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SYNTHESIS OF DIATROPIC HIGHLY BENZANNELATED ANNULENES.[1]

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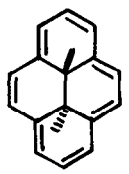
Summary: The first examples of annelated *cis*-dihydropyrenes, **16** , **18** , **19** , together with a number of highly annelated *trans*-dihydropyrenes, **2** - **4** and, **17** , are described. All are diatropic and indicate that higher annelation does not remove the delocalisation in a macrocyclic ring.

Boekelheide's[2] *trans*-15,16-dimethyldihydropyrene[3], **1** , has proved an excellent system to study benzannelation effects[4], since the mono-and dibenzannelated derivatives prepared[5] have all proved reasonably stable, and show clearly discernible diatropicity. Since the internal methyl groups are close to the center of the ring current, they are not only extremely sensitive probes for changes in ring current, but the magnitude of the shielding of such protons seems as great or greater than for any others[6]. Whilst many of the earlier benzannulenes prepared[6], contained three or more benzannelating rings, (which certainly stablised them) none showed diatropicity that could be clearly attributed to a macrocyclic ring current. We thus became interested to determine if diatropic highly annelated annulenes could be prepared. Now, in this paper, we report the synthesis of **2** , **3** and **4** , which are *formally* di, tri, and tetrabenzannelated derivatives of **1** , together with several other examples and their nmr spectra.



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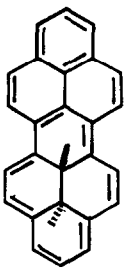

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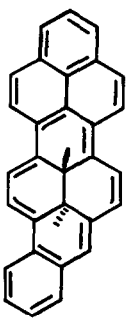

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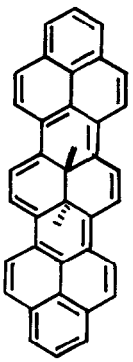

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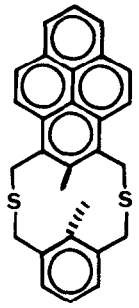
We anticipated that **2** for example might be prepared from the thiacyclophane **5** , by a Wittig rearrangement - Hofmann elimination sequence[7], analogous to **1** . The precursor to **5** however, 1,3-bis(bromomethyl)-2-methylpyrene, and the several pyrene derivatives that lead to it, all proved far too insoluble in common organic solvents for convenient use. We thus preferred to first synthesise the tetrahydropyrene derivative **6** , and subsequently dehydrogenate[8] this. As it turned



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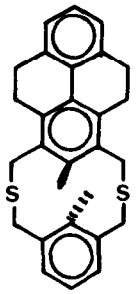

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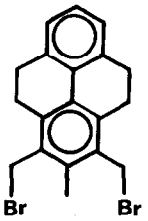

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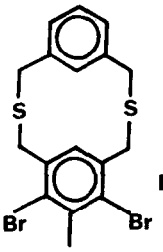

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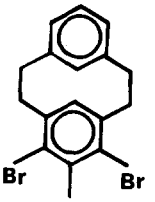

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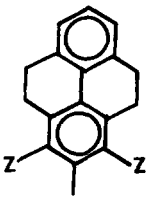
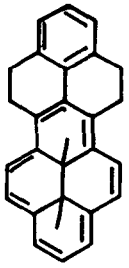


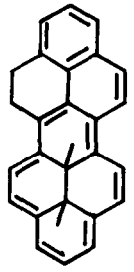
Z
10: Br
11: CN
12: CHO
13: CH_2OH

out, this provided also a number of intermediately annelated compounds, because some partial dehydrogenation occurred.

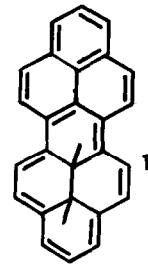
To this end the synthesis of dibromide **7** proceeded from mesitylene in 1·2% yield in 12 steps as follows: bromination of mesitylene in chloroform in presence of Fe powder gave 87% of 2,4-dibromomesitylene[9], which on oxidation with CrO_3-Ac_2O, followed by sulphuric acid hydrolysis gave 22% of 4,6-dibromo-5-methylisophthalaldehyde, mp 172-174°C[10]. Reduction of this dialdehyde with $NaBH_4$ in THF to the dialcohol (mp192-194°C) followed by reflux with conc. HBr gave 85% yield of 2,6-dibromo-3,5-bis(bromomethyl)toluene, mp 120-122°C. Cyclisation[7] of this with *meta*-xylylene dithiol gave 75% yield of the dithiacyclophane **8** , mp 172-173°C. Oxidation to the disulfone, mp 325-327°C(dec)(92% yield, H_2O_2 in acetic acid) followed by thermolysis[11] at 650°C gave 49% of the [2,2]metacyclophane, **9** , mp 115-117°C. In its ^{1}Hmr spectrum, **9** showed its internal hydrogens characteristically shielded as singlets at δ4.41 and 4.27.



15: trans-CH_3
16: cis-CH_3



17: trans-CH_3
18: cis-CH_3



2: trans-CH_3
19: cis-CH_3

Oxidation of **9** to tetrahydropyrene **10** , mp 128-130°C proceeded in 98% yield using[12] Br_2/Fe, and then replacement of the bromines by -CN groups with CuCN in N-methyl-2-pyrrolidinone gave **11** mp 224-226°C in 41% yield. Reduction[13] of **11** with diisobutylaluminum hydride gave dialdehyde **12** mp 147-149°C, in 80% yield, which on further reduction with $NaBH_4$-THF gave dialcohol **13** , mp 180-182°C. in 92% yield. Reflux of this with conc.HBr then yielded 74% of **7** , mp 208-210°C.

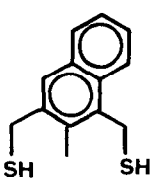
Cyclisation[7] of bromide **7** with 2,6-bis(mercaptomethyl)toluene[13] gave 67% of the *anti*-cyclophane **6** (mp 252-254°C, internal methyl protons at δ1.38 and 1.18) together with 7.3% of the analogous (to **6**) *syn*-cyclophane **14** (mp 198-200°C, internal methyl protons at δ2.48 and 2.44). Wittig rearrangement-Hofmann elimination sequences[7] applied to both **6** and **14** then yielded **15** and **16** respectively together with some of the dehydrogenated compounds **17** - **19** and **2** .

The orange-red, **15** (internal methyl protons at δ-3.81 and -3.89), obtained in about 35% yield, could be subsequently dehydrogenated to **2**, also orange-red, mp 198-199°C, by DDQ(<20% yield) or much better (in 82% yield) simply by boiling in THF solution with potassium t-butoxide.[14] The ^{1}Hmr spectra of **2** and **17** are dramatically different. In **2** the methyl protons appear at δ -4.19 and -4.28, at almost identical position to those of **1** (δ -4.25), whereas in **17** they are at δ -2.78. This demonstrates conclusively the importance of having symmetrical Kekulé structures[5c,6] if maximum diatropicity is to be observed. In **2**, as in **1**, two Kekulé structures for the 14π ring can be written leaving in **2**, in either case, a naphthalenoid ring. Hence, the structures are of equal energy, and maximum delocalisation of the macroring of **2** occurs. In **17** however, in one Kekulé structure the naphthalenoid conjugation is interrupted and hence the two structures do not compete equally, in other words some bond localisation occurs in **17**, with consequent[4] loss of diatropicity.

In the *cis*-series, from **14**, **16**,**18**,**19** were likewise obtained, and represent the first examples of annelated *cis*-dihydropyrenes. The results found were parallel, in that for **19**, the internal methyl protons were at δ -1.85 and -2.14, to be compared with the *cis*-analogue of **1** at δ -2.06[13], whereas those of the monoannelated (naphtho) **18** were substantially less shielded at δ -0.99 and -1.04, consistent with the lesser degree of expected bond delocalisation.

Similarly cyclisation of bromide **7** with thiol[5c] **21** gave *anti*- and *syn*-thiacyclophanes **22** and **23** (mp 204-206°C) in 62% and 11% yields, respectively. *Anti*-**22**, mp 226-227°C (internal CH_3 at δ 1.50 and 0.72), in a similar sequence to above led to what is formally a tribenzannelated dihydropyrene, **3**, internal methyl protons at δ -1.35 and -1.41. Similarly, from **7** and thiol **24**, mp 146-148°C, *anti*-**25** (mp. 289-291°C, 54% yield, internal CH_3 proton at δ1.32) and *syn*-**26** (∿11%, internal CH_3 proton at δ2.14) were obtained, which from **25** gave[15] **4**, internal methyl protons at δ -3.2. The latter result indicates that **4** is the most diatropic of the higher[16] benzannelated annulenes known, and together with that for **3**, conclusively indicates that providing a good probe is chosen (in this case **1**) considerable perturbation of an annulene may be made with still a chance for analysis of effects on diatropicity.[4]

We thank the Natural Sciences Research Council of Canada and the University of Victoria for financial support.



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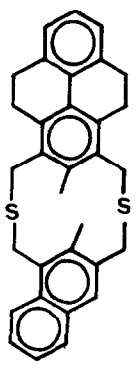
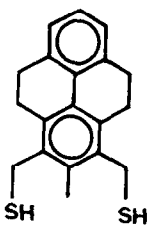


22: anti-CH_3
23: syn-CH_3



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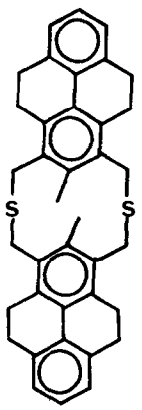

25: anti-CH_3
26: syn-CH_3

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15. The partially dehydrogenated and *cis*-products will be discussed elsewhere.
16. Tribenzo or more.

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