Medium-Sized Cyclophanes. Part 31.[1] Synthesis and Electrophilic Substitution of 8-Substituted [2]Metacyclo[2](1,3)pyrenophanes

Takehiko Yamato,*[a] Akira Miyazawa[b] and Masashi Tashiro*[c]
[a] *Department of Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi 1, Saga 840, Japan*
[b] *Department of Molecular Science and Technology, Graduate School of Engineering Sciences, Kyushu University, 6-1 Kasuga-kohen, Kasuga-shi, Fukuoka 816, Japan*
[c] *Institute of Advanced Material Study, Kyushu University, 6-1 Kasuga-kohen, Kasuga-shi, Fukuoka 816, Japan*

syn- and *anti*-2,11-Dithia[3]metacyclo[3](1,3)pyrenophanes **15** have been obtained by coupling the corresponding 1,3-bis(bromomethyl)pyrene **11** and 1,3-bis(mercaptomethyl)benzenes **14** in ethanol under high-dilution conditions. Oxidation of the obtained thiametacyclophanes **15** with *m*-chloroperbenzoic acid afforded the corresponding *syn*- and *anti*-disulfones **18**. Pyrolysis of the *syn*- and *anti*-disulfones **18** afforded exclusively the corresponding *anti*-[2]metacyclo[2](1,3)pyrenophane **19** in 40–70% yield along with the ring-cleavage product, 7-*tert*-butyl-1,3-dimethylpyrene **8**. The nitration of 5,15-di-*tert*-butyl-8-methyl- **19b** and 5,15-di-*tert*-butyl-8-methoxy-[2]metacyclo[2](1,3)pyrenophane **19d** with 1 mol equiv. of copper(II) nitrate in acetic anhydride solution exclusively occurred on the more reactive pyrene ring to afford 14-nitro derivatives **21a** and **21b** in 83 and 86% yield, respectively. On the other hand, the bromination of substrates **19** with bromide in methylene dichloride solution afforded 13-bromo derivatives **23** along with the transannular cyclization products **24** and **25**. These different orientations for the electrophilic substitution are also discussed.

Although many cyclophanes having a pyrene skeleton **1** and related compounds have been prepared,[2–8] there have been few investigations of their chemical nature in spite of a large number of reports on their spectroscopic properties. Umemoto *et al.*[2] first reported the synthesis of [2.2](1,3)pyrenophane and triple-layered metacyclopyrenophanes in 1975; these are important as model compounds of transannular π-electronic interaction of excimer fluorescence.[3–7] Later on, Mitchell *et al.*[8] synthesized the internally substituted dithiametacyclopyrenophanes as precursors for the preparation of highly annulated *trans*-10b,10c-dimethyl-10b,10c-dihydropyrenes. Recently, Vögtle *et al.*[9] also synthesized [2.2]cyclophanes containing the pyrene unit in order to investigate their chiroptical properties.

In all the three above reports,[2,8,9] in order to construct the pyrene skeleton, the transannular reaction of 4,6-bis(bromomethyl)[2.2]metacyclophane with bromine is an important key step. The preparation of 1,3-disubstituted pyrenes using regioselective electrophilic disubstitution seems to be quite difficult in spite of the fact that electrophilic substitution of pyrene itself occurs at the 1-, 3-, 6- and 8-position.[10–12] For example, Harvey *et al.*[13] reported that the acetylation of pyrene afforded 1,8-diacetylpyrene as a major product along with the 1,6- and 1,3-analogue. Therefore, the selective preparation of 1,3-disubstituted pyrenes by direct electrophilic aromatic substitution was very difficult because of their low yield as well as the difficulty of their separation from the reaction mixture. Recently, Hempenius *et al.*[14] reported the introduction of methyl groups at the 1-, 2- and 3-position, starting from 1*H*-phenalene in ways other than by direct electrophilic substitution of pyrene itself.[15–17] Thus there is substantial interest in investigating the selective introduction of substituents at positions 1 and 3 in electrophilic substitution.

Quite recently, we have found[18] that the $AlCl_3$-catalysed acetylation of 2,7-di-*tert*-butylpyrene **3** with acetyl chloride using the *tert*-butyl group as a positional protective group to afford only the 4,9-diacetylated product, 4,9-diacetyl-2,7-di-*tert*-butylpyrene. This strategy is also suitable for the preparation of 1,3-disubstituted pyrenes, which afforded convenient starting materials for the attempted preparation of 1,3-bridged benzenopyrenophanes.

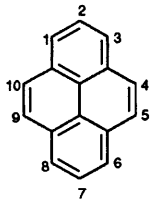


Fig. 1 Numbering scheme for pyrene **1**

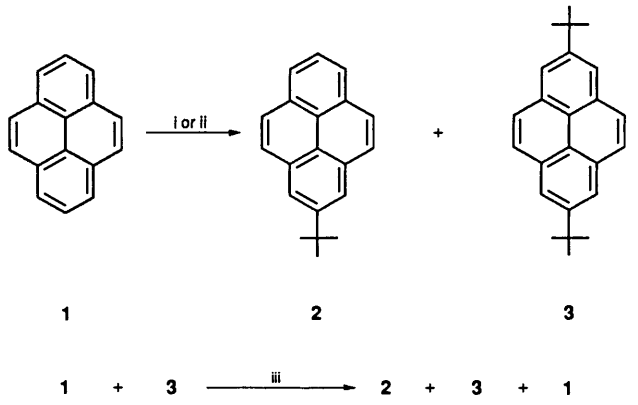
In this paper we report on the first example of the synthesis of a series of 8-substituted [2]metacyclo[2](1,3)pyrenophanes starting from 1,3-bis(bromomethyl)-7-*tert*-butylpyrene, and their reactivity towards electrophilic substitution.

Results and Discussion

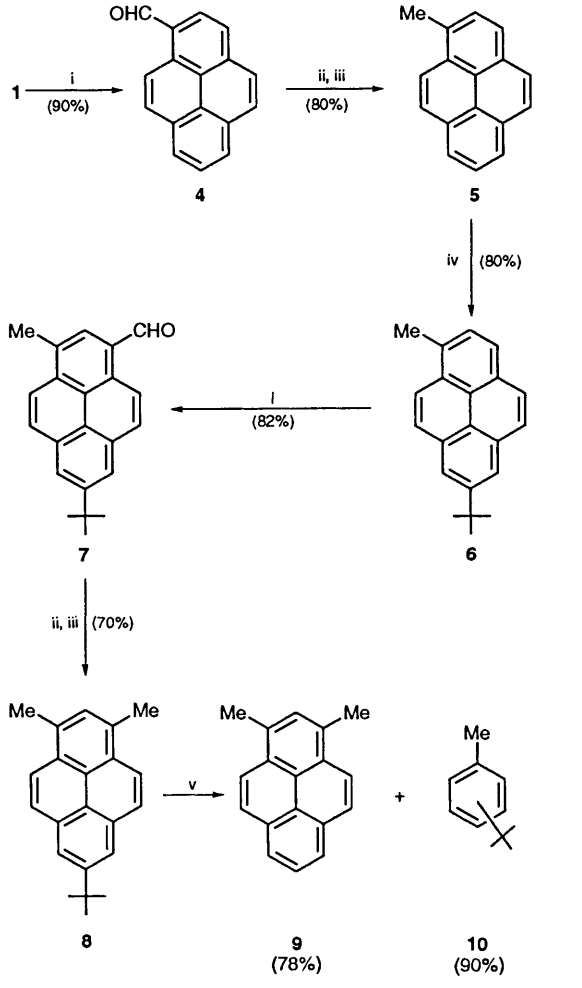
In order to introduce substituents selectively at positions 1 and 3 of the pyrene ring by electrophilic substitution, we have attempted to prepare 2-*tert*-butylpyrene in order to protect one of the active positions of pyrene by a *tert*-butyl group.[19–26]

Attempted mono-*tert*-butylation of pyrene with 1.1 mol equiv. of *tert*-butyl chloride in the presence of various Lewis acids ($AlCl_3$, $TiCl_4$, and $SnCl_4$) led to a mixture of 2-*tert*-butylpyrene **2** and 2,7-di-*tert*-butylpyrene **3** along with recovery of the starting compound, and we were not able to separate these products. The same results were obtained in the case of sulfuric acid-catalysed *tert*-butylation with *tert*-butyl acetate. The attempted $AlCl_3MeNO_2$-catalysed disproportionation of 2,7-di-*tert*-butylpyrene **3** with pyrene also led to the same results (**1**:**2**:**3** = 1:1:2) as shown in Scheme 1.

Since attempted introduction of one *tert*-butyl group on the pyrene ring failed, we next planned the synthetic approach for 1,3-dimethylpyrene **9** as shown in Scheme 2. Thus formylation of pyrene with dichloromethyl methyl ether was carried out in the presence of $TiCl_4$ to afford 1-formylpyrene **4** in 90% yield,



Scheme 1 *Reagents and conditions:* i, Bu'Cl, Lewis acid; ii, Bu'OAc, H_2SO_4; iii, $AlCl_3$–$MeNO_2$, CH_2Cl_2



Scheme 2 *Reagents and conditions:* i, Cl_2CHOMe, $TiCl_4$, CH_2Cl_2; ii, NH_2NH_2, toluene–diethylene glycol, reflux, 1 h; iii, KOH, 180 °C, 3 h; iv, Bu'Cl, $AlCl_3$, room temperature, 1 h; v, Nafion-H, toluene, reflux, 12 h

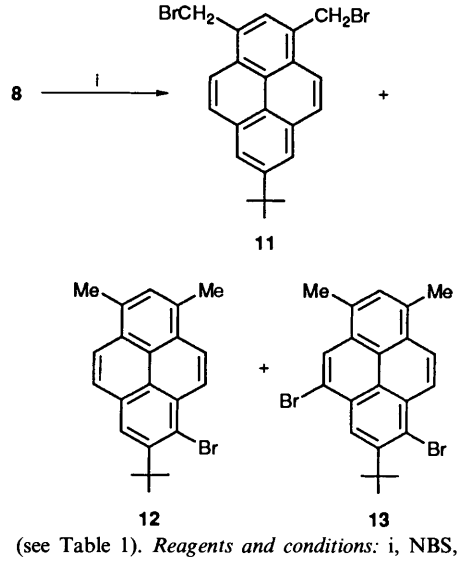
upon which Wolff–Kishner reduction was carried out to give 1-methylpyrene **5** in 80% yield. The $AlCl_3$-catalysed *tert*-butylation of compound **5** with *tert*-butyl chloride afforded 7-*tert*-butyl-1-methylpyrene **6** in 80% yield. 7-*tert*-Butyl-1,3-dimethylpyrene **8** was obtained by the successive formylation of compound **6** with dichloromethyl methyl ether, followed by the reduction of the obtained 7-*tert*-butyl-1-formyl-3-methylpyrene **7**. De-*tert*-butylation of compound **8**, in the presence of Nafion-H as a catalyst,[23–25,27,28] was carried out in boiling toluene to afford the desired 1,3-dimethylpyrene **9** in 78% yield along with *tert*-butyltoluene **10**.

Table 1 Bromination of 7-*tert*-butyl-1,3-dimethylpyrene **8** with NBS

Run	Initiator	Solvent	Conditions	Products (%)[a] 11	12	13
1	BPO	CCl_4	reflux	10	8	5
2	V-65	CH_2Cl_2	reflux	15	11	9
3	AIBN	CH_2Cl_2	reflux	12	15	11
4	V-65	CH_2Cl_2	*hν*[b]	25	18	19
5	V-65	C_6H_6	*hν*[b]	70	5	0
6		CCl_4	r.t.[c]	0	83	8
7[d]		C_6H_6	r.t.[c]	0	7	0

[a] Isolated yields are shown. [b] Tungsten lamp (300 W) was used. [c] Room temperature. [d] Starting compound **8** was recovered (90%).

Bromination of compound **8** with *N*-bromosuccinimide (NBS) to afford 1,3-bis(bromomethyl)-7-*tert*-butylpyrene **11** was carried out under various reaction conditions and the results are compiled in Table 1. As shown in Table 1, when bromination of compound **8** with NBS was carried out in the presence of benzoyl peroxide in carbon tetrachloride at reflux, the desired product **11** was obtained only in 10% yield along with products of the bromination of the pyrene ring, compounds **12** and **13** (Scheme 3). The same results were obtained



Scheme 3 (see Table 1). *Reagents and conditions:* i, NBS, initiator, solvent.

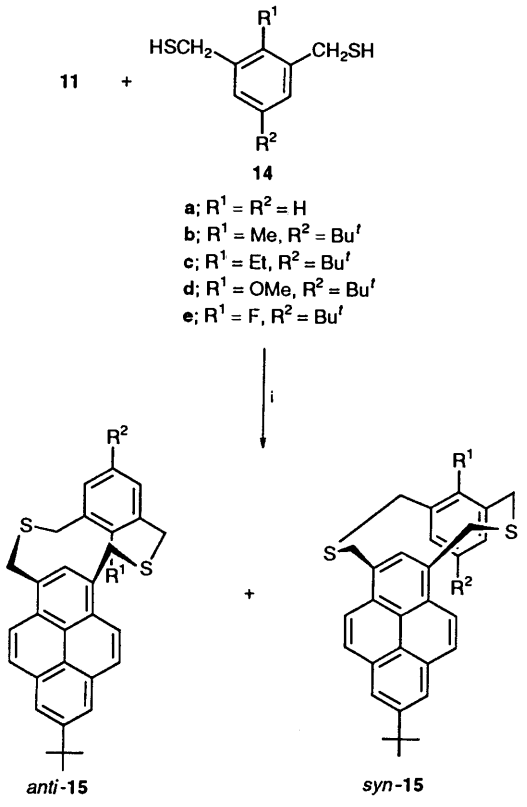
in the presence of a radical initiator such as 2,2'-azo(2,4-dimethylvaleronitrile) (V-65) and azoisobutyronitrile (AIBN) under reflux in methylene dichloride. On the other hand, reaction of compound **8** with NBS in the presence of V-65 in benzene solution under irradiation by a tungsten lamp afforded the desired bis(bromomethyl) compound **11** in 70% yield. However, the same reaction carried out in methylene dichloride solution afforded **11** in only 25% yield. These results seem to indicate that the solvent used might play an important role in this bromination reaction. In fact, the bromination of compound **8** with NBS in carbon tetrachloride or methylene dichloride solution afforded bromides **12** and **13** in 83 and 8% yield, respectively. On the other hand, the same reaction in benzene solution afforded bromide **12** only in 7% yield along with 90% recovery of starting compound. When the same reaction was applied to the bromination of compound **9** with NBS in the presence of V-65 in benzene solution under irradiation by the tungsten lamp, only an inseparable mixture of products was obtained. The total yield of dibromide **11** from pyrene **1** was 26%.

The dithia[3]metacyclo[3](1,3)pyrenophanes **15** were syn-

Table 2 ^{1}H NMR spectral data of [3]metacyclo[3](1,3)pyrenophanes **15**[a]

Compound	Internal pyrene proton, δ	Protons of internal substituent, δ(R)	Benzene protons	*tert*-Butyl protons
syn-**15a**	6.85 (13-H)[b]	6.85 (22-H)[b]	6.85 (18-, 19-, 20-H)[b]	1.57
anti-**15b**	5.85 (22-H)	1.64 (Me)	7.19 (5-, 7-H)	1.02, 1.55
anti-**15c**	6.08 (22-H)	0.85 (Me), 2.49 (CH_2)	7.09 (5-, 7-H)	0.93, 1.56
syn-**15d**	7.64 (22-H)	3.75 (OMe)	6.61 (5-, 7-H)	0.10, 1.56
syn-**15e**	7.63 (22-H)		6.54 (5-, 7-H)	0.12, 1.56

[a] Determined in $CDCl_3$ by using $SiMe_4$ as a reference and expressed in δ(ppm) given. [b] Midpoint value of multiplet.



Yields (%)

a; $R^1 = R^2 = H$	0	38
b; R^1 = Me, R^2 = But	35	0
c; R^1 = Et, R^2 = But	44	0
d; R^1 = OMe, R^2 = But	0	25
e; R^1 = F, R^2 = But	0	41

Scheme 4 *Reagents and conditions:* i, KOH–EtOH, $NaBH_4$, high dilution

thesized by coupling of the 1,3-bis(bromomethyl)-7-*tert*-butylpyrene **11** with 1,3-bis(mercaptomethyl)benzenes **14** under high-dilution conditions in 10% ethanolic potassium hydroxide in the presence of a small amount of sodium borohydride as shown in Scheme 4. *syn*- and *anti*-2,11-Dithia[3]metacyclo[3](1,3)pyrenophane **15** are obtained and the yields of compounds **15** are compiled in Scheme 4.

The structure of compound **15a** was established on the basis of the base peak molecular ion at *m/z* 452 in its mass spectrum, and it was assigned the *syn*-stereochemistry *syn*-**15a** on the basis of its ^{1}H NMR spectrum by comparison with those of the known *syn*-cyclophanes **16** and **17**, since the 13- and 22-aryl protons (Fig. 2) of *syn*-**15a** appear at δ 6.85 (those for **16** are at δ 6.82; those for **17** are at δ 6.73 and 6.94),[29,30] whereas if compound **15a** existed as the *anti* conformer they might be expected to be shielded by the opposite ring to $\delta \sim 5$. Furthermore the 18-, 19-, 20-aryl hydrogens can clearly be seen to be shielded at δ 6.85 by the adjacent ring, a common

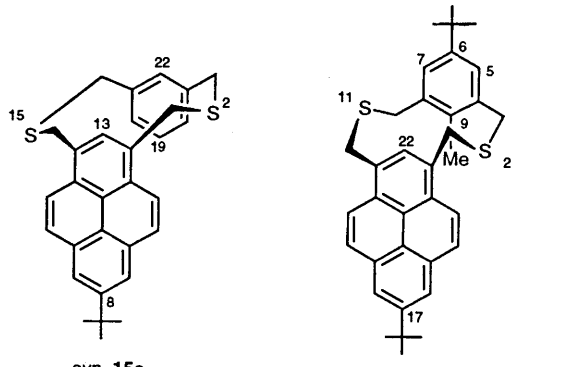
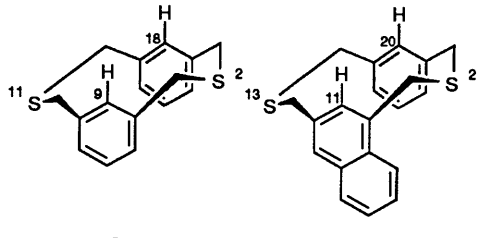


Fig. 2 Numbering scheme for [3]metacyclo[3]pyrenophanes *syn*-**15a** and *anti*-**15b**

consequence with face-to-face benzene rings.[31] The same upfield shift of the 5-, 7-aryl hydrogens was observed in *syn*-**15d** and *syn*-**15e**. Also, one of the *tert*-butyl protons of *syn*-**15d** and *syn*-**15e** was observed upfield, δ 0.10 and 0.12, due to the strong shielding effect of the pyrene ring (see Table 2). In the case of syn-**15e**, the internal pyrene proton (22-H) appeared as a doublet (*J* 2.0 Hz) because of the coupling with the fluorine atom on the opposite benzene ring. These observations strongly suggest that compounds **15a**, **15d** and **15e** adopt the *syn*-conformation.

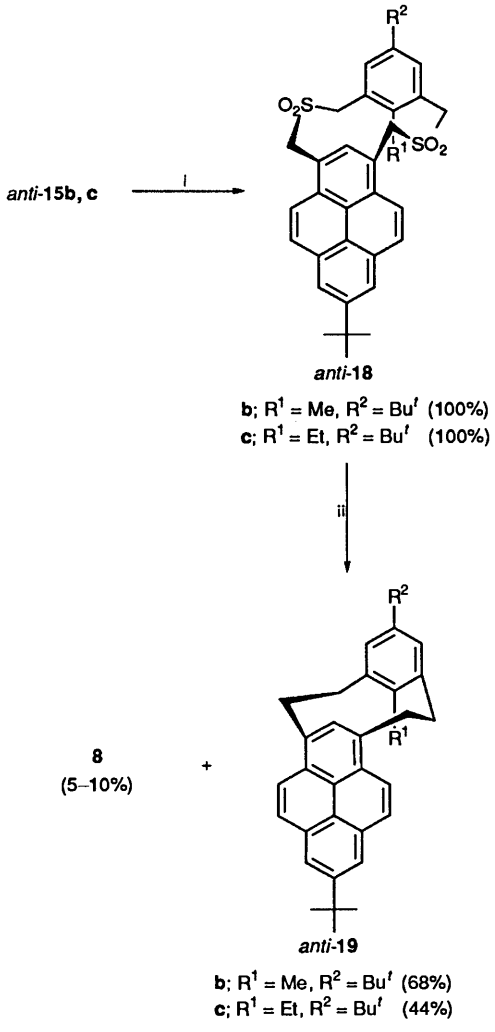
The assignment of structure to *anti*-conformer **15b** was readily apparent from its ^{1}H NMR spectra. Thus, the internal proton of the pyrene ring and methyl protons should show an upfield shift due to the ring current of the opposite aromatic ring for the *anti*-conformation.[32,33] The ^{1}H NMR spectrum of compound **15b** showed the internal proton and methyl protons at δ 5.85 and 1.60. The same upfield shift of the internal proton and ethyl protons was observed in *anti*-**15c**. These observations strongly suggest that compounds **15b** and **15c** adopt the *anti*-conformation.

Dependent on the nature of substituents R^1 and R^2, different yields (inversion of selectivity) of *anti*-**15** and *syn*-**15** were obtained. Thus, 9-methyl (**15b**) and 9-ethyl (**15c**) analogues are exclusively formed in the *anti*-conformer, but other 9-unsubstituted and 9-methoxy and 9-fluoro analogues are exclusively formed as the *syn*-conformers. These findings



suggest that in the case of the 9-methyl and 9-ethyl analogues the aromatic π-π interaction of two opposite benzene rings and the steric crowding at internal positions 9 and 22 may inhibit formation of the *syn*-conformer in the [3.3]MCP (metacyclopyrene) system and, in turn, the C–H–π interaction[34] between the methyl or ethyl group and the opposite aromatic π-electrons may favour the formation of the *anti*-conformer in the process of cyclization. The CH–π interaction involving aliphatic CH moieties is well documented[34a] as either a conformation-controlling intramolecular process or a crystal-structure-controlling intermolecular force, especially for inclusion complexes of calixarene derivatives.[34b–h] In contrast, in the case of the 9-methoxy and 9-fluoro analogues the through-space interaction between the non-bonding electron pairs of the oxygen atom of the methoxy group or the fluorine group and the opposite aromatic π-electrons of the *anti*-conformer may disfavour the formation of the latter.

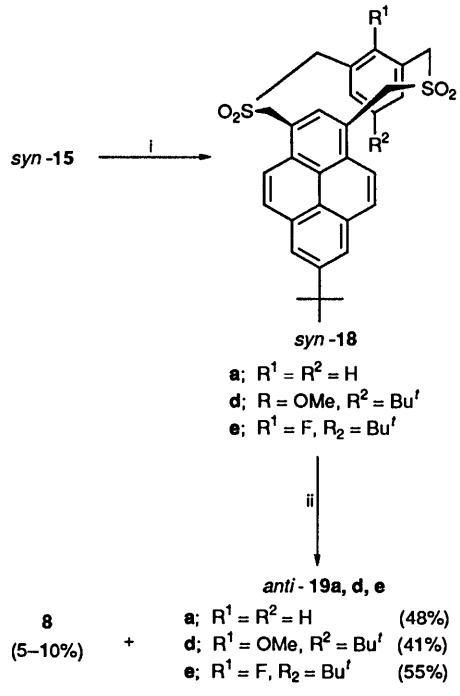
Oxidation of *anti*-**15b** with *m*-chloroperbenzoic acid (MCPBA) at room temp. for 6 h afforded the desired disulfone *anti*-**18b** only in 30% yield along with large amounts of unidentified resinous materials. Treatment of 7-*tert*-butyl-1,3-dimethylpyrene **8** with MCPBA under the same conditions also afforded large amounts of unidentified resinous materials. This result might indicate that, in the reaction of *anti*-**15b** with MCPBA, the oxidation of sulfur atoms competes with the oxidation of the pyrene ring. On the other hand, when oxidation was carried out at −5 °C for 6 h, the disulfone *anti*-**18b** was obtained in almost quantitative yield (Scheme 5).



Scheme 5 *Reagents and conditions:* i, MCPBA, $CHCl_3$, −5 °C, 6 h; ii, 480 °C, 0.8 mmHg

Oxidation of other thiametacyclophanes, *syn*- and *anti*-**15**, furnishes the corresponding sulfones *syn*- and *anti*-**18** in almost quantitative yield (Scheme 5, 6). There is no exchange between the *syn*- and *anti*-conformers during the oxidation of sulfides **15** to sulfones **18**.

Pyrolysis of compounds *anti*-**18** under reduced pressure (0.8 Torr) was carried out according to the reported method[35–37] to afford the corresponding *anti*-8-substituted [2]metacyclo-[2](1,3)pyrenophanes *anti*-**19** in 44–68% yield along with ring-cleavage product **8** in 5–10% yield (Scheme 5). Compounds *syn*-**18a**, **d**, **e** gave the less strained *anti*-conformer of **19** exclusively, the *syn* conformer not being detected by ^1H NMR spectroscopy (Scheme 6).



Scheme 6 *Reagents and conditions:* i, MCPBA, $CHCl_3$, −5 °C, 6 h: ii, 480 °C, 0.8 mmHg

The structures of *anti*-**19** stereoisomers were readily apparent from their ^1H NMR spectra (270 MHz; $CDCl_3$). The chemical shifts of only the internal protons at position 12 or 20 and the internal protons of the substituent at position 8 are summarized in Table 3. The corresponding proton signals of the corresponding proton at position 2 of 7-*tert*-butyl-1,3-dimethylpyrene **8** and protons of the substituent at position 2 of

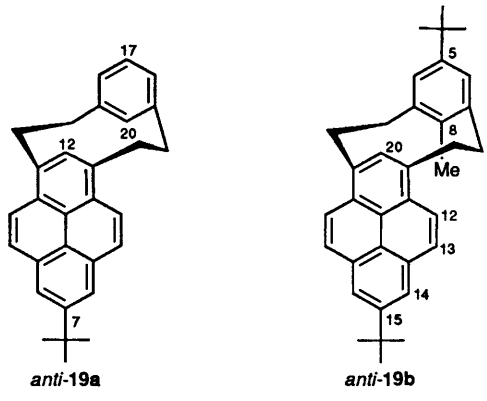
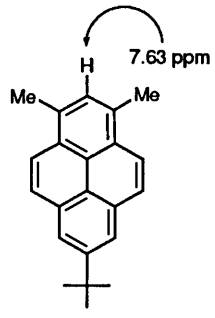


Fig. 3 Numbering scheme for [2]metacyclo[2]pyrenophanes *anti*-**19a** and *anti*-**19b**

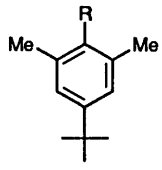
Table 3 ^{1}H NMR spectral data of [2]metacyclo[2](1,3)pyrenophanes **19**[a]

Compound	Internal pyrene proton		Protons of internal substituent		
	δ_H	$\Delta\delta$[b]	δ_{MCP}(R)	δ_{BMX}(R)	$\Delta\delta$(R)[b]
19a	5.09 (12-H)	2.54	3.54 (20-H)	6.79	3.25
19b	4.53 (20-H)	3.10	−0.29 (Me)	2.10	2.39
19c	4.50 (20-H)	3.13	−0.10 (Me), 0.11 (CH_2)	1.07, 2.56	1.17, 2.45
19d	4.86 (20-H)	2.77	2.35 (OMe)	3.65	1.30
19e	5.16 (20-H)	2.47			

[a] Determined in $CDCl_3$ by using $SiMe_4$ as a reference and expressed in δ(ppm) given. [b] $\Delta\delta = \delta$(BMX) − δ(cyclophane).



8



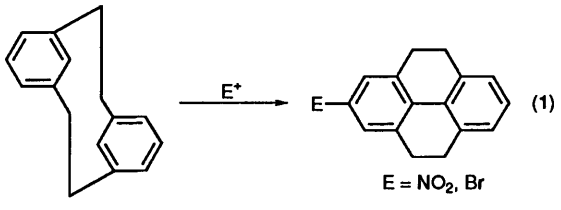
20a; R = H
b; R = Me
c; R = Et
d; R = OMe

2-substituted 5-*tert*-butyl-*m*-xylenes (BMX) **20**[32,33] as well as the differences ($\Delta\delta$) in the chemical shifts of *anti*-**19** from those of BMX are shown in Table 3.

The effect of the ring current of the opposite aromatic ring on the internal protons may be judged by the values of the shift differences ($\Delta\delta$) since there is no ring current in the opposite aromatic ring in the pyrene **8** and BMX **20** systems. The data of Table 3 show that the proton of the internal position 12 or 20 on the pyrene ring is clearly shifted upfield ($\Delta\delta$ 2.47–3.13 ppm) by the ring current in the opposite benzene ring, which values are consistent with that of [2.2]MCP ($\Delta\delta$ 3 ppm).[38] On the other hand, the internal proton 20-H on the benzene ring in *anti*-**19a** shows an upfield shift at δ 3.54 due to the strong ring current in the opposite pyrene ring,[32,33] which is observed at the highest field in the known [2.2]MCPs (δ 4.25). The larger differences ($\Delta\delta$) of the chemical shifts of the protons of internal substituents at position 8 compared with those of the corresponding [2.2]MCPs[32,33] were also observed in *anti*-**19b–d** to be $\delta \sim 0.51$–0.76. These phenomena were attributable to the much stronger ring current effect in the pyrene ring than that in the benzene ring.

Owing to electronic interaction between the two benzene rings, the proximity of the C-8 and C-16 positions, and considerable strain energy, [2.2]MCP is prone to undergo transannular reactions.[39–43] These have usually been rationalized as involving initial dehydrogenation to 4,5,9,10-tetrahydropyrene. Sato *et al.*[44] have reported that the reaction of 8,16-unsubstituted [2.2]MCP with bromine in the presence of iron powder affords the corresponding tetrahydropyrene *via* an addition–elimination mechanism [equation (1)].

Subsequently, we reported[45–47] the unique behaviour of

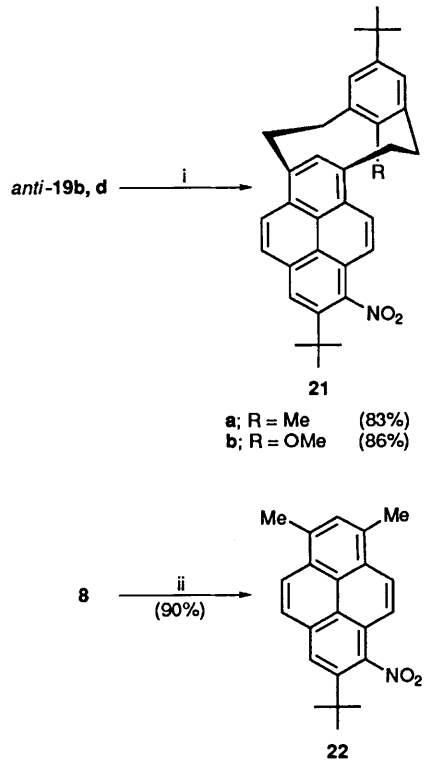


(1)

8-substituted [2.2]MCPs on the electrophilic aromatic substitution affording the corresponding tetrahydropyrenes resulted in the transannular reaction as well as the isomerization. On the other hand, as mentioned previously, although various pyrenophanes have been prepared, their chemistry nature is still largely unknown. The structure of 8-substituted [2]metacyclo-[2](1,3)pyrenophanes **19** formally corresponds with that of 8-substituted [2.2]MCP which is connected at the 1,3-positions of the benzene ring. Thus, there is substantial interest in investigating the effects of the pyrene ring on the electrophilic aromatic substitution of 8-substituted [2]metacyclo[2](1,3)-pyrenophanes **19** prepared in the present paper. Nitration and bromination of pyrenophanes **19** were investigated in order to obtain information about their chemical reactivity towards electrophilic substitution in the present work.

Nitration of *anti*-**19b**, **d** with copper(II) nitrate in acetic anhydride, which is a well known, mild nitrating reagent, was carried out at room temperature to afford 14-nitro substitution products **21a**, **b** in 83 and 86% yield, respectively (Scheme 7). No corresponding transannular cyclization and isomerization products were observed, thus making this reaction different from the nitration of the corresponding 8-methyl- and 8-methoxy-[2.2]MCP, which afforded the transannular and isomerization products.[45] In the case of the nitration of the corresponding 5,13-di-*tert*-butyl-8-methyl- and 5,13-di-*tert*-butyl-8-methoxy-[2.2]MCP, interannular bond formation at the 8- and 16-position is concerted with nitronium ion attack at the *ipso* position of the one *tert*-butyl group of the internally methyl- and methoxy-substituted benzene ring. In contrast, in the case of [2]metacyclo[2](1,3)pyrenophanes **19** the nitronium ion attack exclusively on the pyrene ring occurred due to the higher π-basicity of the pyrene ring compared with that of benzene ring. The π-complex transition state in the normal aromatic nitration[48] may be proposed as a reason for this. The relatively easy electrophilic substitution at a position *ortho* to a *tert*-butyl group (6- or 8-position) on the pyrene ring is remarkable because usually the steric bulkiness of a *tert*-butyl group might direct the substitution towards another position on the pyrene ring. This result is strongly attributable to the high reactivity of the 1-, 3-, 6- and 8-position on the pyrene ring.

The structures **21a** and **21b** were readily apparent from their ^{1}H NMR spectra. For example, the ^{1}H NMR spectral data (270 MHz; $CDCl_3$) of compound **21a** show an original upfield shift of the internal pyrene proton at δ 4.87 and methyl protons at δ −0.43 due to the cyclophane structure, and 4 sets of doublets with the coupling constant J = 9.5 Hz at δ 7.64, 7.90, 8.75 and 8.77, which are assigned to the protons at positions 4, 5, 9, and 10 on the pyrene ring (pyrene numbering). The same ^{1}H NMR spectral pattern was observed in compound **21b**. These data strongly support the assignment of these structures as 14-nitro-[2]metacyclo[2](1,3)pyrenophanes **21a** and **21b**. It was also found that the required reaction time in nitration of pyrenophanes *anti*-**19b** and **19d** was only 30 min for completion of the reaction instead of the 5 h needed in the case of nitration of 7-*tert*-butyl-1,3-dimethylpyrene **8** to give 2-*tert*-butyl-6,8-



Scheme 7 *Reagents and conditions:* i, $Cu(NO_3)_2$, Ac_2O, room temperature, 30 min; ii, $Cu(NO_3)_2$, Ac_2O, room temperature, 5 h

dimethyl-1-nitropyrene **22** under the same conditions. This finding suggests that in metacyclopyrenophane systems an initial σ-complex intermediate would be stabilized by a through-space electronic interaction with the opposing benzene ring, thus accelerating the reaction.

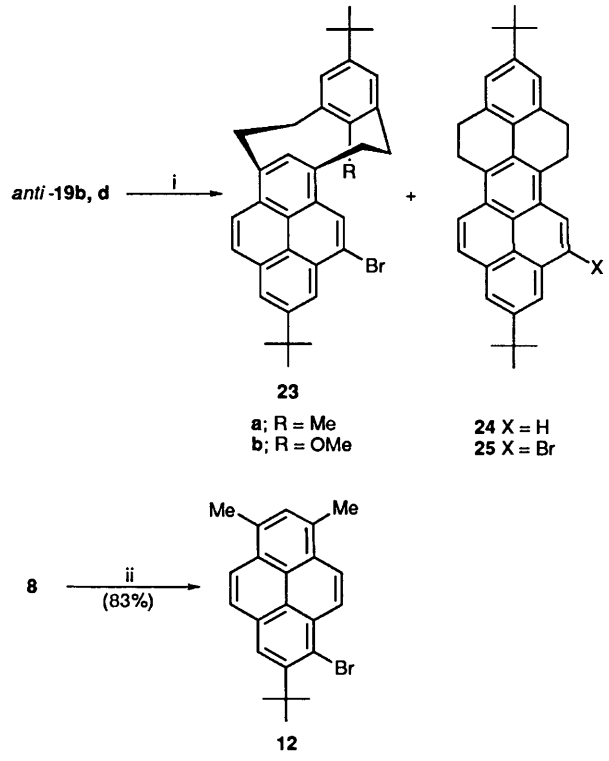
When the 8-methyl[2]metacyclo[2](1,3)pyrenophane (*anti*-**19b**) was treated with 1.1 mol equiv. of bromine in methylene dichloride at 0 °C for 1 min, the monobrominated compound **23a** was obtained in 62% yield along with 20% recovery of the starting compound (Scheme 8). None of the transannular cyclization product was detected as in the nitration of the corresponding 8-methyl[2.2]MCPs.[45] The structure **23a** was readily apparent from the ^1H NMR spectrum. The ^1H NMR spectral data (270 MHz; $CDCl_3$) of compound **23a** show upfield shifts of the internal pyrene proton at δ 4.51 and methyl protons δ −0.28 due to the cyclophane structure, and 2 sets of doublets with the *ortho*-coupling constant (J 9.3 Hz) at δ 8.06 and 8.39 as well as 2 sets of doublets with the *meta*-coupling constant (J 1.8 Hz) at δ 8.24 and 8.60, which are assigned to the protons of positions 9, 10 and 6, 8 on the pyrene ring, respectively. These data strongly support the assignment of the structure as the 13-bromo[2]metacyclo[2](1,3)pyrenophane **23a**.

When the 8-methoxy[2]metacyclo[2](1,3)pyrenophane *anti*-**19d** was treated with 1.1 mol equiv. of bromine in methylene dichloride at 0 °C for 1 min, the 13-monobrominated compound **23b** was obtained in 37% yield along with the transannular cyclization product **24** in 16% yield (Table 4, run 2). Although compound **24** was separated pure by fractional recrystallization of the reaction mixture, attempted isolation of bromide **23b** failed. It was also found that the same bromination carried out with 2.2 mol equiv. of bromine gave 7-bromo-2,9-di-*tert*-butyl-4,5,13,14-tetrahydrodibenzo[*cd*,*lm*]perylene **25** in quantitative yield. These results strongly suggest that compounds **23b** and **24** were the intermediates for the formation of heptacycle **25**. Indeed, a mixture of compounds **23b** and **24** could be treated with 1.1 mol equiv. of bromine

Table 4 Bromination of *anti*-5,15-di-*tert*-butyl-8-substituted [2]metacyclo[2](1,3)pyrenophanes **19** and the dibenzo[*cd*,*lm*]perylene **24**

Run	Substrate	Br_2/Substrate [mol/mol]	Time (t/h)	Products (%)[a]
1	**19b**	1.1	1	**23a** (62)[b]
2	**19d**	1.1	1	**23b** (37), **24** (16)[c]
3	**19d**	2.2	3	**25** (100)
4	**24**	1.1	1	**25** (100)

[a] Isolated yields are shown. [b] Starting compound **19b** was recovered (20%). [c] Starting compound **19d** was recovered (16%).



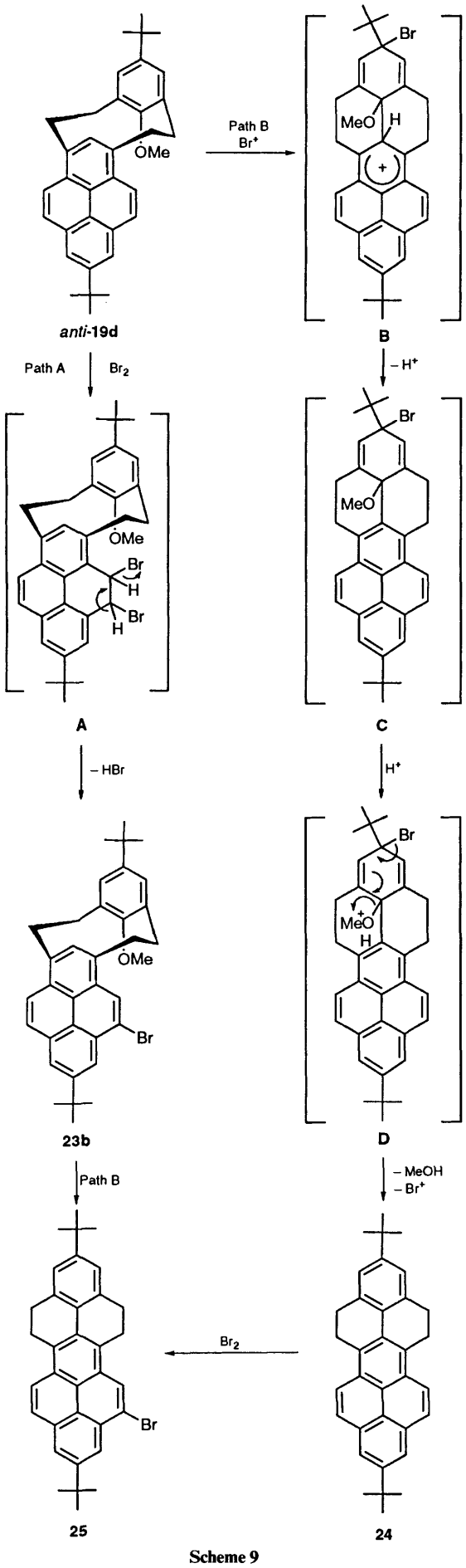
Scheme 8 (see Table 4). *Reagents and conditions:* i, Br_2, CH_2Cl_2, 0 °C; ii, Br_2, CH_2Cl_2, room temperature, 2 h

under the same conditions as above to afford a single product, compound **25**, in almost quantitative yield.

The different orientation of bromination of the pyrene ring of 8-substituted metacyclopyrenophanes **19** were first observed to be different from that in the bromination of 7-*tert*-butyl-1,3-dimethylpyrene to give the corresponding 1-bromopyrene **12** and from the nitration of compounds **19** to give the corresponding 14-nitrometacyclopyrenophane **21**. The only transannular cyclization of 8-methoxy analogue **19d** occurred upon bromination and not upon nitration. A σ-complex intermediate for the transition state of the present bromination, which easily forms because of stabilization by spatial interaction with the second pyrene ring, may be proposed. The correlation between relative rates of certain halogenations and σ-basicities is known to be excellent.[48]

Although the detailed mechanism of formation of the 13-bromometacyclopyrenophane **23** and tetrahydrodibenzo[*cd*,*lm*]perylenes **24**, **25** is not clear, one might assume the reaction pathway shown in Scheme 9.

It is well recognized that the double bond at the 4 and 5 positions of pyrene exhibits olefinic properties. Therefore dichlorocarbene reacts with pyrenes regioselectively at the 4 and 5 positions.[49] Thus, owing to the increased strain in the pyrene ring in the metacyclopyrenophane **19**, the olefinic character of



Scheme 9

the double bond at C-4 and -5 (pyrene-ring numbering) further increased. Subsequently, much more favourable bromine addition to the double bond at C-4 and -5 compared with electrophilic substitution might proceed to form intermediate **A**, from which elimination of hydrogen bromide could occur to afford the 13-bromometacyclopyrenophane **23b**. Elimination of Br^- at position 12 might be favourable over that at C-13 because of the release of its sterically crowded environment between the ethylene bridge as demonstrated by molecular models (Path A in Scheme 9). On the other hand, formation of the transannular reaction product **24** could compete with the above bromine addition as shown in Path B in Scheme 9. Thus, it seems reasonable to assume that interannular bond formation at the 8- and 20-position is concerted with bromophilic attack at the *ipso* position of the *tert*-butyl group to form intermediate **B** *via* the same reaction path as previously reported.[45] The aromatization transforms intermediate **B** into species **C** generating acid which can facilitate removal of the methoxy group and Br^+ from protonated ether **D** accompanied by the restoration of aromaticity. This novel transannular cyclization reaction can be attributed to the methoxy group at the 8-position, which has good leaving-group ability (nucleofugacity), particularly when protonated by acid generated in the system, and so may be important, *e.g.* in preventing reversal of the steps between intermediates **B** and **D**. The formation of the 7-bromo-4,5,13,14-tetrahydrodibenzo[*cd*,*lm*]perylene **25** might come from the competitive reaction of further bromination of heptacycle **24** and the transannular reaction of the MCP **23b** as in Path B.

Conclusions.—The preparation of 8-substituted [2]metacyclo[2](1,3)pyrenophanes **19** using a *tert*-butyl group as a positional protecting group on the aromatic ring appears to be a useful route to such compounds. In the metacyclopyrenophane system an initial σ-complex intermediate would be formed by a through-space electronic interaction with the opposing benzene ring, thus accelerating the reaction in nitration and bromination. The different orientation of bromination of the pyrene ring of 8-substituted metacyclopyrenophanes **19** was first observed in the same bromination of 7-*tert*-butyl-1-3-dimethylpyrene **8** to give the corresponding 1-bromopyrene **12** and in the nitration of compounds **19** to give the corresponding 14-nitrometacyclopyrenophanes **21**. The present transannular reaction of 8-substituted [2]metacyclo[2](1,3)pyrenophanes **19** to afford products **23b** and **24** is strongly affected by the bulkiness and ease of removal of the substituent at the 8-position which increases the strain in the molecule. These results will open up new mechanistic aspects for cyclophane chemistry. Further studies on the electrophilic substitution of [2]metacyclo[2](1,3)pyrenophanes **19** are now in progress.

Experimental

All m.p.s. and b.p.s. are uncorrected. M.p.s. were measured on a Yanagimoto MP-S1. NMR spectra were determined at 270 MHz with a Nippon Denshi JEOL FT-270 NMR spectrometer with $SiMe_4$ as internal reference; *J* values are given in Hz. IR spectra were measured for samples as KBr pellets or a liquid film on NaCl plates in a Nippon Denshi JIR-AQ2OM spectrophotometer. Mass spectra were obtained on a Nippon Denshi JMS-01SA-2 spectrometer at 75 eV using a direct-inlet system through GLC.

Preparation of Pyrene-1-carbaldehyde **4**.—To a stirred solution of pyrene **1** (5.0 g, 25 mmol) and dichloromethyl methyl ether (3.7 g, 32 mmol) in CH_2Cl_2 (200 cm^3) was added, at 0 °C, a solution of titanium tetrachloride (5 cm^3, 45.6 mmol) in CH_2Cl_2 (10 cm^3) and the mixture was stirred for 3 h at room

temperature. The reaction mixture was poured into a large amount of ice–water and extracted with CH_2Cl_2 (200 cm^3 × 2). The organic layer was washed with water (300 cm^3 × 2), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed over silica gel (Wako, C-300; 200 g) with hexane as eluent to give starting compound pyrene **1** (340 mg, 7.8% recovery); elution with benzene as eluent to give a yellow solid, which was recrystallized from hexane to afford the *title compound* **4** (5.1 g, 90%) as pale yellow prisms, m.p. 126–127 °C (lit.,[11] 126 °C).

Preparation of 1-*Methylpyrene* **5**.—To a stirred solution of aldehyde **4** (50 g, 217 mmol) in toluene (150 cm^3)–diethylene glycol (150 cm^3) was added hydrazine hydrate (40.0 g, 800 mmol) and the mixture was refluxed for 1 h. After the toluene and water thus formed had been removed by distillation the reaction mixture was cooled to room temperature. To the mixture was added potassium hydroxide (60.0 g, 1 mol) and the mixture was heated at 180 °C for 3 h. After the reaction mixture had cooled to room temperature, it was poured into a large amount of ice–water and extracted with CH_2Cl_2. The organic layer was separated, washed with water, dried over Na_2SO_4, and concentrated. The residue was chromatographed over silica gel (Wako, C-300; 500 g) with hexane as eluent to give a solid, which was recrystallized from hexane to afford the *title compound* **5** (40.7 g, 80%) as crystals, m.p. 68–70 °C (lit.,[11] 70–71 °C.

Preparation of 7-tert-*Butyl*-1-*methylpyrene* **6**.—To a stirred solution of compound **5** (40.0 g, 187 mmol) and *tert*-butyl chloride (18.5 g, 200 mmol) in CH_2Cl_2 (300 cm^3) was added, at 0 °C, aluminium chloride (25.0 g, 187 mmol) and the mixture was stirred for 2 h at room temperature. The reaction mixture was poured into a large amount of ice–water and was extracted with CH_2Cl_2 (200 cm^3 × 3). The extract was washed with water (200 cm^3 × 2), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed over silica gel (Wako, C-300; 500 g) with hexane as eluent to give a solid, which was recrystallized from hexane to afford the *title compound* **6** (40.7 g, 80%) as prisms, m.p. 99–100 °C; ν_{max}(KBr)/cm^{-1} 3100, 2950, 1590, 1460, 1380, 1360, 1300, 1220, 1170, 1140 and 920; δ_H($CDCl_3$) 1.58 (9 H, s), 2.95 (3 H, s) and 7.70–9.20 (8 H, m); *m/z* 272 (M^+) (Found: C, 92.5; H, 7.4. $C_{21}H_{20}$ requires C, 92.60; H, 7.40%).

Preparation of 7-tert-*Butyl*-3-*methylpyrene*-1-*carbaldehyde* **7**.—To a stirred solution of compound **6** (60.0 g, 220 mmol) and dichloromethyl methyl ether (50.0 g, 440 mmol) in CH_2Cl_2 (600 cm^3) was added, at 0 °C, a solution of titanium tetrachloride (24 cm^3, 218.9 mmol) in CH_2Cl_2 (50 cm^3) and the mixture was stirred for 2 h at room temperature. The reaction mixture was poured into a large amount of ice–water and extracted with CH_2Cl_2 (250 cm^3 × 2). The organic layer was washed with water (300 cm^3 × 2), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed over silica gel (Wako, C-300; 500 g) with benzene as eluent to give a yellow solid, which was recrystallized from hexane–$CHCl_3$ (1 : 1) to afford the *title compound* **7** (54.0 g, 82%) as pale yellow prisms, m.p. 238–238.5 °C; ν_{max}(KBr)/cm^{-1} 3050, 2950, 1670, 1570 and 1470; δ_H($CDCl_3$) 1.60 (9 H, s), 3.00 (3 H, s), 8.22 (1 H, d, *J* 9.3), 8.24 (1 H, d, *J* 9.3), 8.25 (1 H, d, *J* 9.3), 8.26 (1 H, s), 8.33 (2 H, s), 9.33 (1 H, d, *J* 9.3) and 10.77 (1 H, s); *m/z* 300 (M^+) (Found: C, 88.0; H, 6.8. $C_{22}H_{20}O$ requires C, 87.96; H, 6.71%).

Preparation of 7-tert-*Butyl*-1,3-*dimethylpyrene* **8**.—To a stirred solution of aldehyde **7** (20.0 g, 67 mmol) in toluene (50 cm^3)–diethylene glycol (30 cm^3) was added hydrazine hydrate (16.0 g, 320 mmol) and the mixture was refluxed for 1 h. After the toluene and water thus formed had been removed by distillation the reaction mixture was cooled to room temperature. Potassium hydroxide (10.0 g, 192 mmol) was added and the mixture was heated at 180 °C for 3 h, cooled to room temperature, poured into a large amount of ice–water and extracted with CH_2Cl_2. The organic layer was separated, washed with water, dried over Na_2SO_4, and concentrated. The residue was chromatographed over silica gel (Wako, C-300; 500 g) with hexane as eluent to give a solid, which was recrystallized from hexane to afford the *title compound* **8** (13.3 g, 70%) as prisms, m.p. 221–221.5 °C; ν_{max}(KBr)/cm^{-1} 2950, 1600, 1450 and 1380; δ_H($CDCl_3$) 1.51 (9 H, s), 2.86 (6 H, s), 7.63 (1 H, s), 7.98 (2 H, d, *J* 10.1), 8.10 (2 H, s) and 8.12 (2 H, d, *J* 10.1); *m/z* 286 (M^+) (Found: C, 92.5; H, 7.6. $C_{22}H_{22}$ requires C, 92.26; H, 7.74%).

Preparation of 1,3-*Dimethylpyrene* **9**.—A solution of compound **8** (200 mg, 0.70 mmol) in toluene (5 cm^3) containing Nafion-H (200 mg) was refluxed under nitrogen for 12 h. After the reaction mixture had cooled to room temperature, it was filtered and the filtrate was concentrated. The residue was chromatographed over silica gel (Wako, C-300; 50 g) with hexane as eluent to give a solid, which was recrystallized from hexane to afford the *title compound* **9** (125 mg, 78%), m.p. 142–143 °C; ν_{max}(KBr)/cm^{-1} 3050, 2950, 1600, 1450, 1370, 1260, 1180 and 1060; δ_H($CDCl_3$) 2.93 (6 H, s), 7.72 (1 H, s), 7.95 (1 H, d, *J* 7.7), 8.02 (2 H, d, *J* 9.2) 8.13 (2 H, t, *J* 7.7) and 8.20 (2 H, d, *J* 9.2); *m/z* 230 (M^+) (Found: C, 93.8; H, 6.5. $C_{18}H_{14}$ requires C, 93.87; H, 6.13%).

Preparation of 1,3-*Bis*(*bromomethyl*)-7-tert-*butylpyrene* **11**.—A solution of compound **8** (2.2 g, 7.69 mmol), NBS (2.74 g, 15.4 mmol), and V-65 (200 mg) in benzene (150 cm^3) was irradiated with a tungsten lamp for 2 h. The reaction mixture was poured into aq 5% $NaHCO_3$ (300 cm^3) and extracted with benzene (100 cm^3 × 2). The benzene extract was washed with water and dried (Na_2SO_4), and concentrated. The residue was recrystallized from hexane–benzene (1 : 1) which afforded *dibromide* **11** (2.4 g, 70%) as pale yellow needles, m.p. 229–231 °C; ν_{max}(KBr)/cm^{-1} 2950, 2900, 1590, 1380 and 1200; δ_H($CDCl_3$) 1.59 (9 H, s), 5.17 (4 H, s), 7.98 (1 H, s), 8.21 (2 H, d, *J* 9.2), 8.30 (2 H, s) and 8.31 (2 H, d, *J* 9.2); *m/z* 442, 444 and 446 (M^+) (Found: C, 59.4; H, 4.7. $C_{22}H_{20}Br_2$ requires C, 59.49; H, 4.54%).

Preparation of 1-*Bromo*-2-tert-*butyl*-6,8-*dimethylpyrene* **12**.—A solution of compound **8** (2.2 g, 7.69 mmol) and NBS (2.74 g, 15.4 mmol) in carbon tetrachloride (150 cm^3) was stirred at room temperature for 2 h. The reaction mixture was poured into aq. 5% $NaHCO_3$ (300 cm^3) and extracted with CH_2Cl_2 (100 cm^3 × 2). The extract was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako, C-300; 50 g) with hexane–benzene (1 : 1) as eluent to give crude bromination products **12** and **13** as solids. Recrystallization of crude compounds **12** and **13** from hexane–$CHCl_3$ (1 : 1) and from hexane, respectively, afforded bromide **12** (2.33 g, 83%) and dibromide **13** (273.3 mg, 8%), respectively, each as prisms.

1-*Bromo*-2-tert-*butyl*-6,8-*dimethylpyrene* **12**, m.p. 255–257 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2960, 1600, 1580, 1450 and 1380; δ_H($CDCl_3$) 1.80 (9 H, s), 2.92 (6 H, s), 7.71 (1 H, s), 7.97 (1 H, d, *J* 9.2), 8.18 (1 H, d, *J* 9.2), 8.24 (1 H, d, *J* 9.7), 8.25 (1 H, s) and 8.68 (1 H, d, *J* 9.7); *m/z* 364 and 366 (M^+) (Found: C, 72.2; H, 5.85. $C_{22}H_{21}Br$ requires C, 72.33; H, 5.99%).

1,4-*Dibromo*-2-tert-*butyl*-6,8-*dimethylpyrene* **13**, m.p. 265–267 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2950, 1605, 1460, 1360 and 1080; δ_H($CDCl_3$) 1.83 (9 H, s), 2.90 (3 H, s), 2.93 (3 H, s), 7.72 (1 H, s), 8.27 (1 H, d, *J* 9.9), 8.53 (1 H, s), 8.72 (1 H, s) and 8.73 (1 H, d, *J* 9.9); *m/z* 442, 444 and 446 (M^+) (Found: C, 59.5; H, 4.5. $C_{22}H_{20}Br_2$ requires C, 59.48; H, 4.54%).

Cyclization of Dibromide **11** *and Dithiols* **14** *to give Dithiapyrenophanes* **15**.—*Typical procedure.* A solution of dibromide **11** (2.0 g, 4.5 mmol) and 2,6-bis(mercaptomethyl)-4-*tert*-butyltoluene **14b** (980 mg, 4.5 mmol) in benzene (100 cm^3) was added dropwise from a Hershberg funnel under nitrogen to a stirred solution of potassium hydroxide (700 mg, 12.4 mmol) and sodium borohydride (100 mg, 2.5 mmol) in ethanol (3.0 dm^3). When addition was complete (6 h) the reaction mixture was concentrated under reduced pressure and the residue was extracted with CH_2Cl_2 (500 cm^3). The extract was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako, C-300; 100 g) with hexane–$CHCl_3$ (1:1) as eluent to give a solid, which was recrystallized from hexane–benzene (1:1) to yield the desired anti-6,17-*di*-tert-*butyl*-9-*methyl*-2,11-*dithia*[3]*metacyclo*[3]-(1,3)*pyrenophane* anti-**15b** (820 mg, 35%) as prisms, m.p. 228–231.5 °C; ν_{max}(KBr)/cm^{-1} 3050, 2980, 1600, 1480, 1360 and 1230; δ_H($CDCl_3$) 1.02 (9 H, s), 1.55 (9 H, s), 1.64 (3 H, s), 3.83 (4 H, s), 3.89 (2 H, d, *J* 14.8), 4.32 (2 H, d, *J* 14.8), 5.85 (1 H, s), 7.19 (2 H, s), 7.95 (2 H, d, *J* 9.3), 8.03 (2 H, d, *J* 9.3) and 8.13 (2 H, s); *m/z* 522 (M^+) (Found: C, 80.4; H, 7.3. $C_{35}H_{38}S_2$ requires C, 80.41; H, 7.33%).

Compounds *syn*-**15a**, *anti*-**15c**, *syn*-**15d** and *syn*-**15e** were prepared in a similar manner to that described above for *anti*-**15b**. The yields are compiled in Scheme 4.

Preparation of syn-8-tert-*butyl*-2,15-*dithia*[3]*metacyclo*[3]-(1,3)*pyrenophane* syn-**15a**. Prisms (from hexane), m.p. 226–227 °C; ν_{max}(KBr)/cm^{-1} 3030, 2960, 1590, 1480 and 1230; δ_H($CDCl_3$) 1.57 (9 H, s), 3.71 (4 H, s), 4.29 (4 H, s), 6.70–7.00 (5 H, s), 8.02 (2 H, d, *J* 9.5), 8.18 (2 H, d, *J* 9.5) and 8.19 (2 H, s); *m/z* 452 (M^+) (Found: C, 79.6; H, 6.4. $C_{30}H_{28}S_2$ requires C, 79.60; H, 6.23%).

Preparation of anti-6,17-*di*-tert-*butyl*-9-*ethyl*-2,11-*dithia*[3]-*metacyclo*[3](1,3)*pyrenophane* anti-**15c**. Prisms [(from hexane–benzene (1:1)], m.p. 224–226 °C; ν_{max}(KBr)/cm^{-1} 3050, 2980, 1590, 1360 and 1230; δ_H($CDCl_3$) 0.85 (3 H, t, *J* 7.6), 0.93 (9 H, s), 1.56 (9 H, s), 2.49 (2 H, q, *J* 7.6), 3.84 (2 H, d, *J* 13.5), 3.98 (2 H, d, *J* 13.5), 4.07 (2 H, d, *J* 15.0), 4.39 (2 H, d, *J* 15.0 Hz), 6.08 (1 H, s), 7.09 (2 H, s), 7.98 (2 H, d, *J* 9.2), 8.10 (2 H, d, *J* 9.2) and 8.16 (2 H, s); *m/z* 536 (M^+) (Found: C, 80.45; H, 7.5. $C_{36}H_{40}S_2$ requires C, 80.55; H, 7.51%).

Preparation of syn-6,17-*di*-tert-*butyl*-9-*methoxy*-2,11-*dithia*-[3]*metacyclo*[3](1,3)*pyrenophane* syn-**15d**. Prisms [from hexane–benzene (1:1)], m.p. 241–244 °C; ν_{max}(KBr)/cm^{-1} 3050, 2950, 1590, 1480, 1260 and 880; δ_H($CDCl_3$) 0.10 (9 H, s), 1.56 (9 H, s), 3.54 (2 H, d, *J* 14.3), 3.75 (3 H, s), 4.28 (2 H, d, *J* 15.0), 4.48 (2 H, d, *J* 14.3), 4.56 (2 H, d, *J* 15.0), 6.61 (2 H, s), 7.64 (1 H, s), 7.95 (2 H, d, *J* 9.2), 8.12 (2 H, s) and 8.17 (2 H, d, *J* 9.2); *m/z* 538 (M^+) (Found: C, 77.95; H, 7.0. $C_{35}H_{38}OS_2$ requires C, 78.02; H, 7.11%).

Preparation of syn-6,17-*di*-tert-*butyl*-9-*fluoro*-2,11-*dithia*-[3]*metacyclo*[3](1,3)*pyrenophane* syn-**15e**. Prisms [from hexane–benzene (1:1)], 181–182 °C; ν_{max}(KBr)/cm^{-1} 2950, 1590, 1480 and 1260; δ_H($CDCl_3$) 0.12 (9 H, s) 1.56 (9 H, s), 3.49 (2 H, d, *J* 15.4), 4.26 (2 H, d, *J* 15.4), 4.37 (2 H, d, *J* 15.4), 4.55 (2 H, d, *J* 15.4), 6.54 (2 H, d, *J* 6.5), 7.63 (1 H, d, *J* 2.0), 7.95 (2 H, d, *J* 9.5), 8.13 (2 H, d, *J* 9.5) and 8.12 (2 H, s); *m/z* 526 (M^+) (Found: C,77.05; H, 6.6. $C_{34}H_{35}FS_2$ requires C, 77.52; H, 6.70%).

Oxidation of Bissulfides **15** *to give Dithiapyrenophane S,S,S',S'-Tetraoxides* **18**.—*Typical procedure.* To a solution of *anti*-**15b** (1.29 g, 2.5 mmol) in $CHCl_3$ (60 cm^3) was added MCPBA (2.5 g, 12.5 mmol) at −5 °C. After the reaction mixture had been stirred at −5 °C for 6 h, the solvent was evaporated off under reduced pressure. The residue was washed successively with 10% aq. $NaHCO_3$ (30 cm^3 × 2), water (30 cm^3 × 2), and ethanol (5 cm^3 × 2) to yield the desired anti-6,17-*di*-tert-*butyl*-9-*methyl*-2,11-*dithia*[3]*metacyclo*[3](1,3)*pyrenophane* S,S,S',S'-*tetraoxide* anti-**18b** (1.46 g, 100%) as a powder, m.p. 310 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3000, 1600, 1480, 1460, 1360, 1320 and 1230; *m/z* 586 (M^+) (Found: C, 71.7; H, 6.55. $C_{35}H_{38}O_4S_2$ requires C, 71.64; H, 6.53%).

Compounds *anti*-**18a**, *anti*-**18c**, *syn*-**18d** and *syn*-**18e** were prepared in a similar manner to that described above for *anti*-**18b**. The yields are compiled in Schemes 5 and 6.

Preparation of anti-8-tert-*butyl*-2,15-*dithia*[3]*metacyclo*-[3](1,3)*pyrenophane* S,S,S',S'-*tetraoxide* anti-**18a**. Powder, m.p. 310 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2960, 1590, 1320 and 1110; *m/z* 516 (M^+) (Found: C, 66.9; H, 5.3. $C_{30}H_{28}O_4S_2 \cdot H_2O$ requires C, 67.39; H, 5.66%).

Preparation of anti-6,17-*Di*-tert-*butyl*-9-*ethyl*-2,11-*dithia*[3]-*metacyclo*[3](1,3)*pyrenophane* S,S,S',S'-*tetraoxide* anti-**18c**. Powder, m.p. 350 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2960, 1590, 1310 and 1110; *m/z* 600 (M^+) (Found: C, 70.95; H, 6.6. $C_{36}H_{40}O_4S_2 \cdot 1/2H_2O$ requires C, 70.90; H, 6.78%).

Preparation of syn-6,17-*Di*-tert-*butyl*-9-*methoxy*-2,11-*dithia*-[3]*metacyclo*[3](1,3)*pyrenophane* S,S,S',S'-*tetraoxide* syn-**18d**. Powder, m.p. 360 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2960, 1600, 1320, 1270 and 1120; *m/z* 602 (M^+) (Found: C, 69.8; H, 6.4. $C_{35}H_{38}O_5S_2$ requires C, 69.74; H, 6.35%).

Preparation of syn-6,17-*di*-tert-*butyl*-9-*fluoro*-2,11-*dithia*-[3]*metacyclo*[3](1,3)*pyrenophane* S,S,S',S'-*tetraoxide* syn-**18e**. Powder, m.p. 335 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2960, 1600, 1330 and 1120; *m/z* 590 (M^+) (Found: C, 68.8; H, 5.7. $C_{34}H_{35}FO_4S_2$ requires C, 69.13; H, 5.97%).

Pyrolysis of Bis-sulfones **18** *to give* [2]*Metacyclo*[2](1,3)-*pyrenophanes* **19**.—*Typical procedure.* The sulfone *anti*-**18b** (940 mg, 1.6 mmol) was pyrolysed at 480 °C/0.8 Torr according to the literature.[34–36] The sublimed product was collected and chromatographed on silica gel with hexane as eluent to give the pyrene **8** (28 mg, 6.1%) as prisms and the desired anti-5,15-*di*-tert-*butyl*-8-*methyl*[2]*metacyclo*[2](1,3)*pyrenophane*† anti-**19b** (500 mg, 68%) as pale yellow prisms (from hexane), m.p. 246–248 °C; ν_{max}(KBr)/cm^{-1} 3050, 2980, 1600, 1480, 1460, 1230, 1180 and 880; δ_H($CDCl_3$) −0.29 (3 H, s), 1.44 (9 H, s), 1.59 (9 H, s), 2.38 (2 H, m), 2.63 (2 H, m), 3.11 (2 H, m), 4.21 (2 H, m), 4.53 (1 H, s), 7.23 (2 H, s), 8.04 (2 H, d, *J* 9.2), 8.18 (2 H, s) and 8.37 (2 H, d, *J* 9.2); *m/z* 458 (M^+) (Found: C, 91.5; H, 8.3. $C_{35}H_{38}$ requires C, 91.65; H, 8.35%).

Compounds *anti*-**19a** and *anti*-**19c–e** were prepared according to the method described above. The yields are summarized in Schemes 5 and 6.

Preparation of anti-7-tert-*butyl*[2]*metacyclo*[2](1,3)*pyrenophane* anti-**19a**. Pale yellow prisms (from hexane), m.p. 194–195 °C; ν_{max}(KBr)/cm^{-1} 3050, 2950, 1590, 1460, 1390, 1250 and 1230; δ_H($CDCl_3$) 1.59 (9 H, s), 2.14 (2 H, m), 2.36 (2 H, m), 3.24 (2 H, m), 3.54 (1 H, s), 4.26 (2 H, m), 5.09 (1 H, s), 7.18 (2 H, dd, *J* 1.5 and 7.3), 7.36 (1 H, t, *J* 7.3), 8.07 (2 H, d, *J* 9.2), 8.20 (2 H, s) and 8.37 (2 H, d, *J* 9.2); *m/z* 388 (M^+) (Found: C, 92.9; H, 7.2. $C_{30}H_{28}$ requires C, 92.74; H, 7.26%).

Preparation of anti-5,15-*di*-tert-*butyl*-8-*ethyl*[2]*metacyclo*-[2](1,3)*pyrenophane* anti-**19c**. Pale yellow prisms (from hexane), m.p. 267–268 °C; ν_{max}(KBr)/cm^{-1} 3040, 2950, 1590, 1460, 1360, 1275 and 1230; δ_H($CDCl_3$) −0.10 (2 H, t, *J* 7.5), 0.11 (3 H, d, *J* 7.5), 1.43 (9 H, s), 1.59 (9 H, s), 2.35 (2 H, m), 2.75 (2 H, m), 3.10 (2 H, m), 4.15 (2 H, m), 4.50 (1 H, s), 7.22 (2 H, s), 8.04 (2 H, d, *J* 9.2), 8.19 (2 H, s) and 8.37 (2 H, d, *J* 9.2); *m/z* 472 (M^+) (Found: C, 91.1; H, 8.4. $C_{36}H_{40}$ requires C, 91.47; H, 8.53%).

Preparation of anti-5,15-*di*-tert-*butyl*-8-*methoxy*[2]*metacyclo*[2](1,3)*pyrenophane* anti-**19d**. Pale yellow prisms (from hexane), m.p. 302–305 °C; ν_{max}(KBr)/cm^{-1} 3050, 2980, 1590, 1480, 1360, 1280 and 1250; δ_H($CDCl_3$) 1.42 (9 H, s), 1.59 (9 H, s), 2.35 (2 H, m), 2.39 (3 H, s), 2.65 (2 H, m), 2.96 (2 H, m), 4.20 (2 H, m), 4.86 (1 H, s), 7.20 (2 H, s), 8.01 (2 H, d, *J* 9.2), 8.16 (2

H, s) and 8.36 (2 H, d, *J* 9.2); *m/z* 474 (M^+) (Found: C, 88.4; H, 8.0. $C_{35}H_{38}O$ requires C, 88.56; H, 8.07%).

Preparation of anti-5,15-*di*-tert-*butyl*-8-*fluoro*[2]*metacyclo*-[2](1,3)*pyrenophane* anti-**19e**. Pale yellow prisms (from hexane), m.p. 260–263 °C; ν_{max}(KBr)/cm^{-1} 3050, 2950, 1590, 1480, 1290, 1230 and 1120; δ_H($CDCl_3$) 1.42 (9 H, s), 1.58 (9 H s), 2.36 (2 H, m), 2.60 (2 H, m), 2.94 (2 H, m), 4.25 (2 H, m), 5.16 (1 H, s), 7.20 (2 H, d, *J* 5.9), 8.04 (2 H, d, *J* 9.2), 8.18 (2 H, s) and 8.37 (2 H, d, *J* 9.2); *m/z* 462 (M^+) (Found: C, 88.6; H, 7.5. $C_{34}H_{35}F$ requires C, 88.27; H, 7.63).

Nitration of Compounds anti-**19b, d** with $Cu(NO_3)_2$ *in Acetic Anhydride.—Typical procedure.* A solution of *anti*-**19b** (100 mg, 0.22 mmol) in acetic anhydride (5 cm^3)–benzene (2 cm^3) was added copper(II) nitrate (50 mg, 0.22 mmol) at room temperature. After the reaction mixture had been stirred for 30 min at room temperature, it was poured into a large amount of ice–water and extracted with CH_2Cl_2 (50 cm^3 × 2). The extract was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako, C-300; 100 g) with hexane–$CHCl_3$ (3:1) as eluent to give a pale yellow solid, which was recrystallized from hexane to afford anti-5,15-*di*-tert-*butyl*-8-*methyl*-14-*nitro*[2]*metacyclo*[2](1,3)*pyreno-phane* **21a** (91 mg, 83%) as pale yellow prisms, m.p. 258–260 °C; ν_{max}(KBr)/cm^{-1} 2980, 1600, 1530, 1450 and 1360; δ_H($CDCl_3$) −0.43 (3 H, s), 1.42 (9 H, s), 1.62 (9 H, s), 2.27 (2 H, m), 2.57 (2 H, m), 3.05 (2 H, m), 4.05 (2 H, m) 4.87 (1 H, s), 7.19 (2 H, s), 7.64 (1 H, d, *J* 9.5), 7.90 (1 H, d, *J* 9.5), 8.17 (1 H, s), 8.75 (1 H, d, *J* 9.5) and 8.77 (1 H, d, *J* 9.5); *m/z* 503 (M^+) (Found: C, 83.6; H, 7.4; N, 2.8. $C_{35}H_{37}NO_2$ requires C, 83.46; H, 7.41; N, 2.78%).

Compounds **21b** and **22** were also obtained, from substrates *anti*-**19d** and **8** under various conditions, in 86 and 90% yield, respectively.

anti-5,15-*Di*-tert-*butyl*-8-*methoxy*-14-*nitro*[2]*metacyclo*[2]-(1,3)*pyrenophane* **21b**. Pale brown prisms [(from hexane–benzene (1:1)], m.p. 310–312 °C; ν_{max}(KBr)/cm^{-1} 3050, 2980, 1520, 1480 and 1360; δ_H($CDCl_3$) 1.43 (9 H, s), 1.65 (9 H, s), 2.35 (2 H, m), 2.38 (3 H, m), 2.60 (2 H, m), 2.95 (2 H, m), 4.20 (2 H, m), 4.93 (1 H, s), 7.21 (2 H, s), 7.72 (1 H, d, *J* 9.5), 7.99 (1 H, d, *J* 9.2), 8.23 (1 H, s), 8.47 (1 H, d, *J* 9.2) and 8.49 (1 H, d, *J* 9.5); *m/z* 519 (M^+) (Found: C, 80.5; H, 7.3; N, 2.65. $C_{35}H_{37}NO_3$ requires C, 80.89; H, 7.18; N, 2.69%).

2-tert-*Butyl*-6,8-*dimethyl*-1-*nitropyrene* **22**. Pale yellow prisms (from hexane), m.p. 290–292 °C; ν_{max}(KBr)/cm^{-1} 3000, 2980, 1530, 1370 and 1260; δ_H($CDCl_3$) 1.64 (9 H, s), 2.94 (3 H, s), 2.95 (3 H, s), 7.70 (1 H, d, *J* 9.5), 7.77 (1 H, s), 7.98 (1 H, d, *J* 9.2), 8.24 (1 H, s), 8.26 (1 H, d, *J* 9.2) and 8.29 (1 H, d, *J* 9.5); *m/z* 331 (M^+) (Found: C, 80.0; H, 6.5; N, 4.35. $C_{22}H_{21}NO_2$ requires C, 79.73; H, 6.39; N, 4.22%).

Bromination of compounds anti-**19b, d** *with Bromine in Methylene Dichloride.—Typical procedure.* To a solution of hydrocarbon *anti*-**19b** (50 mg, 0.11 mmol) in CH_2Cl_2 (5 cm^3) was added a solution of bromine (20 mg, 0.11 mmol) in CH_2Cl_2 (2 cm^3) at 0 °C. After the reaction mixture had been stirred for 1 min at 0 °C, it was poured into a large amount of ice–water and extracted with CH_2Cl_2 (50 cm^3 × 2). The extract was washed successively with 10% aq. sodium thiosulfate (10 cm^3 × 2) and water (20 cm^3 × 2), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako, C-300; 50 g) with hexane and then with hexane–$CHCl_3$ (3:1) as eluent to give the starting compound (10 mg, 20% recovery) as a solid, and crude bromide **23a** as a pale yellow solid.

Recrystallization of crude compound **23a** from hexane afforded anti-13-*bromo*-5,15-*di*-tert-*butyl*-8-*methyl*[2]*meta-cyclo*[2](1,3)*pyrenophane* **23a** (36 mg, 62%) as pale yellow prisms, m.p. 232 °C; ν_{max}(KBr)/cm^{-1} 2960, 1600, 1480, 1450 and 1360; δ_H($CDCl_3$) −0.28 (3 H, s), 1.43 (9 H, s), 1.61 (9 H, s), 2.38 (2 H, m), 2.63 (2 H, m), 3.15 (2 H, m), 4.17 (2 H, m), 4.51 (1 H, s), 7.23 (2 H, s), 8.06 (1 H, d, *J* 9.3), 8.24 (1 H, d, *J* 1.8), 8.39 (1 H, d, *J* 9.3), 8.60 (1 H, d, *J* 1.8) and 8.73 (1 H, s); *m/z* 536, 538 (M^+) (Found: C, 78.4; H, 6.85. $C_{35}H_{37}Br$ requires C, 78.20; H, 6.94%).

Compounds **23b**, **24**, **25** and **12** were also obtained from substrates *anti*-**19d** and **8** under various conditions (see Table 4 and Scheme 8). However several attempts to isolate compound **23b** as a pure product failed.

2,9-*Di*-tert-*butyl*-4,5,13,14-*tetrahydrodibenzo*[cd,lm]*perylene* **24**. Pale yellow prisms (from hexane), m.p. > 300 °C; ν_{max}-(KBr)/cm^{-1} 3050, 2950, 1600, 1430, 1390 and 1360; δ_H-($CDCl_3$) 1.40 (9 H, s), 1.58 (9 H, s), 3.07 (4 H, m), 3.59 (4 H, m), 7.23 (2 H, s), 8.01 (2 H, d, *J* 9.2), 8.14 (2 H, s) and 8.30 (2 H, d, *J* 9.2); *m/z* 442 (M^+) (Found: C, 92.3; H, 7.25. $C_{34}H_{34}$ requires C, 92.26; H, 7.74%).

7-*Bromo*-2,9-*di*-tert-*butyl*-4,5,13,14-*tetrahydrodibenzo*[cd,-lm]*perylene* **25**. Pale yellow prisms (from hexane), m.p. 305–308 °C ν_{max}(KBr)/cm^{-1} 2950, 1590, 1480, 1360 and 1220; δ_H($CDCl_3$) 1.41 (9 H, s), 1.61 (9 H, s), 3.08 (4 H, s), 3.58 (4 H, s), 7.24 (2 H, s), 8.05 (1 H, d, *J* 9.2), 8.20 (1 H, d, *J* 1.8), 8.34 (1 H, d, *J* 9.2), 8.56 (1 H, d, *J* 1.8) and 8.69 (1 H, s); *m/z* 520, 522 (M^+) (Found: C, 78.3; H, 6.5. $C_{34}H_{33}Br$ requires C, 78.30; H, 6.38%).

References

1 Part 30, T. Yamato, N. Sakaue, L. K. Doamekpor and M. Tashiro, submitted to *J. Chem. Res.* (*S*), in press.
2 T. Umemoto, T. Kawashima, Y. Sakata and S. Misumi, *Chem. Lett.*, 1975, 837.
3 T. Umemoto, S. Satani, Y. Sakata and S. Misumi, *Tetrahedron Lett.*, 1975, 3159.
4 T. Hayashi, T. Suzuki, N. Nagata, Y. Sakata and S. Misumi, *J. Phys. Chem.*, 1977, **81**, 424.
5 R. H. Mitchell, R. J. Carruthers and J. C. M. Zwinkels, *Tetrahedron Lett.*, 1976, 2685.
6 H. Irngartinger, R. G. H. Kirrstetter, C. Krieger, H. Rodewald and H. A. Staab, *Tetrahedron Lett.*, 1977, 1425.
7 T. Kawashima, T. Otsubo, Y. Sakata and S. Misumi, *Chem. Lett.*, 1978, 5115.
8 R. H. Mitchell and R. Mahadevan, *Tetrahedron Lett.*, 1981, **22**, 5131.
9 F. Vögtle, A. Ostrowicki, B. Begemann, M. Jansen, M. Nieger and E. Niecke, *Chem. Ber.*, 1990, **123**, 169.
10 E. Clar, *Polycyclic Hydrocarbons*, Academic Press, New York, 1964, vol. 2.
11 H. Vollmann, H. Becker, M. Correl and H. Streeck, *Justus Liebigs Ann. Chem.*, 1937, **531**, 1.
12 A. Streitwieser, R. G. Lawler and D. Schwaab, *J. Org. Chem.*, 1965, **30**, 1470.
13 R. G. Harvey, J. Pataki and H. Lee, *Org. Prep. Proced. Int.*, 1984, **16**, 144.
14 M. A. Hempenius, J. Lugtenburg and J. Cornelisse, *J. Chem. Soc., Perkin Trans. 1*, 1991, 635.
15 A. M. Braken-van Leersum, J. Cornelisse and J. Lugtenburg, *J. Chem. Soc., Chem. Commun.*, 1987, 1156.
16 S. C. Agarwal and B. L. Van Durren, *J. Org. Chem.*, 1975, **40**, 2307.
17 M. Moyl and E. Ritchie, *Aust. J. Chem.*, 1958, **11**, 211.
18 T. Yamato, A. Miyazawa and M. Tashiro, *Chem. Express*, 1993, **8**, 301.
19 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1978, **43**, 1413.
20 M. Tashiro, *Synthesis*, 1979, 921.
21 M. Tashiro, T. Yamato, K. Kobayashi and T. Arimura, *J. Org. Chem.*, 1987, **52**, 3196.
22 T. Yamato, T. Arimura and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1.
23 A. Miyazawa, T. Yamato and M. Tashiro, *Chem. Express*, 1990, **5**, 381.
24 A. Miyazawa, A. Tsuge, T. Yamato and M. Tashiro, *J. Org. Chem.*, 1991, **56**, 4312.
25 A. Miyazawa, T. Yamato and M. Tashiro, *J. Org. Chem.*, 1991, **56**, 1334.
26 T. Yamato, J. Matsumoto, K. Tokuhisa, K. Suehiro and M. Tashiro, *Chem. Ber.* 1992, **125**, 2443.

27 G. A. Olah, G. K. S. Prakash, P. S. Iyer, M. Tashiro and T. Yamato, *J. Org. Chem.*, 1987, **52**, 1881.
28 T. Yamato, C. Hideshima, M. Tashiro, G. K. S. Prakash and G. A. Olah, *J. Org. Chem.*, 1991, **56**, 6248.
29 W. Anker, G. W. Bushnell and R. H. Mitchell, *Can. J. Chem.*, 1979, **57**, 3080.
30 R. H. Mitchell, R. J. Carruther, L. Mazuch and T. W. Dingle, *J. Am. Chem. Soc.*, 1982, **104**, 2544.
31 R. H. Mitchell and V. Boekelheide, *J. Am. Chem. Soc.*, 1974, **96**, 1547.
32 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 4556.
33 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1983, **48**, 1461.
34 (*a*) M. Nishio and M. Horita, *Tetrahedron*, 1989, **45**, 7201; (*b*) C. D. Andreetti, R. Ungaro and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1979, 1005; (*c*) R. Ungaro, A. Pochini, C. D. Andreetti and O. Domiano, *J. Chem. Soc., Perkin Trans. 2*, 1985, 197; (*d*) M. A. McKervey, E. M. Seward, G. Ferguson and B. L. Ruhl, *J. Org. Chem.*, 1986, **51**, 3581; (*e*) D. J. Cram, S. Karbach, H.-E. Kim, C. B. Knobler, E. F. Marverick, J. L. Ericson and R. C. Helgeson, *J. Am. Chem. Soc.*, 1988, **110**, 2229; (*f*) P. Soncini, S. Bonsignore, E. Dalcanale and F. Ugozzoli, *J. Org. Chem.*, 1992, **57**, 4608; (*g*) J. L. Atwood, S. G. Bott, C. Jones and C. L. Raston, *J. Org. Chem., Chem. Commun.*, 1992, 1349; (*h*) K. Kobayashi, Y. Asakawa, Y. Kikuchi, H. Toi and Y. Aoyama, *J. Am. Chem. Soc.*, 1993, **115**, 2648.
35 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 1543.
36 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1985, **50**, 2939.
37 T. Yamato, J. Matsumoto, K. Tokuhisa, K. Tsuji, K. Suehiro and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2675.
38 D. J. Wilson, V. Boekelheide and R. W. Griffin, Jr., *J. Am. Chem. Soc.*, 1960, **82**, 6302.
39 R. W. Griffin, Jr., *Chem. Rev.*, 1963, **63**, 45.
40 B. H. Smith, *Bridged Aromatic Compounds*, Academic Press, New York, 1964.
41 V. Boekelheide, *Top. Curr. Chem.*, 1983, **113**, 87.
42 N. L. Allinger, M. A. DaRooge and R. B. Hermann, *J. Am. Chem. Soc.*, 1961, **83**, 1974.
43 N. L. Allinger, B. J. Gordon, H.-E. Hu and R. A. Ford, *J. Org. Chem.*, 1967, **32**, 2272.
44 T. Sato, M. Wakabayashi, T. Okamura, T. Amada and K. Hata, *Bull. Chem. Soc. Jpn.*, 1967, **40**, 2363.
45 M. Tashiro, S. Mataka, Y. Takezaki, M. Takeshita, T. Arimura, A. Tsuge and T. Yamato, *J. Org. Chem.*, 1989, **54**, 451.
46 T. Yamato, S. Ide, K. Tokuhisa and M. Tashiro, *J. Org. Chem.*, 1992, **57**, 271.
47 T. Yamato, J. Matsumoto, S. Ide, K. Tokuhisa, K. Suehiro and M. Tashiro, *J. Chem. Res. (S)*, 1992, 420.
48 G. A. Olah, *Acc. Chem. Res.*, 1971, **4**, 240; J. H. Ridd, *Acc. Chem. Res.*, 1971, **4**, 248; R. B. Moodie and K. Schofield, *Acc. Chem. Res.*, 1976, **9**, 287.
49 E. Muller and H. Kessler, *Tetrahedron Lett.*, 1965, 2673.

Paper 3/03516F
Received 18*th June* 1993
Accepted 25*th August* 1993