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Syntheses of Dihydropyrenes and Triple-Layered [2.2]Metacyclophanes

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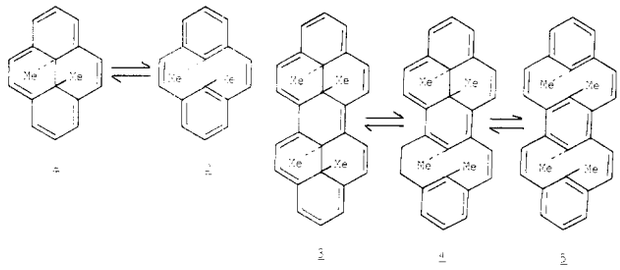
Two synthetic routes have been explored for the possible synthesis of a bridged [22]annulene (**3**) of the peropyrene type. Although the synthesis of **3** was not achieved, a number of *cis*- and *trans*-1,2,3-trisubstituted-15,16-dimethyldihydropyrenes were prepared. Also the triple-layered [2.2]metacyclophane derivative **24** has been synthesized and shown to have a staircase-type geometry.

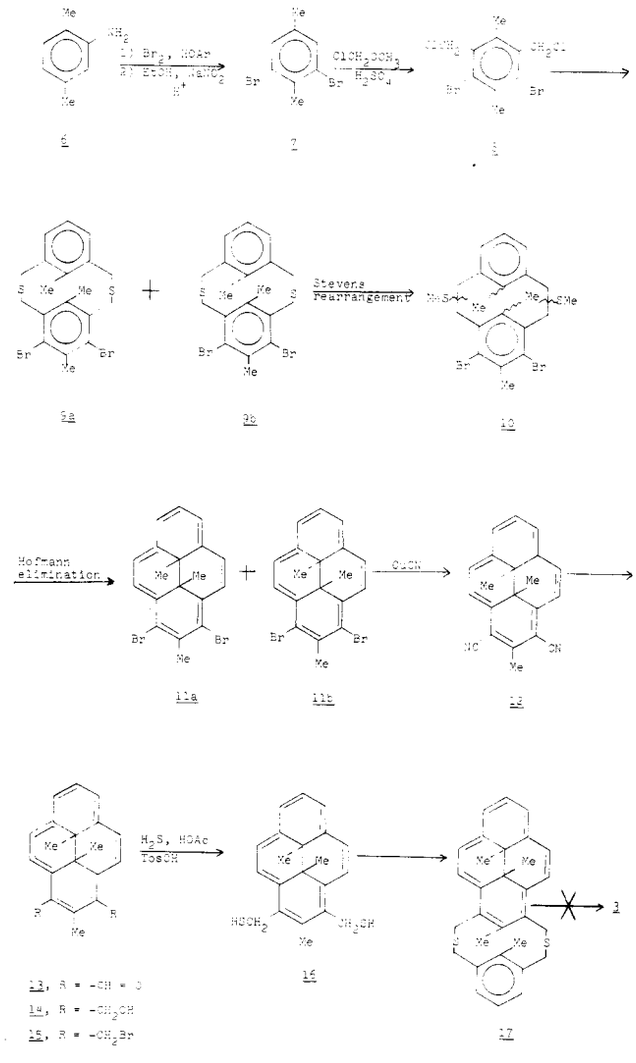
One of the important outstanding problems in Hückel molecular orbital theory is the experimental definition of whether, and at what ring size, the larger [4*n* + 2]annulenes will lose aromaticity and simply show polyene character. As has been discussed elsewhere,[1] bridged [4*n* + 2]annulenes are probably the best experimental models for testing this upper limit. In Haddon's system for empirically evaluating aromaticity by measuring effective ring currents, *trans*-15,16-dimethyldihydropyrene (**1**) is an exceptionally good example



of aromaticity in annulenes and was selected as the reference standard for comparing other molecules.[2] It seemed, therefore, that, in trying to assess the aromaticity of a bridged [22]annulene, a peropyrene structure such as **3**, having a double *trans*-15,16-dimethyldihydropyrene moiety, would be particularly appropriate. Aside from having the desirable features of the dihydropyrenes, structure **3** offers some intriguing possibilities for valence tautomerization. It is well known that the dihydropyrenes readily undergo valence tautomerization (**1** ⇌ **2**) both thermally and photochemically.[3] A similar valence tautomerization of **3** could yield both **4** and **5**, molecules whose relative thermodymamic stability would be of some interest.

The first approach we investigated for the synthesis of **3** is outlined in Scheme I and is based on methods previously developed for the synthesis of *trans*-dihydropyrene derivatives.[4] The steps in the conversion of 2,5-dimethylaniline (**6**) to **8** proceeded in good yield and require no comment. The coupling reaction of **8** with 2,6-bis(mercaptomethyl)toluene gave a mixture of the syn and anti isomers (**9a** and **9b**) of 2,11-dithia-5,7-dibromo-6,8,18-trimethyl[3.3]metacyclophane in an overall yield of 84%, but with a ratio of syn to anti isomers of 1.3:1.0. This is in sharp contrast to the parent example, where the ratio of syn to anti isomers is 1.0:7.0.[4] As has been discussed elsewhere,[5] the relative ratios of syn to anti isomers formed in these coupling reactions is very dependent on what substituents are present. Electron-withdrawing substituents, such as the bromine atoms present in **8**, greatly increase the relative amount of syn isomer formed, presumably due to charge-transfer stabilization of the transition state leading to the syn isomer. The formation of such a large fraction of the syn isomer was unfortunate, both because the anti isomer is the one needed as precursor for the synthesis of **3** and because of the additional difficulties in separation and purification of **11b** from the mixture.

Scheme I



In practice, it proved expedient to carry along the mixture of isomers, **9a** and **9b**, through the Stevens rearrangement and the Hofmann elimination steps, and then effect the separation and purification at the dihydropyrene stage. In this way the *cis*- and *trans*-1,3-dibromo-2,15,16-trimethyl-15,16-dihydropyrenes, **11a** and **11b**, were isolated in the pure state in yields of 20 and 10%, respectively. Both are deep green, crystalline compounds, which can readily be distinguished by comparison of their NMR spectra with that of the parent *cis*- and *trans*-15,16-dimethyldihydropyrenes.[4] The chemical shift values for the protons of the internal methyls of **11a** are τ 11.97 and 11.89, whereas the protons of the internal methyl groups of **11b** appear at τ 13.98 and 13.93.

Although the von Braun reaction in using a pure sample of **11b** gave **12** in 77% yield, the more convenient use of the crude mixture of **11a** and **11b** in the von Braun reaction led to the desired trans isomer **12** in only 15% yield plus the corresponding cis isomer in 18% yield. Reduction of **12** with diisobutylaluminum hydride in benzene gave **13** in 96% yield and this, in turn, with sodium borohydride led to the diol **14** in 99% yield.

Normally, the next step would have been the conversion of the diol **14** to the corresponding dibromide **15**. However, we were surprised to find that none of the standard procedures for effecting this transformation were successful. In each case polymeric black tars resulted. Apparently, the dihydropyrene moiety is such a good electron donor that the dibromide **15**, when first formed, readily yields the corresponding carbonium ion, which undergoes self-alkylation leading to polymerization. To circumvent this the diol **15** was dissolved in acetic acid containing *p*-toluenesulfonic acid and saturated with hydrogen sulfide. Under these circumstances the carbonium ion derived from **15** is captured by the nucleophilic hydrogen sulfide and the desired dimercaptan **16** was formed in 47% yield.

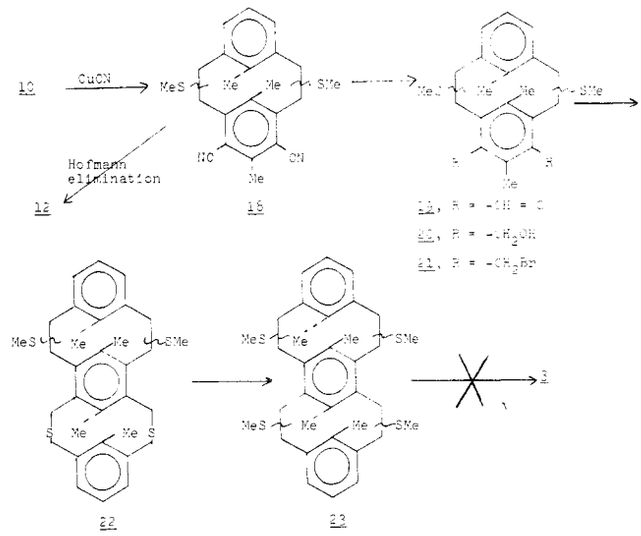
The coupling reaction between **16** and 2,6-bis(bromomethyl)toluene proceeded in high yield to give a mixture of the two possible *anti*-dithiacyclophanes of which **17** appeared to be the predominant isomer. The assignment of anti geometry to the mixture is based on the close correspondence of its NMR spectrum to that of 8,16-dimethyl-2,11-dithia[3.3]metacyclophane.[4] The protons of the internal methyl groups of **17** appear as two singlets at τ 14.17 and 13.58. Also, examination of molecular models suggests that the syn isomer analogous to **17** would be subject to severe steric interactions and so be unlikely to form.

Attempts to convert **17** to **3** by all of the standard methods of ring contraction and sulfur elimination were in each case unsuccessful. The reaction of **17** with dimethoxycarbonium fluoroborate[4] led to immediate tars, presumably via formation of a dihydropyrenyl carbonium ion followed by self-alkylation. However, both the benzyne–Stevens rearrangement[6] and the Wittig rearrangement[7] were also unsuccessful.

In view of our lack of success in effecting the conversion of **17** to **3** and the apparent instability of the dihydropyrene moiety toward the reaction conditions required in the final stages, we decided to try a modified approach starting from **10**, in which both dihydropyrene units would be introduced during the same final reaction. This modified approach is summarized in Scheme II.

When the mixture of stereoisomers from the Stevens rearrangement, depicted by the overall structure **10**, was subjected to the von Braun reaction, only the mixture of isomers having anti geometry, as shown by **18**, could be isolated and it was formed in 52% yield. In support of this assignment **18**, underwent a Hofmann elimination to give only *trans*-1,2-dicyano-2,15,16-trimethyldihydropyrene (**12**), a somewhat more efficient route for the synthesis of **12** than that described earlier. Since the final step in Scheme II was expected to lead

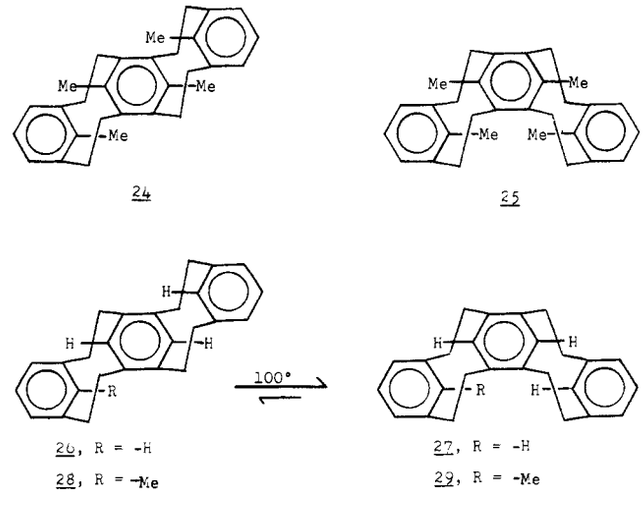
Scheme II



to only one isomer, it was decided not to try to separate the mixture of stereoisomers at this stage, but simply to carry through the intermediate steps with mixtures of stereoisomers.

The conversion, then, of **18** in successive steps to **19**, **20**, and **21** proceeded well following the usual pattern. The coupling of **21** with 2,6-bis(mercaptomethyl)toluene occurred in 65% yield to give the dithiacyclophane **22**. A Wittig rearrangement of **22**, using *n*-butyllithium followed by addition of methyl iodide, proceeded well, giving **23** in 89% yield. Although **23** was obtained as a complicated mixture of isomers, the lack of any signal in the region of τ 3.5, where the aromatic protons of *syn*-[2.2]metacyclophanes appear, rules out the presence of any isomers having syn geometry. Thus, the mixture of isomers represented by **23** appeared to be a suitable precursor for **3**. Unfortunately, however, the standard methods for removing sulfur with concomitant introduction of carbon–carbon double bonds, both the Hofmann elimination and the pyrolysis of the corresponding tetrasulfoxide, were completely unsuccessful in converting **23** to **3**.

As additional proof for the structural assignment made to **23**, it was subjected to desulfurization using Raney nickel. As expected, this gave the triple-layered [2.2]metacyclophane **24**. The question of whether the triple-layered cyclophane should be assigned the conformation shown by **24** or that of **25** was of some interest. It is now known that for benzene rings, in contrast to cyclohexane rings, it requires less energy to deform the ring to a boat than to a chair conformation.[8-10] This is due to the fact that the benzene π-orbital overlap is



more favorable in the boat than in the chair conformation. Umemoto, Otsubo, and Misumi provided the first experimental evidence for this preference when they prepared the two conformations, **26** and **27**, of the triple-layered [2.2]metacyclophane and showed that equilibration between these two conformations occurred readily at 100 °C with **27** being strongly favored.[11] In **27** all three benzene rings have boat conformations, whereas in **26** the central benzene ring is forced into a chair conformation. The driving force for the isomerization of **26** to **27** is the change in the central benzene ring from a chair to a boat conformation. Since Gschwend has shown that the energy barrier for conformational flipping for simple [2.2]metacyclophanes is about 33 kcal/mol,[12] it is remarkable that the isomerization of **26** to **27** should occur so readily.

Furthermore, this same study by the Osaka group showed that even with an internal methyl substituent, as in **28** and **29**, equilibration again occurred at 100 °C giving a mixture of **28** and **29** in a ratio of 1:17. In the case of **29**, a strong nuclear Overhauser effect was observed for the internal methyl and hydrogen substituents, which are forced into close proximity in the up–down conformation. In contrast, **28** does not exhibit a nuclear Overhauser effect. The differences in geometry between **28** and **29** are also evident in their NMR spectra; the signal for the internal methyl protons of **28** appear at τ 9.42, whereas in **29** they are seen at τ 8.93. Our product from the Raney nickel desulfurization of **23** was purified by sublimation at 150 °C and was a single compound. Its NMR spectrum showed the protons of the internal methyl groups as two singlets at τ 9.34 and 9.54. These values are in accord with that of **28** and permit the assignment of the staircase-type geometry of **24** to our tetramethyl derivative. Examination of molecular models suggests that the up–down conformation **25** would have severe, if not prohibitive, steric interactions between the internal methyl groups.

Experimental Section[13]

1,4-Dimethyl-2,6-dibromo-3,5-bis(chloromethyl)benzene (8) The bromination of 2,5-dimethylaniline was carried out as described by Bures and Meskan[14] and on a 4 M scale gave 2,4-dibromo-3,6-dimethylaniline, mp 58–59 °C (lit.[14] mp 61 °C), in 92% yield. This was then subjected to deamination following the procedure of Coleman and Talbot[15] to give 2,6-dibromo-*p*-xylene as a yellow oil [bp 82–88 °C (2 mm)] in 56% yield. A solution of 30.0 g of 2,6-dibromo-*p*-xylene in 75 mL of chloromethyl methyl ether was boiled gently under reflux while 30 mL of fuming sulfuric acid (30%) was added dropwise over a period of 30 min. A precipitate formed during the reaction and this was collected by filtration followed by a brief wash with water on the filter. The resulting solid was recrystallized from carbon tetrachloride to give 35.0 g (94%) of colorless needles: mp 185–187 °C; NMR, singlet at τ 5.2 (4 H, $-CH_2Cl$), and singlets at 7.30 and 7.40 (3 H each, $-CH_3$); mass spectrum *m/e* 361. Anal. Calcd for $C_{10}H_{10}Br_2Cl_2$: C, 33,26; H, 2.77. Found: C, 33.12; H, 2.75.

***syn*- and *anti*-2,11-Dithia-5,7-dibromo-6,9,18-trimethyl[3.3]metacyclophanes (9a and 9b).** A solution of 8.44 g of 1,4-dimethyl-2,6-dibromo-3,5-bis(chloromethyl)benzene (**8**) and 4.30 g of 2,6-bis(mercaptomethyl)toluene[4] in 700 mL of benzene was added dropwise with stirring to a boiling solution of 4.2 g of potassium hydroxide in 2 L of ethanol under a nitrogen atmosphere. After the addition was complete (3 days), the solvent was removed under reduced pressure and the residual solid was extracted with benzene. After concentration of the benzene extract, there separated 9.35 g (84%) of a colorless solid whose NMR spectrum showed it to be a mixture of the syn and anti isomers, **9a** and **9b**, in a ratio of 1.3:1.0. The two isomers could be separated by TLC, but it proved more convenient to allow the mixture to crystallize from benzene and then mechanically separate the syn (plates) and anti (needles) isomers.

In this way the syn isomer (**9a**) was isolated as colorless plates: mp 236–238 °C; NMR, an A_2B multiplet at τ 3.0–3.4 (3 H, ArH), two AB multiplets at 4.95 and 6.44 (4 H, J = 15 Hz, $ArCH_2-$) and at 5.93 and 6.15 (4 H, J = 15 Hz, $ArCH_2-$), and singlets at 7.32, 7.33, and 7.40 (3 H each, CH_3-); mass spectrum *m/e* 472. Anal. Calcd for $C_{19}H_{20}S_2Br_2$: C, 48.32; H, 4.27. Found: C, 48.41; H, 4.25.

The trans isomer (**9b**) was isolated as colorless needles: mp 234–236 °C; NMR, an A_2B multiplet at τ 2.6–2.9 (3 H, ArH), two AB multiplets at 5.94 and 6.30 (4 H, J = 15 Hz, $ArCH_2-$) and 6.26 and 6.30 (4 H, J = 15 Hz, $ArCH_2-$), and singlets at 7.11, 8.37, and 8.90 (3 H each, $-CH_3$); mass spectrum *m/e* 472. Anal. Calcd for $C_{19}H_{20}S_2Br_2$: C, 48.32; H, 4.27. Found: C, 48.41; H, 4.27.

Stevens Rearrangement to Give 10. To a solution of 13.7 g of the mixture of **9a** and **9b** from the above experiment in 400 mL of methylene chloride held at −20 °C was added portionwise with stirring 10.1 g of dimethoxycarbonium fluoroborate.[16] After several hours the solution was allowed to warm to room temperature and the solvent was removed by decantation. The crystalline residue was washed several times with methyl formate and dried to give 18.2 g (93%) of white crystals, mp 209–213 °C dec. Anal. Calcd for $C_{21}H_{26}S_2Br_2B_2F_8$: C, 37.31; H, 388. Found: C, 37.64; H, 3.90.

The bissulfonium salt (18.2 g) was dissolved in 300 mL of dry tetrahydrofuran and then 6.2 g of potassium *tert*-butoxide was added all at once. After addition of dilute aqueous hydrochloric acid, the organic layer was extracted with ether, dried, and concentrated to give 12.6 g (93%) of a pale yellow oil. The NMR spectrum of **10** was very complicated, showing it to be a mixture of stereoisomers of both syn and anti geometry. The high-resolution mass spectrum of **10** showed the parent molecular ion at 497.970 (calcd for $C_{21}H_{24}S_2Br_2$: 497.969). Anal. Calcd for $C_{21}H_{24}S_2Br_2$: C, 50.41; H, 4.83. Found: C, 50.54; H, 4.88.

Hofmann Elimination to Give 11a and 11b. To a solution of 12.6 g of **10** in 150 mL of methylene chloride held at 0 °C under a nitrogen atmosphere there was added 8.9 g of dimethoxycarbonium fluoroborate.[16] After the mixture had warmed to room temperature, it was stirred for 24 h and then 50 mL of ethyl acetate was added. The solvent was removed by decantation and the residue was washed with methyl formate and dried to give 16.0 g (90%) of a pale brown glass. Anal. Calcd for $C_{23}H_{30}S_2Br_2B_2F_8$: C, 39.24; H, 4.30. Found: C, 39.40; H, 4.47.

To a solution of 1.3 g of sodium hydride in 400 mL of dry tetrahydrofuran was added 15.0 g of the bissulfonium salt with stirring under a nitrogen atmosphere. In those runs where the solution did not turn an immediate deep green, the solvent was removed by decantation and replaced by fresh, dry tetrahydrofuran containing the appropriate amount of sodium hydride. When there was no longer any change in color, the solution was filtered and the filtrate was concentrated. The resulting green solid was taken up in petroleum ether (30–60 °C) and chromatographed over silica gel.

***trans*-1,3-Dibromo-2,15,16-trimethyldihydropyrene (11b)** was isolated from the first eluate fraction and, after recrystallization from pentane, was obtained as 800 mg (10%) of deep green, nearly black, crystals: mp 187–188 °C; NMR, an AB at τ 1.02 and 1.32 (4 H, J = 8 Hz, ArH), an A_2B at 1.42 (2 H, J = 8 Hz, ArH) and 1.93 (1 H, J = 8 Hz, ArH), and singlets at 6.58, 13.93, and 13.98 (3 H each, $-CH_3$); mass spectrum *m/e* 404, 389, and 374. Anal. Calcd for $C_{19}H_{16}Br_2$: C, 56.47; H, 3.99. Found: C, 56.50; H, 4.02.

***cis*-1,3-Dibromo-2,15,16-trimethyldihydropyrene (11a)** was isolated from the second fraction of eluate and, after recrystallization from pentane, was obtained as 1.60 g (20%) of deep green crystals: mp 178–180 °C; NMR, an AB at τ 0.83 and 1.28 (4 H, J = 8 Hz, ArH), an A_2B at 1.81 (2 H, J = 8 Hz, ArH) and 2.50 (1 H, J = 8 Hz, ArH), and singlets at 6.33, 11.89, and 11.97 (3 H each, $-CH_3$); mass spectrum *m/e* 404, 389, and 374. Anal. Calcd for $C_{19}H_{16}Br_2$: C, 56.47; H, 3.99. Found: C, 56.38; H, 3.89.

***cis*- and *trans*-1,3-Dicyano-2,15,16-trimethyldihydropyrenes (12).** The crude mixture of **11a** and **11b** (ratio of 2:1) from the Hofmann elimination reaction, weighing 4.66 g, was dissolved in 30 mL of *N*-methylpyrrolidone containing 11.3 g of cuprous cyanide and heated at 110 °C for 20 h under a nitrogen atmosphere. The warm dark solution was poured into 500 mL of a 1:1 mixture of water and concentrated aqueous ammonium hydroxide solution. After the solution had been stirred for 3 h, the solid was collected by filtration and dried. It was then mixed with silica gel, placed at the top of a silica gel column, and eluted with a 1:1 mixture of benzene and carbon tetrachloride.

***trans*-1,3-Dicyano-2,15,16-trimethyldihydropyrene (12)** was recovered from the first fraction of eluate and, after recrystallization from a benzene–hexane mixture, gave 290 mg (15%) of deep green plates: mp 197 °C; NMR, an AB at τ 0.95 and 1.14 (4 H, J = 8 Hz, ArH), an A_2B at 1.19 (2 H, J = 8 Hz, ArH) and 1.74 (1 H, J = 8 Hz, ArH), and singlets at 6.50, 13.94, and 13.98 (3 H each, $-CH_3$); mass spectrum *m/e* 296, 281, and 266. When the above experiment was repeated using pure **11b**, the yield of **12** was 77%. Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 84.95; H, 5.48; N, 9.24.

***cis*-1,3-Dicyano-2,15,16-trimethyldihydropyrene** was recovered from the second fraction of eluate and, after recrystallization from

a benzene–hexane mixture, gave 360 mg (18%) of deep green crystals: mp 185–187 °C; NMR, an AB at τ 0.74 and 0.99 (4 H, J = 8 Hz, ArH), an A_2B at 1.52 (2 H, J = 8 Hz, ArH) and 2.24 (1 H, J = 8 Hz, ArH), and singlets at 6.72, 11.88, and 11.96 (3 H each, $-CH_3$); mass spectrum m/e 296, 281, and 266. The cis isomer reacts readily with oxygen in the presence of light, even indirect laboratory lighting.[17] Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 84.87; H, 5.39; N, 9.32.

***trans*-1,3-Diformyl-2,15,16-trimethyldihydropyrene (13).** To a solution of 420 mg of **12** in 100 mL of dry benzene was added dropwise with stirring a 20% solution of diisobutylaluminum hydride in benzene. After the solution had been stirred at room temperature for 10 min, there was added successively 5 mL of methanol, 20 mL of dilute aqueous hydrochloric acid, and 500 mL of benzene. Hydrolysis of the aldimine was complete in about 30 min, whereupon the benzene layer was separated, dried, and concentrated to give 410 mg (96%) of deep green crystals: mp 190–192 °C; NMR, a singlet at τ −1.58 (2 H, –CHO), an AB at 0.60 and 1.28 (4 H, J = 8 Hz, ArH), an A_2B at 1.36 (2 H, J = 8 Hz, ArH) and 1.92 (1 H, J = 8 Hz, ArH), singlets at 6.54, 13.61, and 13.78 (3 H each, $-CH_3$); mass spectrum m/e 302, 287, and 272. Anal. Calcd for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.32; H, 5.94.

***trans*-1,3-Bis(hydroxymethyl)-2,15,16-trimethyldihydropyrene (14).** To a solution of 400 mg of **13** in 250 mL of dry tetrahydrofuran at room temperature was added 100 mg of sodium borohydride. After the mixture had been stirred for 4 h, it was cooled to 0 °C and dilute aqueous hydrochloric acid was added, followed by ether. The organic layer was separated, dried, and concentrated to give 400 mg (99%) of green crystals: mp 210–212 °C; NMR, an AB at τ 1.11 and 1.36 (4 H, J = 8 Hz, ArH), an A_2B at 1.44 (2 H, J = 8 Hz, ArH) and 1.97 (1 H, J = 8 Hz, ArH), an AB at 4.16 (2 H, J = 12 Hz, $ArCH_2OH$) and 4.30 (2 H, J = 12 Hz, $ArCH_2OH$), and singlets at 6.73, 13.99, and 14.08 (3 H each, $-CH_3$); mass spectrum m/e 306. Anal. Calcd for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.06; H, 7.16.

***trans*-1,3-Bis(mercaptomethyl)-2,15,16-trimethyldihydropyrene (16).** A solution of 165 mg of **14** in 150 mL of glacial acetic acid was saturated with dry hydrogen sulfide and 40 mg of *p*-toluenesulfonic acid was added in one portion. The mixture was stirred at room temperature for 3 h while bubbling hydrogen sulfide through the mixture. After addition of 200 mL of water, the mixture was extracted with benzene and the benzene extract was washed with water and dried. Concentration of the benzene extract followed by chromatography of the residual solid over deactivated silica gel using a 1:1 mixture of benzene–petroleum ether (30–60 °C) for elution gave 85 mg (47%) of green crystals: mp 103–105 °C; NMR, an AB at τ 1.37 and 1.41 (4 H, J = 8 Hz, ArH), an A_2B at 1.49 (2 H, J = 8 Hz, ArH) and 2.00 (1 H, J = 8 Hz, ArH), an ABX at 5.08 and 5.34 (4 H, J_{AB} = 14 and J_{AX} = 7 Hz, $ArCH_2SH$), a triplet at 8.04 (2 H, J = 7 Hz, –SH), and singlets at 6.86, 13.97, and 14.07 (3 H each, $-CH_3$); mass spectrum m/e 338. Anal. Calcd for $C_{21}H_{22}S_2$: C, 74.53; H, 6.55. Found: C, 74.23; H, 6.32.

Dithiacyclophane 17. A solution of 17 mg of **16** and 14 mg of 2,6-bis(bromomethyl)toluene in 35 mL of benzene was added dropwise with stirring under a nitrogen atmosphere to a solution of 30 mg of potassium hydroxide in 500 mL of ethanol held at room temperature. When the addition was complete (5 h), the solution was concentrated and the solid residue was extracted with benzene. Concentration of the benzene extract gave 27 mg (100%) of deep green crystals melting over a broad range. This appeared to be a mixture of the two possible anti isomers having the overall structure shown by **17**. Since the usual methods of separation and purification of these isomers by chromatography were not effective, the mixture of isomers was used directly in the attempts to synthesize **3**. The mixture showed an NMR spectrum having a multiplet in the region of τ 1.4–2.2 (ArH), a multiplet at 2.7–2.9 (ArH), two sets of AB patterns at 5.11 and 5.66 (J_{AB} = 15 Hz, $ArCH_2S$–) and 6.03 and 6.48 (J_{AB} = 14 Hz, $ArCH_2S$–), and singlets at 8.28, 8.73, 9.20, 13.58, and 14.17 (CH_3–); high-resolution mass spectrum m/e 454.180 (calcd for $C_{30}H_{30}S_2$: 454.179).

When a solution of the mixture of anti isomers corresponding to the **17** in methylene chloride was treated with dimethoxycarbonium fluoroborate, immediate formation of a black, polymeric tar occurred. So it was not possible to effect a normal Stevens rearrangement. Similarly, the benzyne–Stevens rearrangement procedure[6] gave no useful product. Furthermore, an attempt to effect a Wittig rearrangement[7] was likewise unsuccessful.

von Braun Reaction with 10 to Give 18. A solution of 2.47 g of the mixture of isomers corresponding to **10** and 8.0 g of cuprous cyanide in 60 mL of *N*-methylpyrrolidone was heated at 165 °C for 21 h. It was then poured into 400 mL of a 1:1 mixture of water and concentrated aqueous ammonium hydroxide. After the resulting mixture had been stirred with cooling for 3 h, the solid precipitate was collected by filtration, washed with water, and dried. The resulting solid was mixed with silica gel, placed at the top of a silica gel column, and eluted with methylene chloride. From the eluate there was isolated 1.01 g (52%) of a yellow oil: NMR, an A_2B multiplet at τ 2.2–3.0 (3 H, ArH), a multiplet at 5.8–6.9 (6 H, $ArCH_2$– and ArCH–), a singlet at 7.28 (3 H, $-CH_3$), a singlet at 7.72 (6 H, CH_3S–), and singlets at 8.6 and 9.4 (3 H each, CH_3–); high-resolution mass spectrum m/e 392.137 (calcd for $C_{23}H_{24}N_2S_2$: 392.138). From the NMR spectrum it is clear that **18**, although a mixture of stereoisomers, has entirely the anti geometry.

Treatment of **18** under the conditions for the Hofmann elimination, as described earlier, gave *trans*-1,3-dicyano-2,15,16-trimethyldihydropyrene (**12**) in 25% yield as deep green crystals, mp 197 °C, identical in all respects with the sample of **12** described previously.

Conversion of 18 to 19, 20, 21, and 22. To a solution of 1.01 g of **18** in 50 mL of dry benzene was added dropwise with stirring 5 mL of an 18% solution of diisobutylaluminum hydride in benzene. After the mixture had been stirred at room temperature, it was coooled and successive additions with stirring were made of 10 mL of methanol, 5 mL of water, and 30 mL of dilute aqueous hydrochloric acid. The organic layer was separated, washed with water, dried, and concentrated to give 500 mg (49%) of a pale orange oil: NMR, a singlet at τ −0.68 (2 H, –CHO), an A_2B multiplet at 2.2–3.1 (3 H, ArH), a broad multiplet at 4.7–8.2 (15 H, ArCH<, $ArCH_2$–, $-CH_3$, CH_3S–), and broad singlets at 8.7 and 9.5 (6H, $-CH_3$); high-resolution mass spectrum m/e 398.137 (calcd for $C_{23}H_{26}S_2O_2$: 398.137). The spectral data are fully in accord with the assignment of structure **19** to this oil.

A mixture of 500 mg of **19** and 45 mg of sodium borohydrde in 15 mL of dry tetrahydrofuran was stirred at room temperature for 3 h. It was then decomposed by the addition of dilute aqueous hydrochloric acid. The organic layer was extracted with ether, dried, and concentrated to give 507 mg (100%) of a pale yellow oil: NMR, a multiplet at τ 2.1–3.1 (3 H, ArH), a broad singlet at 5.10 (4 H, $-CH_2OH$), a multiplet at 5.0–7.9 (15 H, ArCH<, $ArCH_2$–, $-CH_3$, CH_3S–), a broad singlet at 8.24 (2 H, –OH), and broad singlets at 8.7 and 9.5 (3 H each, $-CH_3$); high resolution mass spectrum m/e 402.168 (calcd for $C_{23}H_{30}S_2O_2$: 402.169). The spectral data are fully in accord with the assignment of structure **20** to this oil.

To a stirred solution of 107 mg of **20** in 15 mL of dry benzene there was added dropwise a solution of 63 mg of phosphorus tribromide in 3 mL of benzene. After the mixture had been stirred for 2 h, it was washed with ice water, dried, and concentrated to give 94 mg (67%) of a yellow oil: NMR, a multiplet at τ 2.1–3.0 (3 H, ArH), a multiplet at 5.28 (4 H, $-CH_2Br$), a multiplet at 4.6–7.0 (6 H, ArCH<, $ArCH_2$–), a multiplet at 7.0–7.8 (9 H, CH_3–), broad singlets at 8.7 and 9.5 (6 H, CH_3–); mass spectrum m/e 526, 528, and 530 (the relative peak intensities correspond to the expected bromine isotope distribution for $C_{23}H_{28}S_2Br_2$). These spectral data are in accord with the assignment of structure **21** to this oil.

A solution of 94 mg of **21** and 32 mg of 2,6-bis(mercaptomethyl)-toluene in 20 mL of benzene was added dropwise with stirring to a solution of 98 mg of potassium hydroxide in 500 mL of ethanol. When the addition was complete (5 h), the mixture was stirred an additional 12 h and then concentrated. The residue was taken up in benzene and chromatographed over silica gel to give 65 mg of a pale yellow oil: NMR, a multiplet at τ 2.1–3.1 (6 H, ArH), a multiplet at 5.3–8.0 (20 H, ArCH<, $ArCH_2$–, CH_3S–), and a series of broad singlets at 8.5–9.6 (12 H, $-CH_3$); high-resolution mass spectrum m/e 550.185 (calcd for $C_{32}H_{38}S_4$: 550.186). These spectral data are fully in accord with the assignment of structure **22** to this product.

Wittig Rearrangement of 22 to Give 23. To a solution of 51 mg of **22** in 3 mL of dry tetrahydrofuran there was added by syringe 0.10 mL of a 2 N solution of *n*-butyllithium in hexane. After 10 min, 0.03 mL of methyl iodide was added, followed by 5 mL of water. The organic layer was extracted with methylene chloride, washed with water, dried, and concentrated to give 48 mg (89%) of a yellow oil; NMR, a multiplet at τ 2.1–3.1 (6 H, ArH), a multiplet at 5.9–8.0 (12 H, ArCH<, $ArCH_2$–), a series of singlets at 7.8–7.9 (12 H, CH_3S–), and a series of singlets at 8.4–9.6 (12 H, CH_3–); mass spectrum m/e 578. These data are in accord with the assignment of structure **23** to this oil.

Triple-Layered [2.2]Metacyclophane 24. A solution of 48 mg of **23** in 40 mL of a 3:1 mixture of absolute alcohol and benzene containing commercial Raney nickel was boiled under reflux for 18 h. After removal of the Raney nickel and concentration of the filtrate, the residue was taken up in hexane and chromatographed over silica gel. The main fraction of eluate gave 2.5 mg (8%) of colorless crystals. These were purified by sublimation at 150 °C (10^{-4} mm) to give white crystals: mp 320 °C (sealed tube); NMR, an A_2B multiplet at τ 2.88 (4 H, d, J_{AB} = 7 Hz, ArH) and 3.20 (2 H, t, J_{AB} = 7 Hz, ArH), a multiplet at 6.5–7.9 (16 H, $ArCH_2$–), and singlets at 9.34 and 9.54 (6 H each, CH_3–); high-resolution mass spectrum m/e 394.265 (calcd for

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

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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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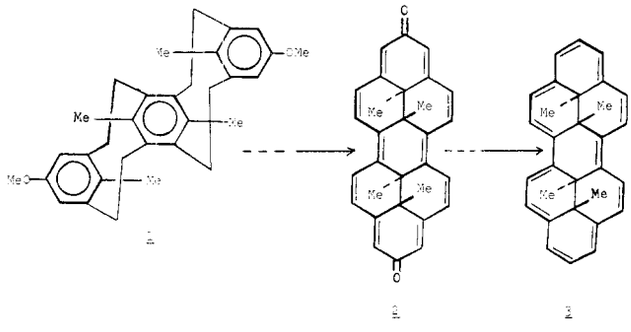
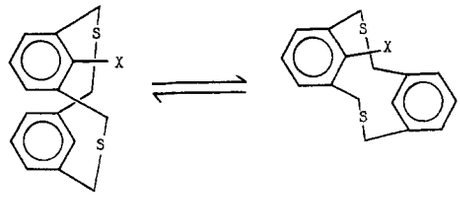
A study has been made of the effect of substituents in influencing the relative amounts of syn and anti isomers formed in the coupling reaction to give substituted 2,11-dithia[3.3]metacyclophanes. Photolytic extrusion of sulfur from *syn*-2,11-dithia-5,7-dicyano-15-methoxy-6,9,18-trimethyl[3.3]metacyclophane (**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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