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Nonplanar Aromatic Compounds. 6. [2]Paracyclo[2](2,7)pyrenophane. A Novel Strained Cyclophane and a First Step on the Road to a “Vögtle” Belt†

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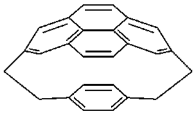
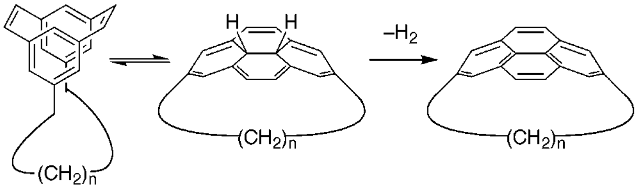
ABSTRACT



A benzene ring nestled into the concave face of a bent pyrene characterizes the title compound in the crystal. The synthesis of this compound was accomplished using the valence isomerization–dehydrogenation (VID) method and marks the official launch of our journey en route to aromatic belts first proposed by Prof. Vögtle.

We have recently developed a general route to the [*n*](2,7)-pyrenophanes **3**[1] and several analogues containing oxygen atoms in the bridge.[2−4] The lynchpin of this strategy is the conversion of a tethered *syn*-[2.2]metacyclophanediene system **1** to the corresponding pyrenophane **3** by a valence isomerization−dehydrogenation (VID) protocol (Scheme 1).

Scheme 1



1 **2** **3**

Noteworthy features of this strategy are the mild conditions (reflux in benzene) required to generate the severely distorted polycyclic aromatic hydrocarbon (PAH) moieties during the key step and the availability of gram quantities of the pyrenophanes using this approach.

With reliable access to bent pyrenes, the application of the VID methodology to the challenging goal of preparing aromatic belts consisting of a repeating pyrene motif, i.e., **4** (Figure 1) can now be targeted realistically. The 5-fold symmetric belt **4a** manifests itself in the equators of the fullerenes D_{5h} C_{70}[5] and D_{5d} C_{80},[6] whereas the 6-fold sym-

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† Part 5 in this series: Bodwell, G. J.; Bridson, J. N; Chen, S.-L.; Poirier, R. A. *J. Am. Chem. Soc.* **2001**, *123*, 4704-4708.

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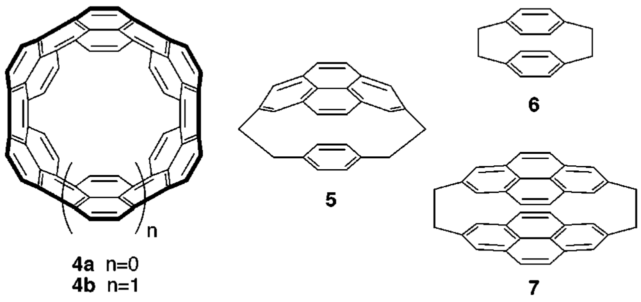


Figure 1.

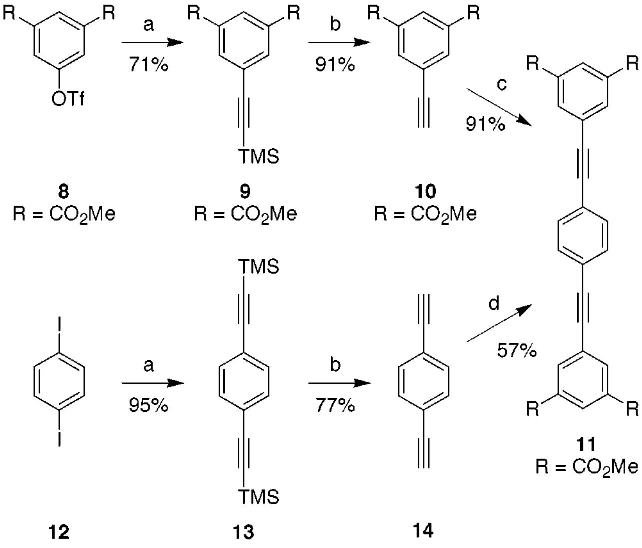
metric homologue **4b** can be excised from the equator of D_{6h} C_{84}.[7] Higher homologues ($n > 1$) are not fullerene fragments but constitute, as do **4a** and **4b**, small sections of nanotubes. With remarkable foresight, Vögtle[8] first proposed these belts as "interesting targets" prior to the discovery of the fullerenes and nanotubes. We suggest the name "Vögtle belts" to denote the architectural motif of **4**.

To progress from the current state of affairs toward a successful synthesis of a Vögtle belt, the obvious task at hand is to replace the aliphatic bridge of **3** with appropriate aromatic units. Doing so in one fell swoop would be ideal, but this approach brings with it a number of knotty synthetic complications. Although we are actively pursuing this avenue of investigation, a stepwise approach to the problem is also being pursued. This approach involves the partial replacement of the aliphatic bridge of **3** with aromatic units to afford pared down versions of **4** as stepping stones en route to the full belts.

The first step in this direction is the incorporation of a single *p*-phenylene unit, and [2]paracyclo[2](2,7)pyrenophane **5** was consequently identified as the first target. This compound is also interesting in that it can be viewed as a hybrid between [2.2]paracyclophane **6**[9] and [2.2](2,7)-pyrenophane **7**.[10] A strong indication that **5** was a viable synthetic target came from the AM1 calculated bend angle (θ) of its pyrene moiety (100.4°),[3] which is well below those of the more distorted [*n*](2,7)pyrenophanes that have already been prepared.[1−3]

The early stages of the synthesis (Scheme 2) involved the construction of diyne **11**, which contains all of the carbon atoms required for the construction of **5**. This was assembled from triflate **8**,[1] 1,4-diiodobenzene **12**, and trimethylsilylacetylene using Sonogashira chemistry[11] by two complementary routes. In the first of these, **8** was coupled with trimethylsilylacetylene to provide diester **9** (71%), which was protodesilylated to give **10** (91%). Coupling of **10** and **12** led to the formation of **11** in 91% yield. In the second route,

Scheme 2[a]



[a] (a) TMS−C≡CH, Pd(PPh$_3$)$_2$Cl$_2$, CuI, DBU, benzene, rt; (b) K$_2$CO$_3$, MeOH, rt; (c) **12**, Pd(PPh$_3$)$_2$Cl$_2$, CuI, DBU, benzene, rt; (d) **8**, Pd(PPh$_3$)$_2$Cl$_2$, CuI, DBU, benzene, rt.

coupling of **12** and trimethylsilylacetylene afforded **13** (95%), and protodesilylation then gave diyne **14** (77%). (WARNING! Purification of this compound by sublimation led in one instance to explosive decomposition.) The coupling of **8** and **14** then furnished **11** (57%). Although the second route worked very well, the explosion hazard associated with **14** led us to discontinue its use.

The remainder of the synthesis (Scheme 3) involved the manipulation of the existing carbon skeleton. Catalytic hydrogenation of **11** afforded tetraester **15** (95%), and this was reacted with LiAlH$_4$ and then HBr/HOAc to provide tetrabromide **16** in 85% yield from **15**. Treatment of **16** with Na$_2$S/Al$_2$O$_3$[12] to produce dithiacyclophane **17** proceeded in a disappointingly low yield of 28%. Bridge contraction of **17** was accomplished by methylation of the sulfur atoms with (MeO)$_2$CHBF$_4$ (Borch reagent) and then Stevens rearrangement. The resulting mixture of isomers **18** (70%, crude) was immediately reacted with Borch reagent and then subjected to the normal Hofmann elimination conditions. From this was obtained a ca. 1:1 mixture of cyclophanediene **19** and the desired pyrenophane **5**[13] in ca. 16% combined yield from **17**. Treatment of this mixture with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in benzene at room temperature gave **5** in 14% overall yield from **17**. The majority of the

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(8) Vögtle, F. *Top. Curr. Chem.* **1983**, *115*, 157−159.

(9) (a) Brown, C. J.; Farthing, A. C. *Nature* **164**, 915−916. (b) de Meijere, A.; König, B. *Synlett* **1997**, 1221−1232.

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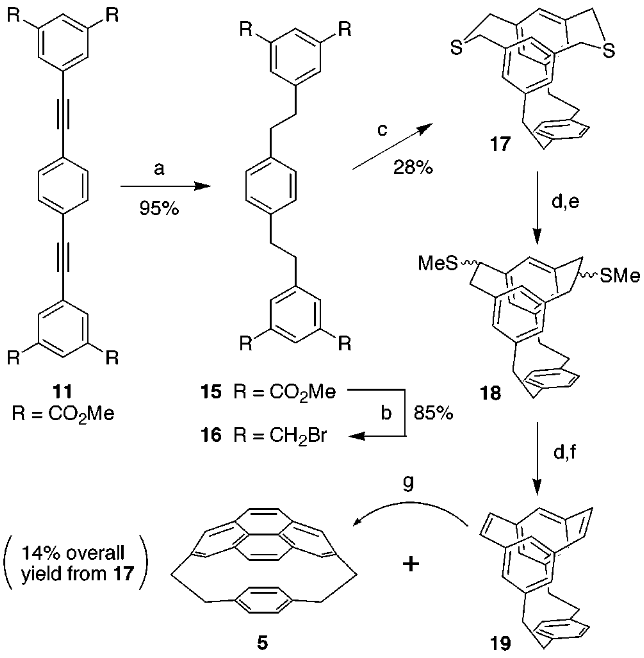
(12) Bodwell, G. J.; Houghton, T. J.; Koury, H. E.; Yarlagadda, B. *Synlett* **1995**, 751−752.

(13) Data for **5**: mp 216−219 °C, ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.67 (s, 4H), 7.40 (s, 4H), 5.54 (s, 4H), 2.99 (AA′XX′ half spectrum, 4H), 2.32 (AA′XX′ half spectrum, 4H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 135.7, 134.2, 131.3, 129.3, 128.6, 128.0, 126.1, 36.5, 33.8; MS (EI, 70 eV) *m/z* (%) 332 (11, M$^+$), 228 (100).

Scheme 3[a]



[a] (a) H_2, Pd(OH)/C, benzene, rt; (b) (i) $LiAlH_4$, THF, reflux, (ii) 30% HBr/HOAc, HOAc, reflux; (c) Na_2S/Al_2O_3, 10% EtOH/CH_2Cl_2, reflux; (d) $(MeO)_2CHBF_4$, CH_2Cl_2, rt; (e) *t*-BuOK, THF, rt; (f) *t*-BuOK, 1:1 THF/*t*-BuOH, rt; (g) DDQ, benzene, rt.

losses during the conversion of **17** into **5** were suffered during the transformation of **18** into **19**. In line with previous experience,[1−4] this step continues to be problematic.

The formation of some **5** during the Hofmann elimination and the ease of the conversion of cyclophanediene **19** to **5** were somewhat surprising. Earlier studies[1,4] have shown that even pyrenophanes with considerably lower bend angles than that of **5** (vide infra) do not form as easily as **5**. The reactivity of **19** is likely a consequence of the rigidity of the *p*-xylyl unit in the tether, which forces open (and thus strains) the *syn*-[2.2]metacyclophanediene system. A result of this is that the two internal carbon atoms are pushed toward one another.

A noteworthy feature of the synthesis is the manner in which the ethano bridges were installed. To the best of our knowledge, this is the first example of the application of such an approach to the preparation of a [2.2]cyclophane.

A single-crystal X-ray structure determination of **5**[14] (Figure 2) revealed a number of unusual and interesting structural features. The bend angle (θ)[3] in the pyrene moiety is 89.7°, which is an anomalously large 10.7° below the AM1 calculated angle of 100.4°. Up to now, the AM1 calculations have consistently exceeded the measured bend angles by just 4−7°.[1,3] On the other hand, the β angles,[15] at 16.1° {C(26)−C(1)−Du(1)[16]} and 16.3° {C(17)−C(15)−Du(2)[16]}, are considerably higher than those previously observed (<9.0°)[1−3] and those in the AM1 calculated structure (11.0°).

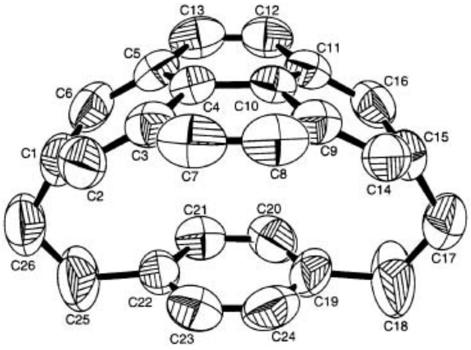


Figure 2. ORTEP representation of **5** in the crystal. The crystallographic numbering shown differs from the systematic numbering. Selected bond lengths (Å) and angles (deg): C(1)−C(26) 1.495(8), C(26)−C(25) 1.468(9), C(25)−C(22) 1.519, C(15)−C(17) 1.522(7), C(17)−C(18) 1.439(8), C(18)−C(19) 1.509(7); C(1)−C(26)−C(25) 112.7(5), C(22)−C(25)−C(26) 123.7(5), C(15)−C(17)−C(18) 111.9(5), C(17)−C(18)−C(19) 124.8(6).

The isolated benzene ring is essentially planar (α angles[15] $< 1°$), but the β angles of 4.0° {C(25)−C(22)−Du(3)[16]} and 4.6° {C(18)−C(19)−Du(4)[16]} are significant. The direction of this distortion is such that the *p*-xylyl unit is bowed *toward* the concave face of the pyrene unit. Although this effect is small, it is opposite to what is normally observed in small cyclophanes, in which face-to-face situated arenes are bowed away from one another.[17] In fact we are not aware of any other "spoons-like" arrangement of arenes within the same molecule.

The bridges are close to being fully eclipsed, the torsion angles about the central C−C bonds being 1(1)° {C(1)−C(26)−C(25)−C(22)} and 7(1)° {C(15)−C(17)−C(18)−C(19)}. As a result, the pyrene and benzene decks are almost perfectly aligned. The most striking feature of the bridges is the unusually large bond angles at the carbon atoms benzylic to the benzene ring.[18] These are 123.7(5)° {C(22)−C(25)−C(26)} and 124.8(6)° {C(17)−C(18)−C(19)}, which is

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[14] Crystal data for **5**: colorless prism ($0.30 \times 0.15 \times 0.40$ mm^3) from heptane, $C_{26}H_{20}$, $M_r = 332.44$, orthorhombic, $P2_12_12_1$ (No. 19), $a = 12.451(2)$, $b = 15.773(3)$, $c = 9.203(2)$ Å, $V = 1807.4(5)$ Å^3, $Z = 4$,_$d_{\mathrm{calc}} = 1.222$ g cm^{-3}, $F(000) = 704$, μ(Cu Kα) = 5.20 cm^{-1}, $T = 299$ K, Rigaku AFC6S diffractometer, graphite-monochromated Cu Kα radiation ($\lambda = 1.54178$ Å), ω-2θ scan type with ω scan width $= 0.84 + 0.14 \tan \theta$, ω scan speed 4.0° min^{-1} (up to five rescans for weak reflections), 1577 reflections measured, empirical absorption correction (max, min corrections = 1.00, 0.93), secondary extinction correction (coefficient = 1.79589×10^{-5}), giving 1556 with $I > 0.00\sigma(I)$. Solution and refinement by direct methods using the teXsan package (Molecular Structure Corporation); all non-hydrogen atoms refined anisotropically; hydrogens included in calculated positions but not refined; full matrix least squares refinement on F^2 with 284 variable parameters led to $R1 = 0.059$, $wR2 = 0.085$, GOF = 1.84. CCDC-160393.

[15] The angles α and β used here are directly analogous to those used for smaller cyclophanes, such as the [*n*]paracyclophanes. See ref 17.

[16] In determining β angles, the following dummy atoms (Du) were placed in the structure: Du(1) at the C(2)−C(6) centroid; Du(2) at the C(14)−C(16) centroid; Du(3) at the C(21)−C(23) centroid; Du(4) at the C(20)−C(24) centroid.

[17] (a) *Cyclophanes, Vols. 1 and 2*; Keehn, P. M., Rosenfeld, S. M., Eds.; Academic Press: New York, 1983. (b) Vögtle, F. *Cyclophan-Chemie*; B. G. Teubner: Stuttgart, 1990. (c) Diederich, F. N. *Cyclophanes*; Royal Society of Chemistry: London, 1991. (d) Hopf, H. *Classics in Hydrocarbon Chemistry*; Wiley-VCH: Weinheim, 2000.

substantially higher than those in the AM1 calculated structure (117.7° for both). It would appear as though the origin of these large bond angles is related to the inward bowing effect discussed above. Normal tetrahedral angles about C(18) and C(25) would cause the benzene deck to be pushed up well into the concave face of the pyrene deck. Repulsions between the π clouds of the opposing arenes presumably disfavor the adoption of this arrangement, and the bond angles at C(18) and C(25) are forced open as the benzene ring is repelled from the pyrene moiety. A further unusual feature of the bridge is the unexpectedly short bond lengths in the central bonds, i.e., 1.468(9) Å for C(25)−C(26) and 1.439(8) Å for C(17)−C(18).[18] The remaining bond lengths in the bridges are within the normal range (1.50−1.52 Å). The AM1 calculations on **5** do not predict any unusual bond lengths in the bridges.

The ^1H NMR spectrum of pyrenophane **5** contains signals for the pyrene system at δ 7.67 and 7.40, which are comparable to those of [8](2,7)pyrenophane[1] ($\theta = 80.8°$, δ 7.84 and 7.59), and 1,8-dioxa[8](2,7)pyrenophane ($\theta = 87.8°$, δ 7.84 and 7.44).[2] However, the signal for the benzene deck is observed at δ 5.54, roughly 1.5 ppm upfield from the corresponding signals of *p*-xylene (δ 7.07). That pyrene is, as a whole, much broader than benzene accounts for the observation that the protons of the benzene ring are shielded by the pyrene moiety, but those of the pyrene moiety appear to experience little magnetic anisotropy from the benzene ring.

Having established that **5** is an accessible system, we are now working toward the synthesis of related systems that will bring us closer to our ultimate goal of the Vögtle belts. Pyrenophane **20** has the same basic skeleton of **5** and is a direct precursor (via valence isomerization of the Dewar benzene moieties to benzene systems) to a 34-carbon fragment of D_{5h} C_{70}, which is a belt consisting of a (2,7)-pyrenyl and three *p*-phenylene units (Figure 3). The synthesis of **20** poses a stiff challenge, but cyclophanediene **21** or related systems, which may be accessible using an approach similar to that described above, may serve as useful progenitors. We are also pursuing the synthesis of pyrenophanes such as **22**, in which two *p*-phenylene units have been inserted into the bridge of **3**.

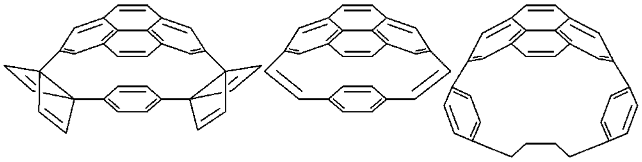
20 **21** **22**

Figure 3.

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[18] The somewhat large thermal ellipsoids at C(25) and (especially) C(18) mean that the exact values of the measured bond angles and lengths should not be viewed with a high degree of confidence, but there is little doubt that the bond angles are indeed unusually large and the bonds unusually short.