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A NEW ENTRY TO [6](1,4)NAPHTHALENOPHANE AND [6](1,4)ANTHRACENOPHANE: SYNTHESIS OF PERI-SUBSTITUTED DERIVATIVES

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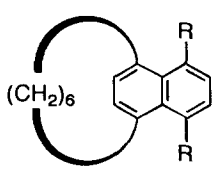
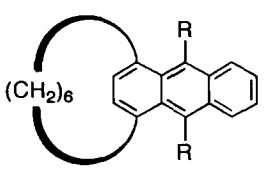
Abstract: [6](1,4)Naphthalenophane (**1a**), [6](1,4)anthraceniophane (**2a**), and the peri-substituted derivatives **1b**, **1c**, and **2b** were prepared by the benzoannelation method. The conformational behavior of **1b**, **1c**, and **2b** suggests that their bridged aromatic rings are more distorted than those of the parent systems **1a** and **2a**.

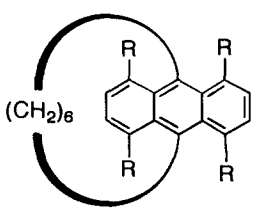
While the chemistry of small [*n*]paracyclophanes has been explored extensively during the last decade,[1] little has been learned about [*n*]cyclophanes of condensed benzenoid aromatics. We synthesized the smallest 1,4-bridged naphthaleno- and anthracenophanes, [6](1,4)naphthalenophane (**1a**) and [6](1,4)anthracenophane (**2a**), and studied their structure and reactivity.[2] Recently, we also succeeded in the synthesis of a derivative of the smallest (9,10)anthracenophane, 1,4,5,8-tetramethyl[6](9,10)anthracenophane (**3b**) and the spectroscopic characterization of the unstable parent hydrocarbon (**3a**).[3] In this communication, we disclose a new synthetic route to **1a** and **2a** which is based on the benzoannelation method starting from bromo[6]paracyclophane (**4**).[4] We also synthesized the derivatives **1b**, **1c**, and **2b** having substituents at the peri positions by using the same mothod.[5] It has been well documented that polynuclear aromatic hydrocarbons are deformed from planarity by the steric repulsion between the peri substituents and that they exhibit unusual properties because of the distortion.[6] In this respect, it may well be anticipated that the acenophane derivatives **1b**, **1c**, and **2b** are more distorted than the parent systems **1a** and **2a**.



1a R=H
1b R=Ph
1c R=Me



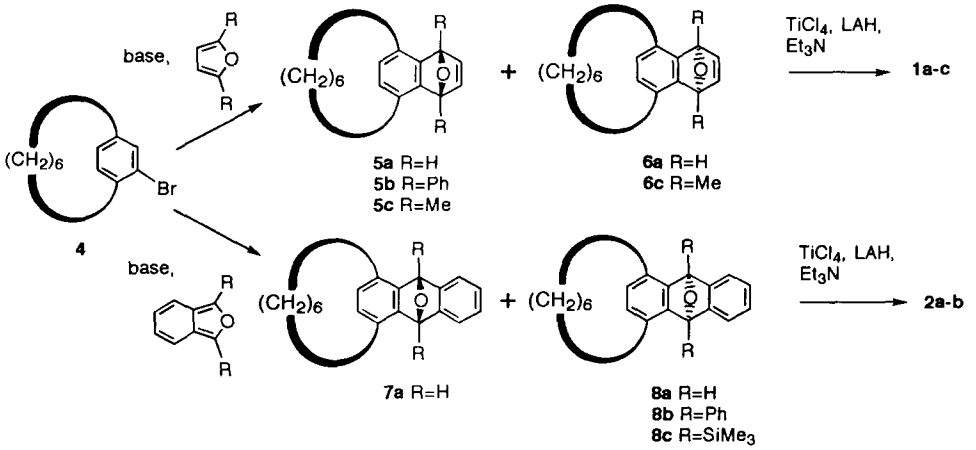
2a R=H
2b R=Ph



3a R=H
3b R=Me

Treatment of bromo[6]paracyclophane (**4**) with a mixed strong base composed of sodium amide and sodium *t*-butoxide in THF in the presence of furan afforded two isomeric [4+2] adducts *syn*- **5a** and *anti*- **5b** in a ratio of 6:1 (41% yield).[7] Reductive deoxygenation of the major isomer **5a** with a low valent titanium reagent prepared from titanium tetrachloride, lithium aluminum hydride, and triethylamine (7:2.5:1)[8] in THF gave the naphthalenophane **1a** in 52 % isolated yield. Similarly, treatment of **4** with $NaNH_2/NaOBu^t$ in the

presence of *in situ* prepared isobenzofuran[9] yielded the [4+2] adducts *syn*- **7a** and *anti*- **8a** in a ratio of 1:2 (66 % yield).[7] The major isomer **8a** was also prepared by desilylation of **8c** (88 %), which was obtained as a sole product from the reaction of **4** and 1,3-bis(trimethylsilyl)isobenzofuran[10] in 50 % yield.[7] Deoxygenation of **8a** with the titanium reducing reagent gave the anthracenophane **2a** in 51 % yield. The present method of preparation of **1a** and **2a** is as convenient as the previous method[2a] with respect to the total steps and yields from the starting material. However this route is advantageous from the fact that (i) both **1a** and **2a** can be prepared from the common advanced intermediate **4**, and (ii) the peri-substituted derivatives such as **1b**, **1c**, and **2b** can be prepared as described below.



Cycloaddition of the benzyne species generated from **4** with 2,5-diphenylfuran[11] or 2,5-dimethylfuran afforded *syn*- **5b** (19 %) or *syn*- **5c** and *anti*- **6c** (3:4; 28 % yield).[7] Reaction with 1,3-diphenylisobenzofuran gave *anti*- **8b** in 30 % yield.[7] Except for the case of diphenylfuran, the amount of the syn isomers decrease relative to that of the anti isomers presumably because of the greater steric repulsion between the benzyl methylenes and the peri substituents in the syn isomers. The reason for the absence of *anti*- **6b**, however, is not certain. Deoxygenation of **5b** or a mixture of **5c** and **6c** with the titanium reducing agent yielded the peri-substituted naphthalenophanes **1b**[12] (87 %) or **1c**[12] (60 %). Moreover, reduction of **8b** under the similar conditions furnished diphenylanthracenophane **2b**[12] in 59 % yield.

As in the case of the parent hydrocarbons **1a** and **2a**,[2a] the derivatives **1b**, **1c**, and **2b** exhibit temperature dependent NMR behavior due to the flipping of the methylene bridge. The barriers of the flipping were determined either by the line shape analysis or from the coalescence temperature (Table 1). As shown in Table 1, the barriers for **1b**, **1c**, and **2b** are smaller than those of the corresponding parent compound by about 1.5 kcal/mol.[13] The decrease of the energy barrier implies that the out-of-plane distortion of the bridged aromatic rings of the peri-substituted compounds is greater than that of the parent systems.

At low temperatures (-50 to -85 °C) the conformation of the methylenes is frozen on the NMR time scale. The signals of the methylene protons were assigned on the basis of the H-H COSY experiment as listed in Table 2. There is not much difference between the chemical shifts of the methylene protons of **1a** and those of **1c** except for Ha which exhibited upfield shift of 0.32 ppm. On the other hand, the benzyl protons (Ha-Hd) and homobenzyl protons (He-Hh) of **1b** and **2b** exhibit remarkable upfield shift relative to those of **1a**

and **2a** due to the anisotropic shielding effect of the peri-substituted phenyl groups. In particular, the proximate benzyl protons Ha and Hd show upfield shift of 1.18, 1.31 ppm (Ha of **1b** and **1b**, respectively) and 1.40, 1.89 ppm (Hd of **1b** and **2b**, respectively).

Table 1. Barriers for the Flipping of the Methylene Bridges of Naphthalenophanes **1a-c** and Anthracenophanes **2a-b**.

compd	$\Delta G^{\neq}$, kcal/mol (temp, K)
1a	13.6 (273)[a,b]
1b	12.2 (283)[a]
1c	12.1 (298)[c]
2a	13.4 (268)[a,b]
2b	12.0 (298)[d]

[a] Determined from the coalescence temperature. [b] Reference 2a. [c] Determined by the line shape analysis of the signals of the methyl protons. [d] Determined by the line shape analysis of the signals of the aromatic protons H5 and H8 which were decoupled by irradiation of the signals of H6 and H7.

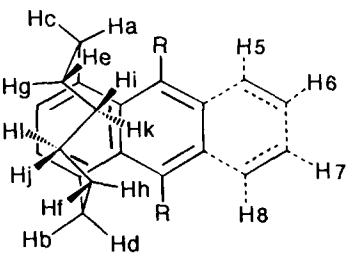


Table 2. ^{1}H NMR Chemical Shifts of Naphthalenophanes **1a-c** and Anthracenophanes **2a-b**.[a]

	compd				
proton	**1a**[b]	**1b**[c]	**1c**[d]	**2a**[b]	**2b**[c,e]
Ha	2.86	1.68	2.54	3.00	1.69
Hb	2.27	1.82	2.19	2.36	1.69
Hc	3.01	2.48	2.97	3.08	2.25
Hd	3.49	2.09	3.50	3.58	1.69
He	1.74	1.33	1.56	1.77	1.36
Hf	1.58	1.14	1.56	1.60	1.17
Hg	0.71	0.53	0.66	0.80	0.61
Hh	0.34	-0.04	0.10	0.38	0.17
Hi	0.79	0.53	0.66	0.71	0.61
Hj	1.11	1.01	1.16	1.14	1.17
Hk	-1.84	-1.92	-1.87	-1.81	-1.60
Hl	-0.47	-0.51	-0.36	-0.31	-0.29

[a] Chemical shifts are in δ ppm. [b] Measured at -50 °C in $CDCl_3$ (reference 2a). [c] Measured in CD_2Cl_2 at -80 °C. [d] Measured in CD_2Cl_2 at -85 °C. e The signals are still broader than those of the other compounds at -80 °C presumably because of hindered rotation of the peri-substituted phenyl groups.

In summary, a new synthetic route to **1a**, **2a**, and their peri-substituted derivatives **1b**, **1c**, and **2b** was developed based on the benzoannelation method. Currently we are investigating the reactivity of the peri-substituted acenophanes.

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7. The orientation of the oxygen atoms of the benzyne-furan adducts was determined on the basis of the shielding effect of the double bond or fused benzene ring on the central methylene protons. The validity of this assignment was verified by X-ray crystallographic structure analyses of bis(2,5-dimethylfuran)-adducts reported in ref. 3a. Details will be reported elsewhere.
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12. **1b**: mp 176-177 °C; ^{13}C NMR (CD_2Cl_2, -80 °C) δ 143.4 (s), 143.2 (s), 142.9 (s), 139.6 (s), 139.3 (s), 138.1 (s), 137.0 (s), 134.2 (s), 133.8 (d), 129.8 (d), 128.8 (d, 2C), 128.7 (d, 2C), 127.79 (d), 127.76 (d), 127.64 (d), 127.62 (d), 127.3 (d), 127.2 (d), 126.6 (d, 2C), 38.0 (t), 36.4 (t, 2C), 31.9 (t), 27.4 (t), 24.0 (t); UV λ_{max} (cyclohexane) 346 (log ε 3.60), 255 (4.59), 249 (4.58) nm
1c: mp 69-72 °C; ^{13}C NMR (CD_2Cl_2, -85 °C) δ 142.4 (s), 139.7 (s), 139.2 (s), 133.5 (s), 132.8 (d), 130.5 (s), 129.6 (s), 128.7 (d), 127.4 (d), 127.2 (d), 38.0 (t), 36.7 (t), 34.9 (t), 32.0 (t), 27.8 (t), 23.8 (t), 23.8 (q), 23.7 (q); UV λ_{max} (cyclohexane) 324 (log ε 3.82), 252 (4.60) nm.
2b: mp 194-196 °C; ^{13}C NMR (CD_2Cl_2, -80 °C) δ 143.5 (s), 141.3 (s), 141.0 (s), 139.4 (s), 139.0 (s), 134.4 (s), 133.4 (s), 133.5 (s), 132.8 (d), 131.2 (d), 131.0 (d), 130.1 (d), 129.8 (d), 129.4 (d), 129.0 (s), 128.85 (d), 128.83 (s), 128.7 (d), 127.6 (d), 127.2 (d), 126.8 (d), 126.6 (d), 126.1 (d), 125.6 (d), 124.8 (d), 124.6 (d), 37.8 (t), 36.7 (t), 34.8 (t), 31.4 (t), 28.0 (t), 23.7 (t); UV λ_{max} (cyclohexane) 403 (log ε 4.05), 273 (4.93) nm.
13. The barrier for the methylene flipping of the tetramethyl derivative **3b**, which might possess the steric repulsion about twice as much as that of **1c**, is smaller than that of **3a** by ca. 4 kcal/mol.[3]

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