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A Perylene Bisimide Cyclophane as a "Turn-On" and "Turn-Off" Fluorescence Probe**

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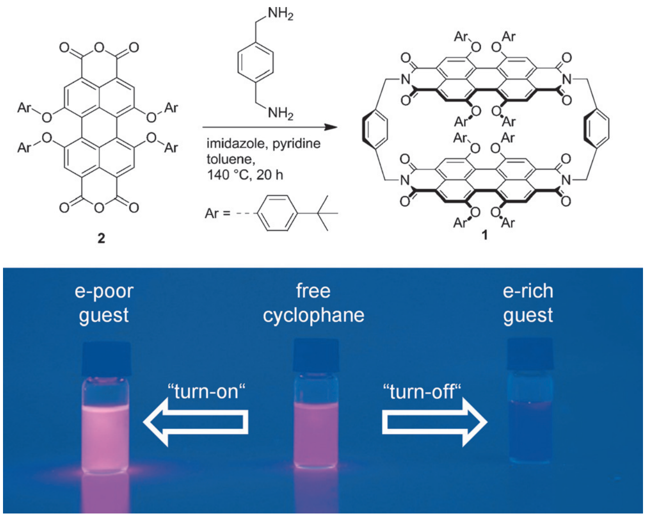
Dedicated to Professor E. W. Meijer on the occasion of his 60th birthday

***Abstract:** A rigid, covalently linked perylene-3,4:9,10-tetracarboxylic acid bisimide (PBI) cyclophane was synthesized by imidization of a bay-substituted perylene bisanhydride with p-xylylenediamine. The interchromophoric distance of approximately 6.5 Å establishes an ideal rigid cavity for the encapsulation of large aromatic compounds such as perylene and anthracene with binding constants up to $4.6\times10^{4}\,\mathrm{M}^{-1}$ (in $CHCl_3$). For electron-poor guest molecules, the complexation process is accompanied by a significantly increased fluorescence, whereas the emission intensity is dramatically quenched by more electron-rich guests because of the formation of charge-transfer complexes. Furthermore, the influence of the PBI core twist on the binding constant results in a remarkable selectivity towards more flexible aromatic guest molecules.*

Highly organized and well-defined porous cavities that are capable to encapsulate particular guest molecules provide a unique environment for the investigation of noncovalent interactions.[1] Whereas most of the initial studies on host–guest phenomena were concerned with the complexation of relatively small molecules and ions, recent publications focus on the incorporation of larger functionalized compounds such as fullerenes[2] and other aromatic hydrocarbons.[3] In the latter case, cyclophanes containing two parallelly arranged aromatic subunits in a well-defined distance have evolved as particularly versatile host molecules to intercalate planar aromatic guests by noncovalent π–π interactions. Thus, several neutral covalently linked cyclophanes composed of pyromellitic or naphthalene bisimides that are suitable to host a variety of small aromatic compounds have been reported.[4] Furthermore, recent examples are concerned with multiple charged systems such as the "ExBox", which was introduced by the group of Stoddart and can be used as a scavenger for polycyclic aromatic hydrocarbons (up to the size of coronene) in both aqueous and organic media.[5] Moreover, multicomponent cyclophanes were self-assembled by noncovalent metal ligand interactions and applied in host–guest chemistry.[6]

Cyclophanes derived from perylene-3,4:9,10-tetracarboxylic acid bisimides (PBIs) should be of particular interest as host systems because of their potential applications in catalysis,[7] sensing,[8] or transport processes.[9] Their unique photophysical properties are highly sensitive to environmental changes and therefore these systems should be useful to gather information about the corresponding host–guest complexes. Among all PBI-based cyclophanes reported to date, there is no example in which the encapsulation of aromatic hydrocarbons into the porous cavity could be achieved.[10,11] A reasonable explanation for this observation can easily be provided based on the fact that the length of the spacer unit between both chromophores determines the size of the accessible void. Short π–π distances certainly provide insufficient space,[10] whereas long and flexible spacer units facilitate an intramolecular PBI–PBI self-aggregation process that efficiently prevents guest intercalation.[11] Therefore, we postulated that the introduction of a more rigid spacer unit with an appropriate length would overcome both of these problems. We present herein the synthesis of the *para*-xylylene bridged PBI cyclophane **1** (Scheme 1) that can be used for the selective encapsulation of polycyclic aromatic molecules. Moreover, we investigated the photophysical properties of the corresponding host–guest complexes and demonstrate that cyclophane **1** serves as a dual fluorescence



Scheme 1. Synthesis of the *para*-xylylene bridged PBI cyclophane **1** (top) and representative photograph for the "turn-on" (phenylnaphthalene@**1**) and "turn-off" (carbazole@**1**) fluorescence sensing of electron-poor and electron-rich aromatic hydrocarbons (bottom).

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probe that distinguishes electron-poor and electron-rich aromatic guests.

PBI cyclophane **1** was synthesized in one step by imidization of 1,6,7,12-tetrakis-4-*tert*-butylphenoxyperylene-3,4:9,10-tetracarboxylic acid bisanhydride (**2**) with *para*-xylylenediamine under standard conditions in a mixture of imidazole and pyridine[12] (Scheme 1). After purification of the crude product by column chromatography, **1** was isolated in pure form as a red solid in 7 % yield, together with larger macrocycles and some linear oligomers that were difficult to separate. To increase the yield of the desired cyclophane, the reaction conditions were optimized which afforded the best results by dilution with toluene ($c(\mathbf{2}) = 0.5$ mM) which obviously facilitates the intramolecular dimerization by a template effect (for rationale see below). Remarkably, the yield of cyclophane **1** could thus be improved to 18 %.

The optical properties of PBI cyclophane **1** were studied by fluorescence and absorption spectroscopy. A significantly decreased fluorescence quantum yield of 21 % (in $CHCl_3$) was observed for **1** in comparison to 97 % for the monomeric PBI **3** that bears two benzyl substituents at the imide position (Figure S3 and Figure S4 in the Supporting Information). This can be explained on the basis of spatial proximity of the PBI units in cyclophane **1** that give rise to a weak interchromophoric interaction. In accordance with this theory, the ratio of the 0–0 and 0–1 vibronic transition ($A_{0\text{–}0}/A_{0\text{–}1}$) for cyclophane **1** is considerably reduced to 1.25 in contrast to 1.66 for **3**. Nevertheless, molecular modelling (Figure S5 a) suggests that the interchromophoric distance of approximately 6.5 Å should be ideally suited for the encapsulation of planar aromatic guest molecules, and indeed the fluorescence quantum yield of **1** is substantially increased to 64 % in the aromatic solvent toluene (the quantum yield of **3** in toluene is 99 %). This effect can be explained in terms of intercalation of toluene molecules between both PBI chromophores leading to a reduced intramolecular π–π interaction. Obviously, embedding of toluene between two PBIs is also the reason for increased yields of cyclophane **1** in this particular solvent (see above).

To investigate the capability of **1** to serve as a host for other more complex aromatic hydrocarbons, UV/Vis absorption and fluorescence ($\lambda_{ex} = 530$ nm) titration experiments were performed by adding an excess of the particular guest to a solution of **1** in chloroform ($c(\mathbf{1}) = 5.8\times10^{-5}$ M; Figure S6). Therefore, different rigid and flexible aromatic substrates were applied to determine the factors that influence the complexation behavior. The titration of cyclophane **1** with electron-poor guest molecules such as naphthalene, biphenyl, 9-fluorenone, anthraquinone, phenanthrene, phenylnaphthalene, and triphenylene resulted in only small changes of the PBI absorbance. Several isosbestic points indicated the formation of single well-defined host–guest complexes. Most interestingly, the intercalation of the guest molecules between the cofacially arranged π surfaces of the PBI chromophores significantly increased the emission intensity up to 100 % by virtue of a reduced electronic coupling between the two PBI units (see above; Figure 1 a, red squares). In contrast, the complexation of more electron-rich substrates such as carbazole, anthracene, pyrene, and perylene further quenches the PBI fluorescence because of charge-transfer (CT) interactions between the guest and the electron-poor PBI chromophores.[2b] Additionally, the emission maxima of the host–guest complexes are strongly red-shifted to 650, 657, and 690 nm for carbazole, pyrene, and anthracene, which can presumably be attributed to emissions originating from CT states.

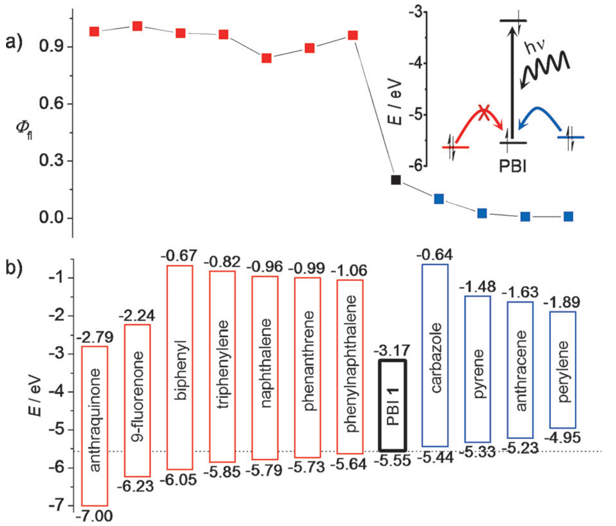

Figure 1. (a) Plot of the fluorescence quantum yield Φ_{fl} of the host-guest complexes. Electron-poor guests (red), electron-rich guests (blue), and the free cyclophane **1** (black); inset: schematic representation of the oxidative fluorescence quenching mechanism; (b) calculated HOMO–LUMO levels of the guest molecules; DFT calculations, Gaussian09W, B3LYP/6-31G(d).

Since the oxidative fluorescence quenching is related to an intermolecular charge transfer from the highest occupied molecular orbital (HOMO) of the guest molecule to the HOMO of the photoexcited host (inset in Figure 1 a), cyclophane **1** can be used as both "turn-on" and "turn-off" fluorescence probe depending on the electronic character of the encapsulated aromatic hydrocarbon. Considering the energy level of ferrocene/ferrocenium with respect to the vacuum level[13] and the oxidation potential of cyclophane **1** ($E_{1/2}^{ox}$ ($\mathbf{1}/\mathbf{1}^+$) = 0.84 V, Figure S7), the HOMO level of **1** can readily be estimated as $-(4.8+0.84)$ eV $= -5.64$ eV (-5.55 eV from DFT calculations). Thus, guest molecules with a HOMO that is higher in energy than that of cyclophane **1** will quench the PBI emission. Whilst aromatic hydrocarbons with a lower lying HOMO level obviously increase the cyclophane fluorescence because the guest molecules keep the two PBIs at distance, preventing structural relaxation in the excited state towards increased intermolecular PBI–PBI coupling that constitutes a common fluorescence quenching pathway of these dyes (Figure 1).[14] Furthermore, new bathochromically shifted CT bands at higher wavelength can be observed for electron-rich guest molecules beside the original PBI absorption maxima in the UV/Vis spectra (Figure 2).

According to Benesi and Hildebrand, who developed a simple mathematical approach for the determination of equilibrium constants of noncovalent host–guest complexes,

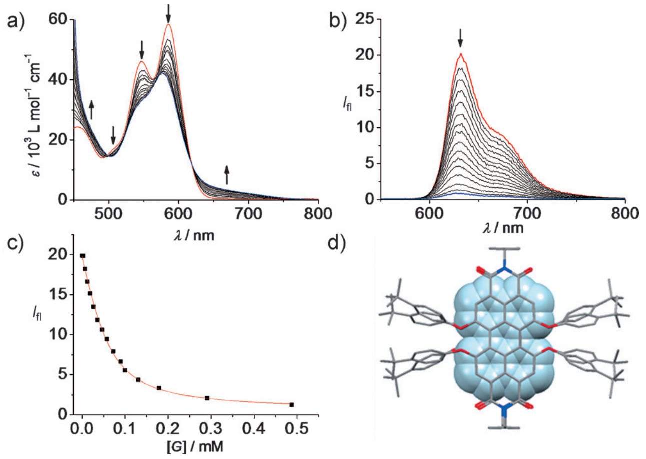

Figure 2. Changes in a) UV/Vis absorption and b) emission spectra of PBI **1** upon titration with perylene; $c(\mathbf{1}) = 5.8 \times 10^{-5}$ M in $CHCl_3$; red line: spectra before the first guest addition; blue line: spectra after 15 equivalents of perylene were added; arrows indicate spectral changes; c) nonlinear least squares fit of the fluorescence intensity vs. guest concentration; d) geometry-optimized structure of the 1:1 complex perylene@**1** in the top view obtained by force field optimization (Maestro 9.3, MacroModel 9.8, $CHCl_3$, MM2*).

$\Delta I_{\mathrm{fl}}^{-1}$ was plotted versus $[G]^{-1}$ which suggested the formation of 1:1 complexes for all applied guests (Figure S6).[15] The respective binding constants were accordingly determined using a 1:1 binding model by nonlinear least squares fitting (Figure S6) and the results are summarized in Table S1 (see the Supporting Information).[16]

For a presumed prevalence of dispersion interactions in these host–guest complexes, it is reasonable to assume that the affinity of **1** towards aromatic guest molecules correlates to the host–guest π surface that is in direct contact by the noncovalent interaction (Figure 3).[17] Thus, the dimension of the PBI π surface apparently defines the maximal binding strength and increasing number of C=C bonds within the substrate should result in larger binding constants until the aromatic PBI core becomes saturated and the guest molecule too extended to be encapsulated.[18] This tendency can be corroborated considering that the binding constant K_a continuously increases in the order naphthalene ($26.8\,\mathrm{M}^{-1}$) ≪ carbazole ($940\,\mathrm{M}^{-1}$) ≈ anthraquinone ($1.5 \times 10^3\,\mathrm{M}^{-1}$) ≈ 9-fluorenone ($1.6 \times 10^3\,\mathrm{M}^{-1}$) < anthracene ($9.9 \times 10^3\,\mathrm{M}^{-1}$) < phenylnaphthalene ($1.1 \times 10^4\,\mathrm{M}^{-1}$) < perylene ($4.6 \times 10^4\,\mathrm{M}^{-1}$) where the binding strength reaches its maximum (marked as dotted line in Figure 3). The similar values for similarly sized electron-rich and electron-poor guest molecules (e.g., carbazole and fluorenone) also corroborate the view that the binding energy is indeed governed by dispersion and not by charge-transfer forces. As a consequence of the particularly strong interaction between perylene and PBI host **1** (see above), the corresponding perylene@**1** complex could also be investigated by mass spectrometry (MALDI-MS, Figure S8).

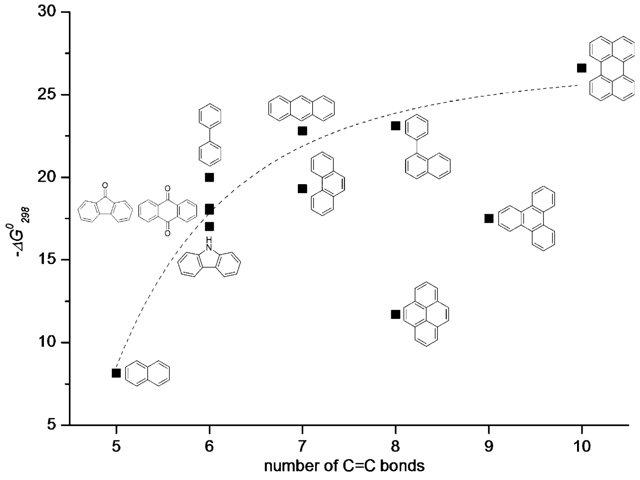

Figure 3. Plot of $-\Delta G^0_{298}$ versus the number of C=C bonds of the guests' π scaffold; the dotted line shows the trend between binding strength and interacting π orbitals that reaches a maximum for perylene.

Considering the number of C=C bonds that should be involved in the complexation of phenanthrene and triphenylene the observed binding constants are apparently lower than one might expect. However, for the geometry-optimized structures of phenanthrene@**1** (Figure S5 d) and triphenylene@**1** (Figure S5 e), this observation seems to be rather reasonable since both guest molecules are partially displaced from the cavity because of the core twisting of bay-substituted PBIs.[19] Therefore, the number of C=C bonds that contribute to the binding interaction in both complexes is reduced to approximately six, which is consistent with our experimental findings. The twist of the aromatic PBI core results in the cavity of cyclophane **1** being indeed somewhat distorted (Figure S5), and consequently exhibits a certain selectivity towards more flexible guest molecules which are capable to screen the surface of the inner void. The binding constant between **1** and pyrene ($114\,\mathrm{M}^{-1}$), which acts as a representative for relatively rigid and more discoid aromatic hydrocarbons, is thus significantly decreased (K_a is 100 times lower than that for phenylnaphthalene). In contrast, substrates with a high intrinsic flexibility such as biphenyl can readily adapt the geometry of the cavity, thus resulting in a comparatively high equilibrium constant of $K_a = 7.1 \times 10^3\,\mathrm{M}^{-1}$ that is four times higher than those for the planarized analogues 9-fluorenone, carbazole, and anthraquinone. Molecules such as 1,1′-binaphthyl and 1,1′-binaphthole, which are axially too twisted, or substrates such as tetracene and *trans*-stilbene, which are larger than the cavity of the PBI cyclophane itself, could not be encapsulated by **1**. This observation provides further evidence that the complexation indeed takes place within the cavity and not at the outer PBI π surface.

In summary, we have reported the synthesis of the rigid *para*-xylylene bridged cyclophane **1** that exhibits an ideal interchromophoric distance for the encapsulation of aromatic hydrocarbons with binding constants up to $4.6 \times 10^4\,\mathrm{M}^{-1}$. Since the emission properties of the complexes are highly dependent on the electronic structure of the substrate, cyclophane **1** could be used as both "turn-on" and "turn-off" fluorescence probe distinguishing electron-rich and electron-poor aromatic molecules.

Keywords: cyclophanes · dyes/pigments · fluorescence probes · host–guest chemistry · perylene bisimides

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