^{-1}; MS (EI) M$^+$·, *m/e* 380 (14), 301 (100), 222 (8), 207 (15), 192 (15). Anal. Calcd for $C_{17}H_{18}Br_2$: C, 53.46; H, 4.75. Found: C, 53.66; H, 4.78.

Bis(3-(mercaptomethyl)-2-methylphenyl)methane 7B (X = CH_2, Y = CH_2SH). The dibromide **7F** (X = CH_2, Y = CH_2Br) (5.36 g, 14 mmol) and thiourea (2.14 g, 28 mmol) were added to 95% ethanol (150 mL) and the mixture was heated under reflux for 3 h. After the mixture had cooled, about $^3/_4$ of the solvent was removed under reduced pressure, and then the remainder was cooled in a freezer for 1 h before the colorless crystals of the bis(isothiouronium) salt were collected. (When dried, 7.45 g, mp 290 °C dec.) The salt (which may be used without drying) was then stirred under reflux with KOH (23.5 g, 0.42 mol) in H_2O (120 mL) for 4 h under N_2. After the mixture had been ice cooled, concentrated H_2SO_4/H_2O (1:1, 40 mL) was slowly added. The acidic mixture was then extracted with ether and the organic layers were washed, dried, and evaporated. The residual yellow semisolid was preadsorbed onto silica gel (30 g) and filtered through a column of silica gel with pentane–dichloromethane (1:1) as eluant to yield 3.90 g (97%) of the mercaptan **7B** as white crystals: mp 66.5–67.5 °C; ^{1}H NMR (90 MHz) δ 7.41–6.85 (m, 6 H, Ar H), 4.03 (s, 2 H, Ar_2CH_2), 3.83 (d, *J* = 8 Hz, 4 H, C*H*$_2$SH), 2.30 (s, 6 H, Ar CH_3), 1.68 (t, *J* = 8 Hz, 2 H, SH); IR (KBr) 1455, 1432, 1079,

781, 734, 720 cm^{-1}; MS (EI) M$^+$·, *m/e* 288 (86), 255 (85), 222 (44), 221 (62), 220 (38), 209 (40), 208 (31), 207 (100), 206 (36), 205 (26), 193 (66), 192 (47), 191 (30). Anal. Calcd for $C_{17}H_{20}S_2$: C, 70.78; H, 6.99. Found: C, 70.91; H, 7.02.

9,16,25,32-Tetramethyl-10-oxo-2,18-dithia[3.1.3.1]metacyclophane 5A (X = CO, Y = CH_2). A solution of the dibromide **7A** (X = CO, Y = CH_2Br) (990 mg, 2.5 mmol) and the dimercaptan **7B** (X = CH_2, Y = CH_2SH) (721 mg, 2.5 mmol) in N_2 purged benzene (125 mL) was added dropwise over 10 h to a well stirred solution of KOH (421 mg, 7.5 mmol) in N_2 purged 90% ethanol (400 mL) at 20 °C under N_2. After the mixture had stirred for an additional 6 h, the bulk of the solvent was removed by evaporation and H_2O and dichloromethane were added to the residue. The organic layer was washed, dried, and evaporated, and the residue was preadsorbed into silica gel (5 g) and chromatographed over silica gel with dichloromethane as eluant to yield 1.05 g (80%) of cyclophane **5A** which on recrystallization from benzene gave colorless crystals: mp 297–299 °C dec; ^{1}H NMR (90 MHz) δ 7.40–6.80 (m, 12 H, Ar H), 3.95 (s, 2 H, Ar_2CH_2), 3.74 (s, 8 H, CH_2S), 1.97 (s, 6 H, $ArCH_3$), 1.85 (s, 6 H, $ArCH_3$); IR (KBr) 1660 (C=O), 1580, 1450, 1372, 1300, 1275, 1075, 948, 792, 782, 758, 732, 722 cm^{-1}; MS (CI) MH$^+$, *m/e* 523 (100), 489 (21), 477 (21), 299 (33). Anal. Calcd for $C_{34}H_{34}OS_2$: C, 78.11; H, 6.56. Found: C, 77.98; H, 6.61.

Stevens Rearrangement of Cyclophane 5A (X = CO, Y = CH_2). (a) Preparation of sulfonium salt **9**. A suspension of the dithiacyclophane **5A** (X = CO, Y = CH_2) (131 mg, 0.25 mmol) in dichloromethane (5 mL) was added to a suspension of $(CH_3O)_2CHBF_4$[18] (121 mg, 0.75 mmol) in dichloromethane (10 mL) under N_2 at −30 °C. The mixture was then stirred without further cooling for 3 h and then ethyl acetate (3 mL) was added and the mixture was stirred an additional 12 h. The fine white crystals of bis(sulfonium) salt **9** were collected and dried to give 175 mg (96%), mp >300 °C dec.

(b) Rearrangement. Potassium *tert*-butoxide (56 mg, 0.5 mmol) was added to a stirred suspension of the salt **9** (160 mg, 0.22 mmol) in dry THF (25 mL) under N_2 at 20 °C, and the mixture was stirred for 45 min. Dilute aqueous HCl and dichloromethane were then added, and the organic layer was washed, dried, and evaporated. The resulting yellow solid was chromatographed over silica gel with pentane–dichloromethane (7:3) as eluant to yield 61 mg (50%) of **10A** (X = CO, Y = CH_2, Z = SCH_3) as a mixture of stereoisomers: ^{1}H NMR (90 MHz) δ 8.0–6.0 (m, Ar H), 4.0–3.2 (m, C*H*(SCH_3)), 2.8–2.1 (m, CH_2CHS and Ar CH_3)) 1.90 (s, SCH_3), 1.35–1.25 (singlets, Ar CH_3); MS (CI) MH$^+$, *m/e* 551 (64), 503 (100). M_r calcd for $C_{36}H_{38}OS_2$, 550.2364; found (MS), 550.2388.

8,15,23,30-Tetramethyl-9-oxo[2.1.2.1]metacyclophane-1,16-diene 6A (X = CO, Y = CH_2). Method a. Through the sulfoxide **10C** (X = CO, Y = CH_2, Z = $SOCH_3$). A solution of Br_2 (1.32 mmol) in dichloromethane (5 mL) was added via a syringe to a vigorously stirred mixture of 10% aqueous $KHCO_3$ solution (15 mL), the mixed isomers of **10A** (X = CO, Y = CH_2, Z = SCH_3) (331 mg, 0.6 mmol), and dichloromethane (10 mL) at 20 °C. After 15 min, more dichloromethane (50 mL) was added, and the organic layer was washed, dried, and evaporated. The resulting yellow solid was filtered through a column of silica gel with dichloromethane and the methanol as eluants, to yield 345 mg (99%) of mixed isomers of sulfoxides **10C**: ^{1}H NMR (90 MHz) δ 7.9–6.1 (m, Ar H), 4.7–3.0 (m, C*H*($SOCH_3$)), 2.9–2.1 (m), 1.7–1.3 (singlets, Ar CH_3); MS (EI) M$^+$·, *m/e* 552 (38), 503 (55), 455 (100).

This mixture of isomers (1.012 g, 1.75 mmol) was dissolved in *N*-methyl-2-pyrrolidinone (50 mL) and heated at reflux for 12 h. After cooling, the mixture was poured into benzene (200 mL) and water (200 mL) was added. The organic layer was separated, washed thoroughly, dried, and evaporated and the residue was preadsorbed onto silica gel (10 g) and chromatographed over silica gel (3 × 35 cm) with pentane and then pentane–dichloromethane (3:2) as eluants. Eluted first was the *major isomer* of **6A** (X = CO, Y = CH_2) (originally assigned structure **13**): 311 mg (39%); mp 291–293 °C; ^{1}H NMR (90 MHz) (−20 °C) δ 7.47–6.98 (m, 6 H, anti Ar H), 6.87 (AB, *J* = 11.5 Hz, CH_A=CH_B), 6.77 (AB, *J* = 11.5 Hz, CH_A=CH_B), 6.68–6.13 (m, 6 H, syn Ar H), 4.09 (AB, *J* = 15 Hz, CH_AH_B), 3.51 (AB, *J* = 15 Hz, CH_AH_B), 2.37 and 2.28 (s, 3 H each, syn Ar CH_3), 1.18 and 1.09 (s, 3 H each, anti Ar CH_3); IR (KBr) 1670 (C=O), 1578, 1442, 1292, 1272, 1258, 945, 888, 850, 825, 818, 772, 758, 730, 712, 686 cm^{-1}; MS (CI) MH$^+$, *m/e* 455 (100). Anal. Calcd for $C_{34}H_{30}O$: C, 89.83; H, 6.65. Found: C, 89.87; H, 6.70.

Eluted next was a mixture of major and minor isomers of **6A**, 169 mg (21%).

Eluted last was the *minor isomer* of **6A** (X = CO, Y = CH_2) (originally assigned structure **14**), 50 mg (6%), which gave after recrystallization from cyclohexane colorless crystals: mp 286–288 °C; ^{1}H NMR (90 MHz) δ 7.83–7.13 (m, 12 H, Ar H) 6.70 (AB m, only inner lines visible, 4 H, =CH), 4.36 (s, 2 H, CH_2), 1.24 (s, 12 H, Ar CH_3); IR (KBr) 1668 (C=O), 1450, 1290, 948, 773, 756, 732 cm^{-1}; MS (CI) MH$^+$, *m/e* 455 (100). Anal. Calcd for $C_{34}H_{30}O$: C, 89.83; H, 6.65. Found: C, 89.77; H, 6.59.

Method b. Through sulfonium salt **10B** (X = CO, Y = CH_2, Z = $S^+(CH_3)_2BF_4^-$). A solution of the mixtures of isomers of **10A** (X = CO, Y = CH_2, Z = SCH_3) (110 mg, 0.2 mmol) in dichloromethane (5 mL) was added to a stirred suspension of $(CH_3O)_2CHBF_4$[18] (97 mg, 0.6 mmol) in dichloromethane (5 mL) at −30 °C under N_2. After the mixture had stirred for 3 h without further cooling, ethyl acetate (2 mL) was added and the mixture stirred for a further 12 h. The yellow powder of the mixed sulfonium salts **10B** was collected and dried to give 134 mg (89%), mp >300 °C dec.

These salts (61 mg, 0.08 mmol) were suspended in dry THF (10 mL) at 20 °C under N_2 and potassium *tert*-butoxide (27 mg, 0.24 mmol) was added. The reaction mixture was then refluxed 1 h, cooled, and poured into dilute aqueous HCl–dichloromethane. The organic layer was washed, dried, and evaporated and the residue was chromatographed as described for **9** (method a) above to give 20 mg (54%) of mixed isomers of **6A**, identical with those obtained above.

Reaction of Dienes 6A (X = CO, Y = CH_2) with Alkyllithiums. A. With *n*-Butyllithium. *n*-Butyllithium (0.06 mmol) in hexane (0.05 mL) was added via syringe to a solution of mixed dienes **6A** (X = CO, Y = CH_2) (14 mg, 0.03 mol) in dry THF (5 mL) under N_2 at 20 °C. A dark red color formed at once and faded in a few seconds. After 10 min, dilute aqueous HCl was added, and the mixture was extracted with dichloromethane. The organic layer was washed, dried, and evaporated to yield a residue which by TLC contained unchanged **6A** and more polar material, separated by prep TLC and assigned the structure **6E** (X = C(OH)(*n*-Bu), Y = CH_2): MS (CI) MH$^+$, *m/e* 513; ^{1}H NMR δ (butyl protons) 1.28 (s).

B. With *tert*-Butyllithium. From *tert*-butyllithium (0.14 mmol) in pentane (0.07 mL) and **6A** (16 mg, 0.035 mmol) in THF (5 mL) as described in A above, there was obtained mostly unchanged **6A**, but some **6F** (X = C(OH)(*t*-Bu), Y = CH_2): MS (CI) MH$^+$, *m/e* 513; ^{1}H NMR δ (*tert*-butyl protons) 0.95 (s).

Bis(3-(mercaptomethyl)-2-methylphenyl) Ketone 7G (X = CO, Y = CH_2SH). A solution of thiourea (1.005 g, 13.2 mmol) and bromide **7A** (X = CO, Y = CH_2Br) (2.614 g, 6.6 mmol) were refluxed in 95% ethanol (75 mL) for 3 h. About three quarters of the solvent was removed under reduced pressure, and the residue was cooled in a freezer for about 1 h. The white bis(isothiouronium) salt was collected (when dried 3.51 g (97%), mp >300 °C dec, and then was heated under reflux with KOH (10.66 g, 0.19 mol) in H_2O (100 mL) under N_2 for 6 h. The mixture was cooled in an ice bath and concentrated H_2SO_4/H_2O (1:1, 20 mL) was added followed by dichloromethane. The organic extract was washed, dried, and evaporated. The residual oil was preadsorbed onto silica gel with pentane–dichloromethane (1:1) as eluant to yield 1.14 g (57%) of mercaptan **7G**, which after recrystallization from benzene–pentane gave colorless crystals: mp 77–78 °C; ^{1}H NMR (60 MHz) δ 7.53–7.12 (m, 6 H, Ar H), 3.82 (d, *J* = 7 Hz, 4 H, CH_2SH), 2.45 (s, 6 H, Ar CH_3), 1.72 (t, *J* = 7 Hz, 2 H, SH); IR (KBr) 1660 (C=O), 1458, 1435, 1308, 1280, 1255, 950, 821, 808, 762, 730, 720, 685 cm^{-1}; MS (EI) M$^+$·, *m/e* 302 (23), 287 (24), 270 (51), 269 (60), 255 (23), 253 (87), 235 (63), 234 (42), 233 (35), 222 (35), 221 (100), 220 (24), 219 (24), 165 (56). Anal. Calcd for $C_{17}H_{18}OS_2$: C, 67.51; H, 6.00. Found: C, 67.46; H, 5.97.

9,16,25,32-Tetramethyl-10,26-dioxo-2,18-dithia[3.1.3.1]metacyclophane 5B (X = Y = CO). A solution of dibromide **7A** (X = CO, Y = CH_2Br) (1.386 g, 3.5 mmol) and dimercaptan **7G** (X = CO, Y = CH_2SH) (1.059 g, 3.5 mmol) in N_2 purged benzene (175 mL) was added dropwise over 12 h to a well stirred solution of KOH (590 mg, 10.5 mmol) in N_2 purged 90% ethanol (600 mL) at 20 °C under N_2. After the solution had stirred 6 h,

the bulk of the solvent was removed under reduced pressure and dichloromethane and H_2O were added to the residue. The organic layer was washed and dried, silica gel (20 g) was added, and then the solvent was evaporated. The residue was slurried in dichloromethane onto a silica gel column and the product **5B** was eluted with dichloromethane as highly insoluble white crystals: 1.265 g (67%) mp 326–331 °C dec; ^{1}H NMR (90 MHz) δ 7.35–7.15 (m, 12 H, Ar H), 3.67 (s, 8 H, CH_2S), 1.88 (s, 12 H, Ar CH_3); IR (KBr) 1655 (C=O), 1452, 1305, 1280, 1260, 1090, 1025, 950, 799, 760, 735, 728 cm^{-1}; MS (CI) MH$^+$, *m/e* 537 (7), 447 (10), 249 (100), 247 (88). Anal. Calcd for $C_{34}H_{32}O_2S_2$: C, 76.08; H, 6.00. Found: C, 76.23; H, 6.12.

Stevens Rearrangement of 5B (X = Y = CO). A suspension of the thiacyclophane **5B** (161 mg, 0.3 mmol) in dichloromethane (5 mL) was added to $(CH_3O)_2CHBF_4$[18] (145 mg, 0.9 mmol) stirred in dichloromethane (10 mL) under N_2 at −30 °C. The mixture was stirred for 3 h without additional cooling and then ethyl acetate (3 mL) was added and stirring continued for 5 h. The bis(sulfonium) salt was then collected, washed with ethyl acetate, and dried to give 216 mg (97%), mp >300 °C dec. The salt (400 mg, 0.54 mmol) was suspended in dry THF (20 mL) under N_2 and powdered potassium *tert*-butoxide (135 mg, 1.2 mmol) was added at about 20 °C. After 1.5 h, dilute aqueous HCl was added, and then dichloromethane. The organic layer was washed, dried, and evaporated, and the yellow residue was chromatographed over silica gel with dichloromethane as eluant to yield 109 mg (36%) of **10D** (X = Y = CO, Z = SCH_3) as bright yellow crystals and a mixture of stereoisomers: ^{1}H NMR (90 MHz) δ 8.1–6.2 (m, Ar H) 4.9–3.1 (m, C*H*(SCH_3)), 2.9–1.7 (m), 1.95 (s, SCH_3), 1.5–1.0 (singlets, Ar CH_3); MS (CI) MH$^+$, *m/e* 565 (100). M_r calcd for $C_{36}H_{36}O_2S_2$, 564.2156; found (MS), 564.2147.

8,15,23,30-Tetramethyl-9,24-dioxo[2.1.2.1]metacyclophane-1,16-dienes 6B (X = Y = CO). A solution of Br_2 (0.55 mmol) in dichloromethane (~1 mL) was added by syringe to a mixture of the Stevens rearrangement isomers **10D** (X = Y = CO, Z = SCH_3) (141 mg, 0.25 mmol), dichloromethane (10 mL), and 10% aqueous $NaHCO_3$ solution (10 mL) vigorously stirred at 20 °C. After 30 min, dichloromethane was added and the organic layer was washed, dried, and evaporated. The residue was filtered through a short column of silica gel with dichloromethane and then methanol as eluant to yield 144 mg (97%) of mixed isomers of sulfoxides **10E** (X = Y = CO, Z = $SOCH_3$) as white crystals: ^{1}H NMR (60 MHz) δ 7.7–6.2 (m, Ar H), 4.5–3.2 (m, CH($SOCH_3$)) 2.8–1.7 (m), 2.40 (s, $SOCH_3$), 1.5–1.2 (singlets, Ar CH_3). This sulfoxide (543 mg, 0.908 mmol) was heated at 150–160 °C in *N*-methyl-2-pyrrolidinone (20 mL) for 14 h. After cooling the mixture was poured into dilute aqueous HCl and dichloromethane was added. The organic layer was washed well, dried, and evaporated. The residue was preadsorbed onto silica gel (2 g) and chromatographed over silica gel with benzene as eluant which gave firstly 221 mg (52%) of mixed isomers of **6B** (2.5:1 ratio): ^{1}H NMR (90 MHz) δ 7.8–7.1 (m, Ar H), 6.82 (s, C*H*=), 6.8–6.4 (m, Ar H), 2.41, 1.30, 1.14 (s, Ar CH_3). Eluted next was 32 mg (8%) of the pure major isomer of **6B** (originally assigned structure **15**): mp 318–320 °C; ^{1}H NMR (90 MHz) δ 7.5–7.2 (m, 6 H, anti Ar H), 6.82 (s, 4 H, C*H*=C*H*), 6.7–6.4 (m, 6 H, syn Ar H), 2.39 (s, 6 H, syn Ar CH_3), 1.11 (s, 6 H, anti Ar CH_3); IR (KBr) 1670 (C=O), 1445, 1274, 1255, 944, 820, 764, 728, 709 cm^{-1}; MS (CI) MH$^+$, *m/e* 469 (100). Anal. Calcd for $C_{34}H_{28}O_2$: C, 87.15; H, 6.02. Found: C, 87.47; H, 6.11.

9,24-Dihydroxy-8,15,23,30-tetramethyl[2.1.2.1]metacyclophane-1,16-dienes 6D (X = Y = CHOH). A solution of the mixed isomers of diene **6B** (X = Y = CO) (21 mg, 0.045 mmol) in wet THF (15 mL) was added to a suspension of $NaBH_4$ (5 mg, 0.13 mmol) in wet THF (100 mL) and the mixture was heated under reflux for 12 h. After the mixture had cooled, dilute aqueous HCl was added and the product was extracted with ether. The organic layer was washed, dried, and evaporated and the residue was filtered through a short column of silica gel with dichloromethane as eluant to yield 18 mg (84%) of white crystals of mixed isomers of diol **6D**: IR (KBr) 3390 (b, OH), 1450, 1000, 945, 820, 796, 768, 728 cm^{-1}; MS (CI) MH$^+$, *m/e* 473 (45), 454 (100). This sample was used directly to prepare bromide **6C** without further purification.

9,24-Dibromo-8,15,23,30-tetramethyl[2.1.2.1]metacyclophane-1,16-dienes 6C (X = Y = CHBr). PBr_3 (85 μL, 0.72 mmol) was added to a suspension of the dialcohol **6D** (X = Y = CHOH) (17 mg, 0.036 mmol) in dry benzene (5 mL) under N_2 at 20 °C. After stirring for 8 h, ether was added and the mixture was washed with H_2O, aqueous $NaHCO_3$, and H_2O, then was dried, and evaporated. The residue was filtered through a short column of silica gel with pentane–dichloromethane (1:1) as eluant, to give white crystals of dibromide **6C**: 20 mg (92%), mp 247–249 °C sublimed; ^{1}H NMR (90 MHz) δ 7.65–7.10 (m, Ar H), 7.00 (s, CH=CH), 6.90–6.60 (m, Ar H and CHBr), 2.47, 1.43, 1.18 (s, Ar CH_3); IR (KBr) 1450, 1372, 1160, 1080, 960, 800, 782, 718 cm^{-1}; MS (CI) MH$^+$, m/e 597 (40), 517 (100), 438 (38). Anal. Calcd for $C_{34}H_{30}Br_2$: C, 68.24; H, 5.05. Found: C, 68.01; H, 5.00.

20,26-Dihydroxy-9,16,25,32-tetramethyl-2,18-dithia[3.1.3.1]metacyclophane 5C (X = Y = CHOH). A suspension of the diketone **5B** (X = Y = CO) (456 mg, 0.85 mmol) and $NaBH_4$ (161 mg, 4.25 mmol) in wet THF (200 mL) was heated under reflux for 12 h. After the mixture had cooled dilute aqueous HCl was added until the solution was acidic. The bulk of the solvent was then removed under reduced pressure and the residue was stirred with H_2O (200 mL). The white crystals of dialcohol **5C** were collected and dried to give 459 mg (100%): mp >350 °C; IR (KBr) 3400 (b, OH), 1460, 1440, 1228, 1090, 1074, 1060, 1010, 808, 776, 740 cm^{-1}. This sample was used directly to prepare bromide **5D** (X = Y = CHBr) below.

10,26-Dibromo-9,16,25,32-tetramethyl-2,18-dithia[3.1.3.1]metacyclophane 5D (X = Y = CHBr). PBr_3 (0.14 mL, 1.5 mmol) was added to a suspension of crude dialcohol **5C** (X = Y = CHOH) (162 mg, 0.3 mmol) in dry benzene (150 mL) and stirred at 20 °C for 12 h. The mixture was then washed with H_2O, aqueous $NaHCO_3$, and H_2O, then was dried, and evaporated. The residue was stirred with boiling dichloromethane (5 mL) for 15 min and hot filtered to give white crystals of dibromide **5D**: 162 mg (81%); mp >350 °C; ^{1}H NMR (CD_2Cl_2, 90 MHz) δ 7.33–6.54 (m, Ar H and CHBr), 4.24–3.34 (m, CH_2S), 2.13–1.04 (singlets, Ar CH_3); MS (CI) MH$^+$, *m/e* 665 (<1), 585 (5), 506 (5), 442 (10), 382 (100). Anal. Calcd for $C_{34}H_{34}Br_2S_2$: C, 61.26; H, 5.14. Found (extended combustion): C, 61.10; H, 5.00.

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Registry No. **5a**, 90369-85-0; **5b**, 90133-68-9; **5c**, 90369-91-8; **5d**, 90369-92-9; **6a**, 90133-70-3; **6b**, 90133-71-4; **6c**, 90369-90-7; **6d**, 90388-42-4; **6e**, 90388-41-3; **6f**, 90369-87-2; **7** (X = CO; Y = $(NH_2)_2C{=}SCH_2^+Br^-$), 90369-93-0; **7a**, 90369-81-6; **7b**, 90369-84-9; **7c**, 90369-79-2; **7d**, 90369-80-5; **7e**, 90369-82-7; **7f**, 90369-83-8; **7g**, 90369-88-3; **8b**, 54454-12-5; **8c**, 874-27-1; **8d**, 90369-75-8; **8f**, 90369-76-9; **8g**, 90369-77-0; **8i**, 28746-27-2; **8j**, 90369-78-1; **9**, 75397-86-3; **10a** (isomer 1), 90369-86-1; **10a** (isomer 2), 90369-95-2; **10c** (isomer 1), 90388-40-2; **10c** (isomer 2), 90369-96-3; **10d** (isomer 1), 90369-89-4; **10d** (isomer 2), 90369-97-4; **10e** (isomer 1), 90369-94-1; **10e** (isomer 2), 90369-98-5; 2,6-dichlorotoluene, 118-69-4.