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1,8-Pyrenylene–Ethynylene Macrocycles

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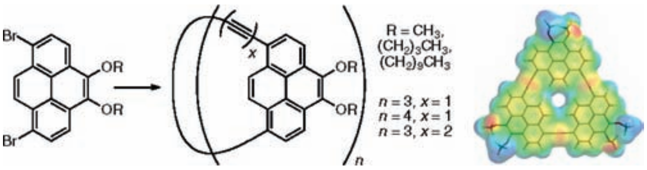
ABSTRACT



A concise, highly regioselective synthesis of 1,8-dibromo-4,5-dialkoxypyrenes has been developed and exploited in the synthesis of some 1,8-pyrenylene–ethynylene macrocycles. The ^{1}H NMR data and NICS calculations indicate that there is little or no macrocyclic ring current. Concentration-dependent UV–visible studies indicate no aggregation at low concentration, but 8b forms dimers with voids suitable for intercalation of small molecules in the solid state.

Arylene–ethynylene macrocycles constitute one of the most important classes of shape-persistent macrocycles.[1] Such systems have attracted interest for a variety of reasons, including their structural, optoelectronic, self-assembly, and liquid crystalline properties. Among the many known arylene–ethynylene macrocycles, benzene is by far the most commonly employed aromatic building block. Other small aromatic and heteroaromatic systems have also been used quite often, e.g. thiophene, pyridine, and naphthalene, but larger aromatic systems,[2] which have larger surfaces and more interesting optoelectronic properties, have been exploited far less often.

Pyrene (**1**), the smallest *peri* condensed polynuclear benzenoid aromatic hydrocarbon, has not previously been incorporated into an arylene–ethynylene macrocycle. Doing so would require access to synthetically useful quantities of appropriately disubstituted pyrenes, but this is nontrivial. For example, electrophilic dihalogenation of pyrene (**1**) is not only limited in the disubstitution patterns it can deliver (1,3-, 1,6-, and 1,8-)[3] but also poorly selective in the ones it provides. Moreover, the resulting isomer mixtures require painstaking separation. We now report a short and completely regioselective synthesis of 1,8-dibromo-4,5-dialkoxypyrenes **5a**–**c** and their use as building blocks for the construction of some 1,8-pyrenylene–ethynylene macrocycles.

The conceptual basis of this work was the premise that substituents at the 4 and 5 positions of pyrene (**1**) would sterically hinder the 3 and 6 positions, thereby enabling regioselective substitution at the 1 and 8 positions. Alkoxy groups were selected because they were expected to both activate the pyrene system toward electrophilic substitution and effectively hinder the 3 and 6 positions.

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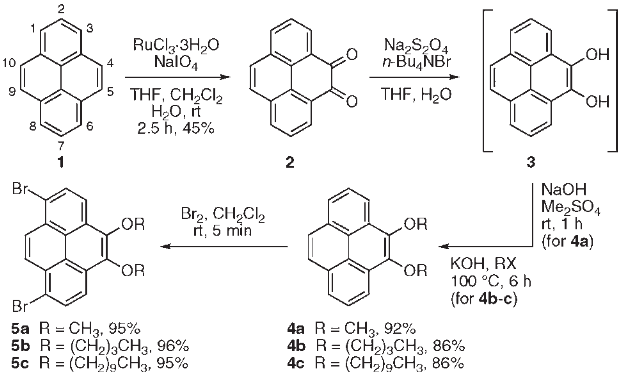
(1) (a) Zhang, W.; Moore, J. S. *Angew. Chem., Int. Ed.* **2006**, *45*, 4416–4439. (b) Zhao, D.; Moore, J. S. *Chem. Commun.* **2003**, 807–818. (c) Marsden, J. A.; Palmer, G. J.; Haley, M. M. *Eur. J. Org. Chem.* **2003**, 2355–2369. (d) Grave, C.; Schlüter, A. D. *Eur. J. Org. Chem.* **2002**, 3075–3098.

(2) Carbazole: (a) Zhao, T.; Liu, Z.; Song, Y.; Xu, W.; Zhang, D.; Zhu, D. *J. Org. Chem.* **2006**, *71*, 7422–7432. Phenanthrene: Morimoto, M.; Akiyama, S.; Misumi, S.; Nakagawa, M. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 857–859. Anthracene: Chen, S.; Yan, Q.; Li, T.; Zhao, D. *Org. Lett.* **2010**, *12*, 4784–4787. 1,10-Phenanthroline: Schmittel, M.; Ammon, H. *Synlett* **1999**, 750–752. [4]Helicene: Nakamura, K.; Okubo, H.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 1097–1099. 10b,10c-Dimethyl-10b,10c-dihydropyrene: Kimball, D. B.; Haley, M. M.; Mitchell, R. H.; Ward, T. R. *Org. Lett.* **2001**, *3*, 1709–1711. Triphenylene: Takeda, T.; Fix, A. G.; Haley, M. M. *Org. Lett.* **2010**, *12*, 3824–3827. Porphyrin: Yu, L.; Lindsey, J. S. *J. Org. Chem.* **2001**, *66*, 7402–7419. Dibenzo[*e*,*l*]pyrene: Höger, S.; Cheng, X. H.; Ramminger, A.-D.; Enkelmann, V.; Rapp, A.; Mondeshki, M.; Schnell, I. *Angew. Chem., Int. Ed.* **2005**, *44*, 2801–2805. Dithieno[3,2-*a*;2,3-*c*]naphthalene: Chen, T.; Pan, G.-B.; Wettach, H.; Fritzsche, M.; Höger, S.; Wan, L.-J.; Yang, H.-B.; Northrop, B. H.; Stang, P. J. *J. Am. Chem. Soc.* **2010**, *132*, 1328–1333. Dibenz[*a*,*j*]anthracene: Chan, J. M. W.; Tischler, J. R.; Kooi, S. E.; Bulovic, V.; Swager, T. M. *J. Am. Chem. Soc.* **2009**, *131*, 5659–5666. BODIPY: Sakida, T.; Yamaguchi, S.; Shinokubo, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 2280–2283. A larger PAH: Liu, W.-J.; Zhou, Y.; Zhou, Q.-F.; Ma, Y.; Pei, J. *Org. Lett.* **2008**, *10*, 2123–2126. Only one reference per aromatic system is given here. A more complete list appears in the Supporting Information.

(3) (a) Minabe, M.; Takeshige, S.; Soeda, Y.; Kimura, T.; Tsubota, M. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 172–179. (b) Grimshaw, J.; Trocha-Grimshaw, J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1622–1623.

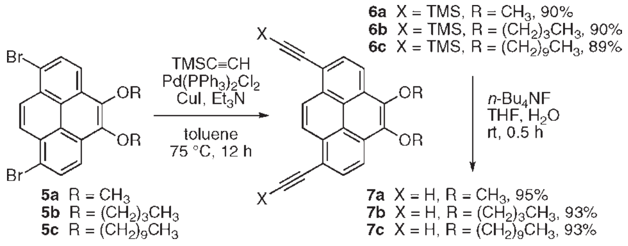
10.1021/ol200485x

Scheme 1. Synthesis of 1,8-Dibromopyrenes **5a−c**



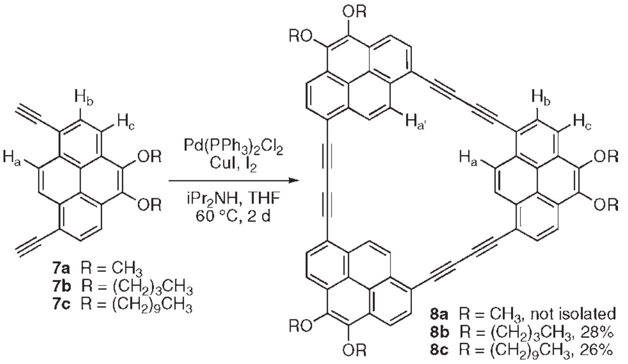
Functionality at the 4 and 5 positions of pyrene (**1**) was introduced selectively by oxidation to dione **2** using a modified version of a recent procedure (Scheme 1).[4] Changing the solvent from acetonitrile to THF allowed the reaction time to be reduced to 2.5 h from 16 h without affecting the yield. Reductive alkylation, which had not previously been reported for **2** (but had been reported for related systems such as phenanthrene-9,10-dione[5]), was then accomplished using a two-step procedure. Reaction of **2** with $Na_2S_2O_4$ afforded 4,5-dihydroxypyrene (**3**),[6] which was immediately di-*O*-alkylated to afford dialkoxypyrenes **4a−c** (86−92% from **2**). Dibromination of **4a−c** using Br_2 (2.2 equiv) was found to occur very readily (< 5 min at rt) with complete selectivity for the 1 and 8 positions to afford dibromides **5a−c** (95−96%). The use of 5 equiv of bromine at room temperature also gave only the 1,8-disubstituted products. Dibromides **5a−c** were then converted into the corresponding 1,8-diethynylpyrenes **7a−c** using a Sonogashira/deprotecion sequence (Scheme 2) in 83−86% overall yield.

Scheme 2. Synthesis of 1,8-Diethynylpyrenes **7a−c**

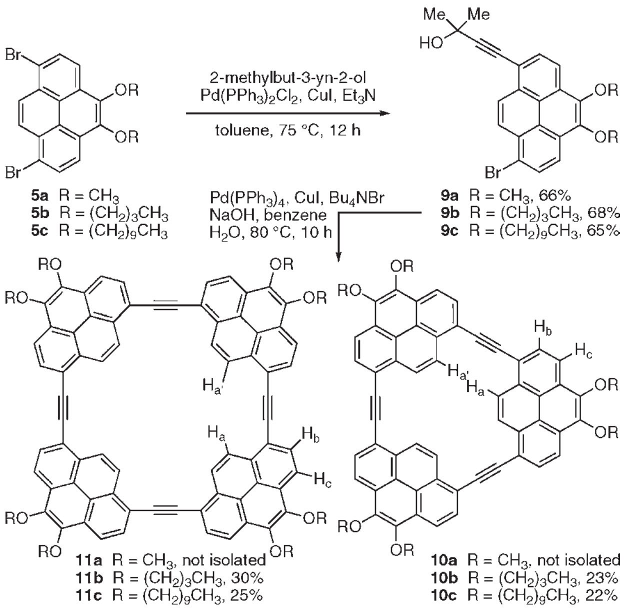


Diynes **7a−c** were subjected to oxidative coupling (Scheme 3).[2a] For **7a**, no cyclic oligomers were isolated, but for **7b−c**, cyclic trimers **8b−c** were obtained in 26−28% yield. No other cyclic oligomers were isolated. Macrocycles **8b−c** are dark red compounds, which are soluble in common organic solvents such as hexanes, benzene, dichloromethane, ethyl acetate, and acetone.

Scheme 3. Synthesis of Macrocycles **8b−c**



Scheme 4. Synthesis of Macrocycles **10b−c** and **11b−c**



Pyrenylene−ethynylene macrocycles with a single ethynylene unit connecting the pyrene units were then targeted (Scheme 4). Sonogashira coupling of dibromides **5a−c** with 2-methylbut-3-yn-2-ol (1.1 equiv) gave ynols **9a−c** (65−68%). An *in situ* deprotection and self-Sonogashira reaction[7] of **9a−c** then afforded macrocycles **10b−c** (22−23%) and **11b−c** (25−30%). These are also dark red in color and soluble in a range of common organic solvents. As with **8a**, the methoxy substituted macrocycles **10a** and **11a** were not isolated.

The molecular structures and properties of **8a**, **10a**, and **11a** were calculated at the HF/3-21G//B3LYP/6-31G*

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(4) Hu, J.; Zhang, D.; Harris, F. W. *J. Org. Chem.* **2005**, *70*, 707–708.

(5) Paruch, K.; Katz, T. J.; Incarvito, C.; Lam, K.-C.; Rhatigan, B.; Rheingold, A. L. *J. Org. Chem.* **2000**, *65*, 7602–7608.

(6) 4,5-Dihydroxypyrene (3) has been reported to be very oxygen sensitive (Tintel, C.; Terheijden, J.; Lugtenburg, J.; Cornelisse, J. *Tetrahedron Lett.* **1987**, *28*, 2057–2060), but it was found to be reasonably stable in our hands.

(7) Huynh, C.; Linstrumelle, G. *Tetrahedron* **1988**, *44*, 6337–6344.

level of theory (see Supporting Information). The optimized structures of the cyclic trimers **8a** and **10a** are planar with D_{3h} symmetry, whereas cyclic tetramer **11a** was calculated to have a saddle-shaped D_{2d}-symmetric structure akin to that of tetrabenzocyclooctatetraene.

Weakly diffracting crystals of **8b** suitable for X-ray crystallographic analysis were obtained from a benzene solution, and the structure revealed four chemically identical macrocycles in the asymmetric unit (one is shown in Figure 1, left). Each unique macrocycle deviates slightly from planarity, as characterized by the dihedral angles between pyrene units (3.52(7)° to 16.02(9)°). Ignoring the difference between the alkoxy substitutents, the experimentally determined structure of **8b** was found to be virtually identical to the calculated structure of **8a** (bond lengths ±0.01 Å; bond angles ±1°). Examination of intermolecular interactions shows that dimers with short intercentroid distances (3.40 and 3.41 Å) form between some macrocycles (Figure 1, right). Intercalated solvent benzene molecules are also present, and dimers associate into a slipped columnar arrangement (slippage angle of 69.5°) running parallel to the *a*-axis (see Supporting Information).

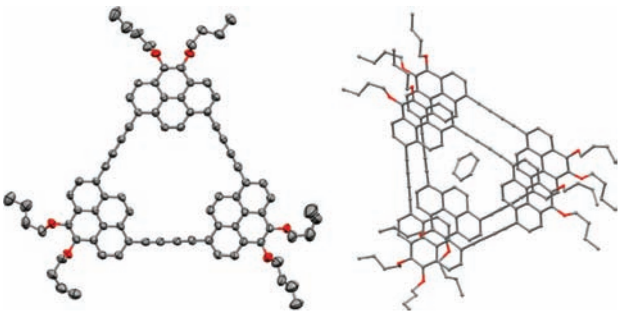

Figure 1. Left: ORTEP representation of macrocycle **8b** with 50% probability displacement ellipsoids; H-atoms omitted for clarity. Right: A dimer of **8b** with associated benzene.

The inner (30π) and outer (42π) edges of **8a**−**c**, as well as all other conjugated pathways through the pyrene systems of these macrocycles, correspond to Hückel aromatic π electron counts. In contrast, **10a**−**c** (inner: 24π, outer: 36π) and **11a**−**c** (inner: 32π, outer: 48π) are formally Hückel antiaromatic systems. Based on the large body of prior work on dehydrobenzannulenes,[1] substantial ring currents in these systems would not be expected, but, at first glance, the ^{1}H NMR spectra of macrocycles **8c**, **10c**, and **11c** (Figure 2)[8,9] appear to provide conflicting evidence.

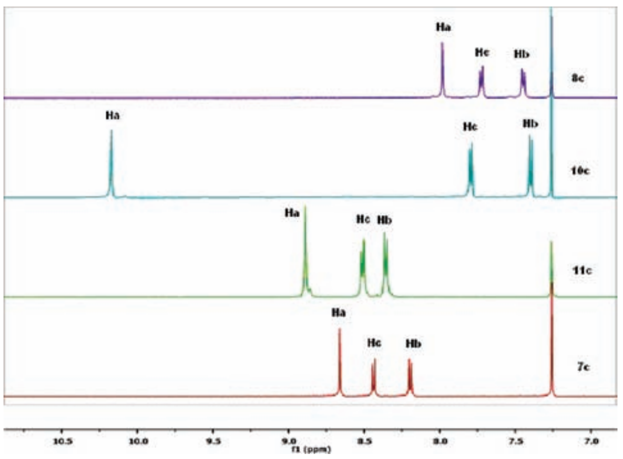

Figure 2. Aromatic regions of the ^{1}H NMR spectra of **7c**, **8c**, **10c**, and **11c**.

In comparison to diyne **7c**, the signals for both the internal and external aromatic protons of nonplanar and formally antiaromatic cyclic tetramer **11c** are observed at somewhat lower field: ($\Delta\delta$ = 0.08−0.25 ppm). Similarly, all aromatic signals for the planar and formally aromatic cyclic trimer **8c** move in the same direction, in this case substantially toward higher field ($\Delta\delta$ = −0.68 to −0.75 ppm). These observations are entirely inconsistent with the existence of a meaningful macrocyclic ring current. On the other hand, the large upfield shift of the external protons ($\Delta\delta$ = −0.65 to −0.80 ppm) and the even larger downfield shift of the internal protons ($\Delta\delta$ = 1.51 ppm) for the planar and formally antiaromatic trimer **10c** are, on the surface, fully consistent with pronounced antiaromatic character. However, considering that the external protons (H_b and H_c) of the two trimeric macrocycles (**8c** and **10c**) have very similar chemical shifts (±0.08 ppm), a weak-to-negligible macrocyclic ring current could still be the case if the low-field chemical shift of the internal protons (H_a) of **10c** is anomalous due to other factors.

In the calculated structure of **10a** (Supporting Information), the internuclear distance between H_a on neighboring pyrene systems (H_a−$H_{a'}$) is 1.94 Å, which is well within the sum of the van der Waals radii (2.4 Å).[10] Thus, a strong steric deshielding of these nuclei would be expected. By comparison, the H_a−$H_{a'}$ distances in the calculated structures of **8a** and **11a** are 4.45 and 3.47 Å, respectively. Moreover, if **10a**−**c** are indeed assemblies of three essentially intact pyrene systems, then each H_a nucleus is situated not only in the deshielding zone of the pyrene system to which it is attached but also in those of the other two pyrene systems, albeit further afield. Since the three pyrene systems are substantially closer to one another in **10a**−**c** than they are in **8a**−**c**, any additional deshielding of H_a from the remote pyrene systems should be strongest in **10a**−**c**.

This notion of cooperative deshielding is supported by NICS calculations (Supporting Information). The NICS_{zz} value at the centroid of **10a** is 17.98. The corresponding

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[8] 1,8-Bis(butadiynyl)-4,5-bis(decyloxy)pyrene was also synthesized, and the aromatic region of its ^{1}H NMR spectrum was virtually identical to that of **7c**.

[9] The nature of the side chain (butoxy vs decyloxy) does not significantly influence the chemical shifts of the pyrene systems, so the discussion of the NMR spectra is limited to the decyloxy substituted macrocycles **8c**, **10c**, and **11c**.

[10] Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.

value for **8a** (5.48) is also positive, but smaller. For **10a**, deletion of the alkynes to leave three isolated pyrene systems[11] gave only a modestly diminshed NICS$_{zz}$ value (14.08). Deletion of the pyrene systems in **10a** to leave three isolated ethyne molecules gave a greatly reduced but still positive NICS$_{zz}$ value (1.26). Summing the NICS$_{zz}$ values for the two sets of isolated components of **10a** (14.08 + 1.26 = 15.34) falls short of the value for **10a** but leaves little room for the influence of effects originating from the intact macrocycle, such as a paratropic macrocyclic ring current.

The aromatic stabilization energy (ASE) of pyrene has recently been calculated to be 74.6 kcal/mol,[12] so it is not surprising that little or no evidence can be found to support the existence of a significant macrocyclic ring current in **8** and **10**. Macrocyclic delocalization would disrupt the aromaticity of all three pyrene systems, costing up to 224 kcal/mol. Thus, all of the macrocycles described here are best viewed as isolated pyrene systems connected by ethynylene bridges,[13] *i.e.* as pyrenophynes.

The UV–vis and fluorescence spectra of **8b**, **10b**, and **11b** are shown in Figure 3.[14] Although the lowest energy $S_0 \rightarrow S_1$ transition for an unsubstituted pyrene is symmetry forbidden, the absorption spectra of **8b**, **10b**, and **11b** do show complex absorption bands with appreciable intensity at longer wavelengths. Clearly, the ethynyl and alkoxyl substituents on the pyrene systems break the symmetry and allow the coupling of the ground- and excited-state wave functions. TD-DFT calculations (Supporting Information) predict transitions with mixed orbital parentage at 524 nm (f_{osc} = 0.002) for **8a** and 596 nm (f_{osc} = 0.0001) for **10a**, in good agreement with the onsets of weak absorption bands observed in their UV–vis spectra. The absorption envelope of **11b** resembles those of the pyrene monomers, indicating considerably disrupted electronic communication as a result of its nonplanar conformation. Optical gaps were estimated from the onset wavelengths of the low-energy absorption bands (**10b**: 2.19 eV, **8b**: 2.33 eV, **11b**: 2.63 eV), which are in line with their calculated HOMO–LUMO gaps (**10b**: 2.56 eV, **8b**: 2.88 eV, **11b**: 3.06 eV). The UV–vis and MO properties indicate weak electronic coupling between the pyrene units via the ethynyl linkages in the ground state, which again points to a small macrocyclic ring current.

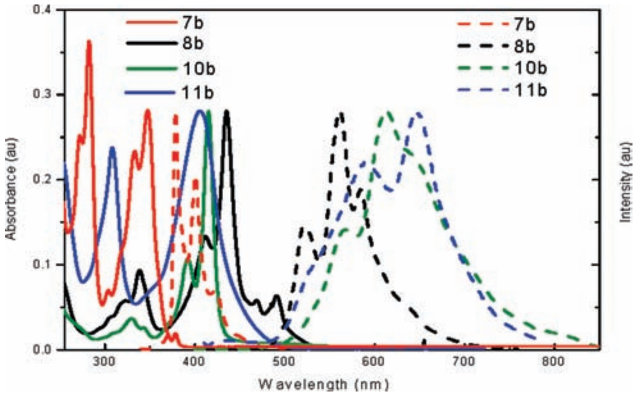

Figure 3. Normalized absorption (solid lines) and emission (broken lines) spectra for **7b**, **8b**, **10b**, and **11b**. λ_{exc} = 300 nm for **7b**; λ_{exc} = 400 nm for **8b**, **10b**, and **11b**. Concentrations: [**7b**] = 2.88×10^{-5} M; [**8b**] = 2.25×10^{-6} M; [**10b**] = 5.45×10^{-6} M; [**11b**] = 8.20×10^{-6} M.

The emission yields for all of the macrocycles ($\phi_{em} \approx 10^{-3}$) are much smaller than those of the diynes **7a–c** ($\phi_{em} \approx 0.13$) or the dialkoxypyrenes **4a–c** ($\phi_{em} \approx 0.2$). Plots of absorbance vs concentration for the macrocyclic systems (Supporting Information) are linear in the 10^{-6} to 10^{-5} M concentration range, which suggests that there is no significant aggregation at these concentrations.

A more detailed investigation of the electronic absorption and emission spectra of the new 1,8-pyrenylene–ethynylene macrocycles is underway, as are studies aimed at the synthesis of other 1,8-pyrenylene-based π systems.

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Supporting Information Available. Experimental procedures, characterization data, ^{1}H and ^{13}C NMR spectra for compounds **2**, **4a–c**, **5a–c**, **6a–c**, **7a–c**, **8b–c**, **9a–c**, **10b–c**, and **11b–c**. MALDI-TOF mass spectra for **8b–c**, **10b–c**, and **11b–c**. UV–vis and fluorescence spectra for **4a–c**, **7a–c**, **8b–c**, **10b–c**, and **11b–c**. Detailed structural description and CIF for **8b**. Computational data for calculated structures of **8a**, **10a**, and **11a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] Hydrogen atoms were used to replace the akynyl groups.

[12] Wu, J.; Cyrański, M. K.; Dobrowolski, M. A.; Merner, B. L.; Bodwell, G. J.; Mo, Y.; Schleyer, P. v. R. *Mol. Phys.* **2009**, *107*, 1177–1186.

[13] A 2,4-pyrenylene–vinylene macrocycle was also found to behave as an assembly of three pyrene "islands". Schnorpfeil, C.; Fetten, M.; Meier, H. *J. Prakt. Chem.* **2000**, *342*, 785–790.

[14] Spectra and detailed spectral data for other compounds are given in the Supporting Information (Figures S4–1 to S4–7).