Synthesis and Adsorption of Shape-Persistent Macrocycles Containing Polycyclic Aromatic Hydrocarbons in the Rigid Framework

SUPPORTING INFORMATION

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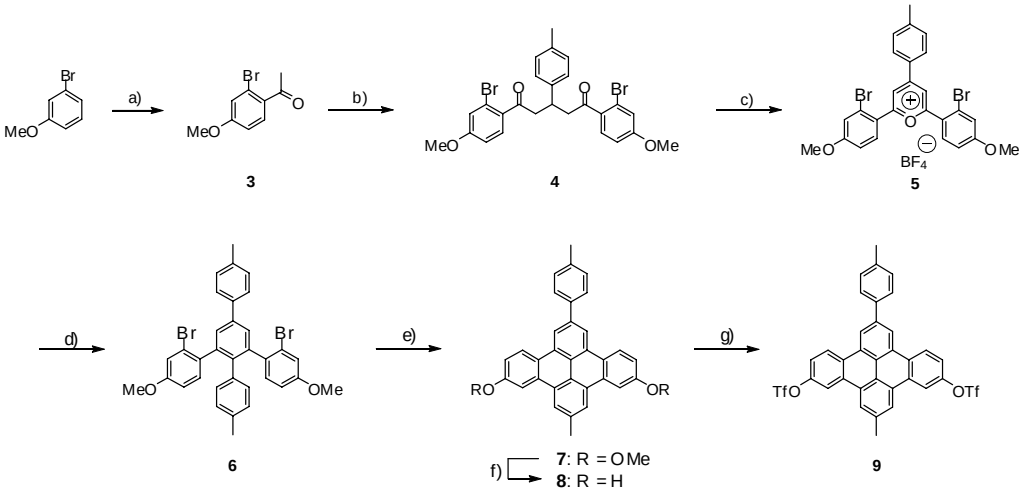
Synthesis.

Results and discussion.

The synthesis of the shape-persistent macrocycles is divided into two parts. The first part is the synthesis of the dibenzonaphthacene bis(triflat) that is capable of undergoing palladium-catalyzed CC-bond formation in order to be used in the second part of the synthesis, the formation of the ring precursors and their oxidative cyclization. The formation of the polycyclic aromatic structure is based on a strategy that we recently described. It uses the possibility to transform pyrylium salts into well defined oligophenylenes.[i] This allows an aromatic CC-bond formation without the need of transition metals, and therefore, the simple construction of halogenated oligophenylenes without the need for sophisticated protective group chemistry. These oligophenylenes can be transformed into polycyclic aromatic building blocks by a transition metal catalyzed dehydrohalogenation. Alkoxy substituents do not interfere with this protocol. Indeed, they support the dehydrohalogenation, as we have shown earlier. Furthermore, they can be transformed in two steps into structures that are capable of undergoing further Pd-catalyzed coupling reactions.[ii]



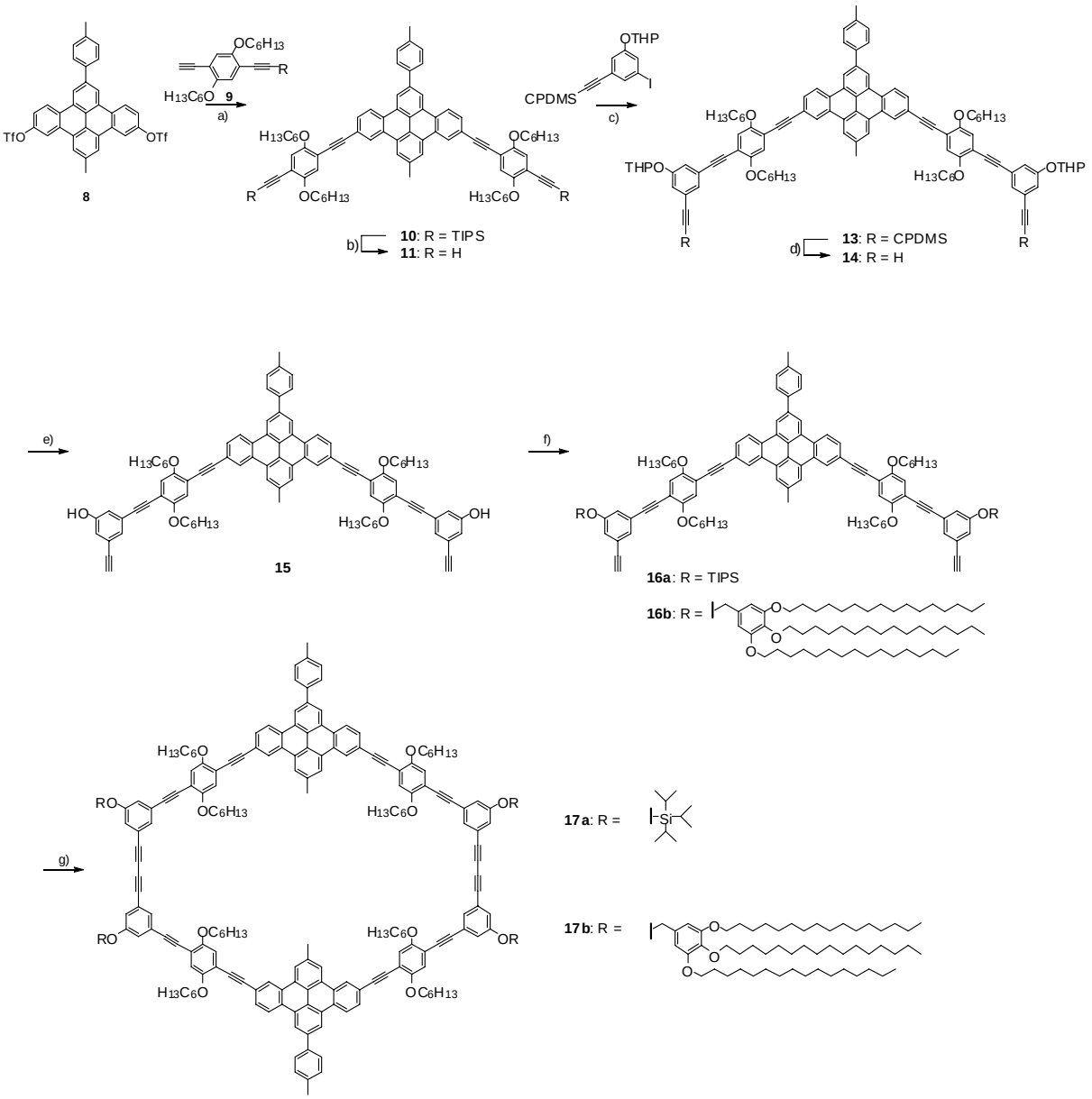
Scheme 1. a) AcCl, $AlCl_3$ (77 %); b) tolylaldehyde, NaOH (59 %); c) chalcone, $BF_3{\cdot}OEt_2$ (82 %); d) sodium tolylacetate (54 %); e) $PdCl_2(PPh_3)_2$, dbu (37 %); f) BBr_3 (92 %); g) Tf_2O, pyridine (57 %).

Starting from commercially available 3-bromoanisole, acylation gave the corresponding acetophenone **3** in 77 % yield (Scheme 1). As we have also observed earlier for pyrylium salts derived from 2-bromo acetophenone, the direct pyrylium salt formation under a variety of

conditions was unsuccessful and gave only non-identified products. However, the two-step procedure by preparing first the 1,5-diketone that was subsequently transformed into the pyrylium salt turned out to be successful. The diketone formation is best performed under solvent-free conditions by intensively grinding two equivalents of the acetophenone and one equivalent of the benzaldehyde with solid sodium hydroxide in a mortar for 20 minutes. After conventional workup, **4** was obtained in 59 % yields after chromatography. Treating of a mixture of **4** and chalcone as hydrogen acceptor with boron trifluoride etherate gave the pyrylium salt **5** (82 %). Condensation of **5** with *p*-tolylacetic acid according to the procedure of Fischer and Zimmermann gave the pentaphenyl **6** (54 %). The Pd-catalyzed dehydrohalogenation was performed with $Pd(PPh_3)_2Cl_2$ and DBU as base in dimethylacetamide at 160 °C over night. The polycylic aromatic **7** was obtained in 37 % yield. According to the ^{1}H-NMR analysis, the crude product contained no unreacted starting material and side product formation occurred mostly due to competing dehalogenation. Although the dibenzonaphthacenes and the side products have similar R_f-values on TLC, the purification of **7** is rather easy performed by recrystallization since it is the least soluble compound in the mixture. Demethylation of **7** using BBr_3 at –78 °C yielded **8** (93 %) that was transformed into the triflate **9** without further purification (57 %).

The synthesis of the macrocycles is displayed in Scheme 2. The polycyclic bistriflate **9** was coupled with the mono protected bisacetylene **10** under Sonogashira-Hagihara conditions to give the bis-triisopropylsilyl (TIPS) protected compound **11** in 80 % yield.

The hexyloxy groups were necessary to ensure sufficient solubility of most of the compounds that were subsequently prepared. Deprotection of **11** by Bu_4NF gave the bisacetylene **12** (87 %). Recent studies in our group have shown that bisacetylenes can be treated with a 7-10-fold excess of an aromatic diiodide under the conditions of the Sonogashira-Hagihara coupling and give the corresponding (enlarged) diiodides in yields up to 80 %.[iii] However, preliminary coupling reactions using the excess strategy and dibenzonaphthacene bisacetylenes were in all cases unsuccessful and gave mostly polymeric products as determined by gel permeation chromatography (GPC). We ascribe that to the tendency of the PAHs to aggregate in solution (see below): After the coupling of the diiodide to the bisacetylene a second bisacetylene is due to the aggregate formation in close proximity and undergoes a second coupling reaction although statistically the large diiodide excess should prevent the oligomer formation.

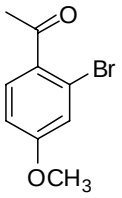


Scheme 2. a) $PdCl_2(PPh_3)_2$, CuI (80 %); b) Bu_4NF (87 %); c) $PdCl_2(PPh_3)_2$, CuI (82 %); d) K_2CO_3/MeOH (41 %) ; e) p-TsOH/MeOH (98 %); f) **1a**: tris(hexadecyloxy)benzyl bromide, K_2CO_3 (83 %); **1b**: TIPSCl/imidazole (81 %); g) **2a**: CuCl/$CuCl_2$, pyridine (41 %); **2b**: CuCl/$CuCl_2$, pyridine (14 %).

Therefore, without testing the behavior of **12**, we avoided the excess reaction and coupled **12** with the monoiodide **13** to yield the protected bisacetylene **14** (82 %). Monoiodide **13** was obtained by a statistical reaction of the THP-protected 3,5-diiodophenol and 3-cyanopropyldimethylsilylacetylene (CPDMS acetylene) in 41 % yield (the CPDMS protecting group has a rather high polarity.[iv] This makes in statistical reactions a separation of

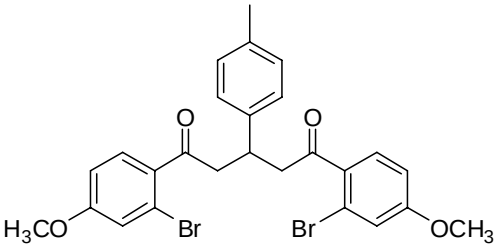
the double coupled side product and remaining starting material even with large material quantities relatively easy). Removing of the CPDMS group can be obtained under mild conditions and treating **14** with potassium carbonate in THF/methanol gave the bisacetylene **15** (41 %).[v] Deprotection of the THP group under slightly acidic conditions resulted in nearly quantitative formation of the bisphenol **13** that was used for the further steps without further characterization. We investigated in our study two compounds with different substituents. Treating **16** with TIPS chloride/imidazole gave **1a** and alkylation of **16** with 3,4,5-tris(hexadecyloxy)benzyl chloride gave the half ring **1b**.[vi] As we have observed before for derivatives of dibenzonaphthacene, the ^{1}H-NMR of the compounds show in dichloromethane a concentration dependence of the chemical shift that suggest an aggregation in solution.[ii] For **1a** we determined the aggregation constant to be 1.2×10^2 M^{-1} under the assumption that the monomer-dimer equilibrium is the predominant process in CD_2Cl_2 solution.

Both compounds were cyclized under pseudo-high dilution conditions, i.e. by adding a solution of **1a** (**1b**) in pyridine slowly into a suspension of the catalysts in the same solvent, to give the macrocycles **2a** and **2b**. **2a** could be obtained in 41 % yield after column chromatography and subsequent recrystallization from chloroform. Contrary, the purification process for **2b** was more tedious and **2b** could only be obtained in 14 % yield after column chromatography and double recrystallization. We expected to observe a larger aggregation constant for the macrocycles compared to the half rings due to the restricted conformational freedom of the compounds. This would be similar to the observation of the ring aggregation by Yamaguchi.[2d(main text)] However, due to the restricted solubility of **2a** in dichloromethane, no aggregation could be observed. On the other hand, a higher solubility was found in tetrachloroethane but no concentration dependence of the ^{1}H-NMR signals could be observed. For **2b** the ^{1}H-NMR signals are broadened in dichloromethane as well as in chloroform and did also not allow the determination of an aggregation constant. Nevertheless, the broad signals in the ^{1}H-NMR spectrum were an indication for the aggregation tendency of the **2b**. Unfortunately, a detailed investigation of the aggregation of **2b** by means of light scattering could not be performed due to the restricted availability of this compound.



3

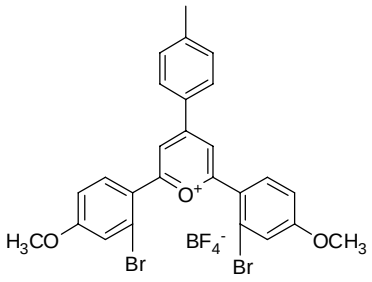
3: (according to Zuber, M.; Percec, V.: *J. Polym. Sci. A* **1992**, *30*, 997-1016) A mixture of 3-bromanisole (37.4 g, 0.2 mmol), anhydrous $AlCl_3$ (32.0 g, 0.24 mol) and 200 ml dry CH_2Cl_2 was cooled below 5 °C by an ice-bath, and acetyl chloride (15.8 g, 0.2 mol) was added drop wise. The mixture was allowed to reach RT and stirred for 1 h., then poured into 250 ml of ice-water containing 40 ml concentrated HCl and stirred to reach RT. The organic phase was separated, and the aqueous layer was washed with CH_2Cl_2 (3× 40 ml). The combined organic phase was washed with H_2O (3× 20 ml), 10 % aqueous NaOH (3×20 ml), H_2O (3×20 ml), brine (3×20 ml), dried over $MgSO_4$, and the solvent was removed in *vacuo*. The residue was purified by recrystallization from petroleum ether (150 ml; at – 15 °C). Yield: 35.2 g (76.9 %); colourless liquid; R_f = 0.36 (petroleum ether /$CHCl_2$ 1:1); $C_9H_9O_2Br$ (cal. 229.07); HRMS (EI) calcd for $C_9H_9O_2Br$ (M^+) 227.98; found 227.9796. ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 7.56 (d, *J* = 8.9 Hz, 1 H), 7.14 (d, *J* = 2.5 Hz, 1 H), 6.88 (dd, *J* = 8.5 Hz, *J* = 2.1 Hz, 1 H), 3.82 (s, 3 H), 2.61 (s, 3 H).



4

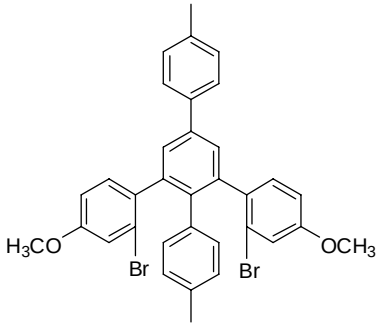
4: With a pestle and mortar, NaOH pellets (4.41 g 0.11mol) were crushed to a fine powder. 2-Bromo-3-methoxyacetophenone (3) (23.9 g, 0.10 mol) and p-tolylaldehyde (6.25 g, 0.052 mol) were added and the mixture was ground for a period of about 25 min. The highly viscous yellow gel was dissolved in Et_2O (300 ml) and water, the ether solution was washed with H_2O (3 × 50 ml), brine (3 × 50 ml), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by preparative centrifugal thin layer chromatography on a Chromototron (Harrison Research) (petroleum ether /CH_2Cl_2 1:1). Yield: 17.1 g (58.6 %); highly viscous yellow oil. R_f = 0.17 (petroleum ether /CH_2Cl_2 1:1); HRMS (EI): calcd for $C_{26}H_{24}O_4Br_2$ (M^{+2}) 560.00; found

560.0005.^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 7.35 (d, *J* = 8.7 Hz, 2 H), 7.12 (d, *J* = 2.4 Hz, 2 H), 7.07 (s, 4 H), 6.86 (dd, *J* = 8.8 Hz, *J* = 2.5 Hz, 2 H), 3.90-3.80 (m, 1 H), 3.82 (s, 6 H) 3.45-3.15 (m, 4 H), 2.28 (s, 3 H).



5

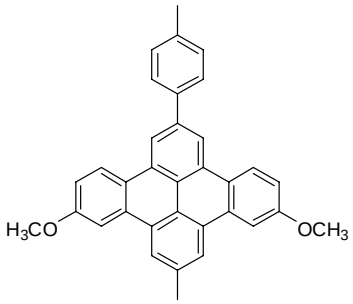
5: A mixture of **4** (15.8 g, 28.2 mmol) and chalcone (5.9 g, 28.2 mmol) was purged with argon. Boron trifluoride etherate (23 ml) was added, the mixture was stirred at 100 °C for 2 h, cooled, and diluted with Et_2O (20 ml). After 12 h, the yellow solid was filtered off and thoroughly washed with ether and used as received.Yield: 14.6 g (82.5 %); yellow solid. ^{1}H-NMR (250 MHz; CD_2Cl_2; *J*/Hz): δ = 8.59 (s, 2 H), 8.05 (d, *J* = 8.9 Hz, 4 H), 7.55 (d, *J* = 8.2 Hz, 2 H), 7.43 (d, *J* = 2.4 Hz, 2H), 7.18 (dd, *J* = 8.5 Hz, *J* = 2.1, 2 H), 3.95 (s, 6 H), 2.53 (s, 3 H).



6

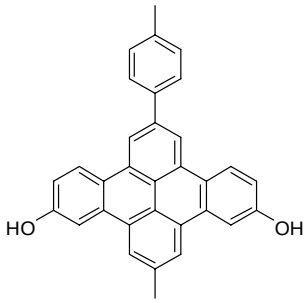
6: A mixture of **5** (7.0 g, 11.2 mmol), sodium 4-methylphenylacetate (19.3 g, 112 mmol) (prepared from 4-methylphenylacetic acid and sodium methanolate in methanol (0.5 M) and evaporation of the solvent), and acetic anhydride (40 ml) was stirred at 150 °C for 2 h. After cooling to RT, the acetic anhydride was removed in vacuo and the residue was dissolved in Et_2O (300 ml). The organic phase was washed with 10 % aqueous NaOH (3×40 ml), H_2O (3×40 ml) and brine (3×40 ml), dried over $MgSO_4$, and then the solvent was removed in vacuo. The

residue was purified by preparative centrifugal thin layer chromatography on a Chromatotron (petroleum ether /CH_2Cl_2 2:1). Yield: 3.80 g (54.0 %); colourless crystals; mp: 133° C; R_f = 0.26 (petroleum ether /CH_2Cl_2 2:1); $C_{34}H_{28}Br_2O_2$ (cal. 628.40), HRMS(EI) calcd for $C_{34}H_{28}Br_2O_2$ (M^{+2}) 626.04; found 626.0467. ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 7.6- 7.53 (m, 4 H), 7.29 (d, *J* = 7.3 Hz, 2 H), 7.10 – 7.05 (m, 3 H), 6.95 - 6.50 (m, 7 H), 3.75 (s, 6 H), 2.42 (s, 3 H), 2.13 (s, 3 H).



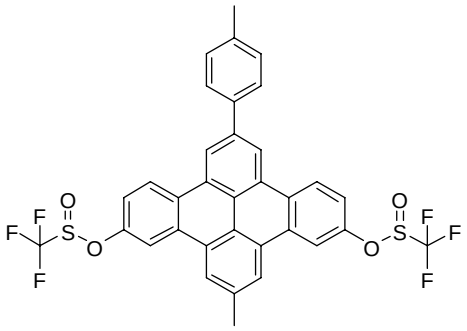
7

7: Under an argon atmosphere, 1,8-diazabicyclo [5.4.0] undec-7-en (2.08 g) was added to a solution of **6** (2.0 g, 3.2 mmol) in dry N,N-dimethylacetamide (30 ml). $PdCl_2(PPh_3)_2$ (0.53 g) was added, the mixture was stirred at 160 °C for 12 h, cooled to RT and poured into CH_2Cl_2 (300 ml). The organic layer was washed with H_2O (3×40 ml), and brine (3×20 ml), dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by recrystallization from $CHCl_3$ (30 ml). Yield: 540 mg (36.5 %); colourless crystals; mp: 284 °C; R_f = 0.21 (petroleum ether /CH_2Cl_2 2:1); $C_{34}H_{26}O_2$ (Cal. 466.57); HRMS (EI) cacld for $C_{34}H_{26}O_2$ (M^{+1}) 467.20; found 467.2018. ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 8.92 (s, 2 H), 8.82 (d, *J* = 9.4 Hz, 2 H), 8.65 (s, 2 H), 8.21 (d, *J* = 2.1 Hz, 2 H), 7.86 (d, *J* = 8.0 Hz, 2 H), 7.45 – 7.35 (m, 4 H), 4.11 (s, 6 H), 2.89 (s, 3 H), 2.31 (s, 3 H).



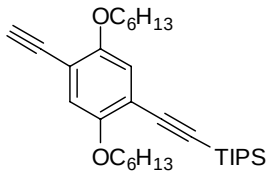
8

8: Under an argon atmosphere, **7** (500 mg, 1.07 mmol) was suspended in dry dichloromethane (40 ml) and cooled to –78 °C. BBr_3 (0.3 ml, 3.21 mmol) was added in one portion. The mixture turned immediately blue, and was stirred at RT overnight. The reaction was quenched by adding a few drops of water. After 1 h stirring, methanol (20 ml) was added, the precipitated product was filtered off and washed with water (10 ml) and methanol (20 ml) and dried in *vacuo* at 40 °C for 4 h. The materials was used as received Yield: 431 mg (92.2 %); colourless solid; mp: >305 °C; $C_{32}H_{22}O_2$ (Cal. 438.5); HRMS (EI) cacld for $C_{32}H_{22}O_2$ (M^{+1}) 439.16; found 439.1609. ^{1}H-NMR (250 MHz; THF-d_8 + D_2O): δ = 8.95 (s, 2 H), 8.81 (d, *J* = 9.2, 2 H), 8.70 (s, 2 H), 8.21 (d, *J* = 2.2 Hz, 2 H), 7.92 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.24 (dd, *J* = 8.7 Hz, *J* = 2.1, 2 H), 2.83 (s, 3 H), 2.43 (s, 3 H).



9

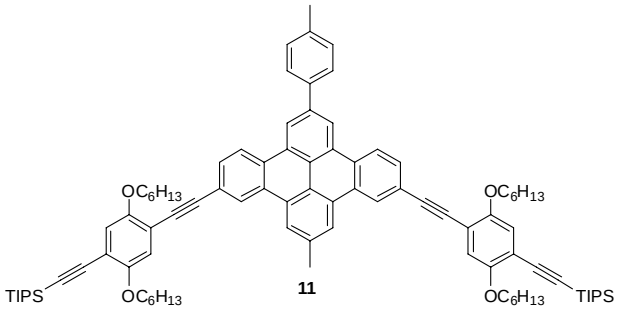
9: Under argon atmosphere, a mixture of **8** (200 mg, 0.46 mmol) in dry pyridine (2.5 ml) was cooled to 0 °C. Trifluormethane sulfonic anhydride (0.4 ml, 2.37 mmol) was added and the mixture was stirred at RT overnight. The reaction was quenched by adding water (10 ml). After 20 min stirring, methanol (20 ml) was added, the precipitated product was filtered off and washed with water (10 ml) and methanol (20 ml) and recrystallized from toluene. Yield: 174.3 mg (56.5 %); colourless crystals; mp: > 305 °C. R_f = 0.34 (petroleum ether /CH_2Cl_2 3:1]. ^{1}H-NMR (250 MHz; THF-d_8): δ = 9.24 (s, 2 H), 9.20 (d, *J* = 9.5 Hz, 2 H), 8.94 (d, *J* = 2.7 Hz, 2 H), 8.91 (s, 2 H), 8.02 - 7.96 (m, 2 H), 7.76 (dd, *J* = 8.6 Hz, *J* = 2.4 Hz, 2 H), 7.41 (d, *J* = 7.7 Hz, 2 H), 2.88 (s, 3 H), 2.46 (s, 3 H).



10

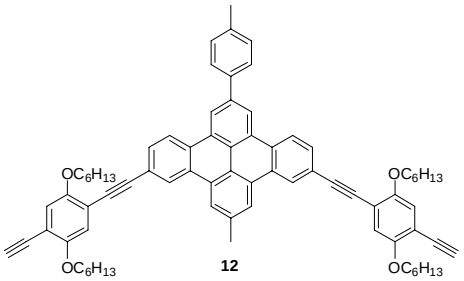
10: **10** was prepared according to ref. 6a (main text) from the corresponding 1,4-dihexyloxy-2-(2-triisopropylsilylethynyl)-5-(2-trimetylsilylethynyl)benzene (3 g, 5.4

mmol) in THF (15 ml) and MeOH (5 ml). After the addition of K_2CO_3 (3 g, 21.8 mmol), the resulting mixture was stirred at RT for 24 h and then poured into ether (150 ml) and H_2O (50 ml). The organic phase was separated, washed with H_2O (3×40 ml), and brine (3×20 ml), dried over $MgSO_4$, and then the solvent was removed in vacuo. Purification of the product was performed by preparative centrifugal thin layer chromatography (petroleum ether/dichlorometnane 4:1). Yield: 2.09 g (80.1 %); colourless crystals; mp: 54 °C; R_f = 0.66 (petroleum ether/dichlorometnane 4:1); $C_{31}H_{50}O_2Si$ HRMS (FAB) cacld for $C_{31}H_{50}SiO_2$ (M^{+1}) 483.36; found 483.3643. ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 7.04 (s, 2 H), 4.10- 3.95 (m, 4 H), 3.48 (s, 1 H), 1.92-1.84 (m, 4 H), 1.66 - 1.42 (m, 12 H), 1.25 (s, 21 H) 1.05 – 0.95 (m, 6 H).



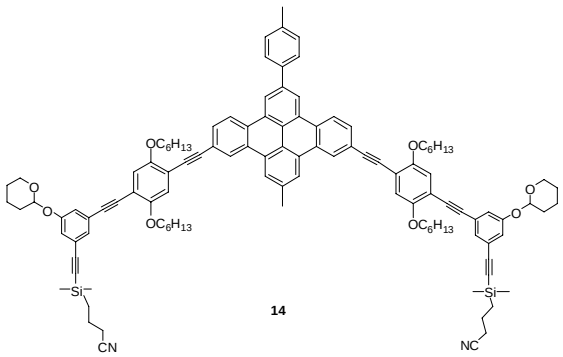
11

11: Under argon atmosphere, **10** (753.7 mg, 1.56 mmol) was dissolved in dry piperidine (25 ml), and then **9** (349 mg, 0.52 mmol), $Pd(PPh_3)_4$ (25 mg) and CuI (13 mg) were added. The yellow suspension was stirred at 50 °C for 8 h, cooled to RT, and poured into CH_2Cl_2 (100 ml). The organic phase was washed with H_2O (3×40 ml), and brine (3×20 ml), dried over $MgSO_4$, and then the solvent was removed in vacuo. The residue was purified by preparative centrifugal thin layer chromatography (petroleum ether/dichlorometnane 3:1). Yield: 567 mg (79.7 %); yellow waxy solid; R_f = 0.32 (petroleum ether /$CHCl_3$ 3:1). ^{1}H-NMR (250 MHz; $CDCl_3$): δ = 8.95 (s, 2 H), 8.91 (br. s, 2 H), 8.76 (d, *J* = 8.5 Hz, 2 H), 8.65 (s, 2 H), 7.81 (m, 4 H), 7.40 (d, *J* = 8.2, 2 H), 7.09 (s, 2 H), 7.01 (s, 2 H), 4.10 –3.90 (m, 8 H), 2.84 (s, 3 H), 2.50 (s, 3 H), 1.22-1.97 (m, 32 H), 1.17 (s, 42 H) 0.90 – 0.75 (m, 12 H,).



12

12: Tetra-n-butyl ammonium fluoride (1M in THF) (1.18 ml, 1.18 mmol) was added to a solution of **11** (402.3 mg, 0.294 mmol) in THF (10 ml). The mixture was stirred at RT for 2 h. Diethyl ether (100 ml) and water (20 ml) were added, the organic phase was separated, washed with H_2O ((3×25 ml), and brine (2×25 ml), dried over $MgSO_4$, and then the solvent was removed in vacuo. After adding methanol (20 ml), the residue was solidified. Then the methanol was decanted and this procedure was repeated for three times. The residue was left under methanol overnight at RT, the precipitate was filtered off and purified by preparative centrifugal thin layer chromatography (petroleum ether/ dichloromethane 4:3). Yield: 269.6 mg (86.9 %); yellow waxy solid; R_f = 0.76 (petroleum ether/ dichlorometnane 1:1]; $C_{76}H_{78}O_4$ calcd 1055.43; found (FD) m/z=1055.0 (M^+). ^{1}H-NMR (400 MHz; $CDCl_3$): δ = 8.97 (s, 2 H), 8.91 (s, 2 H), 8.76 (d, *J* = 8.6 Hz, 2 H), 8.65 (s, 2 H), 7.83 – 7.79 (m, 4 H), 7.41 (d, *J* = 7.4, 2 H), 7.11 (s, 2 H), 7.03 (s, 2 H), 4.08 (m, 8 H), 3.38 (s, 2 H), 2.84 (s, 3 H), 2.49 (s, 3 H), 1.96 – 1.80 (m, 8 H), 1.70 - 1.24 (m, 24 H), 0.92 – 0.80 (m, 12 H).

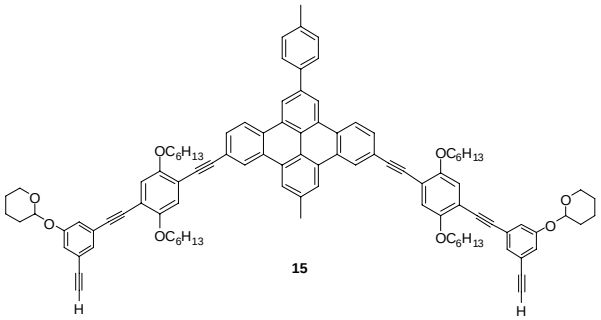


14

13: prepared according to: Ziegler, A.; Mamdouh, W.; Ver Heyen, A.; Surin, M.; Uji-i, H.; Abdel-Mottaleb, M. M. S.; De Schryver, F. C.; De Feyter, S.; Lazzaroni, R.; Höger, S. *Chem. Mater.* **2005**, *17*, 5670-5683

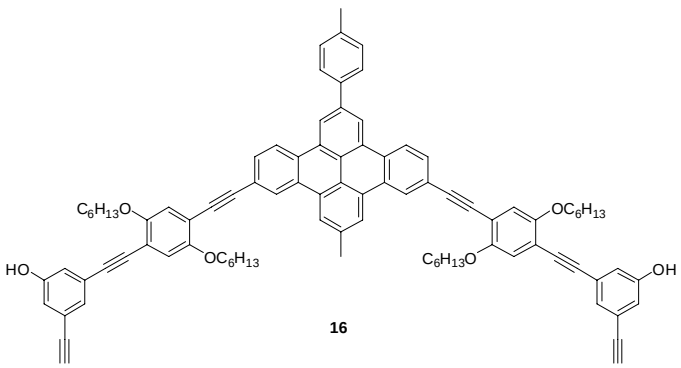
14: Under an argon atmosphere, **12** (269 mg, 0.25 mmol) and **13** (464 mg, 1.00 mmol) was dissolved in dry THF (3 ml) and dry piperidine (0.5 ml). Then $Pd(PPh_3)_4$ (10.4 mg) and CuI (5.2 mg) were added, the mixture was stirred at RT overnight, and then poured into CH_2Cl_2 (100

ml). The organic layer was washed with H_2O (3×40 ml), and brine (3×20 ml), dried over $MgSO_4$, and then the solvent was removed in vacuo. The residue was purified by column chromatography (dichloromethane). Yield: 350 mg (82.0 %); yellow crystals; mp: 54.2 °C; R_f = 0.26 (CH_2Cl_2). ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 8.80 (s, 2 H), 8.73 (s, 2 H), 8.62 (d, *J* = 8.9 Hz, 2 H), 8.47 (s, 2 H), 7.80 – 7.65 (m, 4 H), 7.35 (d, *J* = 8.2 Hz, 2 H), 7.18 (d, *J* = 1.2 Hz, 2 H), 7.14 – 7.12 (m, 2 H), 7.06 (s, 4 H), 6.99 (s, 2 H), 5.39 – 5.37 (m, 2 H), 4.10 – 3.95 (m, 8 H), 3.82 – 3.70 (m, 2 H), 3.60 – 3.48 (m, 2 H), 2.71 (s, 3 H), 2.40-2.30 (m, 7 H), 1.90 - 1.23 (m, 48 H), 0.95 - 0.75 (m, 16 H), 0.18 (s, 12 H).



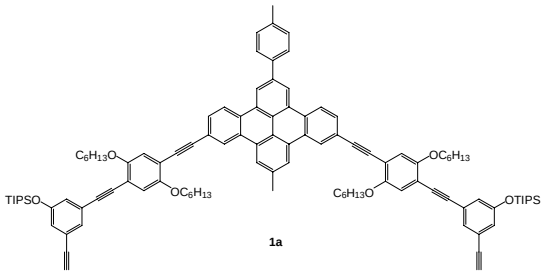
15

15: K_2CO_3 (0.6 g, 4.34 mmol) was added to a solution of **14** (330 mg, 0.193 mmol) in THF/MeOH (1:1, 5 ml), and the mixture was stirred at RT overnight. The mixture was poured into ether and water, and the organic phase was washed with H_2O (3×40 ml), and brine (3×20 ml), dried over $MgSO_4$, and then the solvent was removed in vacuo. The residue was purified by column chromatography (petroleum ether/$CHCl_2$ 2:3). Yield: 114 mg (40.6 %); R_f = 0.8 (petroleum ether/$CHCl_3$ 1:2); yellow crystals; Cr 50.2 °C N 159.8 °C Iso. ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 8.78 (s, 2 H), 8.70 (s, 2 H), 8.80 (d, *J* = 8.6 Hz, 2 H), 8.43 (s, 2 H), 7.80 (d, *J* = 8.0, 2 H), 7.70 (d, *J* = 8.6 Hz, 2 H), 7.40 (d, *J* = 8.0, 2 H), 7.29 – 7.28 (m, 2 H), 7.22 – 7.21 (m, 2 H), 7.18 – 7.17 (m, 2 H) 7.12 (s, 2 H) 7.07 (s, 2 H), 5.48 – 5.44 (m, 2 H), 4.18 – 4.03 (m, 8 H), 3.95 – 3.80 (m, 2 H), 3.68 – 3.55 (m, 2 H), 3.16 (s, 2 H), 2.75 (s, 3 H), 2.49 (s, 3 H), 2.25-1.03 (m, 44 H), 0.98 – 0.82 (m, 12 H).



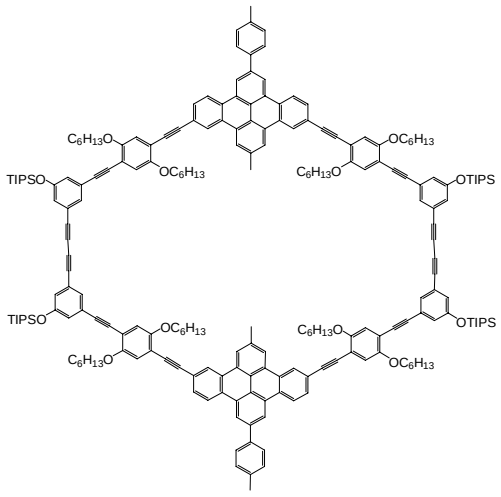
16

16: **15** (163.2 mg, 0.112 mmol) was solved in $CHCl_3$ (25 ml) and MeOH (1.5 ml), p-tolylsulfonic acid (2 mg) was added and the mixture was stirred at RT overnight. Methanol (20ml) was added, the precipitated product was filtered and washed with MeOH (20 mL) and dried. Yield: 140 mg (97.8 %); slightly yellow solid. mp: >250 °C; **16** was used directly without further characterization.



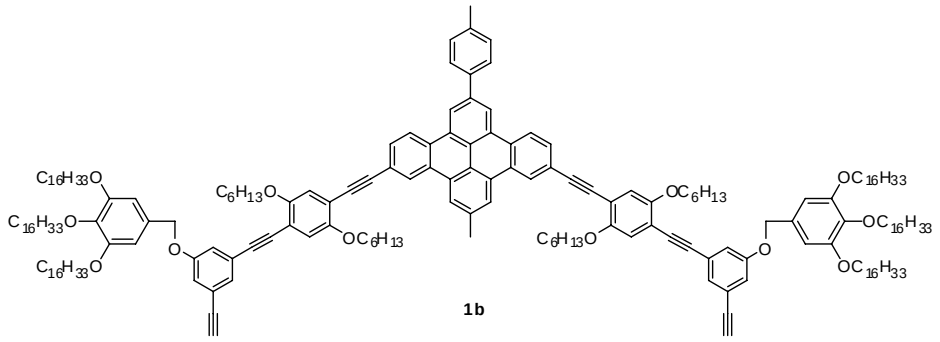
1a

1a: Under an argon atmosphere, **16** (140.1 mg, 0.11 mmol; 1eq) was dissolved in dry DMF (20 ml). Imidazole (88.5 mg; 1.3 mmol, 12 eq) was added, then triisopropylsilyl chloride (251.7 mg, 1.3 mmol; 12 eq) was added dropwise. The mixture was stirred at RT overnight, and then poured into CH_2Cl_2 (100 ml) and H_2O (100 ml). The organic layer was separated and washed with H_2O (3×40 ml), and brine (3×20 ml). After drying over $MgSO_4$ the solvent was removed in *vacuo*. The residue was purified by radial chromatography (petroleum ether/CH_2Cl_2 2:1) to yield **16b** (81.2 mg, 46.1 %) as light yellow crystals. R_f = 0.41 (petroleum ether/CH_2Cl_2 2:1) mp: 132 °C. ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 8.53 (s, 2 H), 8.48 (s, 2 H), 8.36 (d, *J* = 8.5, 2 H), 8.17 (s, 2 H), 7.67 (d, *J* = 8.6, 2 H), 7.54 (d, *J* = 8.8, 2 H), 7.26 (d, *J* = 7.8, 2 H), 7.19 (s, 2 H), 7.02 (s, 2 H), 6.99 (br. s, 4 H), 6.93-6.92 (m, 2 H), 4.08 – 3.90 (m, 8 H), 3.06 (s, 2 H), 2.56 (s, 3 H), 2.38 (s, 3 H), 1.95 - 1.75 (m, 8 H), 1.60 – 1.00 (m, 66 H), 0.95 – 0.75 (m, 12 H).



2a

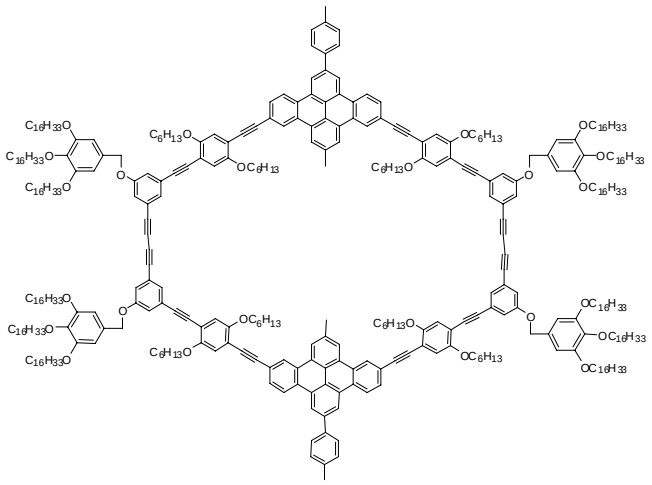
2a: Under an argon atmosphere, **1a** (81.2 mg, 0.051 mmol) in 10 ml dry pyridine was added to a suspension of CuCl (470 mg) and $CuCl_2$ (93 mg) in 20 ml dry pyridine over 96 h at RT. The mixture was poured into $CHCl_3$ (200 ml) and water (100 ml), the organic phase was washed with 25% NH_3 solution, water, 10% acetic acid, water, 10% aqueous NaOH, water and brine and dried over $MgSO_4$. After evaporation of the solvent to 10-20 ml, the coupling product was precipitated by addition of 60 ml MeOH and collected by filtration and washed with MeOH. The crude cyclization product was purified by column chromatrography over silica gel ($CHCl_3$) and subsequently recrystalized from $CHCl_3$. Yield: 67.0 mg (41.4 %); light yellow solid; mp: > 285°C (dec.); $C_{220}H_{248}O_{12}Si_4$ (calcd 3193.79); GPC: single peak at M_w:3400 g mol^{-1}; ^{1}H-NMR (500 MHz; $C_2D_2Cl_4$): δ = 9.10 (s, 4 H), 9.06 (s, 4 H), 8.88 (d, *J* = 9.1 Hz, 4 H), 8.82 (s, 4 H), 7.95 – 7.89 (m, 8 H), 7.48 (d, *J* = 8.2 Hz, 4 H), 7.41 (s, 4 H), 7.19 (s, 4 H), 7.12 (s, 8 H), 7.04 (s, 4 H), 4.20 – 4.10 (m, 16 H), 2.96 (s, 6 H), 2.54 (s, 6 H), 2.05 – 1.85 (m, 16 H), 1.75 – 1.25 (m, 16 H), 1.45 (m, 32 H), 1.17 (m, 84 H), 0.99 (t , *J* = 8.7 Hz, 12 H), 0.93 (t , *J* = 8.8 Hz, 12 H).



1b

1b: Under an argon atmosphere, 3,4,5-trihexadecyloxybenzyl chloride (203.5 mg, 0.24 mmol; 10 eq, prepared analogue to Balagurusamy, V. S. K.; Ungar, G.; Percec, V.; Johansson, G. *J. Am. Chem. Soc.* **1997**, *119*, 1539.) and **16** (30.9 mg, 0.024 mmol) were dissolved in dry DMF (2

ml). K_2CO_3 (100 mg; 0.72 mmol) was added, and the mixture was stirred at 65 °C overnight. The mixture was cooled to RT, then poured into CH_2Cl_2 (100 ml) and H_2O (100 ml). The organic layer was separated and washed with H_2O (3×40 ml), 10% NaOH (3×40 ml), H_2O (3×40 ml), and brine (3×20 ml). After drying over $MgSO_4$ the solvent was removed in vacuo. The residue was purified by column chromatography (petroleum ether/CH_2Cl_2 4:1). Yield: 60 mg (82.5 %), yellow solid; mp: 95 °C; R_f = 0.34 (petroleum ether/CH_2Cl_2 4:1); GPC: single peak at M_w:4500 g mol^{-1}; ^{1}H-NMR (250 MHz; CD_2Cl_2): δ = 8.69 (s, 2 H), 8.61 (s, 2 H), 8.51 (d, *J* = 8.8 Hz, 2 H), 8.34 (s, 2 H), 7.76 (d, *J* = 8.2 Hz, 2 H), 7.59 (d, *J* = 8.8 Hz, 2 H), 7.26 (d, *J* = 8.2 Hz, 2 H), 7.16 – 7.14 (m, 2 H), 7.05 - 6.90 (m, 8 H), 6.50 (s, 4 H), 4.82 (s, 4 H), 4.05 – 3.70 (m, 20 H), 3.04 (s, 2 H), 2.65 (s, 3 H), 2.36 (s, 3 H), 1.95-1.01(m, 200 H), 0.90 - 0.70 (m, 30 H).



2b

2b: Under an argon atmosphere, **1b** (60 mg, 0.0198 mmol) in 6 ml dry pyridine was added to a suspension of CuCl (130 mg) and $CuCl_2$ (25.8 mg) in 15 ml dry pyridine over 96 h by RT. The mixture was poured into CH_2Cl_2 (200 ml) and water (100 ml), the organic phase was washed with 25% NH_3 solution, water, 10% acetic acid, water, 10% aqueous NaOH, water and brine and dried over $MgSO_4$. After evaporation of the solvent to 10-20 ml, the coupling product was precipitated by the addition of 60 ml MeOH and collected by filtration and washed with MeOH. The crude cyclization product was purified by column chromatrography over silica gel ($CHCl_3$) and subsequently recrystalized from CH_2Cl_2. Yield: 8.2 mg (13.7 %), slightly light yellow solid. mp 155°C. GPC: single peak at M_w: 7600 g mol^{-1}. The proton NMR in $CDCl_3$ gave only broadened signals indicating a strong aggregation of the molecules.

[i] Zimmermann, T.; Fischer, G. W. *J. Prakt. Chem.* **1987**, *329*, 975-984.

[ii] a) Cheng, X. H.; Jester, S.-S.; Höger, S. *Macromolecules* **2004**, *37*, 7065-7068; b) Cheng, X. H.; Jester, S.-S.; Höger, S. *Macromolecules* **2004**, *37*, 10217.

[iii] Fischer, M.; Höger, S. *Tetrahedron* **2003**, *59*, 9441-9446;

[iv] Höger, S.; Bonrad, K. *J. Org. Chem.* **2000**, *65*, 2243-2245.

[v] At present we have no explanation for that rather low yield in this step and ascribe that to the difficult purification from minor side products by repeated radial chromatography.

[vi] In our previous reports (cf. ref. 6), the oligo-alkyl side chains were attached to the macrocycles after the ring closure. However, attempts to use the same reaction sequence in the case here failed due to the insolubility of the macrocyclic tetraphenol. Therefore model studies were performed by stirring 3,4,5-trialkoxybenzyloxyphenol in pyrdine/CuCl/$CuCl_2$ that gave even after 7 days at room temperature no indication of an oxidative ether cleavage. These model studies have proven that the 3,4,5-trialkoxybenzyloxy moiety is stable under the cyclization conditions we generally use in our synthesis.