DOI: 10.1002/ejoc.200700683

New Approaches Towards Monoamino Polyglycerol Dendrons and Dendritic Triblock Amphiphiles

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Keywords: Polyglycerol dendrimers / Amphiphiles / Nile Red / Fluorescence / UV/Vis spectroscopy

In order to improve the water solubility of nonpolar compounds such as drugs or dyes, new amphiphilic molecules are needed. In this paper we describe a new class of triblock amphiphiles that we have synthesized by a straightforward convergent approach. These amphiphiles each consist of a nonpolar biphenyl core and a polar shell based on various generations of monoamino polyglycerol dendrons, coupled to the core through amide linkages (**1**). For the synthesis of these monoamino dendrons we applied a simple iterative two-step process based on allylation of an alcohol group and catalytic dihydroxylation. As starting materials, D,L-serine/serinol and – in a second, similar pathway – commercially available triglycerol were used. The transport behavior of these defined triblock amphiphiles was then investigated with the nonpolar dye Nile Red in water.

Introduction

Dendrimers[1] are a unique class of polymers, which are different from all the other macromolecules because of their globular shape, resulting from their highly ordered, perfectly branched architectures and their monodisperse structures.[2] The molecular weight, shape, size and chemical functionality of dendrimers can be controlled through the synthetic methods used for their preparation. So far, two complementary general approaches – divergent and convergent – have been used.[3] The unique properties of dendrimers and dendrons allow for their application as a new scaffold type in drug and dye solubilization.[4]

Among the various polymeric drug carriers known today,[5] dendritic polymers based on polyglycerol (PG), with their defined core-shell-type architectures, have shown good transport capacities for poorly water-soluble drugs. In previous studies, paclitaxel (PTX) was solubilized in water through the use of polyglycerol dendrimers[6] of generations [G4] and [G5].[7] Recently, we have shown that hyperbranched polyglycerol with a biphenyl-functionalized core can be used as a nanocarrier for hydrophobic drugs.[8] Thanks to the π–π interactions between nimodipine or pyrene and the biphenyl moiety, high transport capacities for these systems were observed.

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In view of these results, we decided to design dendritic triblock amphiphiles consisting of biphenyl cores with two carboxylate groups at their 4,4′-positions and shells based on monoamino polyglycerol dendrons (Figure 1). Attractive overlapping through π–π stacking between the aromatic moieties in host and guest made up the rationale for expecting good transport capacities for compounds with structures such as that of Nile Red (**2**). The biocompatibility properties of the aliphatic polyethers, in particular, the high biocompatibility of the polyglycerol oligomers, e.g.,

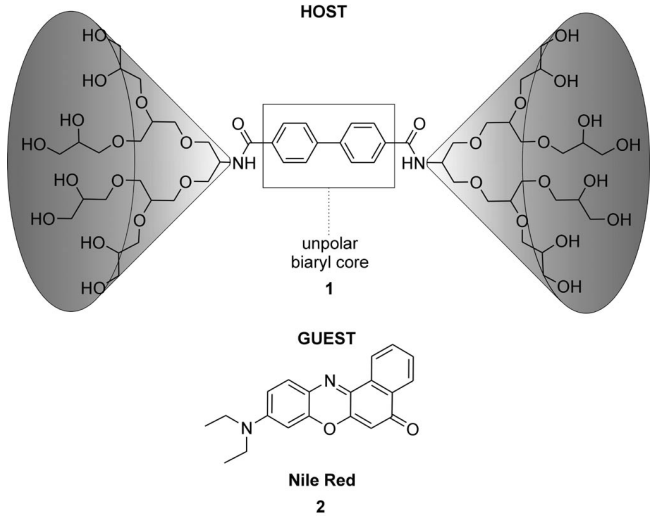


Figure 1. Designed triblock architecture of the amphiphiles with outer polyglycerol blocks and a central biphenyl unit.

food and pharma additives[9] and dendritic polymers[10], are scientifically very interesting for evaluation of new amphiphilic moieties based on polyglycerol dendrons.

Results and Discussion

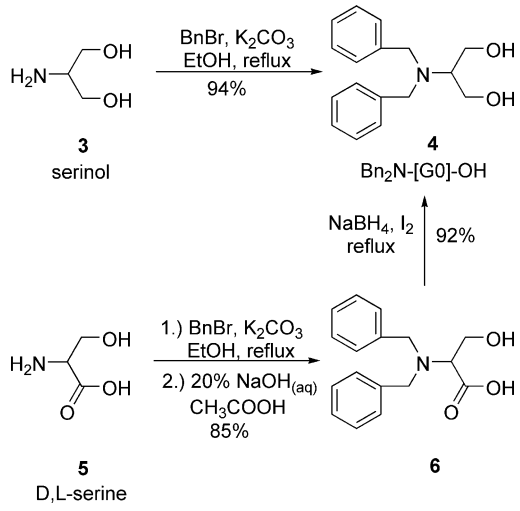
Design of Dendritic Triblock Amphiphiles and Selection of Dyes

The incorporation of focal primary amino units into polyglycerol-based dendrons would allow a modular approach for the generation of various dendritic architectures through amide linkages (**1**). Depending on the molecular geometry of the guest molecule it should then be possible to use the biphenyl core and various sizes of the shell to influence the environment of Nile Red (**2**).

Nile Red, an environmentally sensitive fluorescent dye, was chosen as model compound (Figure 1). This hydrophobic solvatochromic dye is used as a fluorescent probe in many biological and medical studies for localizing and quantitating lipids,[11] identifying hydrophobic sites on the surface of proteins,[12] and detecting ligand binding to enzymes.[13] It is known that the fluorescence of Nile Red strongly depends on the polarity of the environment, being redshifted and strongly quenched in polar solvents and approaching a maximum blueshift and intensity in apolar solvents/environment.[14] The remarkable sensitivity of Nile Red has also been beneficial in studies of the local polarity of bolaamphihiles[15] and micelles[16] and of interactions with cyclodextrins.[17] Small changes in the organization of the surfactants in the solvent system could be monitored by Nile Red,[16c] while the specific properties of Nile Red could also be used to characterize surfactant/amphiphiles self-assembly processes and phase behavior.

Synthesis of Bifunctional Glycerol Dendrons

For the synthesis of bifunctional glycerol dendrons we chose a divergent growth approach based on the application of a reaction sequence similar to the one we had recently developed for the synthesis of glycerol dendrimers.[6,18] We selected a simple iterative two-step process based on allylation[19] of an alcohol functionality under phase-transfer conditions and subsequent catalytic dihydroxylation[20] of the allylic double bond to obtain the desired generations [G1.0–G3.0] of monoamino glycerol dendrons. As starting materials we used either 2-aminopropane-1,3-diol (**3**)/D,L-serine (**5**) (Scheme 1) or, to reduce the number of reaction steps, commercially available triglycerol (**13**; Scheme 3). In both cases it was necessary to protect the amino functionality, which was achieved either by benzyl protection or by using an azide as precursor.

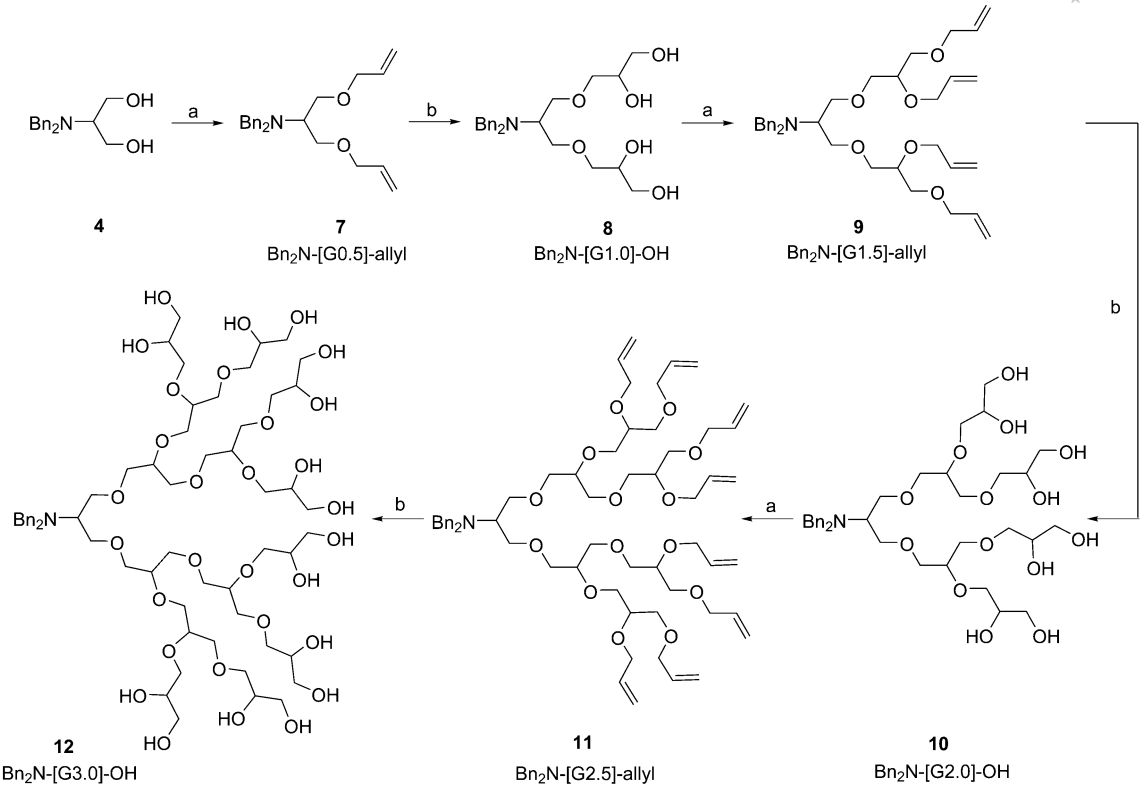


Scheme 1. Preparation of the starting material Bn_2N-[G0]-OH for the construction of monoamino polyglycerol dendrons.

Synthesis of Bifunctional Glycerol Dendrons from D,L-Serine/Serinol

To synthesize the starter Bn_2N-[G0]-OH[21] (**4**), commercially available serinol (2-aminopropane-1,3-diol) (**3**) was treated with benzyl bromide in the presence of K_2CO_3 in ethanol. In spite of a one-step reaction and a very good yield with the use of serinol as the starting material, we decided to use the much cheaper D,L-serine (**5**) as starting material for the up-scaling of the dendrimer synthesis. Protection of the amino functionality of D,L-serine was carried out by using the same conditions as described for serinol. Because of partial ester formation, treatment with aqueous NaOH solution (20%) at 80 °C for 3 h followed by addition of acid was necessary. The resulting *N*,*N*′-dibenzylserine was transformed into the corresponding diol **4** by reduction with $NaBH_4$ and I_2 in THF in high yield (Scheme 1).[22]

Compound Bn_2N-[G0.5]-allyl (**7**; Scheme 2) was obtained in very good yield (80%) by treatment of **4** with allyl bromide and aqueous NaOH (50%) in the presence of a phase-transfer catalyst such as tetrabutylammonium iodide (TBAI). Higher generations (compounds **9** and **11**) were synthesized by this method in 49% and 79% yields, respectively. For the dihydroxylation an optimized Upjohn process, with *N*-methylmorpholine *N*-oxide as a reoxidizing agent, proved to be successful. In the course of optimization it was found that as little as 0.25 mol-% K_2OsO_4 per double bond was sufficient to provide the dendritic polyols in very good yields. The NMR spectra of the crude products showed quantitative conversion of the allyl groups for every generation. The purification of Bn_2N-[G1.0]-OH (**8**), Bn_2N-[G2.0]-OH (**10**) and Bn_2N-[G3.0]-OH (**12**) was achieved by filtration (silica gel, ethanol) and size exclusion column chromatography (Sephadex, methanol).

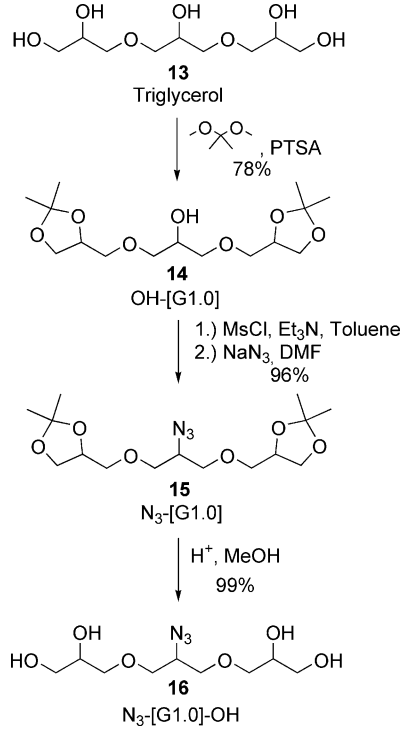


Scheme 2. Reaction sequence for the construction of polyglycerol dendrons with benzyl protection. Reagents and conditions: a) allyl bromide, 50% NaOH, TBAI, 40 °C, 18 h; b) 1 mol-% K_2OsO_4, NMO, acetone/water/*tert*-butyl alcohol, 40 °C, 18 h.

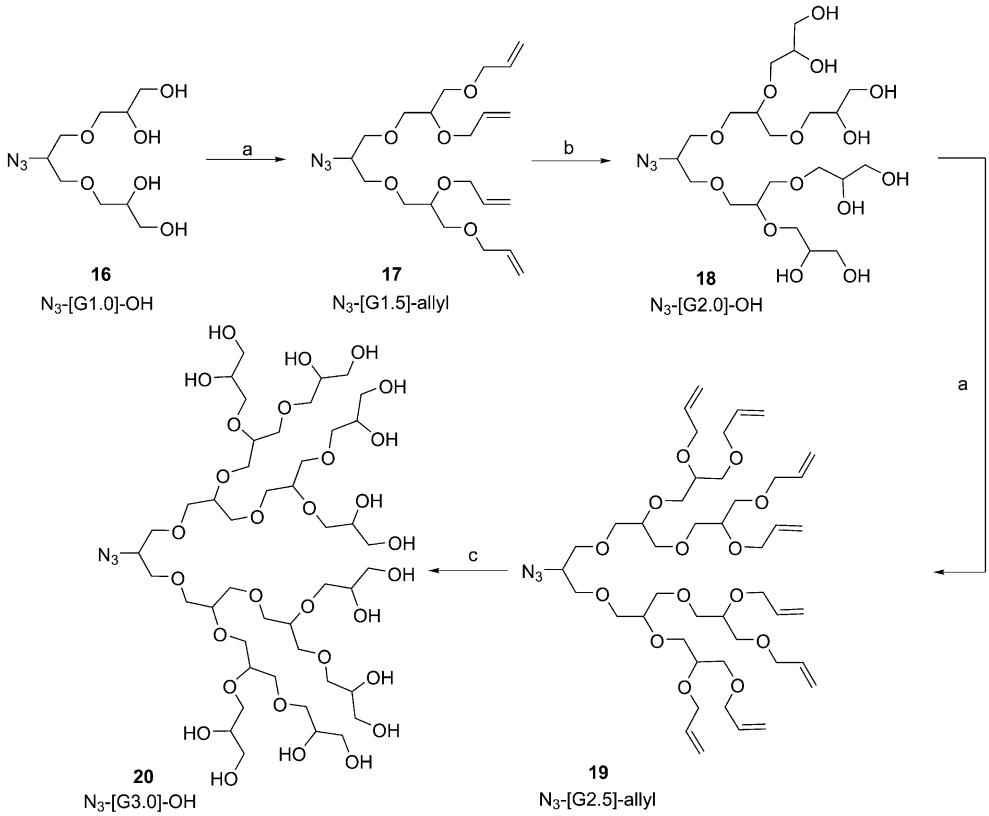
Synthesis of Bifunctional Glycerol Dendrons from Triglycerol

For an alternative approach to bifunctional dendrons with amine groups as focal points, and to reduce the number of steps needed to generate an H_2N-[G3.0]-OH (**23**), we used triglycerol (**13**) as a building block. In view of the high stability of the azide functionality under acidic, basic and oxidative conditions we decided to use it as a precursor for the amino functionality[23] (Scheme 3). We once again applied a reaction sequence based on allylation of the alcohol under phase-transfer conditions and catalytic dihydroxylation of the allylic double bonds (Scheme 4). The commercially available triglycerol (**13**) was protected with acetone dimethylacetal on the terminal diols, the corresponding acetal-protected triglycerol **14** being obtained in 78% yield.[18]

Since triglycerol contains over 20% other oligomers (e.g., diglycerol, tetraglycerol etc.) as impurities, purification by flash column chromatography was necessary. The secondary free hydroxy group of compound **14** was converted into the corresponding mesylate, which was treated without further purification with sodium azide to give N_3-[G1.0] (**15**) in 96% yield over two steps. The acetal protection was removed in almost quantitative yield by stirring with an acidic ion-exchange resin in methanol. The resulting N_3-[G1.0]-OH (**16**) was treated with allyl bromide to give N_3-[G1.5]-allyl (**17**) in 85–94% yield (Scheme 4). Catalytic dihydrox-



Scheme 3. Preparation of the starting material N_3-[G1.0]-OH for the construction of monoamino polyglycerol dendrons.



Scheme 4. Reaction sequence for the construction of polyglycerol dendrons with azide precursor. Reagents and conditions: a) allyl bromide, 50% NaOH, TBAI, 40 °C, 18 h; b) AD-mix-α, water/*tert*-butyl alcohol, 0 °C, 24 h; c) 1 mol-% K_2OsO_4, NMO, citric acid, acetone/water/*tert*-butyl alcohol, 40 °C, 24 h.

ylation of the double bond with osmium tetroxide and NMO was not successful, which was probably due to deactivation of the catalyst by the azide functionality.[24] Therefore, we decided to use AD-mix-α (or AD-mix-β) according to the procedure described by Sharpless et al.,[20c] which led to the formation of new glycerol units on every available allyl functionality in high yield. However, no promoted stereoselectivity was observed in this reaction. Repetition of the allylation and dihydroxylation of the double bond with osmium tetroxide and NMO resulted in N_3-[G3.0]-OH (**20**).

All generations of protected dendrons (from [G1.0] to [G3.0]) were converted into the corresponding monoamino glycerol dendrons **8**, **10** and **12** by a simple hydrogenation procedure with 10% Pd/C (Scheme 5). With benzyl-protected dendrons the reaction was performed under 5 bar of H_2 pressure, but in the cases of compounds **10** and **12** the reactions were still incomplete after 18 h (as determined by ^{1}H NMR), and so further quantities of fresh catalyst were used. Conversion from the azide functionalities to primary amines, on the other hand, was complete under a lower hydrogen pressure and without any extra amount of the catalyst after 24 h. In all cases, purification of **21**–**23** was performed by simple filtration through Celite® pads, yielding pure monoamino dendrons in 85–99% yields.

Synthesis of the Dendritic Triblock Amphiphiles

The resulting polyols **21**–**23** were attached to the 4,4′-biphenyldicarboxylic acid core to give the desired triblock amphiphiles **25**–**27** by DCC coupling. (Figure 2 and Table 1). The carboxylic acid groups were first activated with HOBt (1-hydroxybenzotriazole) or NHS (*N*-hydroxysuccinimide) and a catalytic amount of DMAP, followed by slow addition of DMF solutions of the monoamino poly-

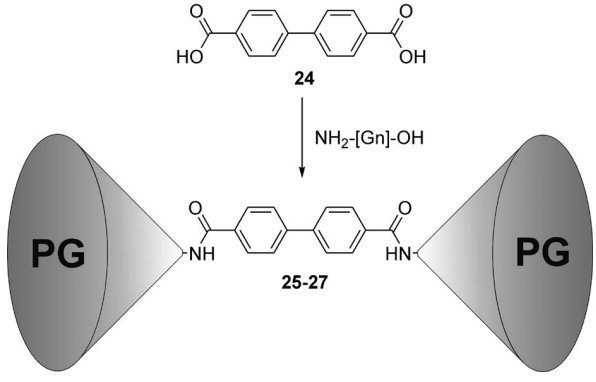
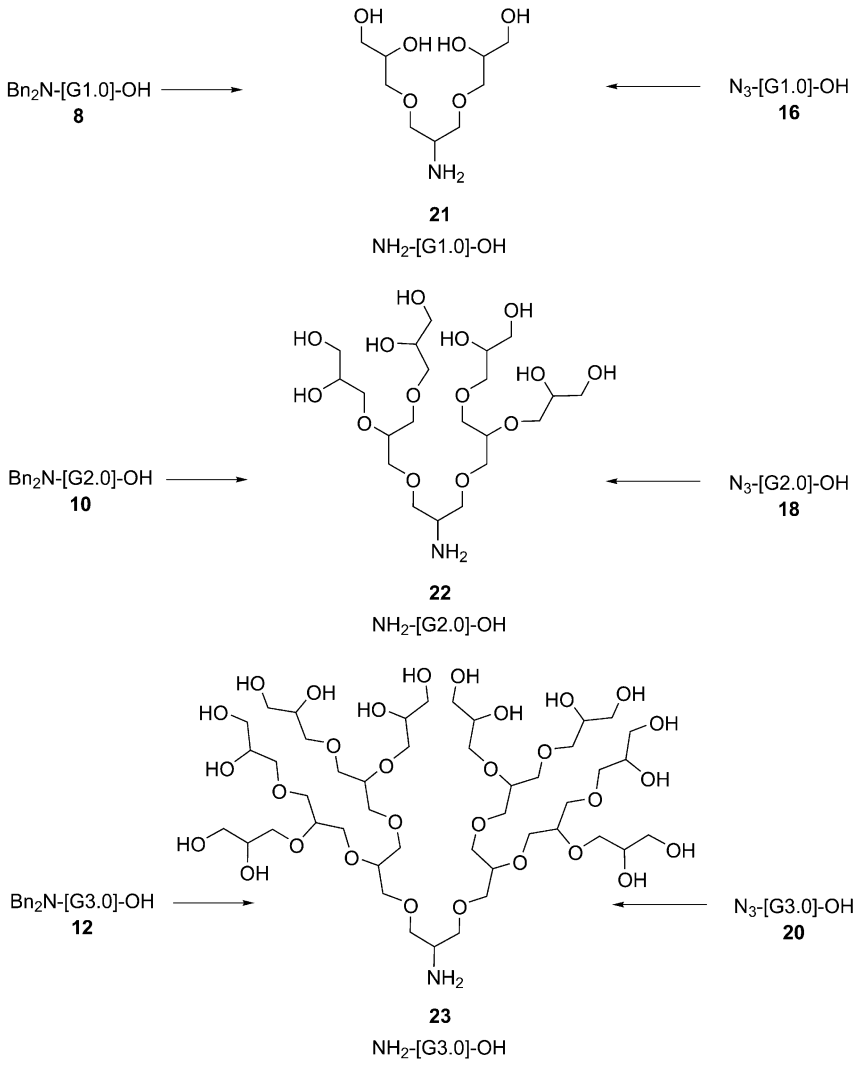


Figure 2. Attachment of the dendrons to the biphenyl core to form triblock amphiphiles.



Scheme 5. Monoamino polyglycerol dendrons: a) 10% Pd/C, MeOH, 5 bar H_2, 24 h; b) twice: 10% Pd/C, MeOH, 5 bar H_2, 24 h; c) 10% Pd/C, MeOH, 1.1 bar H_2, 24 h.

glycerol dendrons. Purification of these dendritic architectures was performed by reversed-phase HPLC (water/methanol, 1:1), as well as by dialysis in methanol. Because of the relatively low yields, an alternative coupling method using 2-ethoxy-*N*-(ethoxycarbonyl)-1,2-dihydroquinoline (EEDQ) by the procedure of Heagy et al.,[25] was tried, but the obtained results were comparable.

Table 1. Attachment of the dendrons to the biphenyl core.

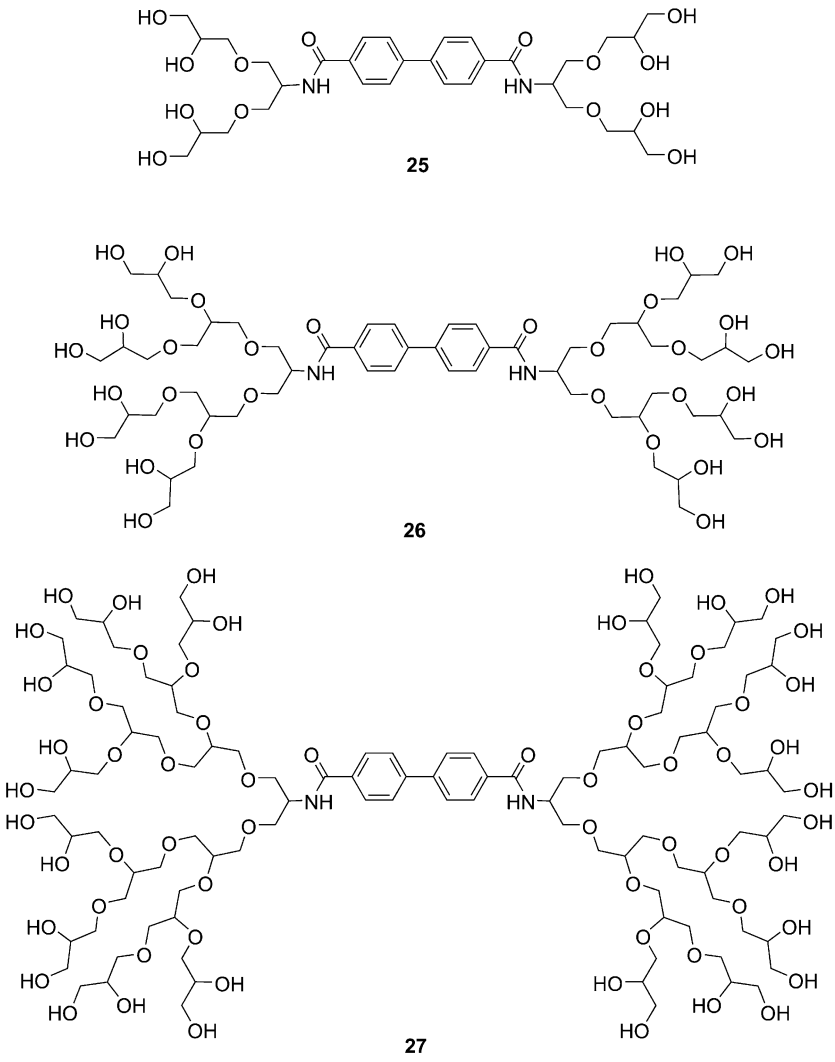
Product	Generation	Coupling reagent	Yield (%)[a]
25	[G1]	3 equiv. HOBt	33
26	[G2]	3 equiv. HOBt	29
27	[G3]	3 equiv. NHS	24

[a] After purification by RP-HPLC (water/methanol, 1:1).

Transport Behavior of the Polyglycerol-Based Triblock Amphiphiles

The dye transport capacities of the obtained [G1] and [G2] dendritic amphiphiles were tested by solid–liquid extraction. Nile Red in powder was added, and the suspensions were stirred vigorously in water.

The result revealed a strong redshift of the absorption band for the Nile Red with the [G1] dendron complex, with λ_{max} = 620 nm, and a strong blueshift for it in the [G2] dendron complex, with λ_{max} = 462 nm (Figure 3). The first shift corresponds to a highly polar environment, such as the PG groups, surrounding the Nile Red. The latter value for Nile Red absorption indicates a highly nonpolar environment of the dye, such as the biphenyl core. The dye/polymer transport ratios were calculated for the highest tested concentration of solutes (10.0 g dm^{-3}), and were 1:292 and 1:4960 for the [G1] and [G2] dendrons, respectively (Scheme 6). The results are strongly opposed to the expected transport capacities. The encapsulation capacity was expected to increase with each dendrimer generation, while the obtained results indicate the opposite tendency. This behavior could be explained by aggregation of the triblock amphiphiles, rather than a unimolecular transport behavior as was initially intended.



Scheme 6. Polyglycerol-based triblock amphiphiles.

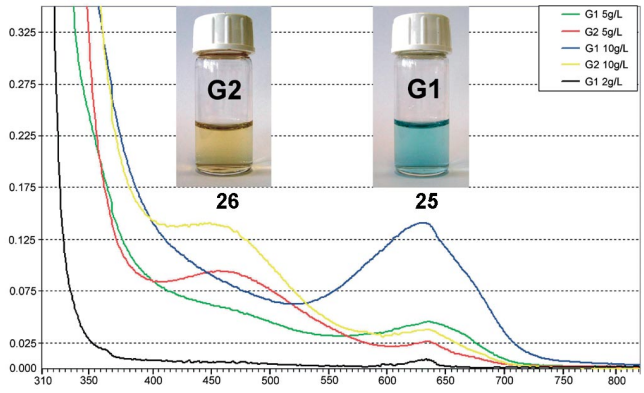


Figure 3. UV absorption of Nile Red encapsulated in [G1] and [G2] dendrimers.

Conclusions

Two new synthetic pathways for the synthesis of monoamino polyglycerol dendrons have been successfully introduced. Although some problems with the scale-up appeared, bifunctional dendrons up to H_2N-[G3.0]-OH (**23**) were produced in good yields. In the dihydroxylation reactions, replacement of NMO by citric acid/H_2O_2 as co-oxidant resulted in almost colorless products.

Our main goal was to achieve an easy route to a variety of well-defined monoamino polyglycerol dendrons, and it was demonstrated that application of different coupling procedures to a biphenyl core results in a new type of triblock amphiphiles based on amide linkages. The transport properties of these macromolecules were tested with the nonpolar guest Nile Red. Also, we have shown that with higher dendron generations the amount of encapsulated Nile Red unexpectedly decreased. However, because the complexes formed between Nile Red (**2**) and the dendritic polyglycerol derivatives **25**–**26** were lower than 1:1 compositions in all cases, the formation of larger aggregates is likely to occur. Further studies will focus on the modification of the core unit in this modular approach and on the size determination of this new class of dendritic triblock amphiphiles.

Experimental Section

General Remarks: Reactions requiring dry conditions were carried out under argon. Dry and analytical-grade solvents were purchased from Acros and used as received. ^{1}H and ^{13}C NMR spectra were recorded with Bruker DRX 400 and DRX 500 spectrometers operating at 300, 400, 500 MHz and 100.5, 125.7 MHz, respectively. The spectra were calibrated on the solvent peak ($CDCl_3$: δ = 7.26 ppm for ^{1}H and δ = 77.0 ppm for ^{13}C. CD_3OD: δ = 4.84 ppm for ^{1}H and δ = 49.05 ppm for ^{13}C. [D_6]acetone: δ = 2.05 ppm for ^{1}H and δ = 30.83 ppm for ^{13}C). Flash chromatography was performed on silica gel 60 (230–400 mesh) with head pressure supplied by compressed air. Infrared spectra (IR) were recorded as thin films between KBr or CaF_2 plates. The instrument used was a Bruker IFS 66 FT-IR spectrophotometer. For ESI measurements a TSQ 7000 (Finnigan Mat) instrument and for MALDI measurements a Voyager-DE PRO BioSpectrometry Workstation were used. High-resolution mass spectra were recorded with a JEOL JMS-SX-102A spectrometer. HPLC was carried out with a Knauer HPLC (pump K-120) with use of a Knauer RI-detector K-2401 and a Eurosphere 100-5C-18 column. UV measurements were carried out with a Specord S100 UV/Vis spectrometer (Analytik Jena) at 25 °C.

Benzyl Protection of 2-Aminopropane-1,3-diol – Bn_2N-[G0]-OH (4): 2-Aminopropane-1,3-diol (3.0 g, 32.9 mmol) and anhydrous potassium carbonate (14.3 g, 0.104 mol, 3.15 equiv.) were suspended in ethanol (120 mL). The mixture was stirred mechanically, and benzyl bromide (16.9 g, 11.8 mL, 98.8 mmol, 3.0 equiv.) was added dropwise over 30 min. After the mixture had been stirred at reflux for 3 h, solids were separated by filtration (EtOAc was used for washings), and volatiles were removed under reduced pressure. The residue was dissolved in EtOAc, and the solution was washed with water, aqueous $NaHCO_3$ and brine. After drying with anhydrous Na_2SO_4 and removal of solvent under reduced pressure, the crude mixture was purified by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1, followed by ethyl acetate/*n*-hexane, 4:1), giving a clean product (8.4 g, 94%). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 7.36–7.20 (m, 10 H, Ph-*H*), 3.74 (s, 4 H), 3.69 (dd, *J* = 10.8, 7.6 Hz, 2 H), 3.59 (dd, *J* = 16.2, 10.8, 5.9 Hz, 2 H), 2.99 (m, 3 H, C*H*, O*H*) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$, 25 °C): δ = 139.2, 128.8, 128.40, 127.38, 59.8, 59.7, 53.9 ppm. IR: ṽ = 3284, 3026, 2927, 2853, 1493, 1452, 743 cm^{-1}. QFT ESI MS: calcd. for $C_{17}H_{21}NO_2$ 271.1572; found 272.1636 [M + H]$^+$.

Benzyl Protection of D,L-Serine (6): D,L-Serine (30.0 g, 0.28 mol) and tetrabutylammonium iodide (TBAI, 10.6 g, 10 mol-%) were dissolved in a solution of potassium hydroxide (39% KOH aq., 300 mL) and EtOH (300 mL). Benzyl chloride (197 mL, 6.0 equiv.) was added dropwise, and the mixture was stirred under reflux conditions for 1 h. Next, after the mixture had cooled to 40 °C, KOH (11.7 g) was added, and the mixture was stirred under reflux conditions for 1 h. The mixture was cooled down to room temperature, and water was added to dissolve the white precipitate. The aqueous layer was extracted with toluene, and solvent was removed by rotary evaporation at aspirator pressure. After the pH value had been adjusted to 5 with acetic acid, the mixture was left overnight for crystallization, yielding white crystals (61 g, 75%); m.p. 133–134 °C. ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 7.34–7.44 (m, 10 H, Aryl-*H*), 4.18 (m, 4 H, Bn-CH_2), 4.08 (dd, *J* = 11.8, 5.8 Hz, 1 H, CH_2), 3.96 (dd, *J* = 11.8, 8.0 Hz, 1 H, CH_2), 3.67 (dd, *J* = 7.8, 5.8 Hz, 1 H, C*H*) ppm. ^{13}C NMR (100 MHz, CD_3OD, 25 °C): δ = 172.3, 136.4, 130.9, 130.0, 129.6, 65.7, 60.5, 56.6 ppm. IR: ṽ = 3410, 3171, 1613, 1497, 1454, 758, 702 cm^{-1}. HR FAB MS: calcd. for $C_{17}H_{19}NO_3$ 285.1365; found 285.1421.

Reduction of 6 to Bn_2N-[G0]-OH (4): The protected D,L-serine (5.47 g, 19.2 mmol) and sodium borohydride (1.72 g, 2.4 equiv.) were dissolved in dry THF in a three-neck round-bottomed flask with mechanical stirrer, condenser and dropping funnel. The mixture was cooled to 0 °C (ice/water bath), and iodine (4.87 g, 1.0 equiv.), dissolved in dry THF (15 mL), was added dropwise with vigorous stirring. Next the mixture was stirred under reflux conditions for 18 h. The solution was cooled to room temperature, and methanol was added until the solution became clear. After 30 min of stirring, the solvent was removed by rotary evaporation at aspirator pressure, and the residual white paste was dissolved in aqueous KOH (20%, 50 mL). The mixture was stirred at 75 °C for 1 h and then extracted with chloroform after cooling down to room temperature. The organic layers were combined, dried with $MgSO_4$, filtered and concentrated by rotary evaporation to provide the product in 92% yield.

General Procedure for the Allylation of Alcohol Groups: Allyl bromide (2.5–5 equiv. per OH group) was added to a solution of the alcohol and TBAI (10–20 mol-%) as phase-transfer catalyst in aqueous NaOH (50% w/v, 2.5–5 equiv. per OH group). The reaction mixture was then stirred at 40–50 °C for 24–72 h. After addition of *n*-hexane and sat. NH_4Cl, the organic phase was separated, washed with water, dried with Na_2SO_4 and concentrated under vacuum. The crude product was further purified by column chromatography on silica gel to give the products as colorless oils (in the case of allylation of the azide derivatives, smaller amounts of reagents were used – 2.5 equiv. per OH group of allyl bromide, 50% NaOH and 10 mol-% of TBAI).

Bn_2N-[G0.5]-allyl (7): Reaction conditions and workup were as described above, with benzylated serinol **4** (2.867 g, 10.57 mmol), TBAI (0.78 g, 2.11 mmol, 20 mol-%), NaOH (50%, 8.5 mL, 0.11 mol, 5 equiv. per OH group) and allyl bromide (9.15 mL, 0.11 mol, 5 equiv. per OH group). Purification was by flash chromatography on silica gel (*n*-hexane/ethyl acetate 10:1), providing title compound **5** (2.97 g, 8.46 mmol, 80%) as a colorless oil. The residue was chromatographed on silica gel with *n*-hexane/ethyl acetate 10:1. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.38 (d, *J* = 7.3 Hz, 4 H), 7.26 (m, 4 H) 7.18 (m, 2 H), 5.89 (m, 2 H), 5.25/5.15 (2 × dd, *J* = 17.9/10.5 Hz, 4 H), 3.93 (d., *J* = 5.5 Hz, 4 H), 3.79 (s, 4 H), 3.62 (m, 4 H), 3.11 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 140.9, 138.2,135.2, 128.8, 126.8, 116.5, 72.1, 69.6, 56.6, 56.4 ppm. IR: ṽ = 3062, 3063, 2852, 1494, 1453, 1361, 1099, 746, 699 cm^{-1}. HR MS: calcd. for $C_{23}H_{29}NO_2$ 351.2198; found 351.2209.

Bn_2N-[G1.5]-allyl (9): Reaction conditions and workup were as described above, with the unpurified alcohol **8** (2.845 mmol), TBAI (0.21 g, 0.57 mmol, 20 mol-%), NaOH (50%, 6.6 mL, 56.9 mmol, 5 equiv. per OH group) and allyl bromide (4.9 mL, 56.9 mmol, 5 equiv. per OH group). Purification was by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 6:1), providing title compound **6** (0.8 g, 1.38 mmol, 49%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.15–7.37 (m, 10 H), 5.89 (m, 4 H), 5.20 (m, 8 H), 4.12 (m, 4 H), 3.98 (m, 4 H), 3.77 (s, 4 H), 3.46–3.65 (m, 15 H), 3.07 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 140.9, 135.4, 134.9, 128.8, 128.3, 126.8, 117.1, 117.0, 77.3, 72.5, 71.5, 70.9, 70.8, 70.5, 55.3, 56.6 ppm. IR: ṽ = 3081, 3025, 2862, 1494, 1453, 1361, 1108, 746, 699 cm^{-1}. HR MS: calcd. for $C_{35}H_{49}NO_6$ 579.3560; found 579.3537.

Bn_2N-[G2.5]-allyl (11): Reaction conditions and workup were as described above, with the unpurified alcohol **10** (0.5 mmol), TBAI (37 mg, 0.1 mmol, 20 mol-%), NaOH (50%, 1.6 mL, 20 mmol, 5 equiv. per OH group) and allyl bromide (1.73 mL, 20 mmol,

5 equiv. per OH group). After 24 h, further allyl bromide (0.5 mL, 12 equiv.) was added and stirring was continued for an additional 36 h. Purification was by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1), providing title compound **7** (0.411 g, 0.479 mmol, 79%) as a colorless oil. ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 7.04–7.19 (m, 10 H), 5.90 (m, 7 H), 5.20 (m, 15 H), 4.12 (m, 8 H), 3.98 (m, 8 H), 3.49–3.79 (m, 35 H), 3.04 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 142.7, 142.1, 136.6 (2×), 136.2, 136.1, 129.8, 129.2, 127.8, 117.2, 117.1, 117.0 (2×), 80.0, 78.9, 78.6, 73.3, 72.7, 72.5, 72.2 (2×), 71.8, 71.3 (2×), 71.2, 58.1, 56.3 ppm. IR: $\tilde{\nu}$ = 2980, 2865, 1494, 1454, 1350, 1108, 924, 747, 700 cm^{-1}. HR MS: calcd. for $C_{59}H_{89}NO_{14}$ 1035.6283; found 1036.6395 $[M + H]^+$. $C_{59}H_{89}NO_{14}$ (1036.34): calcd. C 68.4, H 8.7, N 1.4; found C 68.1, H 8.9, N 1.4.

N_3-[G1.5]-allyl (17): Reaction conditions and workup were as described above, with the alcohol **16** (13.2 g, 49.76 mmol), TBAI (1.84 g, 19.9 mmol, 10 mol-%), NaOH (50%, 39.8 mL, 0.498 mol, 2.5 equiv. per OH group) and allyl bromide (43.1 mL, 0.498 mol, 2.5 equiv. per OH group). Purification was by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1), providing title compound **9** (17.36 g, 40.8 mmol, 82%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.89 (tddd, *J* = 17.2, 10.4, 9.6, 5.6 Hz, 4 H), 5.26 (qdd, *J* = 17.2, 6.0, 1.6 Hz, 4 H), 5.16 (dddd, *J* = 10.4, 6.4, 3.0, 1.3 Hz, 4 H), 4.13 (ddd, *J* = 5.7, 2.6, 1.3 Hz, 4 H), 3.98 (td, *J* = 5.6, 1.3 Hz, 4 H), 3.70–3.51 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 135.0, 134.6, 116.93, 116.88, 76.9, 72.3, 71.61, 71.3, 71.1, 69.8, 60.5 ppm. IR: $\tilde{\nu}$ = 3080, 2866, 2099, 1645, 1271, 1111, 996, 924, 558 cm^{-1}. FAB MS: calcd. for $C_{21}H_{35}N_3O_6$ 425.25; found 448.2 $[M + Na]^+$, 426.3 $[M + H]^+$. $C_{21}H_{35}N_3O_6$ (425.52): calcd. C 59.27, H 8.29, N 9.88; found C 59.29, H 8.30, N 9.68.

N_3-[G2.5]-allyl (19): Reaction conditions and workup were as described above, with the alcohol **18** (1.98 g, 3.525 mmol), TBAI (0.521 g, 1.41 mmol, 10 mol-%), NaOH (50%, 5.64 mL, 70.5 mmol, 2.5 equiv. per OH group) and allyl bromide (6.14 mL, 70.5 mmol, 2.5 equiv. per OH group). Purification was by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 6:1), providing title compound **6** (2.0 g, 2.25 mmol, 64%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.89 (tddd, *J* = 16.7, 10.4, 8.6, 5.6 Hz, 8 H), 5.26 (qdd, *J* = 17.2, 6.0, 1.6 Hz, 4 H), 5.16 (dddd, *J* = 10.4, 6.4, 3.0, 1.3 Hz, 4 H), 4.12 (ddd, *J* = 5.6, 1.2 Hz, 4 H), 3.98 (td, *J* = 5.6, 1.4 Hz, 4 H), 3.70–3.51 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 135.3, 135.3, 134.9, 134.8 (4 C), 117.0, 116.9, 116.89, 116.78 (4 C), 78.6, 72.4, 71.7 (2 C), 71.4 (2 C), 70.5, 70.3, 60.8 ppm. IR: $\tilde{\nu}$ = 3079, 2867, 2099, 1646, 1270, 1109, 997, 924 cm^{-1}. FAB MS: calcd. for $C_{45}H_{75}N_3O_{14}$ 881.52; found 904.3 $[M + Na]^+$. $C_{45}H_{75}N_3O_{14}$ (882.09): calcd. C 61.27, H 8.57, N 4.76; found C 61.16, H 8.68, N 4.73.

General Procedure for the Dihydroxylation of the Allyl Groups: K_2OsO_4 (0.25–0.5 mol-% per allyl group) was added to a solution of the allyl ether and *N*-methylmorpholine *N*-oxide (NMO, 1.1 equiv. per allyl group) in acetone/distilled water/*tert*-butyl alcohol (5:5:1). The mixture was stirred at 30–40 °C for 12–24 h. The volatile compounds were removed under vacuum, and the product was further purified by silica gel column chromatography, Sephadex column chromatography or dialysis.

Bn_2N-[G1.0]-OH (8): Reaction conditions and workup were as described above, with the allyl ether **7** (1 g, 2.845 mmol), NMO (46 mg, 6.26 mmol, 2.2 equiv.) and K_2OsO_4 (10.5 mg, 0.0285 mmol, 1 mol-%) in acetone/distilled water/*tert*-butyl alcohol (13.2 mL). A black viscous oil (1.44 g) was obtained as crude product, part of which was purified by flash column chromatography (methanol/ethyl acetate, 1:4) and characterized. ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 7.16–7.39 (m, 10 H), 3.39–3.77 (m, 18 H), 3.05 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 142.0, 141.8, 129.9, 129.8, 129.2, 129.1, 127.9, 127.8, 73.7, 73.6, 72.3 (2×), 71.5, 70.9, 70.8, 64.7, 64.6, 61.4, 60.0, 59.9, 58.1, 56.1, 55.8 ppm. IR: $\tilde{\nu}$ = 3385, 2928, 2873, 1494, 1453, 1387, 1100, 1072, 1043, 749, 700 cm^{-1}. HR MS: calcd. for $C_{23}H_{33}NO_6$ 419.2308; found 420.2393.

Bn_2N-[G2.0]-OH (10): Reaction conditions and workup were as described above, with the allyl ether **9** (600 mg, 1.03 mmol), NMO (846 mg, 613 mg, 4.532 mmol, 4.4 equiv.) and K_2OsO_4 (3.8 mg, 0.01 mmol, 1 mol-%) in acetone/distilled water/*tert*-butyl alcohol (6.6 mL) with stirring for 12 h. Dialysis in methanol gave a brown oil (428 mg, 0.60 mmol, 58%). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 7.18–7.40 (m, 10 H, Aryl-*H*), 3.50–3.78 (m, 42 H), 3.03 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 142.0, 129.8, 129.2, 127.8, 80.0, 79.9, 75.0, 74.0, 73.0, 72.9, 72.6, 72.5, 72.4, 72.2, 72.1, 71.6 (2×), 64.5 (2×), 58.0, 56.2 ppm. IR: $\tilde{\nu}$ = 3385, 2920, 2876, 1494, 1454, 1362, 1113, 749, 700 cm^{-1}. HR MS: calcd. for $C_{35}H_{57}NO_{14}$ 715.3779; found 716.3868.

Bn_2N-[G3.0]-OH (12): Reaction conditions and workup were as described above, with the allyl ether **11** (100 mg, 0.096 mmol), NMO (115 mg, 0.849 mmol, 8.8 equiv.) and K_2OsO_4 (1.1 mg, 0.0029 mmol, 3 mol-%) in acetone/distilled water/*tert*-butyl alcohol (0.66 mL) with stirring for 16 h. Dialysis in methanol gave a brown oil (116 mg, 0.089 mmol, 92%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 7.15–7.37 (m, 10 H), 3.51–3.76 (m, 80 H), 3.00 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 142.1, 129.9, 129.6, 129.2, 127.9, 80.2 (2×), 80.1, 80.0, 79.9, 74.0 (2×), 73.0, 72.7, 72.5 (2×), 72.4, 72.2, 72.1, 71.7, 71.3, 71.2, 64.5, 58.1, 56.2 ppm. FAB MS: calcd. for $C_{59}H_{105}NO_{30}$ 1307.6721; found 1308.04 $[M + H]^+$.

N_3-[G2.0]-OH (18): A 100 mL round-bottomed flask, containing a magnetic stirrer, was charged with *tert*-butyl alcohol (20 mL), water (20 mL) and AD-mix-α or AD-mix-β (5.6 g, 1.4 g of AD-mix-α/AD-mix-β per 1 mmol of olefin/double bond). The mixture was stirred at room temperature until both phases were clear, and was then cooled to 0 °C. Compound **17** (1 mmol, 0.425 g) was then added in one portion, and the heterogeneous slurry was stirred vigorously at 0 °C until TLC revealed the absence of the starting olefin (24 h). The reaction was quenched at 0 °C by addition of sodium sulfite (1.5 g per 1 mmol of double bond), and the mixture was then warmed to room temperature and stirred for 30–60 min. The reaction mixture was extracted several times with an ethyl acetate/ethanol (4:1) mixture, dried under Na_2SO_4 and concentrated to give a clean product (0.3766 g, 67%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 3.78–3.74 (m, 6 H), 3.73–3.66 (m, 4 H), 3.65–3.51 (m, 21 H), 3.50–3.46 (m, 4 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 80.0, 79.1, 74.0, 73.9, 72.4, 72.2, 71.2, 64.5, 62.6, 62.3 ppm. IR: $\tilde{\nu}$ = 3384, 2877, 2514, 2114, 1458, 1270, 1116, 930, 674 cm^{-1}. FAB MS: calcd. for $C_{21}H_{43}N_3O_{14}$ 561.27; found 583.9 $[M + Na]^+$, 562.0 $[M + H]^+$. $C_{21}H_{43}N_3O_{14}$ (561.58): calcd. C 44.91, H 7.72, N 7.48; found C 44.54, H 7.72, N 7.46.

N_3-[G3.0]-OH (20): Reaction conditions and workup were as described above, with the allyl ether **19** (506 mg, 0.573 mmol), NMO (682 mg, 4.13 mmol) and K_2OsO_4 (8.4 mg, 0.023 mmol, 3 mol-%), and additionally citric acid monohydrate 0.868 g (4.13 mmol, as a cooxidant), in distilled water/*tert*-butyl alcohol (1.0 mL), with stirring for 24 h. Dialysis in methanol gave a light brown oil (563 mg, 85%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 3.78–3.74 (m, 13 H), 3.73–3.66 (m, 12 H), 3.65–3.51 (m, 42 H), 3.50–3.46 (m, 8 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 80.4, 80.2, 79.9,

74.0, 73.97, 73.0, 72.4, 72.3, 72.2, 71.2, 64.5, 62.8 ppm. IR: $\tilde{\nu}$ = 3382, 2877, 2514, 2113, 1463, 1330, 1124, 930, 677 cm^{-1}. ESI TOF MS: calcd. for $C_{45}H_{91}N_3O_{30}$ 1153.5687; found 1176.5615 $[M + Na]^+$.

General Procedure for the Deprotection of the Amino Functionality: Pd/C (10–25 wt.-%) was added to a methanol solution of the polyol, either with benzyl protection or with an azide group, and the mixture was stirred under hydrogen pressure for 24–48 h. The catalyst was filtered through Celite® pads and washed with methanol. The organic layer was concentrated in vacuo, yielding a clean product.

H_2N-[G1.0]-OH (21): Reaction conditions and workup were as described above, with **8** (2.01 g, 4.79 mmol) and Pd/C (500 mg) and stirring at a pressure of 5 bar of H_2 for 18 h. Amine **21** was isolated as a light yellow oil (1.143 g, 99%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 3.85–3.81 (m, 2 H), 3.63–3.38 (m, 12 H), 3.33–3.13 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 73.8 (2×), 73.7 (2×), 72.2 (2×), 64.3, 51.9 ppm. IR: $\tilde{\nu}$ = 3343, 2924, 2287, 1662, 1601, 1456, 1113, 1049 cm^{-1}. HR FAB MS: calcd. for $C_9H_{21}NO_6$ 239.1369; found 240.1475 $[M + H]^+$.

H_2N-[G2.0]-OH (22): Reaction conditions and workup were as described above, with **10** (167 mg, 0.23 mmol) and Pd/C (41 mg) and stirring at a pressure of 5 bar of H_2 for 18 h. Amine **22** was isolated as a light yellow oil (0.218 mg, 95%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 3.74 (m, 4 H), 3.66 (m, 4 H), 3.60–3.38 (br. m, 26 H), 3.06 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 79.8, 74.0, 73.2, 72.9, 72.4, 72.2, 64.4, 51.9 ppm. IR: $\tilde{\nu}$ = 3398, 2931, 2881, 1660, 1464, 1363, 1113, 935, 870 cm^{-1}. ESI TOF MS: calcd. for $C_{21}H_{45}NO_{14}$ 535.2840; found 558.2718 $[M + Na]^+$, 536.2901 $[M + H]^+$.

H_2N-[G3.0]-OH (23): Reaction conditions and workup were as described above, with **12** (650 mg, 0.497 mmol) and Pd/C (163 mg) and stirring at a pressure of 5 bar of H_2 for 18 h. Amine **23** was isolated as a light yellow oil (475 mg, 85%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 3.73–3.44 (m, 75 H), 3.27 (m, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 79.8; 74.0 (2×), 72.9, 72.5, 72.4 (2×), 72.3 (2×), 72.2, 64.4, 49.9 ppm. IR: $\tilde{\nu}$ = 3390, 2922, 2885, 1651, 1464, 1350, 1128, 933 cm^{-1}. ESI TOF MS: calcd. for $C_{45}H_{93}NO_{30}$ 1127.5782; found 1150.5680 $[M + Na]^+$, 1128.5857 $[M + H]^+$.

Acetal Protection of Triglycerol (13) To Give 14: Triglycerol (**13**) (60 g, 0.25 mol) was gently heated with a heat-gun (max. 120 °C) up to the moment at which the substance obtained a liquid consistency. 2,2-Dimethoxypropane (150 mL, 1.25 mol) was added, followed by slow addition of *p*-toluenesulfonic acid (PTSA, 3.0 g, 25 mmol). After stirring for 0.5 h, a homogeneous solution was obtained, and the reaction was allowed to proceed at 30–40 °C overnight. The resulting yellow/orange solution was neutralized by addition of triethylamine (25 mmol) and subsequently stirred at room temperature for 30 min. The solvent was then evaporated in vacuo, and the remaining crude liquid was purified by filtration through silica gel (ethyl acetate/hexane, 1:2, 2:1, 6:1) to give the compound (78%) as a pale yellow oil. (Triglycerol contains ca. 20% other oligomers). ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 4.19 (q, J = 11.9, 6.3 Hz, 2 H), 4.00 (dd, J = 8.2, 6.4 Hz, 2 H), 3.84 (m, 1 H), 3.75 (td, J = 4.9, 1.5 Hz, 1 H), 3.69 (dd, J = 8.2, 6.3 Hz, 2 H), 3.50 (ddd, J = 31.8, 10.1, 5.5 Hz, ddd, J = 17.4, 11.9, 6.3 Hz, 8 H), 2.83 (s, 1 H, OH), 1.33 (s, 6 H, CH_3), 1.28 (s, 6 H, CH_3) ppm. ^{13}C NMR (125 MHz, [D$_6$]acetone, 25 °C): δ = 109.4, 75.6, 73.9, 73.8, 73.14, 73.12, 70.17, 67.4, 27.1, 25.7 ppm. FAB MS (MNBA): calcd. for $C_{15}H_{28}O_7$ 320.18; found 343.2 $[M + Na]^+$, 321.3 $[M + H]^+$. $C_{15}H_{28}O_7$ (320.38): calcd. C 56.23, H 8.8; found C 55.88, H 8.65.

Synthesis of Acetal-Protected Triglycerol Azide 15: Methanesulfonyl chloride (5.06 mL, 65.55 mmol) was added to a solution of **14** (20.0 g, 62.43 mmol) and triethylamine (9.21 mL, 65.55 mmol) in toluene (160 mL), cooled to 0 °C in an ice bath. Progress of the reaction was monitored by TLC. After completion, the precipitate was filtered and the mixture concentrated under vacuum to give an oil as a final product (100%). The crude product was used for the next reaction step. ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 4.83 (q, 1 H), 4.23 (q, 2 H), 4.01 (t, 2 H), 3.72–3.66 (m, 6 H), 3.56–3.51 (m, 4 H), 3.07 (s, 3 H), 1.39 (s, 6 H, CH_3), 1.33 (s, 6 H, CH_3) ppm. ^{13}C NMR (65 MHz, $CDCl_3$, 25 °C): δ = 109.5, 79.8, 74.5, 72.6, 72.4, 70.66, 70.64, 66.3, 38.4, 26.7, 25.3 ppm. Sodium azide (0.157 mol, 10.2 g) was added to a solution of the mesyl triglycerol (65.55 mmol) in dry DMF (150 mL). After the mixture had been stirred at 120 °C under argon for 3 h, the excess of NaN_3 was filtered off, and DMF was removed under high vacuum by cryodistillation. The crude product was purified by filtration through a thin layer of silica gel (ethyl acetate/hexane, 2:1). The [G1.0]-N_3 was obtained as a light yellow, viscous oil in 96% yield over two steps. ^{1}H NMR (500 MHz, [D$_6$]acetone, 25 °C): δ = 4.21 (q, J = 11.7, 6.2, 5.6 Hz, 2 H), 4.03 (ddd, J = 8.2, 6.4, 1.0 Hz, 2 H), 3.76 (m, 1 H), 3.72 (dd, J = 8.2, 6.3 Hz, 2 H), 3.67 (tdd, J = 9.6, 7.8, 4.5 Hz, 2 H), 3.61 (ddd, J = 5.5, 5.0, 2.2 Hz, 2 H), 3.54 (ddd, J = 17.9, 10.3, 5.1 Hz, 4 H), 1.34 (s, 6 H) 1.28 (s, 6 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]acetone, 25 °C): δ = 109.6, 75.51, 75.50, 73.0, 72.9, 71.7, 71.6, 67.2, 61.5, 27.1, 25.7 ppm. IR: $\tilde{\nu}$ = 2987, 2935, 2875, 2100, 1456, 1380, 1371, 1258, 1214, 1081, 1055, 975, 844, 515 cm^{-1}. FAB MS (MNBA): calcd. for $C_{15}H_{27}N_3O_6$ 345.39; found 368.2 $[M + Na]^+$, 346.3 $[M + H]^+$. $C_{15}H_{27}N_3O_6$ (345.39): calcd. C 52.16, H 7.88, N 12.17; found C 52.03, H 7.46, N 11.84.

Synthesis of Triglycerol Azide N_3-[G1.0]-OH (16): Ion-exchange resin Dowex® 50W was added to the acetal-protected triglycerol azide (19.3 g, 55.88 mmol), dissolved in MeOH (100 mL), and the mixture was heated at reflux overnight. After it had cooled down, the resin was filtered off, and the residue was concentrated under vacuum to yield compound **16** (14.81 g, 99%) as a yellow oil. ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 3.78–3.74 (m, 2 H), 3.68–3.46 (m, 12 H), 3.39 (ddd, J = 13.0, 9.8, 3.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 73.84, 73.80, 72.24, 72.20, 72.12, 72.11, 64.4, 62.1 ppm. IR: $\tilde{\nu}$ = 3384, 2876, 2514, 2103, 1457, 1273, 1127, 1047, 929, 665, 558 cm^{-1}. ESI TOF MS: calcd. for $C_9H_{19}N_3O_6$ 265.1274; found 288.1176 $[M + Na]^+$, 304.0824 $[M + K]^+$.

General Procedure for the Coupling of the Amino Dendrons to the Biphenyl Core: Diisopropylamine was added at 0 °C to a mixture of biphenyl-4,4′-dicarboxylic acid, dicyclohexylcarbodiimide (DCC) and hydroxybenzotriazole (HOBt) or *N*-hydroxysuccinimide (NHS) in dry DMF (2 mL). After 5 min of stirring, the amine in dry DMF (1 mL) was added. The reaction mixture was warmed to room temperature and stirred for 1–3 d. The mixture was extracted with diethyl ether and water. The aqueous layer was extracted with diethyl ether (4×). The combined organic layers were concentrated in vacuo. The crude products were purified by HPLC (reversed-phase column, water/methanol, 1:1; flow 9.0 mL min^{-1}).

Coupling of Biphenyl-4,4′-dicarboxylic Acid with H_2N-[G1.0]-OH To Give 25: Reaction conditions and workup were as described above, with the biphenyl-4,4′-dicarboxylic acid (50 mg, 0.21 mmol), **21** (100 mg, 1.25 mmol), diisopropylamine (162 mg, 1.25 mmol), DCC (129 mg, 0.63 mmol) and HOBt (85 mg, 0.63 mmol) in dry DMF (3 mL). The product was purified by RP-HPLC to yield a yellow oil (46 mg, 0.07 mmol, 33%). ^{1}H NMR (500 MHz, CD_3OD,

25 °C): δ = 7.93–7.90 (m, 4 H, Aryl-H), 7.75–7.73 (m, 4 H, Aryl-H), 4.45–4.41 (m, 2 H, 1-H), 3.78–3.48 (m, 28 H, aliphatic H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 169.8, 144.2, 135.0, 131.2, 129.1, 128.1, 73.8, 73.6, 72.2, 72.1, 71.3, 71.2, 64.4, 51.0 ppm. MALDI TOF MS: calcd. for $C_{32}H_{48}N_2O_{14}$ 684.31; found 685.3 $[M + H]^+$.

Coupling of Biphenyl-4,4′-dicarboxylic Acid with H_2N-[G2.0]-OH To Give 26: Reaction conditions and workup were as described above, with the biphenyl-4,4′-dicarboxylic acid (23 mg, 0.09 mmol), **22** (100 mg, 0.186 mmol), diisopropylamine (72 mg, 0.56 mmol), DCC (58 mg, 0.28 mmol) and HOBt (38 mg, 0.28 mmol) in dry DMF (3 mL). The product was purified by dialysis (cutoff 500, 24 h, methanol), and RP-HPLC yielded a yellow oil (35 mg, 0.027 mmol, 29%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 7.96 (d, J = 8.4 Hz, 4 H, Aryl-H), 7.80 (d, J = 8.4 Hz, 4 H, Aryl-H), 4.47–4.44 (m, 2 H), 3.75–3.44 (m, 70 H, aliphatic H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 169.8, 144.4, 135.0, 129.2, 128.2, 79.8, 73.9, 72.9, 72.4 (2×), 72.3, 72.1 (2×), 71.4, 64.3, 51.0 ppm. HR MS:calcd. for $C_{56}H_{96}N_2O_{30}$ 1276.6048; found 1299.5931 $[M + Na]^+$.

Coupling of Biphenyl-4,4′-dicarboxylic Acid with H_2N-[G3.0]-OH To Give 27: Reaction conditions and workup were as described above, with the biphenyl-4,4′-dicarboxylic acid (21.5 mg, 0.09 mmol), **23** (200 mg, 0.177 mmol), diisopropylamine (69 mg, 0.53 mmol), DCC (55 mg, 0.27 mmol) and NHS (31 mg, 0.27 mmol) in dry DMF (3 mL). The product was purified by dialysis (cutoff 500, 24 h, methanol), and RP-HPLC yielded a yellow oil (53 mg, 0.02 mmol, 24%). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 8.11–7.94 (m, 4 H, Aryl-H), 7.87–7.77 (m, 4 H, Aryl-H), 4.52–4.48 (m, 2 H), 3.78–3.44 (m, 150 H, aliphatic H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 170.2, 144.3, 134.8, 129.4, 128.5, 128.1, 79.8, 79.7, 79.5, 73.8, 72.6, 72.3, 72.2 (3×), 72.0, 71.8, 70.8, 64.2, 51.0 ppm. MADLI TOF MS: calcd. for $C_{104}H_{192}N_2O_{62}$ 2461.1933; found 2483.66 $[M + Na]^+$, 2461.22 $[M + H]^+$.

Encapsulation Procedure: The dendritic triblock amphiphiles were dissolved in 5 mL of water at concentrations of 1.0, 5.0 and 10.0 g L^{-1}, Nile Red (5 mg) was added as a fine powder, and the mixtures were stirred for 24 h. Insoluble solid residues of dye were removed by filtration through a 0.45 μm PTFE filter, and the obtained solutions were analysed by UV/Vis spectroscopy. The dye concentration was determined from the corresponding absorption by using a calibration curve (Figure 3).

Acknowledgments

This work was supported by the Studienstiftung des deutschen Volkes (grant for K. M.), the Fonds der Chemischen Industrie (Liebig fellowship for B. P.) and the Deutsche Forschungsgemeinschaft (Emmy-Noether fellowship for B. P.). R. H. is indebted to the Bundesministerium für Forschung und Bildung (BMBF) for a young scientist nanotechnology award. M. W. and R. H. thank Dr. W. Dilla from Solvay Chemicals GmbH for a generous gift of high-purity triglycerol. The authors thank M. Radowski for helpful discussions.

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a simple name system for our bifunctional dendrons. The name of each compound consist of three parts: H_2N-[G1.0]-OH, whereby H_2N- is the core, [G1.0] is the number of the generation, and -OH is the shell.
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Received: July 24, 2007
Published Online: November 15, 2007

