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Strained Aromatic Compounds

Highly Strained Phenylene Bicyclophanes**

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Dedicated to Professor Karl Heinz Dötz on the occasion of his 70th birthday

The self-assembly of rigid organic molecules at the liquid/HOPG (highly oriented pyrolytic graphite) interface enables the bottom-up synthesis of designed two-dimensional (2D) crystalline superstructures with adjustable symmetry and lattice parameters. Enhanced understanding of 2D supramolecular engineering has led to an enhanced understanding of the essential key mechanisms of molecule–surface and molecule–molecule interactions.[1] Usually, aromatic compounds lie flat on the substrate.[2] Architectures with aromatic units aligned perpendicularly to the graphite surface are rarely observed[3] but may become of interest when functionalization towards the volume phase is desired.

Our approach is the construction of a rigid molecular cyclic framework with long alkyl chains that drive adsorption to the graphite surface by van der Waals interactions. The diameter and height of the central lumen cause a central aromatic unit to be confined in an arrangement perpendicular to the overall oblate-shaped molecule structure. The central unit is neither able to rotate, nor able to move into the plane of the structure (Figure 1 b) and will therefore point into the volume phase.[2] We assumed that small cyclic oligo(*meta*-/*para*-phenylene)s with an intraannular central aromatic unit would fulfill these criteria. However, the synthesis of such cyclophanes is challenging owing to their high strain energy.[4]

Herein, we describe a straightforward synthetic approach to the highly strained bicyclic oligophenylene structures **1a**/**b**, **2a**/**b**, and **3a**/**b**, in which the central aromatic unit and the *para*-substituted arylene rings of the bicyclic backbone are aligned perpendicular to the plane of the molecule, as determined by single-crystal X-ray structure analysis. Furthermore, we describe the adsorption of **1b** and **2b** onto HOPG as well as studies of the binding of **1b**, **2b**, and **3b** to appropriate model compounds. All experimental studies are well-supported by state-of-the-art DFT calculations.

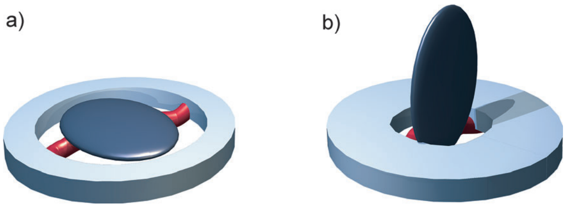

Figure 1. a) Schematic representation of a large framework structure with a central aromatic unit able to move into the plane of the structure when brought into contact with a graphite surface.[2] b) Schematic representation of a large structure with a central aromatic unit confined perpendicularly in a tight and rigid framework.

The synthesis is based on our previously reported convenient route to phenyl-substituted all-*para* quinquephenylenes from readily accessible pyrylium salts (Scheme 1).[5] As the synthesis tolerates halogen substituents, bromo-substituted intermediates can be prepared without the use of protective groups. By the condensation of the triaryl pyrylium salts **4a** and **4c** with sodium 1,4-phenylenediacetate (**5**), tetrabromides **6a** and **6c** were obtained in acceptable yields of approximately 20 %. Compound **6c** was transformed into **6b**, and tetrabromides **6a** and **6b** were treated with bis(1,5-cyclooctadiene)nickel ([Ni(cod)$_2$]) and 2,2′-bipyridine in a mixture of THF and 1,5-cyclooctadiene (COD; Yamamoto conditions)[6] in a microwave oven. When the cyclization reactions were carried out under high-dilution conditions ($c = 10^{-3}$–10^{-4} mol L^{-1}), the formation of higher oligomers was mostly avoided,[7] and the desired bicyclophanes **1a** and **1b** were the main products, as judged by analytical gel permeation chromatography (GPC; **1a** was isolated in 3 % yield owing to its restricted solubility, and **1b** was isolated in 57 % yield, in both cases after purification by recycling GPC). Considering the high strain of the molecules, as suggested by molecular models (see the Supporting Information), the high reaction yield is quite astonishing. The driving force of this exceptional reaction is founded in the preorganization of the phenyl units in the tetrabromo-substituted precursors.[8] After insertion of the transition metal into one of the aryl–bromide bonds, the transmetalation can readily occur prior to the competing dehalogenation.[9] To prove the generality of our synthetic approach, we tested further aromatic diacetates as building blocks for the central unit of the bicyclophanes: Sodium 1,4-naphthylenediacetate (**7**)[10] and 9,10-anthracene-

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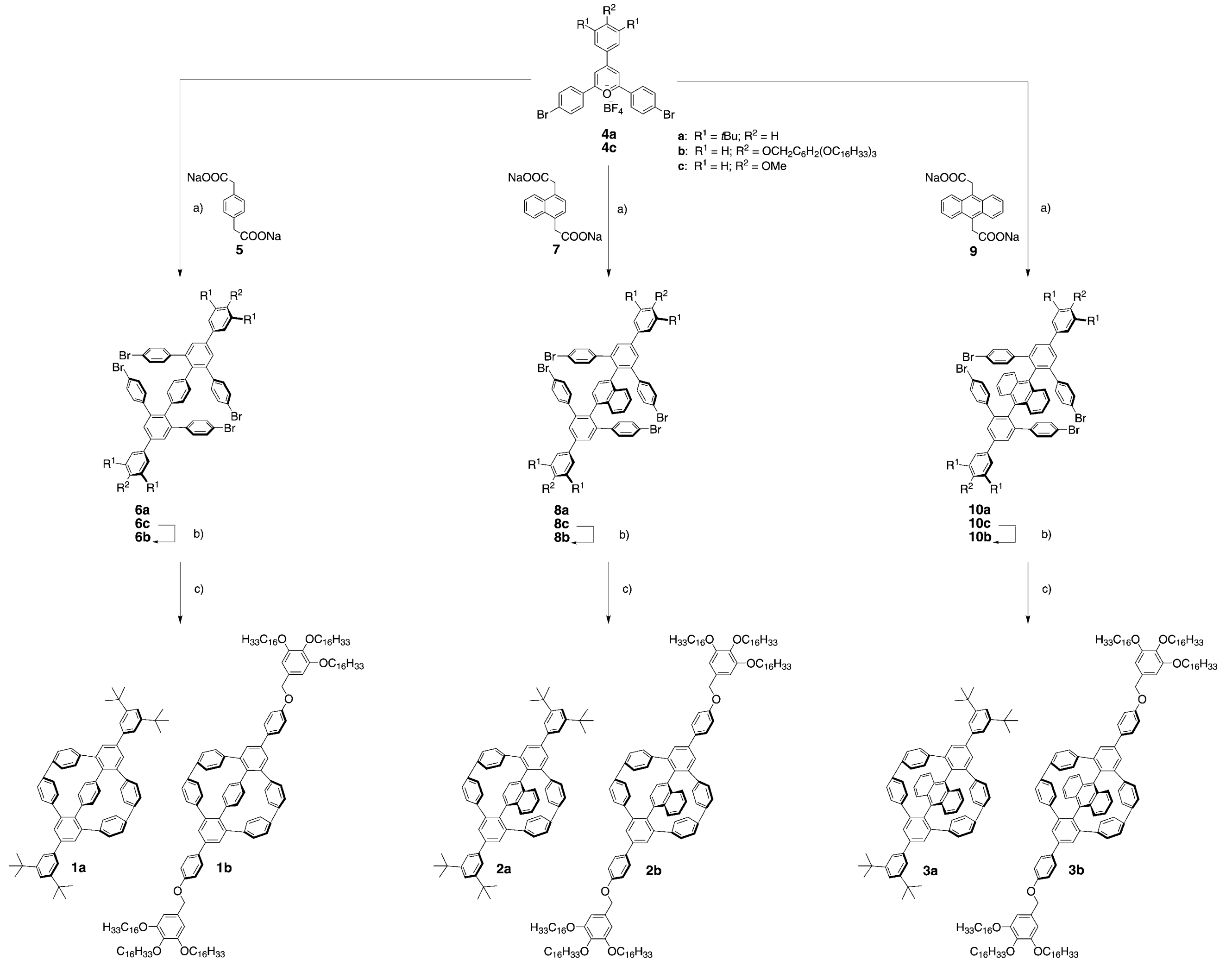

Scheme 1. a) Benzoic anhydride, 150 °C, 3 h; b) 1. BBr_3, CH_2Cl_2, −78 °C→RT, 16 h; 2. 3,4,5-trihexadecyloxybenzyl chloride, Cs_2CO_3, DMF, 110 °C, 48 h; c) $[Ni(cod)_2]$, 2,2′-bipyridine, THF/COD, microwave irradiation, 120 °C, 12 min. DMF = *N*,*N*-dimethylformamide.

diacetate (**9**)[11] were condensed with the pyrylium salts **4a** and **4c**. The reaction gave the desired products, which were subsequently converted into **2a**/**b** (**2a**: 58 %; **2b**: 80 %) and **3a**/**b** (**3a**: 22 %; **3b**: 81 %) by analogous procedures to those used for the synthesis of **1a** and **1b**. The isolation of **3a** was again hindered by low solubility. Owing to its higher solubility in organic solvents, bicylophane **2a** with a central naphthylene moiety was isolated in considerably higher yield.

All six bicyclophanes were white, thermally stable solids. The *tert*-butyl-substituted compounds **1a**, **2a**, and **3a** did not melt below 300 °C, whereas the hexadecyloxy-substituted analogues had lower melting points of 140–145 °C (**1b**), 103 °C (**2b**), and 136 °C (**3b**). NMR and mass spectra together with the analytical GPC data unambiguously proved the structure and purity of the compounds. Furthermore, single crystals of **2a** suitable for X-ray diffraction studies were obtained, and the experimental data (Figure 2) agreed well with dispersion-corrected density functional theory (DFT-D3) calculations (see the Supporting Information); that is, the four *para*-phenylene units in the bicyclophane backbone as well as the central naphthalene unit are oriented almost perpendicularly to the bicyclophane plane. However, a slight twist of the orthogonal phenylene rings D and E was observed. This torsion eliminates H–H contacts that would be too close and leads to a dihedral angle of 12.7° (calculated value: 17.5°).

As the space-filling model shows very impressively (Figure 2b), the central naphthalene ring is clamped between the outer biphenylene bridges and thus is not able to rotate, also in agreement with DFT calculations. For **1a**, the calculated energy difference between the molecular conformations with the central phenylene ring in the orthogonal orientation or in the bicyclophane plane is already 47.3 kcal mol^{-1}, which cannot be overcome under normal conditions. As suggested by the structural formula, the surrounding biphenylene units are not linear but highly curved. The imaginary line through the bridging carbon atoms of phenyl ring D and the neighboring atom in phenyl ring E (Figure 2) encloses an angle $\measuredangle_1$ of 141.3° (calculated value: 142.5°). The corresponding angle $\measuredangle_2$ between the bridging carbon atoms of E and the neighboring atom in D is 144.4° (calculated value: 142.5°). To the best of our knowledge, this deviation from linearity is the largest observed for *para*-substituted biphenylenes (by single-

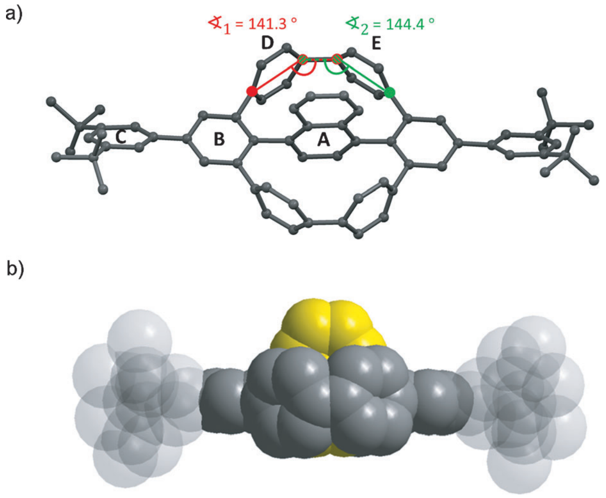

Figure 2. Molecular geometry of **2a**, as determined by single-crystal X-ray diffraction: a) ball-and-stick model with the angles ∡$_1$ and ∡$_2$, which are measures of the high strain of the bicyclophane system; b) space-filling model with the encapsuled naphthalene ring highlighted in yellow.

crystal X-ray analysis; see the Supporting Information). Further evidence of high ring torsion is the aberration of the phenylene rings D and E from planarity: The bridging carbon atoms deviate from the best planes of D and E (defined by their H-substituted carbon atoms) by 17.8 pm (calculated value: 15.8 pm) on average. Comparable values are observed for small *para*-connected cyclophenylenes, for example, [6]cyclo-*para*-phenylene ([6]-CPP).[12] The calculated strain energy of **2a** is 75.2 kcal mol^{-1}.[13] Each of the four bent phenylene units of the surrounding biphenyl bridges contributes 16.6 kcal mol^{-1} to this strain: a contribution similar to the corresponding strain per phenylene unit in [6]-CPP (16.0 kcal mol^{-1}).[14] As the central and four bridging phenylene moieties are oriented perpendicular to the bicyclic plane of the molecule, ten aryl hydrogen atoms point to the top of the molecular plane and a further ten hydrogen atoms point to the bottom of the molecular plane. These hydrogen atoms can in principle bind to polycyclic aromatic hydrocarbons through aryl CH···π interactions.[15]

To confirm this supposed attractive interaction of the bicyclophanes with extended planar π systems, binding with a hexa-*peri*-hexabenzocoronene (HBC) derivative was investigated in solution. HBC can be viewed as a soluble cutout of the honeycomb structure of graphite. Compounds **1b**, **2b**, and **3b** were investigated as complexation partners for hexa-*tert*-butyl-substituted HBC (tBu$_6$-HBC)[16] by means of ^{1}H NMR spectroscopy. When tBu$_6$-HBC was added to solutions of **1b** or **2b** in [D$_8$]THF at room temperature, the ^{1}H NMR signals corresponding to the bicyclic units of the cyclophanes were shifted upfield. For example, the singlet in **2b** at $\delta = 6.07$ ppm moved steadily upfield up to $\delta = 5.85$ ppm as the ratio of tBu$_6$-HBC to **2b** was increased; this shift indicated close proximity between the flat side of the bicyclophane and the π plane of the HBC derivative. In contrast, the NMR signals of **3b** were not influenced by the presence of the HBC derivative, as expected from the structure of the bicyclophane. Owing to the molecular symmetry of **1b** and tBu$_6$-HBC, we expected the formation of infinite alternating stacks, whereas sterical shielding of one side of **2b** should lead to a sandwichlike 2:1 complex in which two bicyclophanes encapsulate one tBu$_6$-HBC unit. As the exchange between the complexes and free hosts and guests is fast on the NMR time scale, the Job method of continuous variation[17] was used to determine the complex stoichiometries (see the Supporting Information). Surprisingly, the maxima in both Job plots were, within the experimental error, at $\chi = 0.5$, which indicated the formation of 1:1 (n:n) complexes in both cases. However, the presence of a small amount of a 2:1 complex cannot be excluded. At present, we ascribe the more or less exclusive formation of the 1:1 complex in both cases to the presence of the long flexible alkoxy chains, which may prevent interaction with a second bicyclophane. Binding constants for the host–guest complexation in THF were found by the double-reciprocal (Benesi–Hildebrand) method to be approximately 70 L mol^{-1}, which corresponds to a free binding energy of −2.5 kcal mol^{-1} (Table 1).[18]

Table 1: Results of Benesi–Hildebrand experiments for **1b** and **2b** with tBu$_6$-HBC.

Host:guest	$\Delta\delta$ [ppm]	K [L^{-1} mol^{-1}]	ΔG [kcal mol^{-1}]
1b:tBu$_6$-HBC	0.241	73 ± 10[a]	−2.6 ± 0.1
tBu$_6$-HBC:**1b**	0.005	72 ± 10[a]	−2.6 ± 0.1
2b:tBu$_6$-HBC	0.219	70 ± 10[a]	−2.5 ± 0.1
tBu$_6$-HBC:**2b**	0.006	66 ± 30[a]	−2.5 ± 0.2

[a] Errors were determined by graphical data analysis (see the Supporting Information).

We performed quantum-chemical computations of bicyclophane–tBu$_6$-HBC complexes at the dispersion-corrected TPSS-D3 level by using def2-TZVP AO basis sets and including corrections derived from the COSMO-RS model for the free energies (298 K) in THF (see the Supporting Information for details).[19] The results reveal significant stacking interactions between **1a′** (a model compound of **1a** in which the tBu substituents are neglected) and tBu$_6$-HBC in the gas phase (ΔE) as well as in solution (ΔG). For **1a′**@tBu$_6$-HBC (Figure 3a), the computed ΔE value (estimated accuracy ± 10 %) is −43.3 kcal mol^{-1}, which is a typical value for two unsaturated hydrocarbons of this size.[20] The binding in the perpendicular conformation (Figure 3c) is significantly less strong (−23.4 kcal mol^{-1}), which excludes such arrangements under normal conditions. As the complexes of **1a′** with tBu$_6$-HBC (in particular, the sandwich complex; Figure 3b) are extremely large for sophisticated DFT computations, we could not afford the largest atomic-orbital basis sets and hence expect a slight systematic overbinding (as a result of the basis set superposition error). For the 1:1 association process leading to **1a′**@tBu$_6$-HBC, we obtained a value for ΔG in solution of −7 kcal mol^{-1}, which compares reasonably well with the experimental values of −2.5 kcal mol^{-1}. We also studied the 2:1 complex and found practically additive interactions; that is, the second association free energy of −7.6 kcal mol^{-1} was very similar to that for the formation of

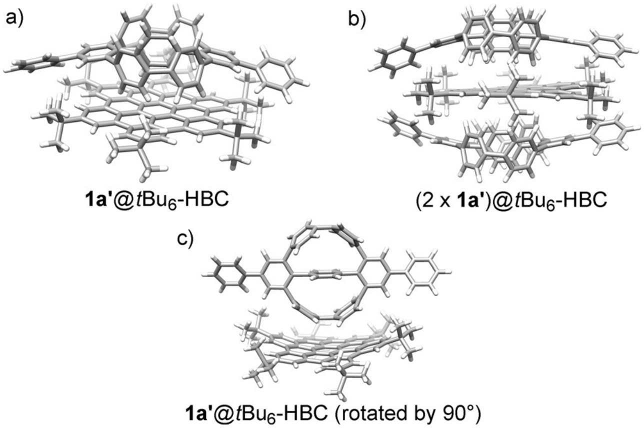

Figure 3. a,b) Computed structures of van der Waals complexes of the 1:1 (a) and 2:1 complex (b) between **1a**′ and tBu$_6$-HBC. The conformation of **1a**′ (except for a bending along the long molecular axis) in the complex is similar to that in the free state. c) The perpendicular conformation is considerably less stable and can be excluded.

the 1:1 complex and hence should be observable under the experimental conditions. At present we can only speculate that the reason for the apparent disagreement between theory and experiment (the 2:1 complex was not observed) is rooted in the presence of the long alkoxy chains of **1b**/**2b**; such chains could not be treated adequately by our ab initio computations (MD simulations would be required). Nevertheless, our computations clearly established substantial noncovalent stacking interactions between **1a**′ and tBu$_6$-HBC that are not quenched in solution and hence can be considered to be form-specific.

These results prompted us to investigate the 2D self-assembly of the bicyclophanes **1b** and **2b** at the liquid/solid interface of 1-phenyloctane (PHO) and HOPG by scanning tunneling microscopy (STM). Both molecules formed crystalline monolayers with domains of lateral extension of more than 100^2 nm^2 (for **2b**, see the Supporting Information). The aromatic backbone and hexadecyloxy side chains were imaged with low and high tunneling resistivity and visualized in bright and dark colors, respectively.[21] Throughout all observed adlayer patterns, regions covered with pairwise-assembled backbones (polymorph A; Figure 4) or continuous lines of densely packed backbones (polymorph B; see the Supporting Information) were separated by lamellar arrangements of hexadecyloxy side chains, which were aligned along an HOPG main axis direction.[22]

As expected, the adsorbate pattern did not depend on the intraannular unit (**1b**: *p*-phenylene; **2b**: *p*-naphthylene). Considering the clear visibility of the macrocyclic units in Figure 4, the observed structures can only be interpreted in such a way that the planes of the cyclophane backbones are aligned in parallel with the HOPG substrate, as also expected from the experimental and theoretical binding studies with the HBC derivative.

In summary, we have synthesized strained phenylene bicyclophanes in good to high yields by intramolecular Yamamoto condensation of the appropriate tetrabromides.

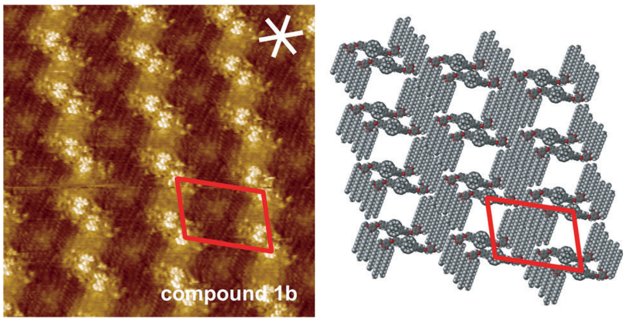

Figure 4. Scanning tunneling microscopy image and molecular model of a self-assembled monolayer of **1b** at the PHO/HOPG interface. Image parameters: 20.1×20.1 nm^2, $c = 10^{-5}$ M, $V_S = -0.8$ V, $I_t = 7$ pA; unit-cell dimensions: $a = (5.9 \pm 0.2)$ nm, $b = (3.9 \pm 0.1)$ nm, $\gamma(a,b) = (73 \pm 2)°$. Red and white lines indicate the unit cell and the HOPG main axis directions, respectively.

The central and four of the six surrounding arylene groups are oriented perpendicular to the plane of the bicyclophane, as verified by single-crystal X-ray structure analysis. The biphenylene moieties are highly bent and show the largest deviation from linearity (141, 144°) measured so far (calculated strain energy of **2a**: 75.2 kcal mol^{-1}). In solution, the bicyclophanes bind through CH⋯π noncovalent interactions to HBC derivatives. STM investigations showed that the molecules adsorb to HOPG in such a way that the central (intraannular) and four of the circumventing phenylene units are oriented perpendicular to the graphite surface. The intraannular unit can be variably substituted at only one side without affecting the graphite adsorption, as shown exemplarily with the naphthylene-centered bicyclophane **2b**. Therefore, this molecular platform may enable volume-phase surface functionalization.

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