Precision host–guest chemistry of polyphenylene dendrimers†

Roland E. Bauer, Christopher G. Clark, Jr. and Klaus Müllen*

Received (in Montpellier, France) 4th December 2006, Accepted 7th March 2007
First published as an Advance Article on the web 26th March 2007
DOI: 10.1039/b617666f

The synthesis of polyphenylene dendrimers with backbone-pendant internal carboxylic acids and nonpolar tetraphenylbenzene chain ends is reported. The host–guest and transport properties of these dendrimers with proflavine, an acridine dye, were investigated. These properties were found not to depend strongly on the number of carboxylic acids, but rather on the structural properties of the stiff dendrimers, binding only 3–4 dyes each for the first- and second-generation dendrimers. The presence of solution accessible polar cavities in the dendrimer provided enhanced solubilization and transport of the polar dyes through a nonpolar phase.

Introduction

The properties of dendrimers to host a number of guest molecules have intensified recent research efforts in their binding and function. In particular, it has been shown that a dendritic shell generates a unique microenvironment within its iteratively branched architecture and influences the optical properties,[1–3] redox chemistry,[4–7] catalysis,[8–12] and molecular recognition[13–15] of the guests. Perhaps the earliest and most studied use of dendrimers as supramolecular hosts was for the solubilization of chromophores in unusual environments by dendritic encapsulation of the chromophores. Three different encapsulation mechanisms have been explored: (1) the sequestration based on the respective solubilities of the dendrimer backbone (interior scaffold), dendrimer chain ends (periphery), guest molecules, and the medium employed;[3,16–18] (2) localized interactions between the dendrimer backbone and guest through ion-pair formation or specific molecular recognition events;[19,20] and (3) the physical or steric trapping of a guest in a dendritic cavity, where the chain ends are too bulky to allow release.[21] Furthermore, stimulus-triggered release of the guests has been achieved.[22] Virtually all of the above-described examples employ a dendrimer with a flexible backbone. The major implication is that for most of the systems, the 3-D position of the guest molecules cannot be explicitly specified, even if it is tethered to a specific site on the dendrimer backbone due to fluctuations in the global and local conformations of the dendrimer, which strongly depend on the environment.[23,24]

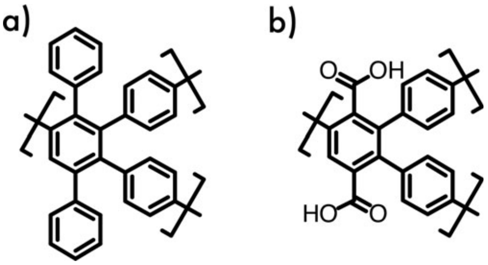
Polyphenylene dendrimers,[25] synthesized stepwise from iterative Diels–Alder syntheses, are structurally perfect, shape-persistent,[26] and thermally stable macromolecules. Accordingly, functionalities have been placed at the core,[27,28] in the backbone at a specific generation,[29,30] or at the chain ends,[31–33] while preserving the shape persistent nature of the dendrimer. Herein, we report the synthesis of polyphenylene dendrimers with backbone-pendant, internal carboxylic acids (Scheme 1) and their properties as a host for binding guest molecules.

Results and discussion

Synthesis

The relative abilities of the different generation polyphenylene dendrimers to solubilize hydrophilic dyes in apolar media were investigated. Accordingly, the main synthetic challenge was the precise placement of polar functional groups into the interior of the polyphenylene scaffold. Divergent dendritic growth proceeds by Diels–Alder cycloaddition of cyclopentadienone **2** (Scheme 2), a key AB_2 dendrimer building block, with a terminal alkyne.[34] Cyclopentadienone **2** carries two masked terminal ethynes for dendritic growth and two methyl ester groups in the α positions, which after dendrimer synthesis are rigidly connected to the branching unit. Ester hydrolysis after dendrimer synthesis was expected to lead to the functionalized dendritic macromolecules with an increased hydrophilic character in the interior.

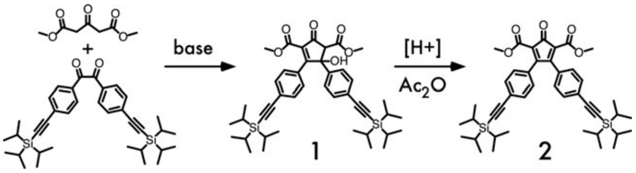
For a more effective isolation of the inner microenvironment, the final generational layer was formed by reaction with the commercially available tetraphenylcyclopentadienone. The key AB_2 cyclopentadienone branching reagent **2** (Scheme 2) was synthesized analogously to 2,5-bis(methylcarboxy)-3,4-diphenylcyclopentadienone.[35,36] The base-promoted double-Knoevenagel condensation of dimethyl acetonedicarboxylate with 4,4′-bis(triisopropylsilylethynyl)benzil[37] yielded cyclo-



Scheme 1 Polyphenylene dendrimer branching units: standard (a) and biscarboxy-functional (b).

Max Planck Institute for Polymer Research, D-55128 Mainz, Germany. E-mail: muellen@mpip-mainz.mpg.de; Fax: +49-6131-379-350; Tel: +49-6131-379-151

† This paper was published as part of the special issue on Dendrimers and Dendritic Polymers: Design, Properties and Applications.



Scheme 2 Synthesis of the key AB$_2$ building block, 2,5-di(methylcarboxy)-3,4-bis(4-triisopropylsilylethynylphenyl)cyclopentadienone, **2**.

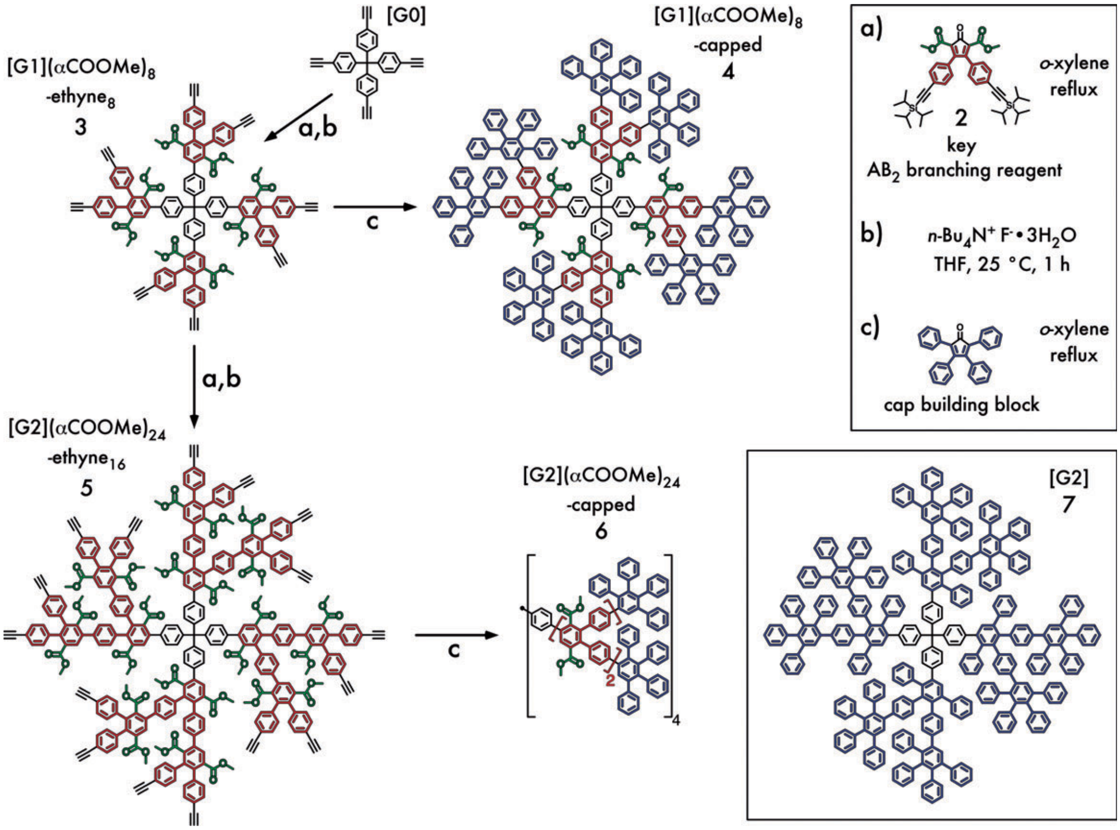
pentenolone **1**, which was dehydrated with catalytic acid in acetic anhydride to produce cyclopentadienone **2**, a bright-orange solid, after purification with column chromatography.

The [**G1**] polyphenylene dendrimer with eight methyl esters in the first-generational layer and capped with tetraphenylbenzene, **4**, was synthesized in two main stages (Scheme 3). First, four Diels–Alder cycloadditions of cyclopentadienone **2** with the tetra(4-ethynylphenyl)methane[34] in refluxing *o*-xylene and subsequent cleavage of the triisopropylsilyl protecting groups with tetrabutylammonium fluoride (TBAF) in THF yielded the first-generation octaethyne **3**. Second, the termination of dendritic growth by eight Diels–Alder cycloadditions with tetraphenylcyclopentadienone yielded the capped first-generation polyphenylene dendrimer **4**.

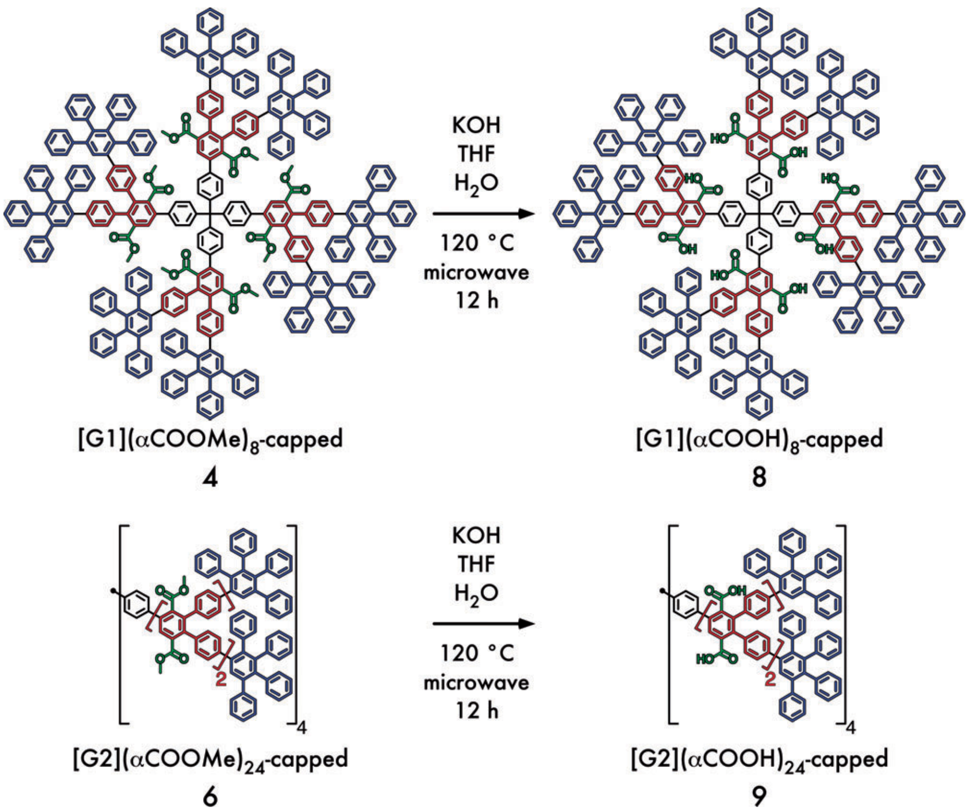
In parallel, the eightfold addition of cyclopentadienone **2** with **3** and subsequent activation of the ethynyl groups with TBAF led to the second-generation polyphenylene dendrimer **5** bearing eight and sixteen methyl ester groups in the first- and second-generational layers, respectively. The peripheral sixteen terminal alkynes of **5**, were then functionalized with tetraphenylcyclopentadienone to yield the [**G2**] dendrimer **6** with 24 methyl esters and capped with a polyphenylene outer layer. Each dendrimer was isolated with column chromatography.

Hydrolysis of the methyl esters in dendrimers **4** and **6** was needed for the preparation of the target carboxy-functional polyphenylene dendrimers **8** and **9** (Scheme 4). Initial alkaline hydrolysis trials with potassium hydroxide in refluxing THF–water were unsuccessful, resulting in incomplete hydrolysis, based on the residual signal of the methyl ester, 3.41 ppm, in the ^{1}H NMR spectra. Hydrolysis conversions were made quantitative by carrying out the reactions in sealed tubes with a microwave reactor with a monomodal microwave cavity. The dendrimers were isolated by precipitation into hydrochloric acid (1 M, aq), washing with water and then methanol. They have good solubilities in organic solvents with moderate polarity, but are sparingly soluble in non-polar solvents such as toluene, indicating that the carboxylic acids are indeed solvent exposed. They are insoluble in water or methanol, demonstrating that the chain ends impart amphiphilicity.

The products were identified by a combination of NMR spectroscopies, MALDI-TOF mass spectrometry, which demonstrated the purity and monodispersity of the synthesized



Scheme 3 Divergent synthesis of [**G1**] polyphenylene dendrimer octa(methyl ester) capped with tetraphenylbenzene, **4**, and [**G2**] polyphenylene dendrimer icositetra(methyl ester) capped with tetraphenylbenzene, **6**. For comparison, the standard [**G2**] polyphenylene dendrimer, **7**, is shown.



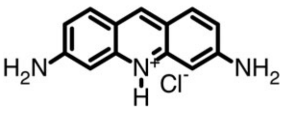
Scheme 4 Synthesis of **[G2]** octa(carboxy)polyphenylene dendrimer capped with tetraphenylbenzene, **8**, and **[G3]** icositetra(carboxy)polyphenylene dendrimer capped with tetraphenylbenzene, **9**.

dendrimers. All synthetic details are given in the Experimental section.

Dye solubilization

A powerful method for monitoring host–guest interactions is with the solubility profile of a spectroscopic probe (guest) in the presence of a host (the carboxy-functionalized dendrimers **8**, and **9**) in a medium in which the guest is sparingly soluble. Host–guest interactions enhance the guest solubility, if it partitions into the soluble dendrimer.[13,38,39] Hydrogen bonding[40–42] and the formation of ion pairs are powerful synthons in supramolecular and host–guest chemistry.

Proflavine hydrochloride (Scheme 5) is a hydrophilic aromatic dye possessing two free amines. The host–guest chemistry of such acridine dyes based on ammonium carboxylates is well established, and they find wide applications as spectroscopic probes.[43,44] Ammonium carboxylate formation (guest uptake) with the polyphenylene dendrimer hosts (Fig. 1) was observed by monitoring spectrophotometric properties of proflavine hydrochloride. A bathochromic shift in absorption for proflavine is associated with increased protonation: the absorption maximum for unprotonated, monoprotonated and diprotonated proflavine in H_2O are *ca.* 390, 445 and 460 nm, respectively.[45]



Scheme 5 Structure of proflavine hydrochloride.

The solubilization of proflavine hydrochloride in chloroform was investigated under conditions of solid–liquid extraction.[38] Accordingly, dendrimer host solutions (10^{-5} M, 4 mL) were mixed with solid proflavine hydrochloride (10 mg) and stirred overnight at room temperature. From the resulting solution, aliquots (0.1 mL) were diluted (50 mL) and filtered, and the degree of dye uptake was measured by UV/vis spectroscopy. The absorption maximum of the dye shifted 14 nm bathochromically from $\lambda_{\max}$ = 440 to 454 nm, upon mixing with the dendrimer host, **9** (Fig. 1), similar to that of encapsulation of proflavine hydrochloride using an acidic endoreceptor.[13,46]

Additionally, a dependence of the amount of solubilized dye (absorption intensity) on the host concentration was observed. Calculations using the relative absorption intensities and reported values for ε_{440}[45] revealed a host **9** to guest ratio of *ca.* 1 : 4. The spectrum of the dye mixed with the smaller dendrimer host **8**, was qualitatively similar to the previous case, but the number of dyes bound to each dendrimer was found to be slightly less, *ca.* 3. Although there are more carboxylic acids in the higher generation dendrimer, **9**, not all are apparently equally accessible due to intradendron hydrogen bonding and the increasingly crowded shape of the dendrimer. The tetrahedral structures have defined clefts at the junction between three dendrons, which apparently accommodate *ca.* one dye molecule each (Fig. 2).

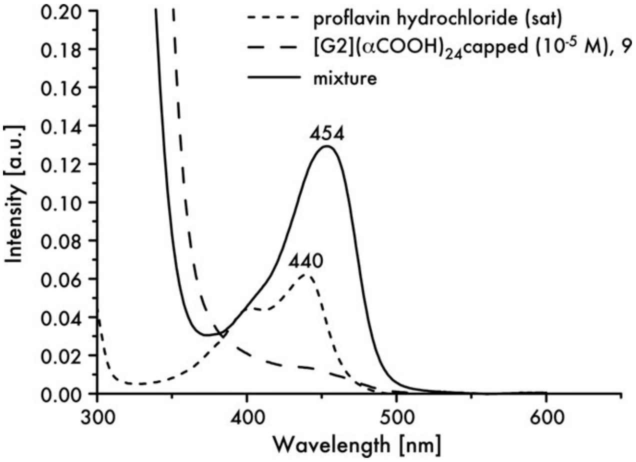


Fig. 1 UV/vis spectra in chloroform of dendrimer **9**, proflavin hydrochloride, and their mixture.

The polydentate nature of the dye may also play a role in blocking multiple sites. That the smaller dendrimer binds less than four dyes is more complex (Fig. 2). It may not be favorable to bind more than three guests in the compact carboxylic acid-rich generational layer as the clefts are more exposed to solvent, and each bound guest contributes to more charge density. A second-generation polyphenylene dendrimer, **7**, lacking carboxylic acids, was mixed with proflavine hydrochloride under the same conditions as already described. As expected, it showed poor uptake of the dye based on the absorption intensity of the solutions, indicating that the carboxylic acid functionalities play the pivotal role in the dye uptake process.

Transport properties

The use of dendritic molecules as transport vehicles or selective extraction systems motivated the further study of the transport of a hydrophilic dye through an apolar phase with subsequent delivery into an aqueous medium. Using solid–liquid–liquid extraction experiment,[13] the hydrophilic dye was mixed with a chloroform solution of the dendritic host (10^{-4} M) below an aqueous phase (Fig. 3). A fritted glass filter with fine porosity was employed as a membrane to prevent the solid dye particles from reaching the aqueous phase. The rate of transport of the dye into the aqueous phase was monitored by UV/vis spectroscopy of the proflavine dye.

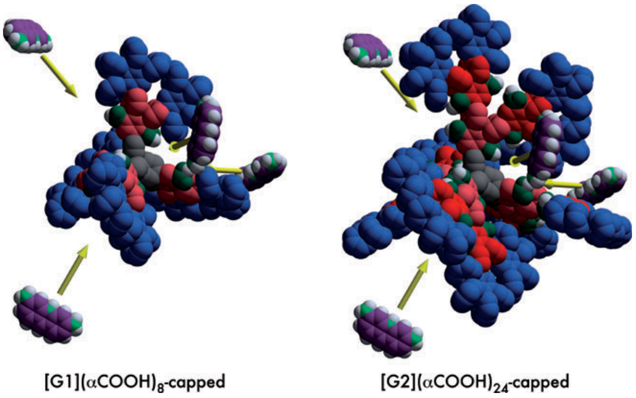


Fig. 2 Proposed proflavin hydrochloride binding regions in dendrimers **8** and **9**. Polyphenylene dendrimer hydrogens, except for those of the carboxylic acids, are omitted for clarity.

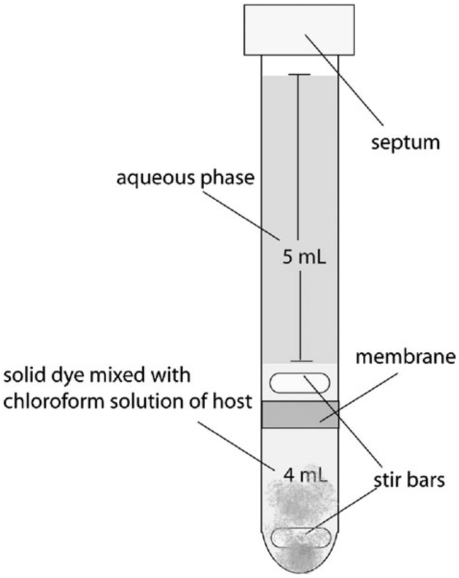


Fig. 3 Setup for measurement of dendrimer-mediated dye transport properties.

Dendrimer hosts **8** and **9** as well as the **[G2]** polyphenylene dendrimer without carboxylic acids were investigated to assess the influence of the generation and functionality over the transport process. The highest transport rate was observed for the highest generation polyphenylene dendrimer **9** with 24 internal carboxylic acids. The transport after 60 min (Fig. 4) was 1.3-fold faster compared with the lower generation host **8** and 9.7-fold faster than the bare dendrimer, **7**. The transport process proceeded over long periods of time, which

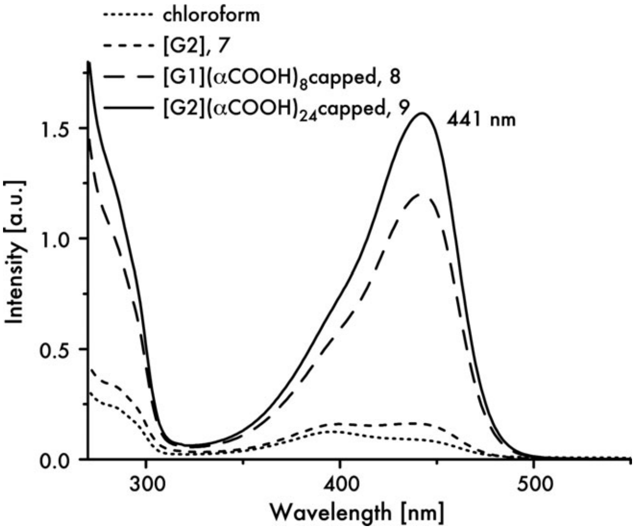


Fig. 4 UV/vis spectra of the aqueous layer in proflavin hydrochloride transport experiments after 1 h using carboxy-functional polyphenylene dendrimers **8**, **9**, as well as the standard polyphenylene dendrimer **7** and pure chloroform (no host) as controls.

demonstrates that the dendritic hosts were continually recycled, not being deactivated after the initial binding.

Diffusion controlled rates are not the rate-limiting factors in the transport as is clearly evident from the results that the largest dendrimer-mediated transport is the fastest. This is further supported by the observation that the dye is sparingly soluble in chloroform. Once dissolved, the diffusion of the dye to the aqueous phase should proceed quickly, but the buildup of dye concentration without a host or with in the presence of the nonpolar host, **7**, in water is foremost slower. The rate-limiting step is apparently the dissolution of the dye into the non-polar phase or the release into the aqueous phase.

One argument is that the [**G2**] dendrimer has deeper pockets for binding, which would better shield the solvent from the guest. This has two fundamental problems. First, it would require the dye-bound host molecule to diffuse all the way from the solid-dye to the aqueous phase and back before it could be recycled. Second, given that ammonium carboxylate formation is enthalpically more favorable (for neutral pH) than the entropy of dye dissociation in water, the earliest stages of the mixture likely feature the filling of the dendrimer with guest, a two-phase, but nonetheless, fast step. Since the larger carboxylic acid containing dendrimer, **9**, maintains faster transport, two issues are relevant: host vacancy and binding efficacy. The higher generation dendrimer, **9**, clearly has more binding sites, but as demonstrated in the previous section, those binding sites are not completely accessible, given that almost the same number of dyes are bound with threefold the carboxylic acid concentration. There is certainly more room in the larger dendrimer, but not enough to accommodate complete binding or even the simultaneous carrying of multiple dyes, which are able to be released. This implies that more guest molecules beyond the primary four are not bound tightly to the dendrimer.

A cooperative modality is that larger dendrimer simply helps to solubilize the dye, but since it is not bound tightly, it quickly diffuses between other dendrimers in solution or unprotected to the aqueous phase. The suggested mechanism is then that the dye bound-dendrimer host is the transient carrier, which is more polar than the solvent alone. This is consistent with the concept that weak secondary interactions between host and guest promote transport.[38] It should be noted that the concentration of a small molecule additive would have to be much higher to achieve the same effect. Although the results of the above experiments are controlled by a multitude of factors, they illustrate that the investigated dendrimers are efficient carrier systems and that the formation or presence of ammonium carboxylates play a crucial role in the transport.

Conclusions

Ammonium carboxylate formation offers a means of binding guests to a dendritic host. For the examples presented herein, the number of bound guests is mediated not only by the number of carboxylic acids, but also by the specific structural properties of the dendrimer, such as porosity or distance between binding sites, which were introduced synthetically in stages. In addition, efficient supramolecular transport of hydrophilic dyes through an apolar phase was mediated by the carboxy-functionalized polyphenylene dendrimers with the slowest diffusing species providing the fastest transport. Finally, the modular synthesis of polyphenylene dendrimers permits the design of host systems with custom peripheries, which opens the way towards supramolecular nanocarriers with tailored solubility and aggregation properties.

Experimental

Instrumentation

Microwave-heated reactions were performed in 10 mL glass tubes using a Discover 300-watt microwave reactor (CEM GmbH) with a single-mode cavity equipped with an infrared temperature sensor, calibrated against DMF at ambient pressure, and an Intellivent pressure transducer. Simultaneous cooling of the reactions was made using a stream of air flowed around the glass vessel at a constant flow rate with a maximum pressure differential of 50 psi. The cooling rate was adjusted to permit the application of maximum microwave power, whereby the microwave power was automatically modulated to maintain a constant reaction temperature.

^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX250, AC300, AMX500 and AMX700 NMR spectrometers using the residual proton of the solvent or the carbon signal of the deuterated solvent as an internal standard.

Field desorption mass spectra (FDMS) were performed with a VG-Instruments ZAB 2-SE-FDP using 8 kV accelerating voltage. MALDI-TOF mass spectra were measured using a Bruker Reflex II, calibrated against poly(ethylene glycol) (3000 g mol^{-1}). Samples for MALDI-TOF MS were prepared by mixing the analyte with the matrix (dithranol) in THF in a ratio of 1 : 250. In some cases, cationization by mixing the matrix with potassium trifluoroacetate (K) or silver trifluoroacetate (Ag) was performed. All reported MALDI-TOF MS measurements were within the experimental error inherent in the technique.

UV/vis absorbance spectra were recorded on a Perkin Elmer Lambda 25 spectrophotometer. Melting points were measured using a Büchi Melting Point Apparatus B545. Elemental analyses were performed by the Microanalytical Laboratory of Johannes Gutenberg University. Elemental analyses were performed on all solids up to the first-generation dendrimers. The nature of the porosity of the dendrimers as hosts for small quantities of solvent impurities as well as incomplete combustion limit the effectiveness of elemental analyses for polyphenylene dendrimer samples. Elemental analyses of dendrimers varied significantly from the expected results. As such, MALDI-TOF in combination with ^{1}H NMR were relied upon more heavily than was the elemental analyses of dendrimers.

Computations were performed with a dual 2 GHz G5 processor PowerMac (Apple Computer, Cupertino) equipped with 2 GB RAM. Semi-empirical AM1 calculations on oligo (phenylene)s were performed with Spartan ‘04 for Macintosh (Wavefunction, Inc., Irvine). Three-dimensional models were constructed in custom-written POV-Ray (www.povray.org) scripts that used the geometric properties obtained from the AM1 calculations.

Materials

Tetra(4-ethynylphenyl)methane[34,47] as well as the second-generation polyphenylene dendrimer [**G2**][34] were synthesized according to the literature. Tetraphenylcyclopentadienone was purchased from Aldrich and used as received. All reactions were performed under a blanket of argon.

Synthesis

2,5-Di(methylcarboxy)-3,4-bis(4-triisopropylsilylethynylphenyl)-cyclopenten-2-one (1). 1,2-Bis{4-[(triisopropylsilanyl)ethynyl]-phenyl}ethane-1,2-dione (5.7 g, 10 mmol), dimethyl acetonedicarboxylate (1.74 g, 10 mmol) and potassium hydroxide (0.1 g) in ethanol (150 ml) were stirred for 20 h under argon at room temperature and then poured into water. The aqueous phase was extracted 2–3 times with dichloromethane, the combined organic phases were dried over $MgSO_4$, and the solvent was removed *in vacuo* to give a yellow–orange solid: 6.9 g Product mixture of **1** and **2**. FDMS: *m*/*z* 726 (65% **1**), 708 (100% **2**), [M$^+$]; calc.: 727.11 (**1**), 709.09 (**2**). The mixture was utilized for further synthesis without purification.

2,5-Di(methylcarboxy)-3,4-bis(4-triisopropylsilylethynylphenyl)-cyclopentadienone (2). The product mixture of the antecedent step (**1**) (6.9 g) was added at room temperature to acetic anhydride (15 ml) containing concentrated sulfuric acid (3 drops). The mixture was heated with stirring until the solid dissolved and then allowed to stir for 0.5 h without additional heating. Subsequently, the solution was added to water (250 ml) under vigorous stirring. When the precipitate had settled, it was filtered off, washed thoroughly with water, and dried under reduced pressure. Additional column chromatography with dichloromethane as eluent yielded an orange solid 4.77 g (64%). mp 112–113.6 °C. ^{1}H NMR (250 MHz, CD_2Cl_2 300 K): δ 7.38 (d, 4H, ^3J = 8.5 Hz, Ar), 7.00 (d, 4H, ^3J = 8.5 Hz, 4H), 3.7 (s, 6H, OCH_3) and 1.12 (s, 42H, $CH(CH_3)_2$) ppm; ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ 188.7 (C=O cyclopentadienone); 167.69 (C4), 159.58 (C=O), 136.31 (C4), 132 (C4), 131 (Ar), 127.43 (Ar), 119.82 (C4), 108.01 (C4), 92.28 (C4), 51.76 (C_{OCH_3}), 19.05 and 12.24 ppm; FDMS: *m*/*z* 709 (100%) [M$^+$]; calc.: 709.09. Anal. Calc. for $C_{43}H_{56}O_5Si_2$: C, 72.84; H, 7.96. Found: C, 71.92; H, 8.17%.

[G1](αCOOMe)$_8$-ethynyl-T*i*PS$_8$ (3a). A mixture of tetra(4-ethynylphenyl)methane (0.1 g, 0.2 mmol) and 2,5-di(methylcarboxy)-3,4-bis(4-triisopropylsilylethynylphenyl)cyclopentadienone (**2**) (0.85 g 0.9 mmol) in *o*-xylene (10 mL) was heated to reflux for 24 h under argon. After cooling to room temperature, the solvent was removed *in vacuo*. The residue was purified by means of column chromatography using petroleum ether–CH_2Cl_2 (1 : 1) as eluent. Upon evaporation of the solvent, a colorless solid was obtained: 0.71 g (89%). mp >300 °C. ^{1}H NMR (250 MHz, CD_2Cl_2 303 K): δ_H 7.88 (s, 4H, Ar), 7.38 (br, 16H, Ar), 7.29 (d, 8H, ^3J = 8.5 Hz, Ar), 7.26 (d, 8H, ^3J = 8.5 Hz, Ar), 6.97 (m, 16 H, Ar), 3.59 (s, 12H, OCH_3), 3.28 (s, 12H, OCH_3) and 1.11 (br s, 144 H, T*i*PS) ppm; ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ_C 169.14, 169.10 (C=O), 142.43, 142.39, 141.38, 137.51, 134.670 (C_4), 128.99, 128.54, 128.16, 127.87 (Ar), 123.01, 122.64, 107.33, 91.96, 89.70 (C_4), 52.67, 52.41 (C_{OCH_3}), 18.89 (C_{CH}) and 11.9 (C_{CH_3}) ppm; FDMS: *m*/*z* 3137 (100%) [M$^+$]; calc.: 3140.86.

[G1](αCOOMe)$_8$-ethyne$_8$ (3b). To an argon purged mixture of [**G1**](αCOOMe)$_8$-ethyne-T*i*PS$_8$ (**3a**) (0.6 g 0.01 mmol) in THF (20 mL) was added a solution of tetrabutylammonium fluoride trihydrate (TBAF) [1.8 mmol (1.2 eq./T*i*PS)] in THF (5 mL). The reaction mixture was stirred at room temperature for 15 min. After quenching with H_2O (5 mL), the mixture was extracted three times with CH_2Cl_2 and the dried ($MgSO_4$) organic phase was concentrated *in vacuo*. The pure product, a colorless solid, was obtained as a result of preparative column chromatography using CH_2Cl_2 as eluent. 0.3 g (85%). t_{decomp} >300 °C. ^{1}H NMR (250 MHz, CD_2Cl_2 303 K): δ_H 7.88 (s, 4H, Ar), 7.38 (br, 16H, Ar), 7.29 (d, 8H, ^3J = 8.5 Hz, Ar), 7.26 (d, 8H, ^3J = 8.5 Hz, Ar), 6.97 (m, 16 H, Ar), 3.59 (s, 12H, H_{OCH_3}), 3.28 (s, 12H, H_{OCH_3}) and 2.93, 2.91 (2s, 8H, ethyne) ppm; ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ_C 169.14, 169.10 (C=O), 142.43, 142.39, 141.38, 137.51, 134.670 (C_4), 128.99, 128.54, 128.16, 127.87 (C_{Phenyl}), 123.01, 122.64, 107.33, 91.96, 90.70 (C_4), 84.64, 77.55, 77.39 (C_{ethyne}), 51.8, 51.41 (C_{OCH_3}); FDMS: *m*/*z* 1889 (100%) [M$^+$]; calc. 1890.10.

[G1](αCOOMe)$_8$-capped (4). Similar to [**G1**](αCOOMe)$_8$-ethyne-T*i*PS$_8$ (**3a**), [**G1**](αCOOMe)$_8$-capped (**4**) was produced as a result of a eightfold Diels–Alder cycloaddition of tetraphenylcyclopentadienone to **3b**. Accordingly a mixture of **3a** (0.1 g, 0.05 mmol) and tetraphenylcyclopentadienone (0.24 g, 0.62 mmol) in *o*-xylene (15 mL) was heated to reflux for 48 h under argon. After cooling to room temperature, the reaction mixture was precipitated into of *n*-pentane (300 mL). The solid was collected; redissolved in dichloromethane (10 mL) and the precipitation (200 mL *n*-pentane) was repeated three to four times. [**G1**](αCOOMe)$_8$-capped (**4**) was obtained as a colorless solid: 0.2 g (81%). t_{decomp} > 300 °C. ^{1}H NMR (250 MHz, CD_2Cl_2, 303 K): δ_H 7.92 (s, 4H, Ar), 7.82, 7.81 (2s, 8H, Ar), 7.52–6.49 (m, 208H, Ar), 3.59 (s, 12H, H_{OCH_3}) and 3.28 (s, 12H, H_{OCH_3}) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ_C 169.17, 169.11 (C=O), 142.46, 142.39, 141.1, 140.79, 139.79, 137.09, 134.67 (C4), 132.08, 130.50, 129.89, 129.67, 128.11, 127.46, 127.38, 127.08, 126.83, 126.19, 125.87 (C_{phenyl}), 51.8 and 51.41 (C_{OCH_3}) ppm. MALDI-TOF (dithranol): exact mass, calc. for $[M + Ag]^+$ $C_{353}H_{244}Ag$: 4849.7, found: 4845.

[G2](αCOOMe)$_{24}$-ethynyl-T*i*PS$_{16}$ (5a). A mixture of **3b** (0.1 g, 0.05 mmol) and 2,5-di(methylcarboxy)-3,4-bis(4-triisopropylsilylethynylphenyl)cyclopentadienone (**2**) (0.28 g, 0.3 mmol) in *o*-xylene (10 mL) was heated to reflux for 48 h under argon. After cooling to room temperature, the reaction mixture was precipitated in *n*-pentane and the solid was collected and purified by means of column chromatography using petroleum ether–CH_2Cl_2 (1 : 1) as eluent to remove unreacted **2**. Evaporation of the solvent produced **5a** as a colorless solid: 0.21 g (94%). t_{decomp} >300 °C. ^{1}H NMR (250 MHz, CD_2Cl_2 303 K): δ_H 7.92 (s, 4H, Ar); 7.82, 7.81 (2s, 8H, Ar); 7.52–6.49 (m, 169H, Ar), 3.59 (s, 12H, OCH_3), 3.55, 3.54 (2s, 24H, OCH_3) 3.33 (s, 12H, OCH_3), 3.24, 3.21 (2s, 24H, OCH_3) and 1.11 (br, 288H; T*i*PS) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ_C 168.9, 168.83, 168.5, 169.11 (C=O), 140.12, 139.99, 139.91, 139.29, 139.26, 139.15, 139.03, 138.49, 138.44, 137.22, 134.01 (C4), 131.90, 130.69, 130.22, 128.32, 127.69, 126.91, 126.26, 125.96 (C_{phenyl}) 123.01, 122.64, 107.33, 107.14, 91.96, 91.70 (C4), 52.67, 52.41 (C_{OCH_3}), 18.98 (C_{CH}), 11.91 (C_{CH_3}); MALDI-TOF (dithranol): exact mass, calc. for $[M]^+$ $C_{465}H_{532}O_{48}$: 7328, found: 7328 (M^+) and 5496 ($\frac{3}{4}M^+$).

[G2](αCOOMe)$_{24}$-ethyne$_{16}$ (5b). A similar procedure as in the case of **3b** was applied: To an argon purged mixture of **5a** (0.2 g, 0.02 mmol) in THF (20 mL) was added a solution of tetrabutylammonium fluoride trihydrate (TBAF) [0.52 mmol (1.2 eq./T*i*PS)] in THF (3 mL). The reaction mixture was stirred at room temperature for 15 min. After quenching with H_2O (5 mL), the mixture was extracted three times with DCM and the dried ($MgSO_4$), and the organic phase was concentrated *in vacuo*. The pure product, a colorless solid, was obtained as a result of preparative column chromatography using CH_2Cl_2 as eluent: 0.11 g (84%); ^{1}H NMR (250 MHz, CD_2Cl_2 303 K): δ_H 7.92 (s, 4H, Ar), 7.82, 7.81 (2s, 8H, Ar); 7.52–6.49 (m, 169H, Ar); 3.59 (s, 12H, OCH_3), 3.55, 3.54 (2s, 24H, OCH_3) 3.33 (s, 12H, OCH_3) 3.24, 3.21 (2s, 24H, OCH_3) and 3.09, 3.12 (2s, 16H, ethyne) ppm; ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ_C 168.92, 168.85, 168.52, 16.14 (C=O), 140.12, 139.99, 139.91, 139.29, 139.26, 139.15, 139.03, 138.49, 138.44, 137.22, 134.01 (C4), 132.08, 131.75, 130.50, 129.89, 129.67, 128.11, 127.46, 126.83, 126.19, 125.87 (C_{phenyl}), 123.01, 122.64, 107.33, 107.14, 91.96, 91.70 (C4), 83.8, 78.21 (C_{ethyne}), 52.54, 52.41, 52.32 (C_{OCH_3}); MALDI-TOF (dithranol): exact mass, calc. for $[M]^+$ $C_{321}H_{212}O_{48}$: 4832, found: 4835 (M^+).

[G2](αCOOMe)$_{24}$-capped (6). The capping of **5b** was conducted under similar reaction conditions as in the case of **4**. The Diels–Alder cycloaddition was carried out in refluxing *o*-xylene (10 mL) using **5b** (0.11 g, 0.02 mmol) and tetraphenylcyclopentadienone (cap building block) (0.209 g, 0.5 mmol). After a reaction time of 72 h the product was isolated by repetitive precipitation in pentane as a colorless solid: 0.21 g (94%); t_{decomp} >300 °C; ^{1}H NMR (250 MHz, CD_2Cl_2 303 K): δ_H 7.91 (s, 4H, Ar), 7.85, 7.84 (2s, 8H, Ar), 7.51–6.50 (m, br, 448H, Ar), 3.57 (s, 12H, OCH_3), 3.41, 3.40 (2s, 24H, OCH_3), 3.33 (s, 12H, OCH_3) and 3.14, 3.12 (2s, 24H, OCH_3) ppm; ^{13}C NMR (75 MHz, CD_2Cl_2, 300 K): δ_C 168.97, 168.88, 169.17, 169.11 (C=O), 144.5, 142.3, 141.6, 140.81, 140.3, 139.52, 139.12, 138.56, 138.24, 133.32 (C4), 132.81, 131.95, 131.32, 130.21, 128.81, 127.75, 127.2, 126.32, 125.61, 112.72, 112.41, 127.08, 126.83, 126.19, 125.82 (C_{phenyl}), 52.70, 52.59, 52.47, 52.35 (C_{OCH_3}); MALDI-TOF (dithranol): exact mass, calc. for $[M + Ag]^+$ $C_{769}H_{532}O_{48}$: 10 635, found: 10 646 $[M + Ag]^+$, 8003 $[\frac{3}{4}M + Ag]^+$, 2740 $[\frac{1}{4}M + Ag]^+$.

[G1](αCOOH)$_{16}$-capped (8). [**G1**](αCOOH)$_{16}$-capped (**8**) was obtained as a result of an alkaline hydrolysis of [**G1**](αCOOMe)$_8$-capped (**4**) in the presence of KOH in a THF–water (5 : 1 v/v) solvent system. Accordingly, **4** (0.1 g, 0.021 mmol) and KOH (0.096 g, 1.73 mmol) in a mixture of THF–H_2O (6 ml, 5 : 1 v/v) were heated in a microwave-reactor (120 °C) in a 10 mL rubber-septum sealed glass tube for 8 h. After cooling to room temperature, the reaction mixture was dropped into diluted HCl (100 mL, 1 M). The solid was collected, washed with water and then methanol and dried under reduced pressure yielding **8** in the form of a colorless powder. 0.086 g (89%); ^{1}H NMR (250 MHz, THF-d_8, 303 K): δ_H 7.67 (s, 4H, Ar), 7.38, 7.34 (s, 8H, Ar) and 7.20–6.47 (br, 108H, Ar) ppm; ^{13}C NMR (75 MHz, THF-d_8, 300 K): 169.14, 169.10 (C=O) 156.9, 144.5, 142.3, 141.6, 140.8, 140.3, 139.5, 139.1, 138.5, 138.2, 137.9, 133.3, 132.9 (C4); 132.8, 131.9, 131.3, 130.2, 127.8, 127.0, 126.2, 125.6, 112.7 and 112.4 (C_{phenyl}) ppm; MALDI-TOF (dithranol): exact mass, calc. for $[M]^+$ $C_{345}H_{228}O_{16}$: 4624, found: 4663 $[M + K]^+$, 4625 $[M]^+$, 3508 $[\frac{3}{4}M + K]^+$.

[G2](αCOOH)$_{24}$-capped (9). Identical procedure as in the case of **8**. A THF–H_2O (5 : 1 v/v) solution of **6** (0.1 g, 0.009 mmol) and KOH (0.125 g, 4.3 mmol) were heated in a microwave-reactor (120 °C) in a 10 mL rubber-septum sealed glass tube for 8 h. After cooling to release temperature the reaction mixture was dropped into diluted HCl 100 mL (1 M). The solid was collected, washed with water and then methanol and dried under reduced pressure yielding **9** in form of a colorless powder 0.08 g (87%); ^{1}H NMR (250 MHz, THF-d_8, 303 K): δ_H 7.98 (s, 4H, Ar), 7.71, 7.69 (2s, 8H, Ar) and 7.47–6.61 (m, br, 448H, Ar) ppm; ^{13}C NMR (75 MHz, THF-d_8, 300 K): δ_C 169.14, 169.12, 169.13, 169.09 (C=O), 142.4, 142.35, 141.35, 141.07, 140.76, 140.7, 139.76, 137.09, 134.64 (C4), 132.04, 131.72, 130.47, 129.86, 129.64, 128.07, 127.43, 127.35, 127.02, 126.79, 126.16 and 125.83 (C_{phenyl}) ppm; IR ν = 3461 (m), 3039 (m), 2958 (m), 1703 (s), 1609 (s); 1593 (s), 1507 (s), 1409 (m), 1332 (s), 1281 (s), 1206 (s), 1174 (m), 1115 (w), 1005 (m), 840 (m), 749 (m), 702 (m) and 567 (w) cm^{-1}; MALDI-TOF (dithranol): exact mass, calc. for $[M + Ag]^+$ $C_{745}H_{484}O_{48}$: 10 192, found: 10 201 $[M + H]^+$, 10 242 $[M + K]^+$.

Host : guest molar ratio

For the calculation of the host : guest molar ratio, the following procedure was applied. Chloroform solutions (100 mL) of the host molecules **8** (5.0 mg, 10×10^{-4} mmol) and **9** (10.0 mg, 9.8×10^{-4} mmol) were prepared in volumetric flasks resulting in solutions with concentrations of 1.07×10^{-5} M and 0.98×10^{-5} M, respectively. Aliquots (4 mL) of the above host solutions were mixed with solid proflavine hydrochloride (10 mg) and stirred overnight (12 h) at room temperature. Subsequently, samples (1 mL) were separated and evaporated to dryness. The residues were redissolved in deionised water, filtered, and diluted (10 mL) in volumetric flasks. The concentrations of proflavine in the obtained aqueous solutions were evaluated by means of UV/vis spectroscopy recording the absorbance intensities at λ = 440 nm (0.15 and 0.18 for the aqueous solutions, obtained in the case of **8** and **9**, respectively). Using a molar extinction value of $\varepsilon_{440} = 4.15 \times 10^4$ mol^{-1} cm^{-1}, the concentration of proflavine was calculated according to the Beer–Lambert law. As such, the initial chloroform samples (1 mL) contained 3.57×10^{-5} and 4.33×10^{-5} mmol of proflavine, respectively. Using the amount of the host dendrimers **8** and **9**, in the chloroform (1 mL) (1.07×10^{-5} and 0.98×10^{-5} mol) the host : guest ratio could be calculated: host **8** : proflavine = 1 : 3.3 (0.3) and host **9** : proflavine = 1 : 4.4 (0.4).

Acknowledgements

The research is supported by the Deutsche Forschungsgemeinschaft (DFG) in the frame of the Sonderforschungsbereich (SFB) 625. This support is gratefully acknowledged by the authors. C. G. C. is grateful for financial support from a U.S. National Science Foundation MPS Distinguished International Postdoctoral Research Fellowship (MPS-DRF) (Award: DMR-0207086) and from the Max Planck Society.

References

1 S. Hecht and J. M. J. Frechet, *Angew. Chem., Int. Ed.*, 2001, **40**, 74–91.
2 T. Gensch, K. Tsuda, G. C. Dol, L. Latterini, J. W. Weener, A. Schenning, J. Hofkens, E. W. Meijer and F. C. De Schryver, *Pure Appl. Chem.*, 2001, **73**, 435–441.
3 G. R. Newkome, C. N. Moorefield, G. R. Baker, M. J. Saunders and S. H. Grossman, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1178–1180.
4 D. Astruc, J. C. Blais, E. Cloutet, L. Djakovitch, S. Rigaut, J. Ruiz, V. Sartor and C. Valerio, in *Dendrimers II*, Springer, Berlin, Heidelberg, 2000, pp. 229–259.
5 C. M. Cardona, S. Mendoza and A. E. Kaifer, *Chem. Soc. Rev.*, 2000, **29**, 37–42.
6 V. Balzani, S. Campagna, G. Denti, A. Juris, S. Serroni and M. Venturi, *Acc. Chem. Res.*, 1998, **31**, 26–34.
7 F. Vögtle, M. Plevöts, M. Nieger, G. C. Azzellini, A. Credi, L. De Cola, V. De Marchis, M. Venturi and V. Balzani, *J. Am. Chem. Soc.*, 1999, **121**, 6290–6298.
8 P. Bhyrappa, J. K. Young, J. S. Moore and K. S. Suslick, *Abstr. Pap. Am. Chem. Soc. Natl. Meet.*, 1995, **210**, 584-INOR.
9 H. Brunner, *J. Organomet. Chem.*, 1995, **500**, 39–46.
10 F. Svec and J. M. J. Frechet, *Science*, 1996, **273**, 205–211.
11 D. Astruc and F. Chardac, *Chem. Rev.*, 2001, **101**, 2991–3023.
12 T. Iwasawa, M. Tokunaga, Y. Obora and Y. Tsuji, *J. Am. Chem. Soc.*, 2004, **126**, 6554–6555.
13 C. Seel and F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 442–444.
14 F. W. Zeng and S. C. Zimmerman, *Chem. Rev.*, 1997, **97**, 1681–1712.
15 G. R. Newkome, L. A. Godinez and C. N. Moorefield, *Chem. Commun.*, 1998, 1821–1822.
16 F. Kohn, J. Hofkens, U. M. Wiesler, M. Cotlet, M. van der Auweraer, K. Müllen and F. C. De Schryver, *Chem. Eur. J.*, 2001, **7**, 4126–4133.
17 C. J. Hawker, K. L. Wooley and J. M. J. Frechet, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1287–1297.
18 G. R. Newkome, C. N. Moorefield, G. R. Baker, A. L. Johnson and R. K. Behera, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1176–1178.
19 F. H. Huang, J. W. Jones, C. Slebodnick and H. W. Gibson, *J. Am. Chem. Soc.*, 2003, **125**, 14458–14464.
20 Y. J. Li, P. L. Dubin, R. Spindler and D. A. Tomalia, *Macromolecules*, 1995, **28**, 8426–8428.
21 J. F. G. A. Jansen, E. M. M. de Brabander-van den Berg and E. W. Meijer, *Science*, 1994, **266**, 1226–1229.
22 J. F. G. A. Jansen, E. W. Meijer and E. M. M. de Brabander-van den Berg, *J. Am. Chem. Soc.*, 1995, **117**, 4417–4418.
23 H. M. Kao, A. D. Stefanescu, K. L. Wooley and J. Schaefer, *Macromolecules*, 2000, **33**, 6214–6216.
24 R. Scherrenberg, B. Coussens, P. van Vliet, G. Edouard, J. Brackman, E. de Brabander and K. Mortensen, *Macromolecules*, 1998, **31**, 456–461.
25 R. E. Bauer, A. C. Grimsdale and K. Müllen, in *Functional Molecular Nanostructures*, 2005, pp. 253–286.
26 (*a*) S. Rosenfeldt, Nico Dingenouts, D. Pötschke, M. Ballauff, A. J. Berresheim, K. Müllen and P. Lindner, *Angew. Chem., Int. Ed.*, 2004, **43**, 109–112; (*b*) S. Rosenfeldt, Nico Dingenouts, D. Pötschke, M. Ballauff, A. J. Berresheim, K. Müllen and P. Lindner, *Angew. Chem.*, 2004, **116**, 111–114.
27 A. Herrmann, T. Weil, V. Sinigersky, U. M. Wiesler, T. Vosch, J. Hofkens, F. C. De Schryver and K. Müllen, *Chem. Eur. J.*, 2001, **7**, 4844–4853.
28 D. Grebel-Koehler, D. J. Liu, S. De Feyter, V. Enkelmann, T. Weil, C. Engels, C. Samyn, K. Müllen and F. C. De Schryver, *Macromolecules*, 2003, **36**, 578–590.
29 T. Weil, E. Reuther and K. Müllen, *Angew. Chem., Int. Ed.*, 2002, **41**, 1900–1904.
30 S. Bernhardt, M. Baumgarten, M. Wagner and K. Mullen, *J. Am. Chem. Soc.*, 2005, **127**, 12392–12399.
31 T. Weil, U. M. Wiesler, A. Herrmann, R. Bauer, J. Hofkens, F. C. De Schryver and K. Müllen, *J. Am. Chem. Soc.*, 2001, **123**, 8101–8108.
32 N. Krasteva, I. Besnard, B. Guse, R. E. Bauer, K. Müllen, A. Yasuda and T. Vossmeyer, *Nano Lett.*, 2002, **2**, 551–555.
33 T. Vossmeyer, B. Guse, I. Besnard, R. E. Bauer, K. Müllen and A. Yasuda, *Adv. Mater.*, 2002, **14**, 238–242.
34 U. M. Wiesler, A. J. Berresheim, F. Morgenroth, G. Lieser and K. Müllen, *Macromolecules*, 2001, **34**, 187–199.
35 R. C. Cookson, J. B. Henstock, J. Hudec and B. R. D. Whitear, *J. Chem. Soc. C*, 1967, 1986.
36 B. Eistert and A. A. Thommen, *Chem. Ber.*, 1971, **104**, 3048.
37 (*a*) F. Morgenroth, E. Reuther and K. Müllen, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 631–634; (*b*) F. Morgenroth, E. Reuther and K. Müllen, *Angew. Chem.*, 1997, **109**, 647–649.
38 G. M. Dykes, L. J. Brierley, D. K. Smith, P. T. McGrail and G. J. Seeley, *Chem. Eur. J.*, 2001, **7**, 4730–4739.
39 M. Fischer and F. Vögtle, *Angew. Chem., Int. Ed.*, 1999, **38**, 885–905.
40 R. E. Gillard, F. M. Raymo and J. F. Stoddart, *Chem. Eur. J.*, 1997, **3**, 1933–1940.
41 D. Philp and J. F. Stoddart, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1155–1196.
42 J.-M. Lehn, *Supramolecular Chemistry – Concepts and Perspectives*, VCH, Weinheim, 1995.
43 S. Y. Bi, C. Y. Qiao, D. Q. Song, Y. Tian, D. J. Gao, Y. Sun and H. Q. Zhang, *Sens. Actuators, B*, 2006, **119**, 199–208.
44 A. M. Wiosetek-Reske and S. Wysocki, *Spectrochim. Acta, Part B*, 2006, **64**, 1118–1124.
45 K. Yamaoka, S. Noji and M. Yoshida, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 31–34.
46 D. K. Smith, *Chem. Commun.*, 1999, 1685–1686.
47 U.-M. Wiesler and K. Müllen, *Chem. Commun.*, 1999, 2293–2294.