Synthesis and Diatropicity of a *trans*-10c-Methyl-10b,10c-dihydropyrene-containing Cyclophane: a Novel Aromatic Molecule with a (1,3)Cyclophane within the π-Cloud of a [14]Annulene

Yee-Hing Lai * and Angeline Hui-Tin Yap
Department of Chemistry, National University of Singapore, Kent Ridge, Republic of Singapore 0511

1,4-Bis(bromomethyl)-2,6-dimethylbenzene (**17**) was obtained by direct bromomethylation of α-bromomesitylene and used for the preparation of 14,18-dimethyl-2,11-dithia[3.3](1,3)(1,4)-cyclophane (**19**). Desulfurization of **19** to afford 12,16-dimethyl[2.2](1,4)cyclophane (**22**) could be achieved *via* two routes. Selective bromination of the methyl groups in **22** followed by coupling with 2,6-bis(mercaptomethyl)toluene led to the double-layered *anti*-dithiacyclophane **26**. Ring contraction *via* a Wittig rearrangement–Hofmann elimination sequence gave the double-layered cyclophanediene **14** which underwent valence isomerization to afford the title compound **15**. A diatropicity study of **15** suggests that it retains 99% of the ring current of the parent system **1**. Protons of the methylene group directly attached to the dihydropyrene moiety in **15** are, however, shifted about 1 ppm downfield compared with those of the corresponding methylene protons in related dihydropyrenes with internal butyl and but-4-enyl groups. This is attributed to a deviation of the methylene carbon concerned in **15** from the central axis of delocalization of the aromatic π-cloud in the dihydropyrene.

The internal methyl protons of **1** appear as a strongly shielded singlet at δ −4.25 in its ^{1}H NMR spectrum,[1] some 5.2 ppm upfield from the chemical shift of the methyl protons (δ 0.97) of the non-delocalized model compound **7**[2] with a very similar molecular geometry. A number of derivatives of **1** with ethyl,[3] propyl,[3] butyl,[4] but-4-enyl[5] and phenyl[6] in place of the methyl groups, namely **2**–**6** respectively, have also been synthesized. An approximate mapping[7] of the ring current of **1**–**4** shows that, with respect to the chemical shift of methyl protons in **7**, the ring current shielding on protons of a linear alkyl group in **1** is quite constant at about 5.1 ppm for protons one atom removed from the bridgehead and about 2.7, 1.5 and 1 ppm for protons two, three and four atoms away from the bridgehead, respectively. The shielding of the phenyl protons in **6**, however, was reported to be about 4.4, 1.3 and 1.0 ppm for the *ortho*, *meta* and *para* protons respectively when compared with the chemical shift of protons in benzene (δ 7.2). The phenyl group in **6**, although free to rotate within the π-cloud of the macroring, is held somewhat vertically at an angle perpendicular to the plane of the periphery. It would thus be interesting to place an internal benzene ring in a plane somewhat parallel to that of the periphery, and thus the π-electron cloud of the dimethyldihydropyrene moiety, to investigate whether there are any significant interactions between the two aromatic rings of a very different nature.

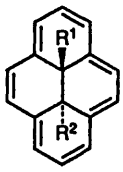
Attempts at synthesizing a cyclophane within the cavity of the dihydropyrene had yet to meet with success. Misumi *et al.*[8] reported that the cyclophanediene **8** failed to valence-isomerize to **9** thermally or photochemically. The benzene rings in [2.2](1,4)cyclophane **12** are known to pucker considerably in a 'boat' form.[9,10] Two such units in **8** would tilt the two 'internal' quaternary carbons away from each other, thus discouraging the ring-closure reaction in forming the dihydropyrene **9**. Even the related system **10** does not undergo valence isomerization to give dihydropyrene **11**.[11] An interesting attempt would be to replace the (1,4)-bridged ring in **10** with a (1,3)-bridged ring. [2.2](1,4)Cyclophane **12** could undergo an isomerization to the less strained [2.2](1,3)(1,4)cyclophane **13**.[12] The 1,4-bridged ring in **13** has also been shown to deviate less from planarity[10] than that in **12**. Thus the cyclophanediene **14** is expected to undergo valence isomerization to afford the dihydropyrene system **15**—perhaps the first example of a novel aromatic molecule with a (1,3)cyclophane within a [14]annulene.

Results and Discussion

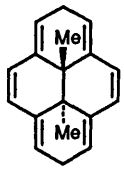
Synthesis of Cyclophane **22**.—Free radical monobromination of mesitylene with *N*-bromosuccinimide (NBS) in CCl_4 was achieved by the method described by Truce *et al.*[13] The product 1-bromomethyl-3,5-dimethylbenzene **16** was then subjected to ring bromomethylation using 1,3,5-trioxane and a mixture of 48% aqueous hydrobromic acid and glacial acetic acid in the presence of a phase-transfer catalyst myristyltrimethylammonium bromide.[14] A mixture of the monobromomethylated product **17**, a dibromomethylated product and starting material **16** were obtained in all attempts. The desired product **17** was only obtained in 22% yield after repeated recrystallization in cyclohexane. The ease of product isolation seemed to improve in large-scale reactions. In order to minimize any unfavourable steric interaction in the subsequent cyclization reaction, the dibromide was first converted into the dithiol **18** which was then coupled with 1,3-bis(bromomethyl)benzene under high dilution conditions.[15] The dithiacyclophane **19**, m.p. 120–122 °C, was isolated in 79% yield. The ^{1}H NMR spectrum of **19** shows only an averaged methyl signal at δ 2.19 consistent with a conformationally mobile (1,3)-bridged ring at room temperature.

Pyrolysis of disulfones has been known to be very useful for the preparation of [2.2]cyclophanes.[16] The disulfone **20** was readily prepared in quantitative yield by oxidation of **19** using hydrogen peroxide. In the mass spectrum of **20**, no molecular ion was observed but the base peak at *m*/*z* 236 corresponding to the cyclophane **22** was present indicating a facile thermal elimination of sulfur dioxide from **20** as desired. The results from actual attempts to convert **20** into **22** by flash vacuum pyrolysis[16,17] were however, rather discouraging. The cyclophane **22** was isolated in variable yields of 15–60% and large-scale (> 300 mg) reactions were found to be less successful.

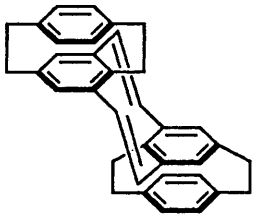
An alternative route to **22** was then investigated *via* a Wittig rearrangement[18] of **19** to afford a mixture of isomers of **21**



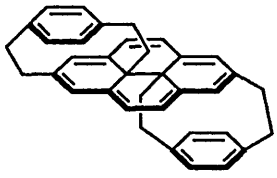
1; $R^1 = R^2 = CH_3$
2; $R^1 = R^2 = CH_2CH_3$
3; $R^1 = R^2 = CH_2CH_2CH_3$
4; $R^1 = CH_2CH_2CH_2CH_3$, $R^2 = CH_3$
5; $R^1 = CH_2CH_2CH{=}CH_2$, $R^2 = CH_3$
6; $R^1 = C_6H_5$, $R^2 = CH_3$



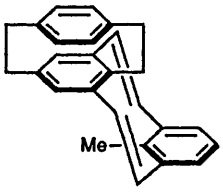
7



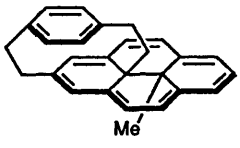
8



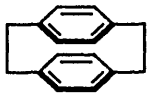
9



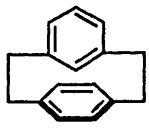
10



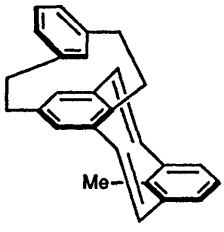
11



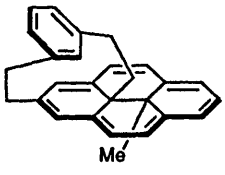
12



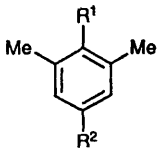
13



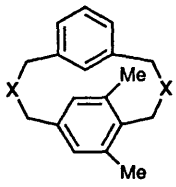
14



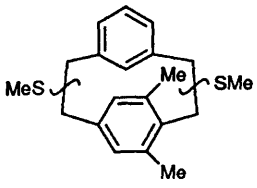
15



16; $R^1 = H$, $R^2 = CH_2Br$
17; $R^1 = R^2 = CH_2Br$
18; $R^1 = R^2 = CH_2SH$



19; X = S
20; $X = SO_2$



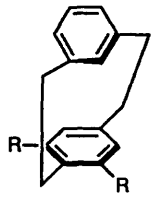
21

followed by reduction[2] of the latter with W-7 Raney nickel.[19] In several separate attempts, the cyclophane **22** could be isolated consistently in *ca.* 30% overall yield. The fact that such a synthetic sequence could be carried out even in 3 g-scale reactions without affecting the product yield made it an obvious choice for the preparation of the cyclophane **22**—a precursor to be used for the subsequent synthetic scheme. In the ^1H NMR spectra of **22** the aryl and methyl protons on the (1,4)-bridged ring appear as two pairs of singlets, respectively. This is clearly consistent with, at room temperature, a rigid conformation in which the aryl proton and methyl protons on one side of the (1,4)-bridged ring are shielded by the tilted (1,3)-bridged ring, similar to results reported for the parent [2.2](1,3)(1,4)-cyclophane.[20]

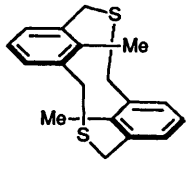
Synthesis of Dihydropyrene **15**.—The most successful synthetic route to **1** involved the use of dithiacyclophane *anti*-**24** as a precursor. A retrosynthetic scheme in our work thus suggests *anti*-**26** as an appropriate precursor to our desired cyclophanediene **14** which is expected to undergo valence isomerization to afford **15**.

Owing to the conformational rigidity in **22**, its bridging methylene groups are not expected to behave chemically as benzylic methylene groups and are unlikely to be functionalized directly. Taking advantage of this unique chemical property, free radical bromination of **22** was carried out by treating it with NBS added in two portions. The dibromide **23** was isolated in good yield (72%) and its structure is supported by a molecular ion at *m/z* 392, with a correct isotope pattern for two bromine atoms, observed in its mass spectrum. In its ^1H NMR spectrum, H-13 is perhaps deshielded to δ 7.36 by the anisotropic effect of bromine but H-15 is significantly shielded by the (1,3)-bridged ring at δ 5.87; H-8, being projected into the π-cloud of the (1,4)-bridged ring, is the most shielded aromatic proton at δ 5.65. Each of the two pairs of methylene protons is, in principle, diastereotopic but one pair is unresolved and appears as a singlet at δ 4.71 which could be assigned to that attached to C-12 [away from the (1,3)-bridged ring]. The other pair is shielded by the (1,3)-bridged ring and clearly resolved into an AB system at δ 4.34 and 3.50, respectively.

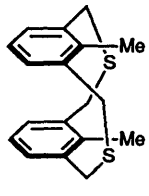
Intermolecular coupling of dibromide **23** with 2,6-bis(mercaptomethyl)toluene **25**[2] under high dilution[15] gave a 32% yield of mainly the double-layered dithiacyclophane *anti*-**26**.



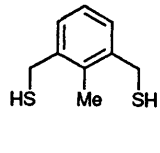
22; R = CH_3
23; R = CH_2Br



anti - **24**

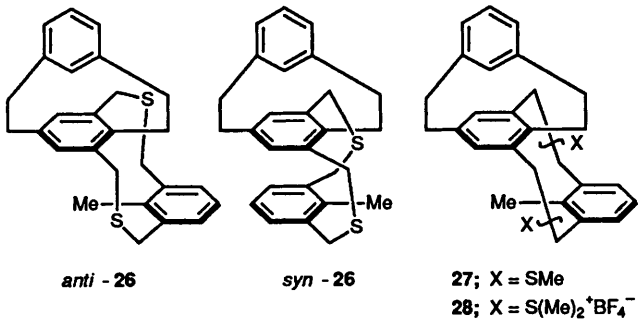


syn - **24**



25

The *anti* stereochemistry is evident by the methyl singlet at δ 1.44, comparable to that observed for *anti*-**24** at δ 1.30,[2] in the ^1H NMR spectrum of **26**. Signals of the ethylene bridges appear as multiplets in the range δ 1.6–3.0 thus any presence of a minor amount of *syn*-**26** (the methyl signal of which is expected to be at δ 2–3 similar to that of *syn*-**24** at δ 2.54)[2] would not be apparent. The general structure of **26** was, however, confirmed by a molecular ion observed at *m/z* 416 in its mass spectrum and the presence of only *anti*-**26** was further indicated by a sharp



anti - **26** *syn* - **26** **27**; X = SMe **28**; X = $S(Me)_2^+BF_4^-$

melting point (170 °C) recorded. One AB system centred at δ 3.78 (the outer two lines are unresolved or too low in intensity for the measurement of the coupling constant) equivalent to four protons could be assigned to the two almost identical pairs of methylene protons at C-1 and C-12. Another AB system centred at δ 3.61 (the outer two lines are again unresolved or too low in intensity for the measurement of the coupling constant) then corresponds to the methylene group at C-3 [away from the (1,3)-bridged ring] while the third well-resolved AB system at δ 3.25 and 2.79 is shielded by the (1,3)-bridged ring.

A mixture of isomers of **27** was obtained in a 68% yield on treatment of *anti*-**26** with lithium diisopropylamide followed by a methyl iodide quench.[19] Although the ^{1}H NMR spectrum of the product mixture is very complicated owing to significant overlapping of signals, the characteristic 'internal' methyl protons of the *anti*-[2.2](1,3)cyclophane system, SMe protons, and shielded ring protons of the [2.2](1,3)(1,4)cyclophane system appear as expected as several singlets in the range δ 1.4–1.6, δ 2.1–2.3 and δ 5.0–5.7, respectively. The general structure of **27** is clearly supported by a molecular ion at *m*/*z* 444 observed in its mass spectrum.

The bis(sulfonium) salt **28**, m.p. > 200 °C, could be prepared in 61% yield by treating the isomers of **27** with dimethoxycarbonium fluoroborate.[21] The first attempt at a Hofmann elimination of **28** to form the cyclophanediene **14**, and thus the dihydropyrene **15**, was carried out with potassium *tert*-butoxide in refluxing THF. An intense orange-red colour was initially observed which faded and disappeared rapidly. The formation of a coloured compound was evident from TLC studies during the initial period of the reaction. The dihydropyrene **1** and its derivatives are known to be intensely coloured and thus the above observation perhaps indicated the presence of the dihydropyrene **15**. Spectral studies of the isolated product mixture, however, did not indicate the presence of either the dihydropyrene **15** or the cyclophanediene **14**. TLC studies suggested the presence of mainly polymeric materials with very small R_f values.

Several attempts at the Hofmann elimination of **28** were then carried out at room temperature with an effort to exclude oxygen by using thoroughly degassed solvents. TLC studies indicated that the orange–red colour, though it faded slowly, persisted during the reaction period. Isolation of the product mixture was carried out rapidly but chromatography on silica gel seemed to cause rapid decomposition. Chromatography on alumina, however, allowed the isolation of an orange oil. The ^{1}H NMR spectrum of the product taken immediately was rather complicated and did not indicate the presence of a clean product mixture. However, a sharp singlet at δ −4.19 and a multiplet centred at δ −3.1 in a 3:2 ratio were clearly observed. These are in reasonable accord with chemical shifts expected of the methyl and C-1′ methylene protons of **15** respectively, the complicated multiplet of the latter being due to a rigid conformation of the (1,3)cyclophane system. Another multiplet centred at δ 0.3 of approximately two protons could be assigned to the C-2′ methylene protons. Signals observed at about δ 1.5

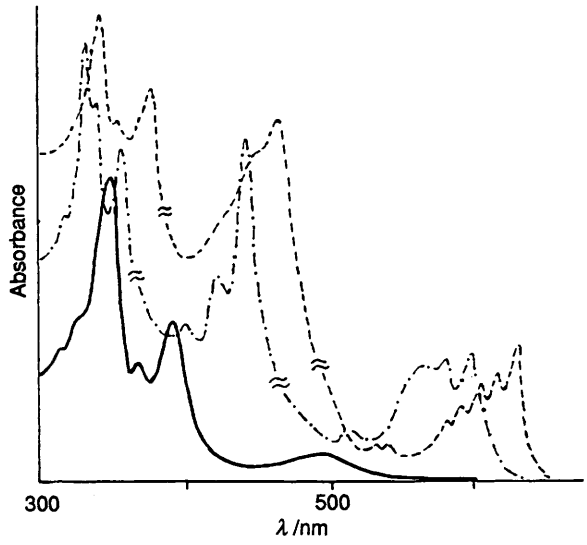
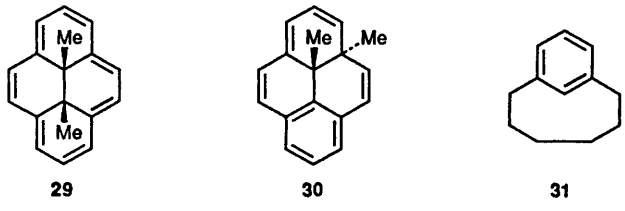


Fig. 1 Qualitative UV–VIS absorption spectrum of a freshly isolated product mixture containing **15** (——) and those of **1** (– – – –) and **29** (— · — ·) reconstructed from literature data[22]

may correspond to the methyl protons of **14** but overlapping of signals at δ 5–9 prevented the identification of olefinic protons of **14**.

The presence of **15** in the isolated mixture was further supported by the mass spectrum determined for a freshly isolated sample. A molecular ion at *m*/*z* 348 was observed with subsequent loss of methyl (*m*/*z* 333) and methane (*m*/*z* 332). Ready fragmentation of part of the (1,3)cyclophane unit was evident when the base peak corresponding to $M - (CH_3) - (CH_2CH_2C_6H_4)$ was observed at *m*/*z* 229. Further evidence for the presence of the dihydropyrene system was obtained from the UV–VIS spectrum (Fig. 1) of the product mixture. Absorptions at λ_{max} 349, 368, 393 and 496 nm observed in the visible region are similar, though shifted to shorter wavelength, relative to those[22] displayed by the parent dihydropyrenes **1** and **29**.



29 **30** **31**

Based on the above spectral data, the desired novel molecule **15** having a (1,3)cyclophane within the π-cloud of a [14]annulene was evidently formed, although all our efforts to isolate a pure sample of **15** failed. Our result, however, justifies the earlier prediction that on going from **8** to **10** to **14**, reduced strains in the (1,3)(1,4)cyclophane unit in cyclophanediene **14** will result in a more favourable geometry, allowing cyclization involving C-8 and C-16 to form the dihydropyrene system **15**.

A sample of the isolated product mixture, however, slowly decomposed even when kept at 0 to −10 °C. The orange colour disappeared after more than 48 h. TLC studies of the sample indicated mainly component(s) with very small R_f value(s). Its ^{1}H NMR spectrum no longer resembled that obtained earlier. The UV–VIS spectrum of the sample shows only absorptions in the UV region and no satisfactory mass spectrum could be obtained. The rate of decomposition seemed to increase thermally or photochemically (254 nm).

Thermal rearrangement of the parent dimethyldihydro-

Table 1 Comparison of the diatropicities in several dihydropyrenes

Compound	δCH_3	δCH_2[a]	δCH_2[b]	$\Delta\delta(CH)_3$[c]	% Ring current
1[1,2,7]	−4.25	—	—	5.22	100
4[4]	−4.3	−4.0	−1.7	5.27	100
5[5]	−4.25	−4.14	0.36	5.22	100
15	−4.19	−3.1	0.3	5.16	99
29[22]	−2.06	—	—	3.03	58

[a] The first methylene group directly bonded to one of the internal tertiary carbons of the dihydropyrene moiety. [b] The second methylene group of the internal substituent. [c] The shielding (in ppm) of the internal methyl protons relative to those in the non-aromatic (non-diatropic) model **7**.

pyrene **1** at 190–210 °C is known to give the product **30**.[23] The diethyl and dipropyl derivatives[3] **2** and **3** have been shown to rearrange at much lower temperatures (boiling cyclohexane). There was however no spectral evidence for the presence of rearranged product(s) in the decomposition product mixture of **15**. The dihydropyrene **15** still sustains as strong a ring current (see later discussion) as that of the parent **1**. This perhaps serves as the main driving force for the ready valence isomerization of **14** to form **15**. Molecular models of **15** however suggest significant angle strains particularly in the (1,3)cyclophane unit which, due to fixed positions of C-2 and C-10b, could be more strained than [6](1,3)cyclophane **31**.[24] Based on the mass spectral data mentioned earlier, a plausible explanation for the decompositon of **15** is that bond strains in the (1,3)cyclophane unit led to homolysis of the C-10b–C-2′ bond forming radicals which result in decomposition and/or polymerization.

Diatropicity Study.—The chemical shifts of the internal methyl protons of **1** and its derivatives have been shown to be sensitive probes for the extent of delocalization (diatropicity) of the macroring.[25] A direct comparison of the observed ^1H NMR data for *trans*-**1**,[1,2,7] **4**,[4] **5**[5] and **15** (Table 1) clearly indicates that all these [14]annulenes sustain an almost identical ring current (diatropicity). Qualitatively, the comparison to the non-aromatic (non-diatropic) system **7** with methyl protons in a similar environment (internal methyl protons at δ 0.97)[2] and the assumption that shielding is proportional to ring current[26] show that **15** sustains about 99% of the ring current of *trans*-**1**. Deviation of the π-periphery from planarity, for example the saucer-shaped **29** (internal methyl protons at δ −2.06),[22] has been shown to exhibit a smaller ring-current effect (Table 1). It is likely that in **15**, despite significant angle/bond strains in the (1,3)cyclophane unit, no appreciable change in the overall geometry of the dihydropyrene moiety is experienced thus sustaining as strong a ring current as that of the parent **1**.

A study of the chemical shifts of the internal ethylene bridge protons (Table 1) of several dihydropyrenes has led to some interesting results. The C-2′ methylene protons (δ 0.3) in **15** appear at a similar chemical shift to those in **5** but are undoubtedly shifted significantly downfield compared with the corresponding methylene protons in **4**. The anisotropic effect of the benzene ring in **15** however must have caused a significant deshielding of the C-2′ methylene protons and thus these protons do not serve as a good probe for the study of the ring current effect. A comparison of proton chemical shifts of the 'first' methylene groups directly attached to the dihydropyrene moiety should give a better indication of the relationship between the relative position in space and the ring current effect.

Molecular models, results from molecular mechanics calculations[25] and X-ray crystallographic data[27] of derivatives of **1** all indicate that the two methyl groups (δ −4.25) in *trans*-**1** rest approximately in the central axis of the dihydropyrene moiety (Fig. 2). The straight-chain substituents in **4** and **5** would also

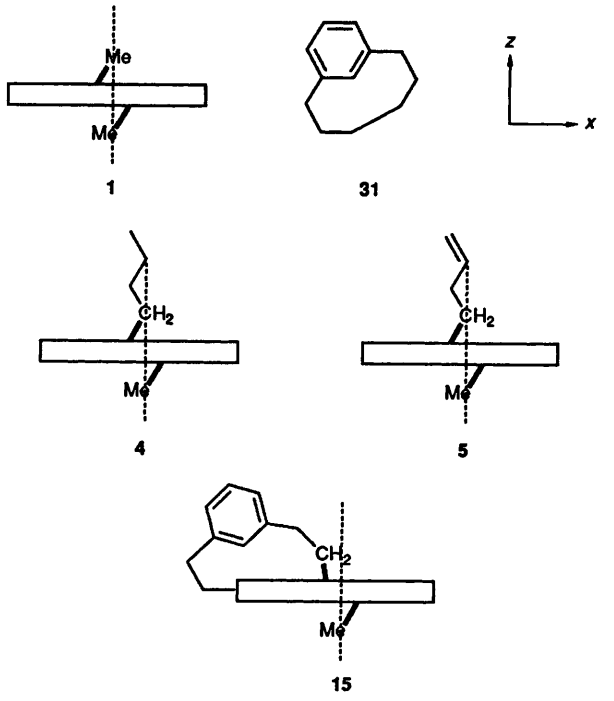


Fig. 2 Diagramatic representations of the relative positions of internal substituents in the dihydropyrene moiety with reference to the averaged plain of the periphery (*x*-axis) and the central axis (*z*-axis)

place the respective 'first' methylene groups approximately in the same axis. Their similar chemical shifts observed at *ca.* δ −4.0 support this argument. This is also consistent with earlier findings[7] that for the same position in space relative to the mean plane of delocalization of the aromatic π-cloud (the *x*-axis; Fig. 2) in dihydropyrene, the magnitude of the ring current effect on the chemical shifts is essentially the same for ^{13}C and for ^1H. Protons of the 'first' methylene group in **15** however are observed at δ −3.1, some 1 ppm downfield from those observed for **4** and **5** (Table 1). Angle/bond strain effects may have caused a change in chemical shift of these methylene protons. Molecular models of **15**, however, indicate a clear deviation of the methylene group concerned from the central axis (Fig. 2). The significant downfield shift may be a result of this change in relative position in space of the methylene group. This serves as the first example to indicate qualitatively that the ring current effect on proton chemical shift depends significantly on the position in space relative to the central axis of delocalization of the aromatic π-cloud (the *z*-axis; Fig. 2) in dihydropyrene **1**.

Experimental

All melting points were determined with a Thomas Hoover capillary melting point apparatus and are uncorrected. ^1H NMR spectra were determined in $CDCl_3$ (unless otherwise stated) on a Perkin-Elmer R32 (90 MHz) spectrometer, a JEOL FX90Q (90 MHz) or a Bruker AC-F 300 (300 MHz) Fourier Transform spectrometer. All chemical shifts are reported in ppm downfield from tetramethylsilane, which was used as an internal standard. *J* values are given in Hz. IR spectra were recorded on a Perkin-Elmer 1310 infrared spectrometer. UV–VIS spectra were determined in cyclohexane and recorded on a Shimadzu UV 240 Graphicord spectrometer. Mass spectra were determined on a VG Micromass 7035 mass spectrometer at 70 eV electron impact ionization being used. Relative intensities are given in parentheses. Only the molecular ion containing ^{79}Br is given for compounds containing bromine. Correct isotope patterns were obtained in all cases. Microanalyses were performed by the Microanalytical Laboratory

of the Department of Chemistry, National University of Singapore. All evaporations were carried out under reduced pressure on a rotary evaporator at *ca.* 40 °C, and all organic layers were washed with water (unless otherwise stated) and dried with anhydrous magnesium or sodium sulfate.

1,4-*Bis*(*bromomethyl*)-2,6-*dimethylbenzene* (**17**).—The bromide **16**[13] (22.18 g, 111 mmol) was added to 48% aqueous hydrogen bromide (27 cm^3) and glacial acetic acid (7 cm^3). To this mixture were added 1,3,5-trioxane (3.34 g, 111 mmol) and myristyltrimethylammonium bromide (0.28 g). The whole mixture was stirred vigorously and heated at gentle reflux for 24 h. It was then cooled to room temperature. The aqueous phase was decanted and the precipitate was repeatedly washed with water. The solid was recrystallized repeatedly from cyclohexane to give colourless crystals of **17**, 6.53 g (22%), m.p. 140–142 °C (Found: C, 41.4; H, 4.1; Br, 54.5. $C_{10}H_{12}Br_2$ requires C, 41.1; H, 4.1; Br, 54.7%); ν_{max}/cm^{-1} 1440, 1410, 1370, 1290, 1180, 1110, 870, 760, 730 and 650; δ_H 7.06 (2 H, s, ArH), 4.35 (2 H, s, CH_2), 4.40 (2 H, s, CH_2) and 2.40 (6 H, s, CH_3); *m*/*z* 292 (M^+, 9%), 213 (81), 211 (77) and 132 (100).

1,4-*Bis*(*mercaptomethyl*)-2,6-*dimethylbenzene* (**18**).—Thiourea (0.89 g, 12.9 mmol) and 1,4-bis(bromomethyl)-2,6-dimethylbenzene **17** (1.88 g, 6.4 mmol) were added to 95% ethanol (80 cm^3). The stirred mixture was heated gently at reflux for 3 h. After cooling to room temperature, the bulk of the solvent was removed under reduced pressure. The intermediate salt was filtered and stirred at reflux with potassium hydroxide (7.4 g, 129 mmol) in water (150 cm^3) for 4 h. The mixture was cooled in an ice-bath and 50% sulfuric acid was added until the solution was acidic. Extraction of the mixture with chloroform followed by washing, drying and concentration under reduced pressure gave a yellow oil. The crude mixture was chromatographed on silica gel using hexane–dichloromethane (1 : 1) as eluent to give the desired product **18** (1.13 g, 83%). A sample recrystallized from cyclohexane afforded colourless crystals of **18**, m.p. 76–78 °C (Found: C, 60.3; H, 7.05; S, 32.6. $C_{10}H_{14}S_2$ requires C, 60.6; H, 7.1; S, 32.3%); ν_{max}/cm^{-1} 2520, 1440, 1370, 1246, 1160, 870, 765, 690 and 670; δ_H 6.98 (2 H, s, ArH), 3.74 (2 h, d, *J* 6.8, CH_2), 3.65 (2 H, d, *J* 7.6, CH_2), 2.38 (6 H, s, CH_3), 1.73 (1 H, t, *J* 7.6, SH) and 1.56 (1 H, t, *J* 6.7, SH); *m*/*z* 198 (M^+, 59%), 165 (100), 132 (81) and 119 (15).

14,18-*Dimethyl*-2,11-*dithia*[3.3](1,3)(1,4)*cyclophane* (**19**).—A solution of 1,3-bis(bromomethyl)benzene (4.13 g, 16 mmol) and **18** (3.10 g, 16 mmol) in benzene (180 cm^3) was added dropwise over a period of 8 h to a vigorously stirred solution of potassium hydroxide (2.67 g, 48 mmol) in 95% ethanol (750 cm^3) at room temperature under nitrogen. After stirring for an additional 18 h, the bulk of the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane, washed, dried and evaporated. The residue was preadsorbed on silica gel and chromatographed using hexane–dichloromethane (3:1) as eluent to afford dithiacyclophane **19** (3.72 g, 79%). A sample was recrystallized from hexane to give colourless crystals of **19**, m.p. 120–122 °C (Found: C, 71.95; H, 6.8; S, 21.6. $C_{18}H_{20}S_2$ requires C, 71.95; H, 6.7; S, 21.3%); ν_{max}/cm^{-1} 1580, 1570, 1440, 1360, 1200, 1160, 1070, 890, 870, 820, 780 and 710; δ_H 7.12–6.88 (3 H, m, 5-, 6- and 7-H), 6.61 (2 H, s, 15 and 17-H), 5.69 (1 H, br s, 9-H), 3.90 (2 H, s, CH_2), 3.74 (2 H, s, CH_2), 3.50 (2 H, s, CH_2), 3.35 (2 H, s, CH_2) and 2.19 (6 H, S, CH_3); *m*/*z* 300 (M^+, 97%), 163 (51) and 133 (100).

Disulfone (**20**) *of* 14,18-*dimethyl*-2,11-*dithia*[3.3](1.3)(1,4)*cyclophane* (**19**).—An excess of 35% aqueous hydrogen peroxide (10 cm^3) was added slowly with stirring to a suspension of (1.00 g, 3 mmol) of dithiacyclophane **19** in acetic acid (30 cm^3). The solution was kept at 100 °C for 5 h. The resulting precipitate was filtered and repeatedly washed with water and dried to give a quantitative yield of the corresponding disulfone **20**, m.p. > 300 °C (Found: C, 59.1; H, 5.5; S, 17.4. $C_{18}H_{20}S_2O_4$ requires C, 59.3; H, 5.5; S, 17.6%); ν_{max}/cm^{-1} 1400, 1310, 1260, 1170, 1110, 900, 880, 860, 840 and 700 cm^{-1}; δ_H 7.1–7.5 (3 H, m, 5-, 6- and 7-H), 6.89 (2 H, s, 15- and 17-H), 5.75 (1 H, br s, 9-H), 4.68 (2 H, s, CH_2), 4.35 (2 H, s, CH_2), 4.10 (2 H, s, CH_2), 4.03 (2 H, s, CH_2) and 2.28 (6 H, s, CH_3); *m*/*z* 236 (M^+, 100%), 221 (29), 206 (4), 131 (66) and 104 (52).

Wittig Rearrangement of Dithiacyclophane **19** *to form* **21**.—Lithium diisopropylamine was prepared by addition of 1.5 mol dm^{-3} butyllithium in hexane (10 cm^3, 15 mmol) to diisopropylamine (2.4 cm^3, 20 mmol) in dry THF (10 cm^3). The base was then added dropwise to a solution of the dithiacyclophane **19** (1.5 g, 5 mmol) in dry THF (20 cm^3) under nitrogen at 0 °C. After 15 min, the green solution was quenched with methyl iodide. Water was added and the resulting mixture extracted with dichloromethane. The organic phase was washed, dried and evaporated. The yellow oil obtained was chromatographed on silica gel using hexane–dichloromethane (1 : 1) as the eluent to give a mixture of isomers of **21** (0.92 g, 56%) (Found: M^+, 328.1317. $C_{20}H_{24}S_2$ requires *M*, 328.1319); ν_{max}/cm^{-1} 1580, 1420, 1380, 1210, 1080, 920, 860, 790 and 730; δ_H 7.0–8.0 (m, ArH), 5.65 (s, 13-H), 5.50 (s, 8-H), 3.2–3.7 (m, CH), 1.8–2.9 (m, CH_2), 2.47 (s, $ArCH_3$), 2.01 (s, SCH_3), 2.00 (s, SCH_3) and 1.68 (s, $ArCH_3$); *m*/*z* 328 (M^+, 48%), 196 (100) and 181 (80).

12,16-*Dimethyl*[2.2](1,3)(1,4)*cyclophane* (**22**).—*Pyrolytic method.* The flash vacuum thermolysis set-up was purchased from the Aldrich Chemical Company. The disulfone **20** (100–300 mg) was placed at the closed end of the quartz tube about 15 cm away from the furnace. The system was evacuated to 200 mTorr and the furnace heated to 600 °C. An external pre-heater was heated to 300 °C and slid towards the sample of disulfone **20**. After 0.5 h, the oil trapped between the furnace and the cold trap was extracted into dichloromethane. The crude product was chromatographed on silica gel using hexane as the eluent to give **22** as a colourless oil (15–60%) which solidified on standing. A sample recrystallized from cyclohexane afforded colourless crystals of **22**, m.p. 56 °C (Found: M^+, 236.1560. $C_{18}H_{20}$ requires *M*, 236.1565. Found: C, 91.0; H, 8.8. $C_{18}H_{20}$ requires C, 91.5; H, 8.5%); ν_{max}/cm^{-1} 1600, 1480, 1380, 1180, 930, 880, 860, 820, 790, 740, 720, 650 and 640; δ_H 6.7–7.0 (3 H, m, 4-, 5- and 6-H), 6.68 (1 H, s, 13-H), 5.64 (1 H, s, 15-H), 5.53 (1 H, br s, 8-H), 3.22–2.01 (8 H, m, CH_2), 2.41 (3 H, s, CH_3) and 1.65 (3 H, s, CH_3); *m*/*z* 236 (M^+, 100%), 221 (56) and 131 (85).

Raney nickel reduction. A mixture of the isomers of **21** (0.35 g, 1 mmol) was added to absolute alcohol (10 cm^3) containing an excess (> 10 equiv.) of W-7 Raney nickel[19] and the mixture was heated at reflux for 24 h. The mixture was cooled and diluted with benzene. The excess nickel was filtered off and the solvent evaporated. The product isolated after column chromatography was identical (m.p., IR, ^1H NMR, MS) with a reference sample obtained previously.

12,16-*Bis*(*bromomethyl*)[2.2](1,3)(1,4)*cyclophane* (**23**).—A catalytic amount of benzoyl peroxide was added to a mixture of the cyclophane **22** (1.34 g, 5.68 mmol) and *N*-bromosuccinimide (1.01 g, 5.68 mmol) in carbon tetrachloride (50 cm^3). The mixture was irradiated with a 200 W tungsten lamp and left at reflux for 2 h, after which a second batch of *N*-bromosuccinimide (1.01 g, 5.68 mmol) was added. After heating at reflux with continuous irradiation for an additional 2 h, the reaction mixture was cooled to room temperature and filtered. The precipitate was washed thoroughly with carbon tetrachloride. Evaporation of the solvent, followed by chromatography on alumina with hexane as the eluent afforded pale yellow crystals

of dibromide **23** (1.75 g, 72%), m.p. 126–128 °C (Found: C, 54.9; H, 4.5. $C_{18}H_{18}Br_2$ requires C, 54.8; H, 4.6%); ν_{max}/cm^{-1} 1440, 1200, 930, 780, 750 and 710; δ_H 7.36 (1 H, br s, 13-H), 6.7–7.3 (3 H, m, 4-, 5- and 6-H), 5.87 (1 H, br s, 15-H), 5.65 (1 H, br s, 8-H), 4.71 (2 H, s, CH_2Br), 3.51, 4.36 (2 H, AB, *J* 10.7, CH_2Br) and 1.7–3.3 (8 H, m, CH_2C); *m/z* 392 (M^+, 22%), 313 (100), 234 (62), 233 (46), 219 (32), 205 (26), 104 (28) and 103 (19).

anti-24-*Methyl*-1,21-*dithia*[3.3](1,3)(1,3)[2.2](2,5)(1,3)*cyclophane* (**26**).—The intermolecular coupling reaction of 12,16-bis(bromomethyl)[2.2]metaparacyclopane **23** (0.81 g, 2.04 mmol) and 2-methyl-1,3-bis(mercaptomethyl)benzene **25**[2] (0.38 g, 2.04 mmol) under high dilution conditions was carried out according to the procedure for the preparation of dithiacyclophane **19**. The crude product was preadsorbed on silica gel and chromatographed using hexane–dichloromethane (2:1) as the eluent to yield pale yellow crystals of dithiacyclophane *anti*-**26** (0.55 g, 32%), m.p. 170 °C (Found: M^+, 416.1639. $C_{27}H_{28}S_2$ requires *M*, 416.1640. Found: C, 77.6; H, 6.1. $C_{27}H_{28}S_2$ requires C, 77.8; H, 6.8%); ν_{max}/cm^{-1} 1580, 1450, 1170, 1070, 930, 780, 760, 740, 710 and 625; δ_H 7.03 (1 H, br s, 13-H), 6.5–7.3 (6 H, m, 4-, 5-, 6-, 21-, 22- and 23-H), 5.71 (1 H, br s, 15-H), 5.23 (1 H, br s, 4-H), 3.78 (4 H, AB with non-observable outer two lines, CH_2S), 3.61 (2 H, AB with non-observable outer two lines, CH_2S), 3.25 and 2.79 (2 H, AB, *J* 14.3, CH_2S), 1.6–3.0 (8 H, m, CH_2C) and 1.44 (3 H, s, CH_3); *m/z* 416 (M^+, 92%), 383 (31), 382 (12), 297 (43), 265 (24), 161 (100) and 117 (34).

Wittig Rearrangement of Dithiacyclophane anti-**26** *to form* **27**.—This reaction was carried out with dithiacyclophane *anti*-**26** (318 mg, 0.76 mmol) according to the procedure for the conversion of **19** into **21**. The product obtained was chromatographed on alumina using hexane–benzene (3:1) as the eluent to give a mixture of isomers of **27** (230 mg, 68%) (Found: M^+, 444.1943. $C_{29}H_{32}S_2$ requires *M*, 444.1945); ν_{max}/cm^{-1} 1560, 1450, 1180, 1020, 930, 860, 780, 750, 710 and 625; δ_H 6.4–7.2 (m, 4-, 5-, 6-, 13-, 20-, 21- and 22-H), 4.95, 5.22, 5.75 (br s, 8- and 15-H), 3.0–4.0 (m, CH), 1.3–4.0 (m, CH_2) and 2.06, 2.07 (s, SCH_3); *m/z* 444 (M^+, 95%), 430 (38), 382 (100), 349 (51), 333 (16), 277 (29), 265 (22), 243 (24), 215 (39) and 133 (59).

trans-10c-*Methyl*-10b,10c-*dihydro*-2,10b-*ethanol*[1,3]*benzenoethanopyrene* (**15**).—A solution of a mixture of isomers of **27** (147 mg, 0.33 mmol) in dichloromethane (5 cm^3) was added dropwise with stirring to a solution of dimethoxycarbonium fluoroborate (160 mg, 0.99 mmol) in dichloromethane (4 cm^3) kept at −30 °C. The mixture was allowed to warm to room temperature and was stirred for an additional 14 h. The salt **28** was separated by decantation and triturated with ethyl acetate to give a yellow solid weighing 130 mg (61%), m.p. > 200 °C. The sulfonium salt **28** was then stirred in degassed dry THF (10 cm^3) at room temperature under nitrogen. Solid (powdered) potassium *tert*-butoxide (68 mg, 0.6 mmol) was added and the mixture was stirred at room temperature for 45 min. The solution turned orange–red. Degassed dilute aqueous HCl and benzene were then added and the organic layer was separated, dried and evaporated. The residue was filtered rapidly through alumina with degassed hexane as the eluent. An orange oil (30 mg) was obtained (Found: M^+, 348.1877. $C_{27}H_{24}$ requires *M*, 348.1878); λ_{max}(cyclohexane)/nm 349, 368, 393 and 496; ν_{max}/cm^{-1} 2920, 2860, 1460, 870, 780 and 720; δ_H, see discussion in text; *m/z* 348 (M^+, 12%), 333 (23), 229 (100), 215 (41), 202 (10), 149 (25), 131 (13) and 91 (21).

Acknowledgements

This work was supported (RP860606) by the National University of Singapore (NUS). A. H.-T. Yap thanks the NUS for the Research Studentship (1988–90). Assistance from the technical staff of the Department of Chemistry, NUS, is gratefully acknowledged.

References

1 V. Boekelheide and J. B. Phillips, *J. Am. Chem. Soc.*, 1967, **89**, 1695.
2 R. H. Mitchell and V. Boekelheide, *J. Am. Chem. Soc.*, 1974, **96**, 1547.
3 V. Boekelheide and T. A. Hylton, *J. Am. Chem. Soc.*, 1970, **92**, 3669.
4 T. D. Harris, B. Neuschwander and V. Boekelheide, *J. Org. Chem.*, 1978, **43**, 727.
5 Y. L. Mao and V. Boekelheide, *J. Org. Chem.*, 1980, **45**, 2746.
6 R. H. Mitchell and W. Anker, *Tetrahedron Lett.*, 1981, **22**, 5139.
7 R. Du Vernt and V. Boekelheide, *Proc. Natl. Acad. Sci. USA*, 1974, **71**, 2961.
8 S. Misumi, Y. Sakata, E. Kobayashi and H. Higuchi, *Tetrahedron*, 1986, **42**, 1731.
9 (*a*) C. J. Brown and A. C. Farthing, *Nature* (*London*), 1949, **164**, 915; (*b*) C. J. Brown, *J. Chem. Soc.*, 1953, 3265; (*c*) K. Lonsdale, H. J. Milledge and K. V. Krishna Rao, *Proc. R. Soc. London, Ser. A*, 1960, **255**, 82; (*d*) K. Lonsdale and H. J. Milledge, *Nature* (*London*), 1959, **184**, 1545.
10 H. Hope, J. Bernstein and K. N. Trueblood, *Acta Crystallogr., Sect. B*, 1972, **28**, 1733.
11 S. Misumi and H. Higuchi, personal communication.
12 (*a*) D. J. Cram, R. C. Helgeson, D. Lock and L. A. Singer, *J. Am. Chem. Soc.*, 1966, **88**, 1324; (*b*) D. T. Hefelfinger and D. J. Cram, *J. Am. Chem. Soc.*, 1971, **93**, 4754.
13 W. E. Truce, B. VanGermert and W. W. Brand, *J. Org. Chem.*, 1978, **43**, 103.
14 R. H. Mitchell and S. I. Vivekanantan, *Synlett*, 1989, **1**, 55.
15 (*a*) L. Rossa and F. Vögtle, *Top. Curr. Chem.*, 1983, **113**, 1; (*b*) P. Knops, N. Sendhoff, H.-B. Mekelburger and F. Vögtle, *Top. Curr. Chem.*, 1991, **161**, 1; (*b*) A. Ostrowicki, E. Koepp and F. Vögtle, *Top. Curr. Chem.*, 1991, **161**, 37.
16 F. Vögtle and L. Rossa, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 515.
17 N. Kannen, T. Otsubo, Y. Sakata and S. Misumi, *Bull. Chem. Soc. Jpn.*, 1976, **48**, 3307.
18 R. H. Mitchell, T. Otsubo and V. Boekelheide, *Tetrahedron Lett.*, 1975, 219.
19 (*a*) M. Adkins and H. R. Billica, *J. Am. Chem. Soc.*, 1948, **70**, 695; (*b*) *Org. Synth. Coll. Vol. III*, 1955, 176.
20 (*a*) F. Vögtle and P. Neumann, *Chimia*, 1972, **26**, 64; (*b*) S. Akabori, S. Hayashi, M. Nawa and K. Shiomi, *Tetrahedron Lett.*, 1969, 3727; (*c*) D. T. Hefelfinger and D. J. Cram, *J. Am. Chem. Soc.*, 1971, **93**, 4767.
21 R. F. Borch, *J. Org. Chem.*, 1969, **34**, 627.
22 R. H. Mitchell and V. Boekelheide, *J. Chem. Soc., Chem. Commun.*, 1970, 1555.
23 V. Boekelheide and E. Sturme, *J. Am. Chem. Soc.*, 1969, **91**, 902.
24 (*a*) S. Hirano, H. Hara, T. Hiyama, S. Fujita and H. Nozaki, *Tetrahedron*, 1975, **31**, 2219; (*b*) S. L. Kammula, L. D. Iroff, M. Jones, Jr., J. W. van Straten, W. H. de Wolf and F. Bickelhaupt, *J. Am. Chem. Soc.*, 1977, **99**, 5815.
25 R. H. Mitchell, *Adv. Theor. Interesting Mol.*, 1989, **1**, 135.
26 (*a*) R. H. Mitchell and J. S. H. Yan, *Can. J. Chem.*, 1978, **55**, 3347; (*b*) Y.-H. Lai, *J. Am. Chem. Soc.*, 1985, **107**, 6681.
27 (*a*) A. W. Hanson, *Acta Crystallogr., Sect. B*, 1965, **18**, 599; (*b*) A. W. Hanson, *Acta Crystallogr., Sect. B*, 1967, **23**, 476.

Paper 2/05747F
Received 28*th October* 1992
Accepted 7*th December* 1992