Synthesis and Molecular Structure of 1,4,5,8-Tetramethyl[6](9,10)anthracenophane: The Smallest 9,10-Bridged Anthracene

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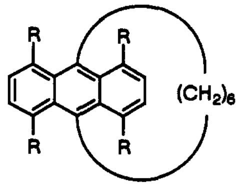
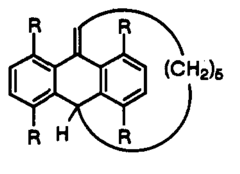
The chemistry of strained small-bridged [*n*]cyclophanes has attracted much interest in recent years; the lower limit of their existence has been explored successfully.[1] By contrast, little has been learned about condensed benzenoid cyclophanes despite the fact that the aromatic character os such a system would be more sensitive to strain imposed by the short bridge.[2] As to [*n*](9,10)anthracenophanes, the smallest known representatives are the 2,7-diketo,[3] 3,6-diketo,[4] and 2,7-dithia compounds with $n = 8$. In contrast to the corresponding benzolog, [8]paracyclophane,[6] these anthracenophanes readily underwent air oxidation although the central aromatic ring of these compounds is only slightly deformed from planarity.[4,5a] Moreover, isomerization to methylenedihydro (isotoluene) type tautomers of dithia[*n*](9,10)-anthracenophanes of $n = 8$–12 under basic conditions has been observed spectroscopically.[5c] Apparently, the decrease of aromatic character by benzannelation markedly enhances the reactivity of these cyclophanes and thus reduces their kinetic stability. We now report the synthesis, isolation, and determination of molecular geometry of the smallest known example of an [*n*](9,10)anthracenophane, the [6](9,10)anthracenophane derivative **2** bearing methyl groups at the four peri positions. We also report the first isolation of bridged methylenedihydroanthracenes (**3** and **4**), isotoluene type tautomers of the parent anthracenophane **1** and its tetramethyl derivative **2**, respectively.

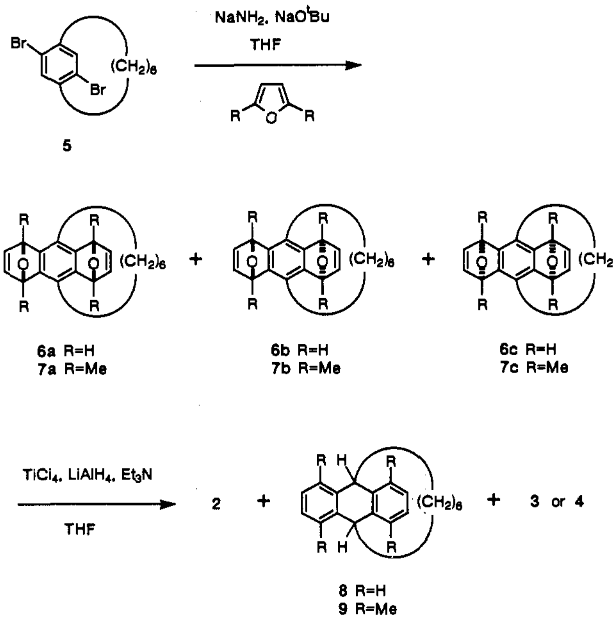


1 R=H
2 R=Me



3 R=H
4 R=Me

Scheme I



Taking into account the expected kinetic lability of **1**, we planned to start from a molecule already having the [6]paracyclophane substructure and to construct thereon the anthracene ring by bis-benzoannelation[7] in the last stage of the synthesis. On the same grounds, we also planned to prepare tetramethyl derivative **2** with the hope that the methyl substituents would sterically protect the reactive central ring of the anthracene core. Dibromoparacyclophane **5**[8] was treated with a large excess of the mixed base $NaNH_2/NaO^tBu$[9] in the presence of excess furan or 2,5-dimethylfuran, giving three isomers **6a–c** (17, 10, and 5% yields, respectively) or **7a–c** (12, 47, and 28% yields, respectively) of [4 + 2] adducts (Scheme I).[10] These were then deoxygenated. Of the several methods examined, the protocol of Wong[11] proved to be the most successful. Treatment of a mixture of **6a–c** with a low-valent titanium reagent prepared from $TiCl_4$, $LiAlH_4$, and triethylamine furnished dihydroanthracenophane **8** and the methylenedihydroanthracene **3** in a ratio of 2:1 (26% total yield). These products are probably derived from **1** by reduction and acid- or base-induced isomerization, respectively, during reaction and workup. No signal assignable to **1** was detected in the ^1H NMR spectra of the crude reaction products. Similar treatment of a mixture of **7a–c**, on the other hand, gave anthracenophane **2** as the major product, along with a small amount of its isomer **4** and the dihydro derivative **9** (11:1:2 ratio; 43% total yield). A pure sample of **2** (mp 161–162 °C was obtained by recrystallization from ether/dichloromethane. It was stable to air but was very sensitive to acid; even trace amounts readily induced its isomerization to **4**.

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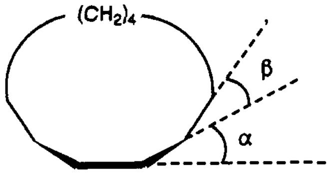
Table I. AM1-Calculated Deformation Angles and Heats of Formation of Anthracenophanes **1**, **2**, and **10** and their Methylenedihydro Tautomers **3** and **4**

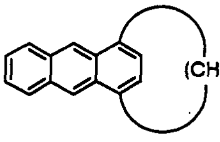


compd		α (deg)[a]	β (deg)[b]	α + β (deg)	$\Delta H_f°$ (kcal/mol)
1	calcd	25.6	16.1	41.7	68.4
3	calcd				49.4
2	calcd	28.8	14.8	43.6	50.0
	exptl[c]	24.7	18.5	43.2	
4	calcd				24.2
10	calcd	25.4	16.0	41.4	66.0
	exptl[d]	21.0	19.5	40.5	

[a] Average out-of-plane flip angle of the para carbons. [b] Average out-of-plane bending angle of the benzyl carbons. [c] This work. [d] Reference 2b.

AM1 calculations[12] predict that anthracenophane **1** is less stable than its tautomer **3** by 19.0 kcal/mol (Table I). Moreover, the tetramethyl derivative **2** is much less stable than **4** (25.8 kcal/mol). These results are inconsistent with the observed stabilities of **1** and **2**. Consequently, we deduce that **2** is kinetically stabilized by steric protection of the reactive central ring of the anthracene core by the four methyl groups protruding from the peri positions.

The ^1H NMR spectrum of **2** (270 MHz, CD_2Cl_2) at 30 °C exhibits just three signals for the methylene protons (δ 3.31, 0.87, and −0.38 ppm), indicating that flipping of the methylene bridge is rapid on the NMR time scale. As the temperature was lowered, these signals broadened and the most shielded methylene proton appeared at δ −1.89 ppm at −90 °C. The chemical shift of this proton is similar to that of the corresponding proton of [6](1,4)-anthracenophane (**10**),[2b] which appears at δ −1.81 ppm, suggesting that these protons in both compounds are located in similar environments. The barrier to flipping the bridge of **2** was estimated to be 9.5 kcal/mol. This is much smaller than that of **10** (13.4 kcal/mol).[2b,13] The UV-vis spectrum of **2** in cyclohexane (λ_{max} 455 nm (log ε 3.6)) exhibits a remarkable bathochromic shift from that of 1,4,5,8,9,10-hexamethylanthracene in heptane (λ_{max} 425 nm (log ε 3.7)).[14]



10

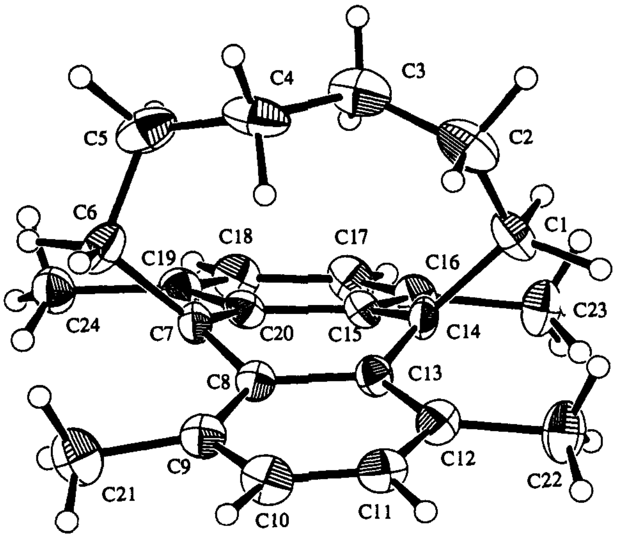


Figure 1. Side view of the molecular structure of **2**.

The crystal structure of **2**, as determined by X-ray crystallography (Figure 1),[15] shows severe deformation of the central ring of the anthracene core; the out-of-plane bending angles (α) of the para carbons are 25.5° and 23.8°, and the bending angles (β) of the benzylic bonds are 18.4° and 18.7°. The total deformation angle (α + β) is 43.2°, which represents the largest deformation angle observed in any small-bridge [*n*]cyclophane. The internal torsion angles of the central ring are −25.8°, −3.8°, −30.6°, 27.8°, 1.8°, and 28.6°. The side rings tilt downward from the central ring, the dihedral angles between the base plane of the central ring and the mean planes of the side rings are 9.3° and 11.4°. Short nonbonded distances were observed between the methyl and benzyl carbons (3.06–3.12 Å), which are well below the sum of the van der Waals radii. Because of this steric repulsion, the side rings are slightly deformed from planarity; the dihedral angles (C(13)–C(8)–C(9)–C(21) and C(20)–C(15)–C(16)–C(23) are −170.8° and −172.5°, respectively. The observed total deformation angle (α + β) is in good agreement with the AM1-calculated value, though this semiempirical method tends to overestimate the angle α. While the calculated deformation angles of **1** are similar to that of **10**, the observed values as well as those calculated for **2** are considerably larger than those for **1** and **10**, indicating that the greater deformation in **2** is due to the additional steric interaction between the methyl groups and the benzyl methylenes of the bridge.

Supplementary Material Available: Spectral properties of compounds **2**, **3**, **4**, **8**, and **9**, fully labeled top view of the structure of **2**, and tables of interatomic bond distances and angles, fractional atomic coordinates, and anisotropic thermal parameters for non-hydrogen atoms of **2** (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(13) The exceptionally small conformational barrier for **2** is probably due to destabilization of the ground-state conformation relative to the transition state of flipping because of steric repulsion between the methyl group and benzyl methylenes.

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(15) Crystal data: $C_{24}H_{28}$, monoclinic $P2_1/c$, $a = 13.620(4)$ Å, $b = 9.286(2)$ Å, $c = 15.645(2)$ Å, $\beta = 115.10(1)°$, $V = 1792.1(6)$ Å^3, $Z = 4$. Data were collected at 23 °C on a Rigaku AFC5R diffractometer with graphite-monochromated Mo Kα radiation giving 4392 unique reflections. The structure was solved by a direct method (SAPI91) to yield $R = 0.066$, $R_w = 0.034$ for 1267 independent reflections with $I > 3\sigma(I)$.