$C_{30}H_{34}$: 394.266).

Acknowledgment. We thank the National Science Foundation for their support of this investigation.

Registry No.—**8,** 66788-12-3; **9a,** 66793-69-9; **9a** bis(methylsulfonium) derivative BF_4 salt, 66788-15-6; **9b,** 66808-49-9; **9b** bis(methylsulfonium) derivative BF_4 salt, 66788-15-6; **9b,** 66808-49-9; **9b** bis(methylsulfonium) derivative BF_4 salt, 66808-11-5; **10,** 66792-73-2; **10** bismethylsulfonium derivative BF_4 salt, 66792-80-1; **11a,** 66788-16-7; **11b,** 66788-17-8; *cis*-**12,** 66788-18-9; **12,** 66788-19-0; **13,** 66788-20-3; **14,** 66788-21-4; **16,** 66788-22-5; **17** isomer 1, 66788-23-6; **17** isomer 2, 66808-12-6; **18,** 66792-74-3; **19,** 66792-75-4; **20,** 66792-76-5; **21,** 66792-77-6; **22,** 66792-78-7; **23,** 66810-82-0; **24,** 66788-24-7; 2,6-dibromo-*p*-xylene, 66788-13-4; 2,6-bis(mercaptomethyl)toluene, 41563-67-1; dimethoxycarbonium fluoroborate, 18346-68-4; 2,6-bis(bromomethyl)toluene, 41563-68-2.

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Syntheses of *syn*-[2.2]Metacyclophanes and Triple-Layered *anti*-[2.2]Metacyclophanes

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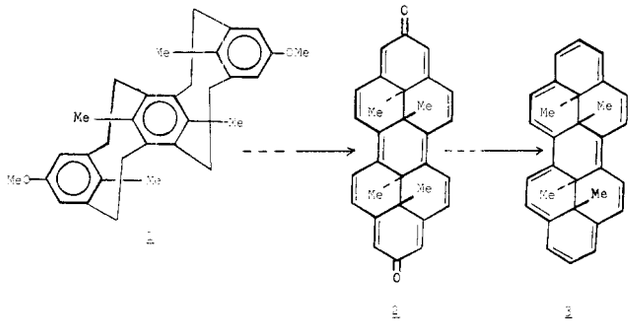
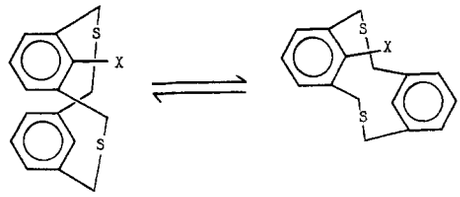
Received January 27, 1978

A study has been made of the effect of substituents in influencing the relative amounts of syn and anti isomers formed in the coupling reaction to give substituted 2,11-dithia[3.3]metacyclophanes. Photolytic extrusion of sulfur from *syn*-2,11-dithia-5,7-dicyano-15-methoxy-6,9,18-trimethyl[3.3]metacyclophane (**11**) has led to the first examples of simple *syn*-[2.2]metacyclophanes. Using the standard methods of 2,11-dithia[3.3]metacyclophane formation followed by ring contraction with sulfur extrusion we have been able to prepare the triple-layered *anti*-[2.2]metacyclophane **1**. Oxidation of **1** readily yields the bisdienone **28,** demonstrating the role of the central benzene ring in such triple-layered *anti*-[2.2]metacyclophanes as a transmitter of electronic effects.

The molecule shown by structure **3** has been proposed as a good model for testing the theoretical prediction that the larger [4*n* + 2]annulenes will lose their aromaticity and simply exhibit polyene character. In an accompanying paper,[1] we have described attempts to synthesize **3** starting either with preformed dihydropyrene derivatives or using the standard sulfur methods developed for synthesizing dihydropyrenes. Unfortunately, **3** does not appear to survive the reaction conditions required for its generation by these routes. An alternate possibility for synthesizing **3** is to employ the quinone approach originally used for the preparation of *trans*-15,16-dimethyldihydropyrene.[2] In this approach the key steps are the conversion of a triple-layered *anti*-[2.2]metacyclophane **1** to quinone **2** and this, in turn, to the peropyrene derivative **3.** In the present paper we describe our experiences in exploring this approach to **3.**



The synthesis of **1** requires anti geometry, and so the factors affecting the ratio of syn to anti isomers in metacyclophane formation were of immediate concern to us. Vögtle, Weider, and Förster have described the effect of substituents on the syn–anti equilibrium of 2,11-dithia[3.3]metacyclophanes, where conformational flipping is readily possible.[3] For example, the equilibrium between **4** and **5** lies completely on the side of the syn conformer **4,** presumably due to the more favorable charge-transfer interaction possible with the syn geometry. However, reduction of the nitro group in **4** to give the amino derivative **6** leads to an equilibration that is completely on the side of the anti conformer **7.**



4, X = $-NO_2$ **5,** X = $-NO_2$
6, X = $-NH_2$ **7,** X = $-NH_2$

With bulky groups such as methyl at the 9 and 18 positions,

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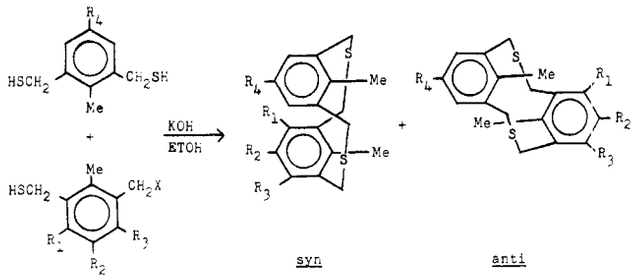


10, R_1=R_3= -Br; R_2= $-CH_3$; R_4= $-OCH_3$
11, R_1=R_3= -CN; R_2= $-CH_3$; R_4= $-OCH_3$

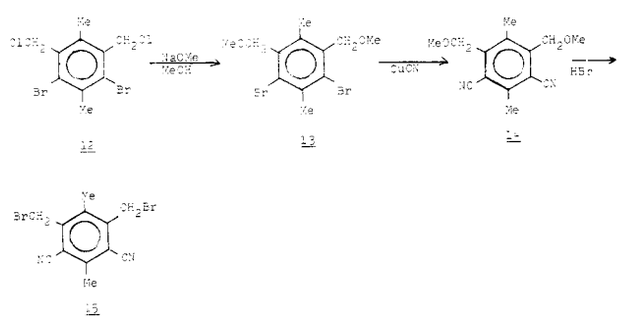
equilibration of the syn and anti isomers of 2,11-dithia[3.3]-metacyclophanes is no longer possible. Thus, for these compounds the ratio of syn to anti isomers will be determined by their relative rates of formation. Again, however, charge-transfer interaction should preferentially lower the energy of activation for formation of the syn isomer and so substituents should play an important role in influencing the relative amounts of syn and anti isomers formed. This is found to be true, and the data available from this and other studies are summarized in Table I.

As can be seen, the ratio of syn to anti isomers varies widely depending upon the substituents present, going from 1:7 for the unsubstituted case to 10:1 where one ring has an electron-donating methoxyl and the other ring has electron-withdrawing cyano groups. Since for our purposes we required both anti geometry and the presence of a methoxyl group in one ring and two cyano groups in the other ring, the 10:1 distribution in the coupling reaction was quite discouraging. However, this distribution was clearly the result of kinetic control and it seemed possible that equilibration under thermodynamic control at a later stage might be much more favorable for providing the anti isomer.

Our first task then was providing 3,11-dithia[3.3]metacyclophanes with the appropriate substitution pattern, regardless of the relative ratios of syn and anti isomers. The coupling reaction of 2,6-bis(mercaptomethyl)-4-methoxytoluene and 2,6-bis(chloromethyl)-3,5-dibromo-1,4-dimethylbenzene occurred in 71% yield to give **10,** having a syn to anti ratio of isomers of 2.5:1.0 as shown in Table I. Unfortunately, the replacement of bromide by cyanide in the von Braun reaction proceeded very poorly with **10;** the syn isomer of **10** gave the syn isomer of **11** in only 5% yield, whereas the anti isomer of **10** gave the anti isomer of **11** in 24% yield. To circumvent this the cyano precursor **15** for the coupling reaction was prepared as outlined in Scheme I.

Although the coupling of **15** with 2,6-bis(mercaptomethyl)-4-methoxytoluene then provided a more efficient route to **11,** the ratio of syn to anti isomers in this coupling reaction was 10:1, as shown in Table I. It was important, therefore, in selecting a route for ring contraction and expulsion of sulfur to choose one that might be expected to give increased amounts of the anti isomer. The photochemical expulsion of sulfur in the presence of trimethyl phosphite is

Scheme I



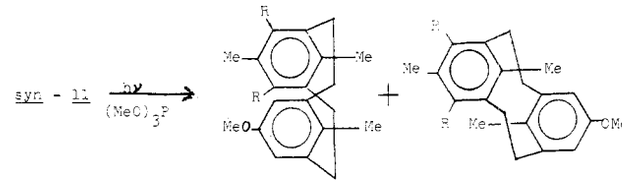
12 13 14

15

Table I. Effect of Substituents on the Relative Amounts of Syn and Anti Isomers Formed in the Coupling Reaction

compd	substituents R_1	R_2	R_3	R_4	syn/anti ratio
7[4]	H	H	H	H	1:7
8[5]	H	H	H	NO_2	1:1
9[1]	Br	CH_3	Br	H	1.3:1
10	Br	CH_3	Br	OCH_3	2.5:1
11	CN	CH_3	CN	OCH_3	10:1

known to involve an intermediate diradical[6-8] and so this was the method selected. Irradiation of the syn isomer of **11** in the presence of trimethyl phosphite gave the *syn*-[2.2]metacyclophane **16** in 20% yield and the corresponding anti isomer **17** in 40% yield.



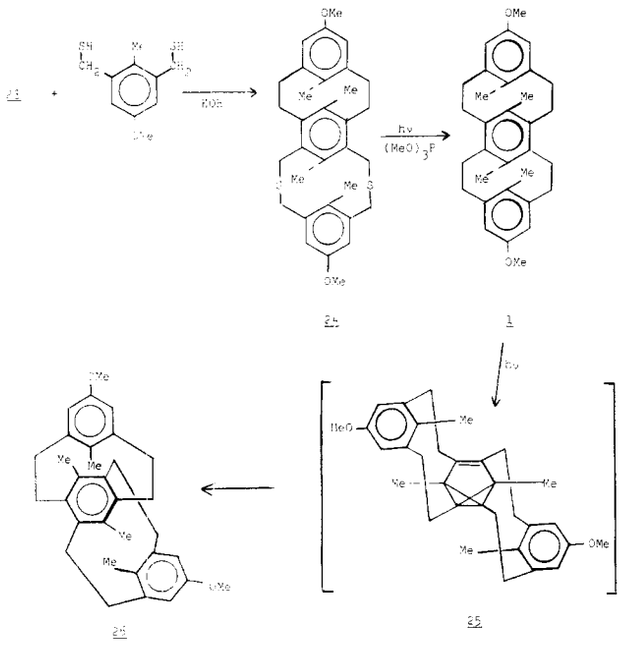
16, R = -CN 17, R = -CN
18, R = -CH=O 21, R = -CH=O
19, R = $-CH_2OH$ 22, R = $-CH_2OH$
20, R = $-CH_2OCH_3$ 23, R = $-CH_2Br$

To our knowledge the isolation of **16** is the first reported example of a simple *syn*-[2.2]metacyclophane.[9] Previously, we had tried to prepare *syn*-8,16-dimethyl[2.2]metacyclophane by the Raney nickel desulfurization of a *syn*-bis(methylthio)-8,16-dimethyl[2.2]metacyclophane, but the product was entirely the *anti*-8,16-dimethyl[2.2]metacyclophane.[4] Similarly, treatment of [2.2.2](1,3,5)cyclophan-1-ene with osmium tetroxide at 0 °C gave entirely the *anti*-5,13-diformyl[2.2]metacyclophane and none of the syn isomer.[10] Intuitively, one would expect the strain energy of *syn*-[2.2]-metacyclophanes to be comparable to that of [2.2]paracyclophane, and Boyd has shown from heats of combustion that the relative strain energies of [2.2]paracyclophane, [2.2]meta-paracyclophane, and *anti*-[2.2]metacyclophane are 32.6, 24.5, and 13.5 kcal/mol, respectively.[11] However, despite the strong driving force for a syn to anti isomerization in the [2.2]metacyclophane series, this would not be expected to occur spontaneously, for Gschwend has shown that the energy barrier to conformational flipping in *anti*-[2.2]metacyclophane is 33.2 kcal/mol,[12] and for derivatives having methyl substituents at the 8 and 16 positions, the barrier must be very much higher.

One possible explanation for the stability of **16** could be that there is an exceptionally strong charge-transfer interaction due to the presence of the two cyano groups. It was of interest, therefore, to make a series of derivatives in which the cyano groups were replaced by other substituents, including electron-donating groups. This was readily done. Reduction of **16** with diisobutylaluminum hydride gave the corresponding diformyl derivative **18,** and sodium borohydride reduction of **18** gave the diol **19.** Treatment of **19** with methanol containing a trace of hydrogen chloride immediately gave the corresponding methyl ether **20.** The syn and anti isomers of [2.2]-metacyclophanes are readily distinguished by their NMR spectra and all of these transformation products, **18, 19,** and **20,** are clearly syn isomers and are stable at ambient temperatures.

Reich and Cram first showed that heating [2.2]paracyclophanes at 200 °C leads to ring opening and isomerization via diradical intermediates.[13] If *syn*-[2.2]metacyclophanes have comparable strain energies to those of [2.2]paracyclophanes, it would be expected that they might show a similar thermal

Scheme II



isomerization. This has been found to be true. When a sample of the syn isomer **16** was heated above its melting point (194–196 °C) in a sealed capillary and held at that temperature for a period of time, the sample recrystallized and, on NMR analysis, was found to have undergone a quantitative conversion to the anti isomer **17.** Similarly, the *syn*-diformyl derivative **18** on being heated at 215 °C was converted quantitatively to the corresponding anti isomer **21.** Thermal isomerization of the syn isomers **19** and **20** to their corresponding anti isomers was also effected, but was accompanied by considerable decomposition. Apparently, the syn geometry in the [2.2]metacyclophane series strongly promotes thermal carbonium ion formation followed by self-alkylation.

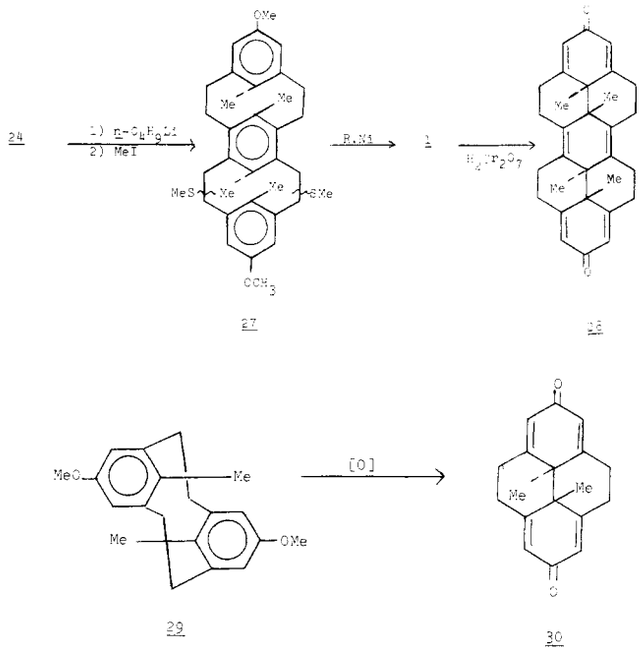
From these data it can be concluded that the influence of substituents on the relative ratios of *syn*- and *anti*-[2.2]metacyclophanes is a result of their effect on reaction rates and that thermodynamically *anti*-[2.2]metacyclophanes are greatly favored over *syn*-[2.2]metacyclophanes regardless of the nature of the substituents. Furthermore, the combination of photochemical extrusion of sulfur followed by thermal isomerization is a practical, efficient route for converting *syn*-2,11-dithia[3.3]metacyclophanes completely to *anti*-[2.2]metacyclophanes.

With the way now clear for preparing the appropriately substituted *anti*-[2.2]metacyclophane **17,** the overall synthetic approach to **1** could be continued. Following the same procedures used with **16,** the transformation of **17** to **21** and then on to **22** proceeded well and in high yield. Treatment of **22** with phosphorus tribomide then gave **23.** A coupling reaction between **23** and 2,6-bis(mercaptomethyl)-4-methoxytoluene gave the dithiacyclophane **24** as a single product in 56% yield (Scheme II). The assignment of a staircase geometry to **24** is based both on its NMR spectrum, which clearly fits an anti isomer, and the assumption that an up–down conformation would require prohibitive steric interactions between the internal methyl groups.

In an attempt to effect ring contraction with sulfur extrusion, a solution of **24** in trimethyl phosphite was irradiated using a medium-pressure mercury lamp. A single product was isolated in 51% yield having the correct composition and molecular weight expected for **1.** However, the spectral properties of the product were inconsistent with those to be expected for a triple-layered *anti*-[2.2]metacyclophane. Its ultraviolet absorption spectrum showed maxima at 211 (ε 53 000), 238 (14 500), and 287 nm (3500), but with none of the longer wavelength absorptions characteristic of the *anti*-[2.2]metacyclophanes of this series. Its NMR spectrum shows the four aromatic protons as an AB pattern at τ 3.44 and 3.52 (J_{AB} = 3 Hz) instead of the singlet to be expected for **1.** Also, there is no signal in the region of τ 9.5 where the internal methyl protons of an *anti*-[2.2]metacyclophane should occur. However, these spectral data are in good accord with those reported by Kannen, Umemoto, Otsubo, and Misumi for triple-layered [2.2]metaparacyclophanes.[14] We have, therefore, assigned structure **26** to this product and its formation is logically explained as a photochemical isomerization of the initially formed **1** going via the benzvalene intermediate **25** to the final product **26.**

Attempts to obtain **1** by using shorter irradiation times with **24** were unsuccessful. However, when a low-pressure mercury lamp was substituted for the medium-pressure lamp, irradiation of **24** did give **1** in low yield. Apparently, the photochemical isomerization of **1** to **26** is wavelength dependent and is favored by the longer wavelengths of light emitted by the medium-pressure lamp. As expected, the ultraviolet absorption spectrum of **1** had, in addition to maxima at 207 (ε 13 000) and 259 nm (6600), bands at 310 (1000) and 340 nm (500) as is characteristic for the *anti*-[2.2]metacyclophanes in this series. Likewise, the four aromatic protons of **1** appear as a singlet at τ 3.28 and the internal methyl protons as two singlets at τ 9.38 and 9.41.

Because of the poor yield in the photochemical conversion of **24** to **1,** an alternate method for this transformation was sought. When **24** was subjected to a Wittig rearrangement, a mixture of stereoisomers corresponding to **27** was formed in



93% yield. Raney nickel desulfurization of **27** then led to **1** but, again, in disappointingly small yield.

An unusual feature of *anti*-5,13-dimethoxy-8,16-dimethyl[2.2]metacyclophane (**29**) is its easy oxidation under mild conditions to the bisdienone **30.**[2] Presumably the first step in this oxidation is the formation of a radical cation which is delocalized over both aromatic rings.[15] Of immediate interest, then, was whether the central aromatic ring of **1** would enter into such a delocalization process and allow the formation of the extended bisdienone **28.** In fact, treatment of **1** with an acetone solution of chromic acid reagent for a few minutes at room temperature effected a complete conversion of **1** to **28.** The central benzene ring in triple-layered *anti*-[2.2]metacyclophanes having a staircase conformation is clearly a very

effective transmitter of electronic effects between the benzene rings at each end.

In the case of **30**, treatment with *N*-bromosuccinimide led smoothly in high yield to the corresponding quinone.[2] However, treatment of **28** with *N*-bromosuccinimide gave only extensive decomposition and none of the desired quinone **2**. Unfortunately, lack of material precluded exploring other possible routes for the conversion of **28** to **2**.

Experimental Section[16]

2,6-Bis(mercaptomethyl)-4-methoxytoluene. To a stirred solution of 1.52 g of thiourea in 59 mL of ethanol was added 3.08 g of 2,6-bis(bromomethyl)-4-methoxytoluene,[2,17] and the mixture was boiled under reflux for 1 h. After removal of the solvent under reduced pressure, a solution of 6.5 g of potassium hydroxide in 25 mL of water was added to the residual solid and the resulting mixture was boiled under reflux for 3 h. When the solution had cooled, it was acidified and extracted with ether. The ether extract was washed with water, dried, and concentrated to give 2.05 g (96%) of a clear oil: NMR, a singlet at τ 3.2 (2 H, ArH), a singlet at 6.20 (3 H, $-OCH_3$), a doublet at 6.25 (4 H, J = 7 Hz, $ArCH_2-$), a singlet at 7.65 (3 H, $ArCH_3$), and a triplet at 8.35 (2 H, J = 7 Hz, –SH); mass spectrum m/e 214.047 (calcd for $C_{10}H_{14}OS_2$: 214.049). Anal. Calcd for $C_{10}H_{14}OS_2$: C, 56.07; H, 6.59. Found: C, 55.93; H, 6.52.

***syn*- and *anti*-5,7-Dibromo-6,9,18-trimethyl-15-methoxy-2,11-dithia[3.3]metacyclophane (10).** A solution of 2.03 g of 2,6-bis(mercaptomethyl)-4-methoxytoluene and 3.42 g of 2,6-dibromo-3,5-bis(chloromethyl)-1,4-dimethylbenzene[1] in 250 mL of benzene was added dropwise with stirring to a boiling solution of 1.6 g of potassium hydroxide in 1.0 L of ethanol. When the addition was complete (24 h), the solution was concentrated and the residual solid was extracted with dichloromethane. Concentration of the dichloromethane extract was followed by chromatography of the residue over silica gel using a 1:2 mixture of benzene–petroleum ether (30–60 °C) as eluent. The first fraction of eluate gave 2.42 g (51%) of the syn isomer of **10** as white needles: mp 254–256 °C; NMR, a singlet at τ 3.47 (2 H, ArH), an AB pattern at 6.30 and 5.20 (4 H, J = 15 Hz, $ArCH_2-$), a singlet at 6.08 (4 H, $ArCH_2-$), a singlet at 6.27 (3 H, $-OCH_3$), and three singlets at 7.42, 7.46, and 7.55 (3 H each, $-CH_3$); mass spectrum m/e 502. Anal. Calcd for $C_{20}H_{22}Br_2OS_2$: C, 47.82; H, 4.41. Found: C, 47.52; H, 4.33.

The second fraction of eluate gave 940 mg (20%) of the anti isomer of **10** as white crystals: mp 235–237 °C; NMR, a singlet at τ 3.05 (2 H, ArH), an AB pattern at 6.37 and 6.27 (4 H, J = 14 Hz, $ArCH_2-$), an AB at 6.21 and 6.07 (4 H, J = 14 Hz, $ArCH_2-$), a singlet at 6.17 (3 H, $-OCH_3$), and singlets at 6.32, 8.58, and 8.68 (3 H each, $-CH_3$); mass spectrum m/e 502. Anal. Calcd for $C_{20}H_{22}Br_2OS_2$: C, 47.82; H, 4.41. Found: C, 47.59; H, 4.47.

2,6-Dibromo-3,5-bis(methoxymethyl)-1,4-dimethylbenzene (13). A solution of 27.0 g of sodium methoxide in 200 mL of methanol was added dropwise with stirring to a solution of 68.6 g of **12** in 450 mL of dry benzene. When the addition was complete, the resulting solution was boiled under reflux for 11 h. After removal of the inorganic precipitate by filtration, the filtrate was washed with water and concentrated to give 66.1 g (98%) of a colorless solid, mp 122–123 °C. A sample recrystallized from methanol gave soft needles: mp 122.5–123.5 °C; NMR, a singlet at τ 5.28 (4 H, $ArCH_2-$), a singlet at 6.58 (6 H, $-OCH_3$), and singlets at 7.31 and 7.48 (3 H each, $-CH_3$). Anal. Calcd for $C_{12}H_{16}Br_2O_2$: C, 40.94; H, 4.58. Found: C, 40.65; H, 4.48.

2,6-Dicyano-3,5-bis(methoxymethyl)-1,4-dimethylbenzene (14). To a solution of 66.0 g of **13** in 200 mL of *N*-methylpyrrolidone was added 50.4 g of cuprous cyanide and the mixture was heated at 170 °C for 66 h. It was then poured into a cold solution of 300 mL of concentrated ammonium hydroxide and 300 mL of water. The gray precipitate was collected by filtration, washed with water, and dried. It was then taken up in dichloromethane and chromatographed over silica gel to give 27.5 g (60%) of colorless crystals. A sample recrystallized from 2-propanol gave white crystals: mp 116–117 °C; NMR, a singlet at τ 5.28 (4 H, $ArCH_2-$), a singlet at 6.53 (6 H, $-OCH_3$), and singlets at 7.21 and 7.51 (3 H each, $-CH_3$). Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.38; H, 6.60. Found: C, 68.64; H, 6.39.

2,6-Dicyano-3,5-bis(bromomethyl)-1,4-dimethylbenzene (15). A solution of 10.0 g of 14 in 30 g of a 30% solution of hydrogen bromide in acetic acid was stirred at room temperature for 48 h. It was then poured into 200 mL of ice water and extracted with dichloromethane. After the dichloromethane extract had been washed with water, it was dried and concentrated. The residual solid was taken up in a 2:1 dichloromethane–hexane mixture and chromatographed over silica gel to give 8.12 g (52%) of white crystals: mp 168–170 °C; NMR, a singlet at τ 5.39 (4 H, $ArCH_2-$), and singlets at 7.22 and 7.49 (3 H each, $-CH_3$); mass spectrum m/e 341.919 (calcd for $C_{12}H_{10}Br_2N_2$: 341.919). Anal. Calcd for $C_{12}H_{10}Br_2N_2$: C, 42.11; H, 2.92. Found: C, 42.01; H, 2.73.

***syn*- and *anti*-5,7-Dicyano-6,9,18-trimethyl-15-methoxy-2,11-dithia[3.3]metacyclophane (11).** A solution of 17.75 g of **15** and 11.10 g of 2,6-bis(mercaptomethyl)-4-methoxytoluene in 1 L of benzene was added dropwise with stirring to a solution of 8.55 g of potassium hydroxide in 6 L of ethanol boiling under reflux. When the addition was complete (5.5 days), the solution was concentrated and the residual semisolid was extracted with hot chloroform. The chloroform extract was concentrated and the residue was chromatographed over silica gel using benzene as eluent.

The first fraction of eluate gave 4.63 g (23%) of the syn isomer of **11** as colorless crystals: mp 276–277 °C; NMR, a singlet at τ 3.56 (2 H, ArH), an AB pattern at 5.39 and 6.17 (4 H, J = 16 Hz, $ArCH_2-$), a singlet at 6.04 (4 H, $ArCH_2-$), a singlet at 6.22 (3 H, $-OCH_3$), and singlets at 7.37, 7.42, and 7.55 (3 H each, $-CH_3$); mass spectrum m/e 394.116 (calcd for $C_{22}H_{22}N_2OS_2$: 394.116). When a sample of the syn isomer of **10** was subjected to the von Braun reaction, as described for the preparation of **14**, the product, formed in only 5% yield, was identical in all respects with this specimen. Anal. Calcd for $C_{22}H_{22}N_2OS_2$: C, 66.99; H, 5.62. Found: C, 67.25; H, 5.55.

The second fraction of eluate gave 505 mg (2%) of the anti isomer of **11** as colorless crystals: mp 291–292 °C; NMR, a singlet at τ 3.09 (2 H, ArH), a multiplet at 5.92–6.38 (8 H, $ArCH_2-$), a singlet at 6.16 (3 H, $-OCH_3$), and singlets at 7.55, 8.56, and 8.68 (3 H each, $-CH_3$); mass spectrum m/e 394.119 (calcd for $C_{22}H_{22}N_2OS_2$: 394.116). When a sample of the anti isomer of **10** was subjected to the von Braun reaction, as described for the preparation of **14**, the product, formed in 24% yield, was identical in all respects with this specimen. Anal. Calcd for $C_{22}H_{22}N_2OS_2$: C, 66.99; H, 5.62. Found: 66.91; H, 5.57.

Photochemical Extrusion of Sulfur to Give *syn*- and *anti*-4,6-Dicyano-5,8,16-trimethyl-13-methoxy[2.2]metacyclophane (16 and 17). A suspension of 1.79 g of the syn isomer of **11** in 100 mL of trimethyl phosphite was irradiated with a 450-W medium-pressure Hanovia lamp for 46 h. The homogeneous solution was then poured onto 200 g of crushed ice and stirred at room temperature for 2 h. The solid, which had precipitated, was collected by filtration, washed with water, and extracted with dichloromethane. The dichloromethane extract was washed with water, dried, and concentrated to give 3 g of a clear oil. This was chromatographed over silica gel using dichloromethane as eluent.

The product from the first fraction of eluate was recrystallized from a mixture of dichloromethane–petroleum ether (30–60 °C) to give 510 mg (33%) of the anti isomer **17** as colorless crystals: mp 291–292 °C; NMR, a singlet at τ 3.24 (2 H, ArH), a singlet at 6.21 (3 H, $-OCH_3$), multiplets at 6.90–7.36 and 6.36–6.56 (8 H, $ArCH_2-$), and singlets at 7.31, 9.21, and 9.41 (3 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 218 (ϵ 49 000), 245 (20 000), and 338 nm (1200); mass spectrum m/e 330.172 (calcd for $C_{24}H_{22}N_2O$: 330.173), 315, and 300. Anal. Calcd for $C_{22}H_{22}N_2O$: C, 79.97; H, 6.71. Found: C, 79.80; H, 6.62.

The product from the second fraction of eluate was recrystallized from ether to give 247 mg (17%) of the syn isomer **16** as colorless crystals: mp 194–196 °C; NMR, a singlet at τ 3.90 (2 H, ArH), a singlet at 6.36 (3 H, $-OCH_3$), a multiplet at 6.46–7.08 (8 H, $ArCH_2-$), and singlets at 7.63, 7.78, and 7.90 (3 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 232 (ϵ 37 000), 292 (2700), and 346 nm (520); mass spectrum m/e 330, 315, and 300. Anal. Calcd for $C_{22}H_{22}N_2O$: C, 79.97; H, 6.71; N, 8.48. Found: C, 79.75; H, 6.57; N, 8.24.

A sample of the syn isomer **16** was sealed under vacuum in a capillary tube and heated just above its melting point for 5 h. At the end of this time **16** was completely converted to the anti isomer **17**, identical in all respects with the sample obtained above.

***anti*-4,6-Diformyl-5,8,16-trimethyl-13-methoxy[2.2]metacyclophane (21).** To a solution of 746 mg of **17** in 22 mL of dry benzene was added at room temperature 4.8 mL of a 20% solution of diisobutylaluminum hydride in benzene. After the solution had stood at room temperature for 2 h, additions were made successively with stirring of 3.5 mL of methanol, 3.5 mL of water, and 10 mL of aqueous 10% hydrochloric acid. The organic layer was extracted with benzene, washed with water, dried, and concentrated. The residual solid was recrystallized from a benzene–hexane mixture to give 744 mg (98%) of pale yellow prisms: mp 191–192 °C; NMR, a singlet at τ – 0.75 (2 H, ArCHO), a singlet at 3.35 (2 H, ArH), a singlet at 6.22 (3 H, $-OCH_3$), multiplets at 6.21–6.32 and 6.86–7.60 (8 H, $ArCH_2-$), and singlets at 7.32, 9.24, and 9.42 (3 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 217 (ϵ 38 000), 253 (2600), and 352 nm (1700); mass spectrum m/e 336. Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19. Found: C, 78.49; H, 7.16.

***syn*-4,6-Diformyl-5,8,16-trimethyl-13-methoxy[2.2]metacy-**

clophane (18). A 405-mg sample of **16** was reduced with diisobutylaluminum hydride following the same procedure described above for preparing **21.** Chromatography of the product over silica gel using dichloromethane as eluent gave 243 mg (59%) of yellow needles: mp 208–210 °C (sealed capillary); NMR, a singlet at τ −0.38 (2 H, ArCH), a singlet at 4.15 (2 H, ArH), two multiplets at 6.14–6.75 and 7.04–7.30 (8 H, $ArCH_2$–), a singlet at 6.48 (3 H, $-OCH_3$), and singlets at 7.57, 7.50, and 7.90 (3 H each, $-CH_3$); UV (cyclohexane), maxima at 212 (ϵ 25 000), 240 (16 000), and 360 nm (440); mass spectrum *m/e* 336.174 (calcd for $C_{22}H_{24}O_3$: 336.173), 321, and 306.

A sample of the syn isomer **18,** sealed under vacuum in a capillary tube, was heated at 215 °C for 5 h. When the tube was cooled, the contents was shown to be completely identical with the anti isomer **21.**

***anti*-4,6-Bis(hydroxymethyl)-5,8,16-trimethyl-13-methoxy-[2.2]metacyclophane (22).** To a stirred solution of 879 mg of **21** in 22 mL of a 2:1 mixture of tetrahydrofuran–2-propanol was added 65 mg of sodium borohydride. After the mixture had been stirred at room temperature for 3.5 h, 10 mL of aqueous 5% hydrochloric acid was added. The organic layer was extracted with chloroform, washed with water, dried, and concentrated to give 889 mg (100%) of white needles: mp 227–230 °C; NMR (Me_2SO-d_6), a singlet at τ 3.16 (2 H, ArH), a singlet at 5.25 (4 H, $-CH_2OH$), a singlet at 6.20 (3 H, $-OCH_3$), two multiplets at 6.4–6.7 and 7.0–7.8 (8 H, $ArCH_2$–), and singlets at 7.57, 9.29, and 9.50 (3 H each, $-CH_3$); mass spectrum *m/e* 340.201 (calcd for $C_{22}H_{28}O_3$: 340.204). Anal. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.47; H, 8.01.

***syn*-4,6-Bis(hydroxymethyl)-5,8,16-trimethyl-13-methoxy-[2.2]metacyclophane (19) and *syn*-4,6-Bis(methoxymethyl)-5,8,16-trimethyl-13-methoxy[2.2]metacyclophane (20).** A 122-mg sample of **18** was reduced with sodium borohydride as described for the preparation of **22.** After crystallization from methanol, there was isolated 117 mg (95%) of white crystals: mp 172–173 °C (sealed capillary); NMR, singlets at τ 4.20 (2 H, ArH), 5.48 (4 H, $ArCH_2OH$), and 6.48 (3 H, $-OCH_3$), two multiplets at 6.50–6.75 and 7.14–7.36 (8 H, $ArCH_2$–), and singlets at 7.82 and 7.84 (9 H, $-CH_3$); UV (tetrahydrofuran), maxima at 275 (ϵ 2500) and 297 nm (1400); mass spectrum *m/e* 340.

When a sample of **19** was heated at 200 °C, the NMR spectrum of the starting material was quickly replaced by that of **22,** but the thermal isomerization was accompanied by decomposition. Anal. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29. Found: C, 77.07; H. 8.19.

A 110-mg sample of **19** in 5 mL of methanol was treated with one drop of concentrated hydrochloric acid. It was then poured into an aqueous solution of sodium bicarbonate and extracted with dichloromethane. After concentration, the residual oil was chromatographed over silica gel using chloroform as eluent. The main fraction of eluate gave **20** as a colorless oil: NMR, singlets at τ 4.20 (2 H, ArH), 5.77 (4 H, $ArCH_2OCH_3$), 6.48 (3 H, $-OCH_3$), and 6.61 (6 H, $-OCH_3$), two multiplets at 6.6–6.8 and 7.2–7.4 (8 H, $ArCH_2$–), and singlets at 7.81, 7.86, and 7.94 (9 H, $-CH_3$); mass spectrum *m/e* 368.236 (calcd for $C_{24}H_{32}O_3$: 368.235).

A sample of **20** heated above 200 °C quickly had its NMR spectrum replaced by a new one, apparently corresponding to the anti isomer of **20,** but considerable decomposition occurred.

***anti*-4,6-Bis(bromomethyl)-5,8,16-trimethyl-13-methoxy-[2.2]metacyclophane (23).** To a stirred suspension of 720 mg of **22** in 22 mL of dry benzene there was added with stirring 0.25 mL of phosphorus tribromide. After the solution had stood at room temperature for 1 h, it was poured into 50 mL of water and the organic layer was extracted with benzene. The benzene extract was washed successively with water, aqueous bicarbonate, and water before it was dried and concentrated. The residual oil was chromatographed over silica gel using dichloromethane as eluent. The product from the main fraction of eluate was recrystallized from a 1:4 mixture of benzene–hexane to give 423 mg (41%) of white prisms: mp 160–163 °C; NMR, singlets at τ 3.25 (2 H, ArH), 5.25 (4 H, $-CH_2Br$), and 6.21 (3 H, $-OCH_3$), two multiplets at 6.55–6.78 and 6.92–7.48 (8 H, $ArCH_2$), and singlets at 7.58, 9.33, and 9.47 (3 H each, $-CH_3$); mass spectrum *m/e* 466.035 (calcd for $C_{22}H_{26}OBr_2$: 466.033). Compound **23** is unstable to oxygen and light, but can be stored in the dark under nitrogen.

4^2-Methyl-4^5-methoxy-4[1,3],$8^{3,6}$-dimethyl-8^u[1,5,2,4],11^2-methyl-11^5-methoxy-11^u[1,3]-tribenzospiro[7.5]-2,6-dithiatridecaphane[18] (24). A solution of 76 mg of **23** and 35 mg of 2,6-bis(mercaptomethyl)-4-methoxytoluene in 60 mL of benzene was added dropwise with stirring to a solution of 35 mg of potassium hydroxide in 125 mL of ethanol. When the addition was complete (9 h), the mixture was concentrated and the residue was extracted with dichloromethane. After the dichloromethane extract had been washed with water, dried, and concentrated, the residual solid was chromatographed over silica gel using dichloromethane as eluent. The product from the main fraction of eluate was recrystallized from a benzene–hexane mixture to give 47 mg (56%) of colorless crystals: mp 254–257 °C; NMR, singlets at τ 3.06 (2 H, ArH), 3.48 (2 H, ArH), 6.18 (3 H, $-OCH_3$), and 6.21 (3 H, $-OCH_3$), multiplets at 6.04–6.25 and 6.30–6.42 (8 H, $ArCH_2$–) and multiplets at 6.48–6.75 and 7.04–7.48 (8 H, $ArCH_2$–), and singlets at 8.74, 8.77, 9.24, and 9.58 (3 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 207 (ϵ 41 000), 247 (25 000), 303 (3320), and 327 nm (640); mass spectrum *m/e* 518.229 (calcd for $C_{32}H_{38}O_2S_2$: 518.231).

3^2-Methyl-3^5-methoxy-3[1,3],$6^{3,6}$-dimethyl-6^u[1,5,2,4],9^2-methyl-9^5-methoxy-9^u[1,3]-tribenzospiro[5.5]undecaphane[18] (26). A suspension of 118 mg of **24** in 100 mL of trimethyl phosphite was irradiated for 27 h using a 450-W medium-pressure Hanovia lamp. The solution was then poured onto 200 g of crushed ice and stirred at room temperature for 2 h. The organic matter was extracted with dichloromethane, washed with water, dried, and concentrated. The residual oil was then chromatographed over silica gel using dichloromethane as eluent. The main fraction of eluate gave 53 mg (51%) of a colorless oil: NMR, an AB pattern at τ 3.44 and 3.52 (4 H, J = 3 Hz, ArH), a singlet at 6.21 (6 H, $-OCH_3$), two multiplets at 6.64–7.56 and 7.80–8.62 (16 H, $ArCH_2$–), and singlets at 8.04 and 9.94 (6 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 211 (ϵ 53 000), 238 (14 500), and 287 nm (3500); mass spectrum *m/e* 454, 439, 424, 409, 394, and 379. Anal. Mol wt calcd for $C_{32}H_{38}O_2$: 454.287. Found (high-resolution mass spectrum): 454.285.

3^2-Methyl-3^5-methoxy-3[1,3],$6^{3,6}$-dimethyl-6^u[1,5,2,4],9^2-methyl-9^5-methoxy-9^u[1,3]-tribenzospiro[5.5]undecaphane[18] (1).

A. Via the Wittig Rearrangement of 24 to 27 and Desulfurization. To a stirred solution of 42 mg of **24** in 3 mL of dry tetrahydrofuran was added 0.125 mL of a 1.5 M solution of *n*-butyllithium in hexane at room temperature. After the solution had been stirred for 10 min, 0.2 mL of methyl iodide was added. The mixture was then poured into 10 mL of water and extracted with dichloromethane. After the dichloromethane extract had been washed with water, dried, and concentrated, it gave 41 mg (93%) of a mixture of isomers of **27** as a yellow oil: NMR, a singlet at τ 3.28 (4 H, ArH), multiplets at 5.96–6.44 and 7.00–7.80 (14 H, ArCH< and $ArCH_2$–), a singlet at 7.85 (6 H, $-SCH_3$), and four singlets at 9.00–9.55 (3 H each, $-CH_3$); mass spectrum *m/e* 546 and 499.

To a solution of 41 mg of **27** in 10 mL of a 1:1 absolute ethanol–benzene mixture was added a spatula of commercial Raney nickel and the mixture was boiled under reflux for 11 h. The catalyst was removed by filtration and washed with dichloromethane. The combined dichloromethane washings were concentrated and the solid residue was purified by preparative thin-layer chromatography using benzene as eluent. The band at R_f 0.5 gave 2.6 mg of **1** as colorless crystals: NMR, a singlet at τ 3.28 (4 H, ArH), a singlet at 6.22 (6 H, $-OCH_3$), multiplets at 6.50–6.70 and 7.00–7.40 (16 H, $ArCH_2$), and two singlets at 9.38 and 9.41 (6 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 207 (ϵ 13 000), 259 (6600), 310 (1000), and 340 nm (500); mass spectrum, *m/e* 454, 439, 424, 409, 394, 379, and 364. Anal. Mol wt calcd for $C_{32}H_{38}O_2$: 454.287. Found (high-resolution mass spectrum): 454.289.

B. Via Irradiation of 24. A suspension of 21 mg of **24** in 0.5 mL of trimethyl phosphite in a 5-mm quartz tube was irradiated using a low-pressure Rayonet mercury resonance lamp for 2 days. The solution was then poured into water, stirred at room temperature for 2 h, and extracted with dichloromethane. After the dichloromethane extract had been washed with water, it was dried and concentrated. Preparative thin-layer chromatography over silica gel using dichloromethane as eluent gave a band at R_f 0.6 which yielded 2 mg (11%) of a colorless solid, whose spectral properties agreed in all respects with the specimen obtained in A.

Oxidation of 1 to Give the Bisdienone 28. To a stirred suspension of 4 mg of **1** in 0.5 mL of acetone was added 0.01 mL of a prepared chromic acid reagent.[2] After the deep green solution had been stirred at room temperature for 5 min, 2 mL of water and 2 mL of dichloromethane were added. The aqueous layer was separated and extracted with dichloromethane. The combined dichloromethane extract and organic layer was washed successively with aqueous bicarbonate solution and water. The dichloromethane solution was then dried and concentrated to give 3.4 mg (92%) of a yellow oil: NMR, a singlet at τ 3.75 (4 H, C (=O)CH=C<), a broad multiplet at 6.90–7.70 (16 H, $-CH_2$–), and two singlets at 8.81 and 8.83 (6 H each, $-CH_3$); UV (tetrahydrofuran), maxima at 223 (ϵ 22 000), 277 (23 000), 332 (1800), and 355 nm (1400); mass spectrum *m/e* 424, 409, 394, 379, and 364. Anal. Mol wt calcd for $C_{30}H_{32}O_2$: 424.240. Found (high-resolution mass spectrum): 424.236.

Acknowledgment. We thank the National Science Foundation for their support of this investigation.

Registry No.—1, 66793-10-0; *syn*-10, 66793-11-1; *anti*-10, 66808-40-0; *syn*-11, 66793-12-2; *anti*-11, 66808-41-1; 12, 66788-12-3; 13, 66793-13-3; 14, 66793-14-4; 15, 66793-15-5; 16, 66793-16-6; 17, 66808-42-2; 18, 66793-17-7; 19, 66793-18-8; 20, 66793-19-9; *anti*-20, 66808-43-3; 21, 66808-44-4; 22, 66808-45-5; 23, 66793-20-2; 24, 66793-21-3; 26, 66793-22-4; 27, 66792-72-1; 28, 66793-23-5; 2,6-bis(mercaptomethyl)-4-methoxytoluene, 66793-24-6; 2,6-bis(bromomethyl)-4-methoxytoluene, 14542-73-5.

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(16) Elemental and mass spectral analyses were determined by Dr. R. Wielesek, University of Oregon Microanalytical Laboratories. Melting points are uncorrected and were taken with a Mel-Temp apparatus, visible and ultraviolet spectra were measured with a Cary 15, NMR spectra were measured using deuteriochloroform with tetramethylsilane as an internal standard and were obtained with a Varian HA-100 or XL-100 instrument, and all mass spectra were taken using a CEC Model 21-110 spectrometer at 70 eV.
(17) We thank Dr. F. Häfliger and the Geigy Research Laboratories for a generous gift of 2,6-bis(bromomethyl)-4-methoxytoluene.
(18) At present there is no accepted system of nomenclature for the multilayered cyclophanes. The name given to compounds **24**, **26**, and **1** follow from the system proposed by H. Lehner (*Monatsh. Chem.*, **107**, 565 (1976)). However, Lehner did not provide for the conformational isomerism possible in the triple-layered [2.2]metacyclophane, and so to his system we have added the use of superscripts u and o to designate whether that aromatic ring is under or over the previous ring. This follows the pattern of up–down nomenclature used by Misumi (*Mem. Inst. Sci. Ind. Res., Osaka Univ.*, **33**, 53 (1976).

Chemical Behavior of *cis*-15,16-Dimethyldihydropyrene

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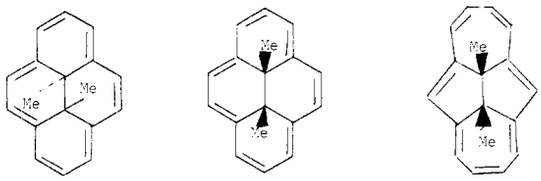
Received January 27, 1978

The synthesis of *cis*-15,16-dimethyldihydropyrene derivatives has been reexamined and 2-nitro-*cis*-15,16-dimethyldihydropyrene (**8**) has been prepared both by nitration of *cis*-15,16-dimethyldihydropyrene (**2**) and by independent synthesis. Acetylation of *cis*-15,16-dimethyldihydropyrene gives both the 1- and 2-acetyl derivatives (**10** and **11**) in a ratio of 2:1. In contrast to the trans series, *cis*-15,16-dimethyldihydropyrene (**2**) readily reacts with oxygen to give a nonaromatic diepoxide.

The development of the dithiacyclophane–sulfur extrusion route for the synthesis of *trans*-15,16-dimethyldihydropyrene (**1**) made possible the concomitant synthesis of *cis*-15,16-dimethyldihydropyrene (**2**), albeit in poor yield.[1] For purposes of comparing the chemical properties of the *cis*-



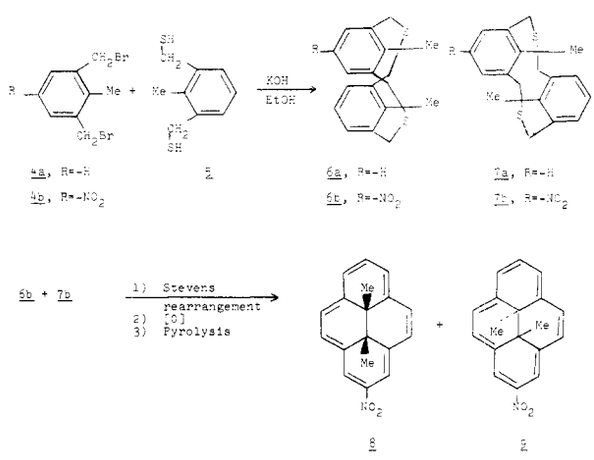
1 2 3

and *trans*-15,16-dimethyldihydropyrenes, as well as making a comparison of the physical and chemical properties of **2** with 1,6:8,13-ethanediylidene[14]annulene (**3**),[2,3] where both types of molecules have the same saucer-shaped geometry but different perimeter contours, we needed additional quantities of *cis*-15,16-dimethyldihydropyrene.

The difficulty in the previous synthesis was the coupling reaction of **4a** and **5** which, although it proceeds in about 75% overall yield, gives the syn and anti isomers of 9,18-dimethyl-2,11-dithia[3.3]metacyclophane (**6a** and **7a**) in a ratio of about 1:7.[1] For the synthesis of **2** only the syn isomer is useful and so the unfavorable syn to anti isomer distribution in the coupling reaction is a severe disadvantage. Subsequently, it was found that substituents present in **4** or **5** affect the ratio of syn to anti isomers formed and the role of substituents in such coupling reactions is discussed in an accompanying paper.[5] On the assumption that the presence of a nitro group, as in **4b**, would improve the syn to anti isomer ratio and that the nitro group could be removed as a final step, we undertook the synthesis of 2-nitro-*cis*-15,16-dimethyldihydropyrene (**8**), as shown in Scheme I.

To obtain the requisite 2,6-bis(bromomethyl)-4-nitrotoluene (**4b**), 2-methylisophthalaldehyde was nitrated and then converted by standard procedures to **4b**. The coupling reaction of **4b** and **5** proceeded in 47% overall yield, giving a mixture whose NMR spectrum showed the ratio of syn to anti isomers (**6b**/**7b**) to be 1:1. Since the Stevens rearrangement

Scheme I



4a, R=H; 4b, R=NO_2 5 6a, R=H; 6b, R=NO_2 7a, R=H; 7b, R=NO_2

6b + 7b 8 9

