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# A Convergent Approach to Biocompatible Polyglycerol "Click" Dendrons for the Synthesis of Modular Core–Shell Architectures and Their Transport Behavior

**Monika Wyszogrodzka and Rainer Haag*[a]**

**Abstract:** Dendrimers are an important class of polymeric materials for a broad range of applications in which monodispersity and multivalency are of interest. Here we report on a highly efficient synthetic route towards bifunctional polyglycerol dendrons on a multigram scale. Commercially available triglycerol (**1**), which is highly biocompatible, was used as starting material. By applying Williamson ether synthesis followed by an ozonolysis/reduction procedure, glycerol-based dendrons up to the fourth generation were prepared. The obtained products have a reactive core, which was further functionalized to the corresponding monoazido derivatives. By applying copper(I)-catalyzed 1,3-dipolar cycloaddition, so-called "click" coupling, a library of core–shell architectures was prepared. After removal of the 1,2-diol protecting groups, water-soluble core–shell architectures **24**–**27** of different generations were obtained in high yields. In the structure–transport relationship with Nile red we observe a clear dependence on core size and generation of the polyglycerol dendrons.

**Keywords:** biocompatibility · click chemistry · core–shell structures · dendrimers · host–guest systems · polyglycerol dendrons

## Introduction

Dendrimers and dendrons have been known for 30 years and have entered many research areas, from gene and drug delivery to diagnostics, as well as nanoengineering.[1] This relatively new type of macromolecular architecture is successfully used in many applications such as surface modification,[2] materials science, and catalysis.[3] By taking advantage of the multivalency of dendrimers and the possibility to use almost any type of chemistry for their post-synthetic chemical modification, they may be used as antiviral, antibacterial, and antitumor agents.[4]

In spite of the attractive properties of dendrimers, only two types, namely, polyamidoamine (PAMAM, Starburst, DNT) and poly(propylene imine), PPI (Astramol, DSM), have been commercialized, because of their tedious, stepwise, and time-consuming synthesis. So far, two complementary general methods—the divergent approach initiated by Vögtle et al.,[5] Tomalia et al.,[6] and Newkome et al.[7] and the convergent approach of Hawker and Fréchet—[8] have been developed for their preparation. The problem of the structural purity of single molecules in the divergent approach has been overcome by the convergent growth approach,[9] wherein the synthesis of dendrimers starts from the periphery to a polyfunctional core, and thus reduces the number of reactions performed on a single molecule. Consequently, in the convergent method, each molecule has a precise molecular weight and structure and can easily be purified from the incomplete coupling products. Also, the dendrons can be modified at both ends: the focal point and the shell.

Dendritic oligoethers[10] have found a wide range of applications.[11] Much effort has been devoted to the preparation of dendrimers that are water-soluble and biocompatible. For example, Fréchet and co-workers synthesized a dendritic analogue of the highly biocompatible poly(ethylene glycol) (PEG), which is a promising structural skeleton for many biological applications.[12] Dendritic polyethers based on glycerol dendrimers prepared by us are also of interest for biomedical applications due to their high biocompatibility.[13] Yamamoto et al. reported the convergent preparation of glycerol-based dendrons by applying Williamson ether formation between a benzyl/dendritic alcohol and epichlorohydrin.[14] A carborane unit was linked to these dendrons to

[a] Dipl.-Ing. M. Wyszogrodzka, Prof. Dr. R. Haag
Institut für Chemie und Biochemie
Freie Universität Berlin
Takustrasse 3, 14195 Berlin (Germany)
Fax: (+49) 30-838-53357
E-mail: haag@chemie.fu-berlin.de

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produce a water-soluble carborane that was used in boron neutron-capture therapy.

We previously reported an efficient divergent method towards polyglycerol dendrimers involving a repetitive sequence of allylation and dihydroxylation steps.[15] Recently, we described a divergent route for the synthesis of bifunctional monoamino glycerol dendrons,[16] in which we also applied a sequence based on allylation and catalytic dihydroxylation with osmium tetroxide, and obtained [G3] monoamino glycerol dendrons in good yields. Park et al. showed that [G4.0] and [G5.0] polyglycerol dendrimers can solubilize the poorly water-soluble drug paclitaxel (PTX). The solubility of PTX increased with increasing generation of dendritic PG.[17] On the other hand, core–shell-type architectures obtained by simple modification of hyperbranched PG with a biphenylic unit enhanced the solubilization of highly hydrophobic drugs such as Nimodipine.[18]

Since linear and hyperbranched polyglycerol proved to be highly biocompatible[19] and might be used for many biomedical applications, any heavy-metal content would be a problem. Therefore, an alternative synthetic route to metal-free dendrimers was our goal. Additionally, optimization of the reaction and purification steps may improve the synthetic pathway and enable the preparation of large quantities. Nevertheless, one major drawback remains, that is, the tremendous effort required to obtain these perfect structures. Furthermore, the ability to execute considerable structural control by imparting bifunctionality with easy synthetic steps is required.

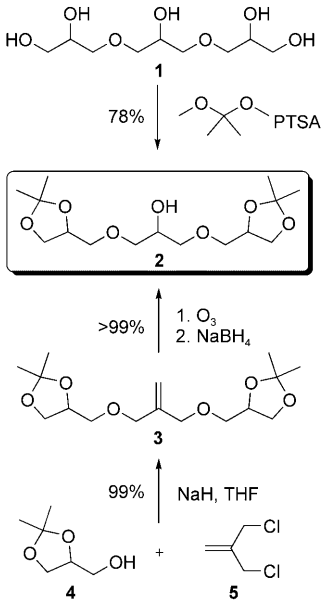
The [2+3] Huisgen cycloaddition, rediscovered by Sharpless et al.,[20] is growing in impact and has found many applications in most areas of modern chemistry. The beauty of this reaction resides in its simplicity, reliability, specificity, and biocompatibility. Moreover, this copper(I)-catalyzed formation of triazoles tolerates a wide range of functional groups and many solvents (including water). Recently, Hawker et al. introduced click coupling into dendrimer synthesis, and demonstrated for the first time the power and efficiency of this methodology in macromolecular chemistry.[21] Since then, Huisgen 1,3-dipolar cycloaddition of azides and alkynes has been utilized in fields of chemistry ranging from drug discovery to materials science.[22]

Here we describe the convergent synthesis of a new family of core–shell dendrimers with an aliphatic polyether backbone based on glycerol units. Such well-defined dendrons have great potential owing to multifunctional chain ends stemming from an easily functionalizable focal point. In addition, polyglycerol dendrons with their glycerol building blocks are biocompatible and can be made water-soluble or water-dispersible by varying their shell functionality.

## Results and Discussion

**Synthesis of bifunctional, clickable glycerol dendrons**: In contrast to the divergent approach, convergent protocols allow us to attain considerable structural control and variable bifunctionality using easy synthetic steps. We achieved our goals by applying a combination of two previously described protocols.[23] We used 3-chloro-2-chloromethyl-1-propene (methallyl dichloride or MDC) as monomer, because its allylic functionality makes nucleophilic substitution of both electrophilic sites more attractive. In addition, the double bond at the focal point can be converted easily and in high yields to the primary or secondary alcohol by a standard hydroboration/oxidation protocol[10b,23a] or ozonolysis/reduction sequence,[23b] respectively. Using Williamson ether synthesis and an ozonolysis/reduction sequence for subsequent activation and growth steps allowed us to prepare bifunctional polyglycerol dendrons up to the fourth generation in high yields. Additionally, ozonolysis and hydride reduction, as opposed to hydroboration with 9-borabicyclo-[3.3.1]nonane (9-BBN) and oxidation with $H_2O_2$, proceeded smoothly in all cases and gave the desired compounds in pure form.

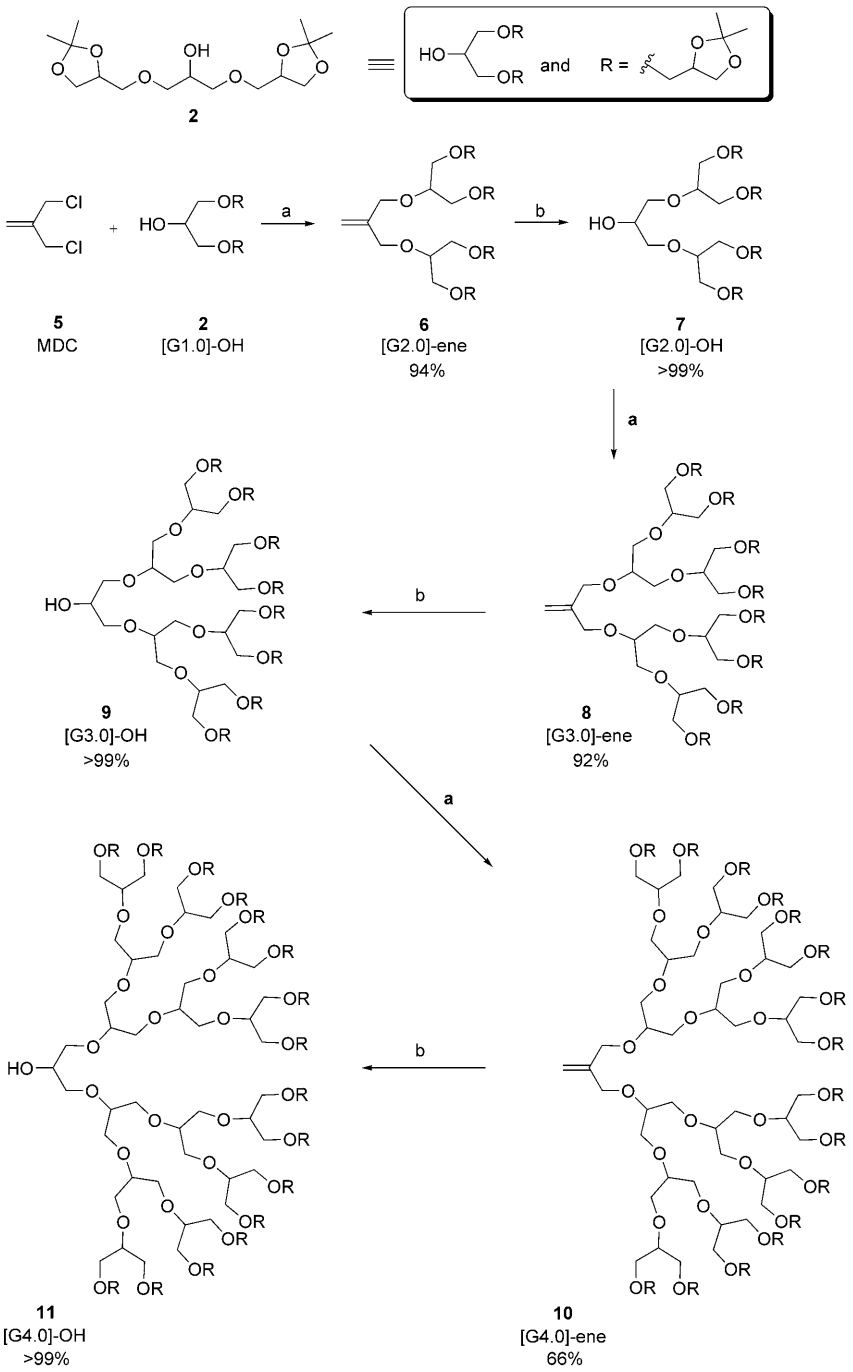
As a starting material we chose commercially available triglycerol (**1**), the terminal diol units of which were converted to the corresponding diacetal by catalytic reaction with acetone dimethylacetal.[24] The acetal protecting group is stable under strongly basic, reductive, and oxidative conditions.[25] In addition, deprotection of the terminal hydroxy groups, which can be further modified if desired, can be performed under mild acidic conditions. Even though triglycerol contains a considerable amount of other oligomers, such as di- and tetraglycerol, we decided that this concept is the more straightforward approach for scaleup. After acetal protection [G1.0]-OH (**2**) can be obtained on a scale of up to 600 g in highly pure form. Alternatively, **2** can also be obtained from acetal-protected glycerol by the procedure shown in Scheme 1 (bottom).




Scheme 1. Syntheses of acetal-protected triglycerol.

Second-generation [G2.0]-ene (**6**) was synthesized by reaction of 2.1 equiv of [G1.0]-OH (**2**) with a suspension of sodium hydride and MDC in dry THF in the presence of catalytic amounts of KI, [15]crown-5, and [18]crown-6 (Scheme 2). The presence of [15]crown-5 during deprotonation of the OH group and subsequent addition of [18]crown-6/KI allows us to generate a more reactive secondary alcoholate in the core and to improve the coupling yields dramatically. Therefore, we did not observe any formation of monosubstituted MDC. Due to the similar polarity of starting material **2** and [G2.0]-ene (**6**), purification by column chromatography on a multigram scale was incomplete. Therefore, on large scales (up to 100 g), we used HPLC with 2-propanol/*n*-hexane as eluent to separate all [G*n*]-ene products. The unsaturated compound was then ozonolyzed and reduced to the secondary alcohol by treatment with sodium borohydride, and [G2.0]-OH (**7**) was obtained by simple extraction in excellent yield and in very pure form. For all other dendron modifications column filtration was sufficient for purification.




Scheme 2. Convergent approach to bifunctional polyglycerol dendrons. a) NaH, [15]crown-5, MDC, [18]crown-6, KI, THF, reflux, 24 h; b) 1. $O_3$, $CH_2Cl_2$/MeOH (1/1), 2. $NaBH_4$.

To synthesize the next generations, compound **7** was again treated with MDC in THF, followed by the $O_3$/$NaBH_4$ reaction. Both [G3.0]-ene (**8**) and [G3.0]-OH (**9**) were obtained in very high yields. Up to generation [G4.0] monosubstitution of MDC was not observed, but a significant decrease in yield for [G4.0]-ene (**10**) was. This was attributed to steric hindrance after the attack of the first dendritic alcohol group of compound **9** on MDC and to difficulties in purification. All [G*n*]-ene and [G*n*]-OH compounds were isolated as transparent, slightly yellow or colorless viscous oils. We also tried to synthesize [G5.0]-ene, but due to difficulties in purification we were only able to detect the desired product by ESIMS.

Identification of the focal functionality by NMR and IR spectroscopy facilitated characterization of these dendritic structures, especially for higher generations. The integration ratio calculated from $^1$H NMR between acetal groups and focal functionality verified retention of protecting groups and the number of generations. The purity of polyether dendrons was assessed by elemental analysis and high-resolution mass spectroscopy. A single species was observed in the mass spectrum corresponding to the expected isotopic ratio for $[M+H]^+$, $[M+Na]^+$, and $[M+K]^+$. In some cases, the presence of $[M+NH_4]^+$ and

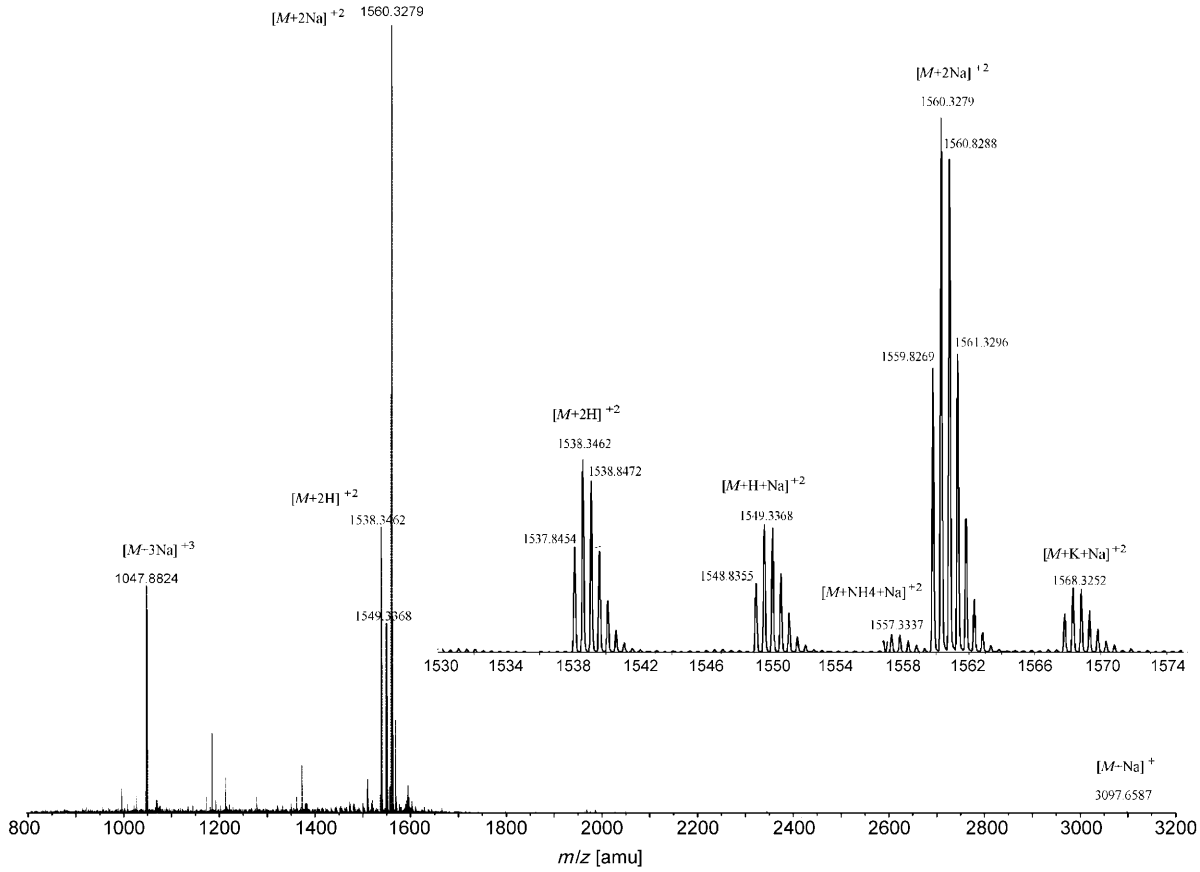
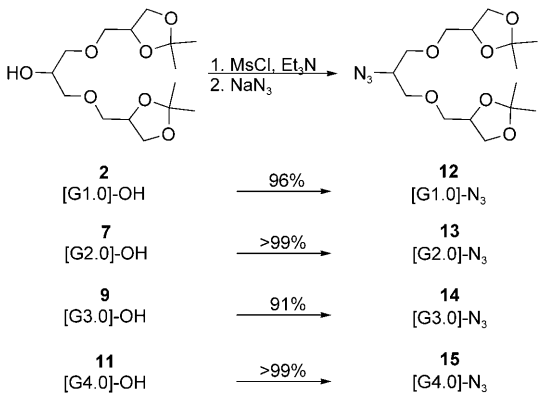



Figure 1. ESI-TOF mass spectrum of **25c** ($m/z$ 3073.6852).

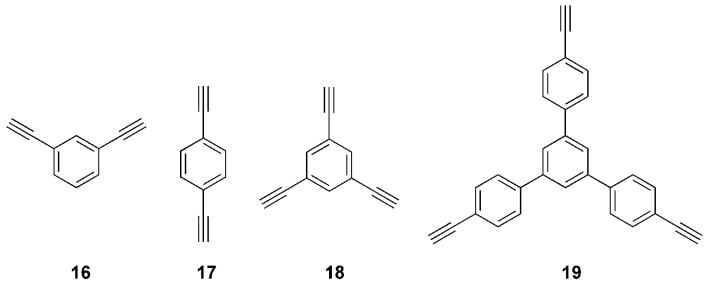
very strong signals of doubly charged ions were observed (e.g., ESI-TOF-MS of **25c**, Figure 1).

We previously reported a divergent approach to bifunctional glycerol dendrons with azide functionality in the core.[16] We used the same reaction sequence to functionalize the focal point of all polyglycerol dendrons with azo groups (Scheme 3). The free secondary hydroxyl group of [G1.0]-OH was converted to the corresponding mesylate[26] and without further purification treated with sodium azide[27] to give [G1.0]-$N_3$ in 96% yield over two steps. The same reaction sequence was applied to the higher generations of polyglycerol dendrons, and the desired monoazides were obtained in excellent yields.

**Design and synthesis of modular core–shell architectures with click dendrons**: In designing dendrimers for functionalization by click chemistry, multifunctional azide- or acetylene-terminated core molecules are required. Initially, commercially available aromatic oligoacetylene cores **16–18** were chosen for our modular approach with monoazido dendrons (Scheme 4). In addition, **19** was synthesized according to the procedure described by Müllen et al.[28] starting from 1,3,5-tris(4-bromophenyl)benzene.[29]




Scheme 3. Synthesis of monoazido glycerol dendrons.




Scheme 4. Oligoacetylene aromatic cores.

The first click reactions between compounds **16–18** and [G1.0]-$N_3$ were performed according to the procedure described by Sharpless et al.[30] with 5 mol% $CuSO_4$, 10 mol% ascorbic acid/10 mol% NaOH (to form sodium ascorbate in situ) in water/THF (1/1) at room temperature. However, the reaction times were very long and the conversions incomplete. Additionally, cleavage of acetal groups was observed, probably due to incomplete salt formation. Hence, we modified the coupling procedure, first by excluding the presence of acid and second by using additional catalyst to shorten the reaction times. In the course of optimization, we found that 5–15 mol% of $CuSO_4$, 10–30 mol% of sodium ascorbate, and 10–30 mol% of diisopropylethylamine (DIPEA) were sufficient to generate the desired core–shell structures in very good yields (Table 1, Scheme 5). As shown in Table 1, the yields of **20–23** isolated from the coupling of [G3.0]-$N_3$ to aromatic cores **16–18** were in the range of 30–44%, mainly due to the steric hindrance of dendrons and core and difficulties in purification.

Table 1. Yields for click coupling of monoazido glycerol dendrons to the aromatic cores and after removal of acetal groups.

| Entry | Aromatic core | [G*n*]-$N_3$ | Coupling product | Yield[a] [%] | Deprotection product | Yield[a] [%] |
|---|---|---|---|---|---|---|
| 1 | **16** | [G1.0] | **20a** | 96 | **24a** | 86 |
| 2 | **16** | [G2.0] | **20b** | 97 | **24b** | 99 |
| 3 | **16** | [G3.0] | **20c** | 32 | **24c** | 99 |
| 4 | **17** | [G1.0] | **21a** | 97 | **25a** | 88 |
| 5 | **17** | [G2.0] | **21b** | 78 | **25b** | 95 |
| 6 | **17** | [G3.0] | **21c** | 30 | **25c** | 98 |
| 7 | **18** | [G1.0] | **22a** | 98 | **26a** | 96 |
| 8 | **18** | [G2.0] | **22b** | 91 | **26b** | 84 |
| 9 | **18** | [G3.0] | **22c** | 44 | **26c** | 92 |
| 10 | **19** | [G1.0] | **23a** | 99 | **27a** | 87 |
| 11 | **19** | [G2.0] | **23b** | 87 | **27b** | 87 |
| 12 | **19** | [G3.0] | **23c** | 75 | **27c** | 91 |

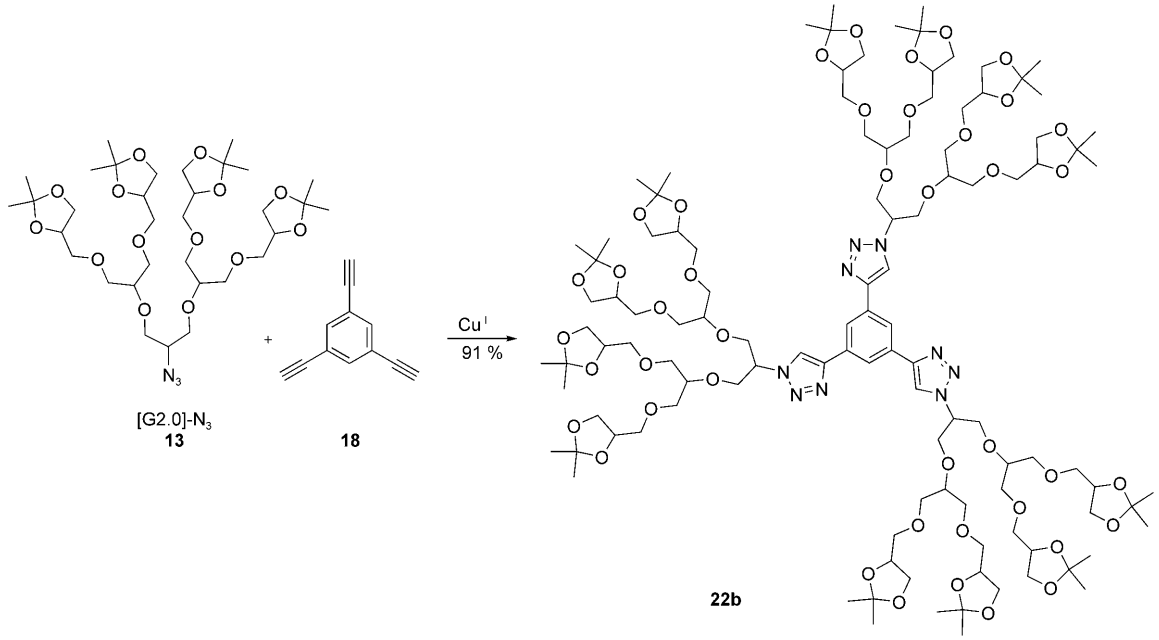
[a] Yields of isolated products.

Traces of copper salts in the products were easily removed by washing with a saturated solution of ethylenediaminetetraacetic acid (EDTA). To obtain high conversions, we tried to use stoichiometric amounts of the azides (2–3 equiv depending on core functionality), but formation of byproducts was observed. Therefore, in all cases an excess of 0.1 equiv of monoazido dendrons per triple bond was used. Purification was performed by flash column chromatography or HPLC.

Finally, the acetal protecting groups were removed in almost quantitative yield by stirring with an acidic ion-exchange resin in methanol to obtain the water-soluble core–shell architectures (Scheme 6). Because 1,2,3-triazole is a weak base, the ion-exchange beads were washed with 5% $Et_3N$ in MeOH in order to obtain the desired water-soluble dendrimers **24–27** in 84–99% yield (Table 1).

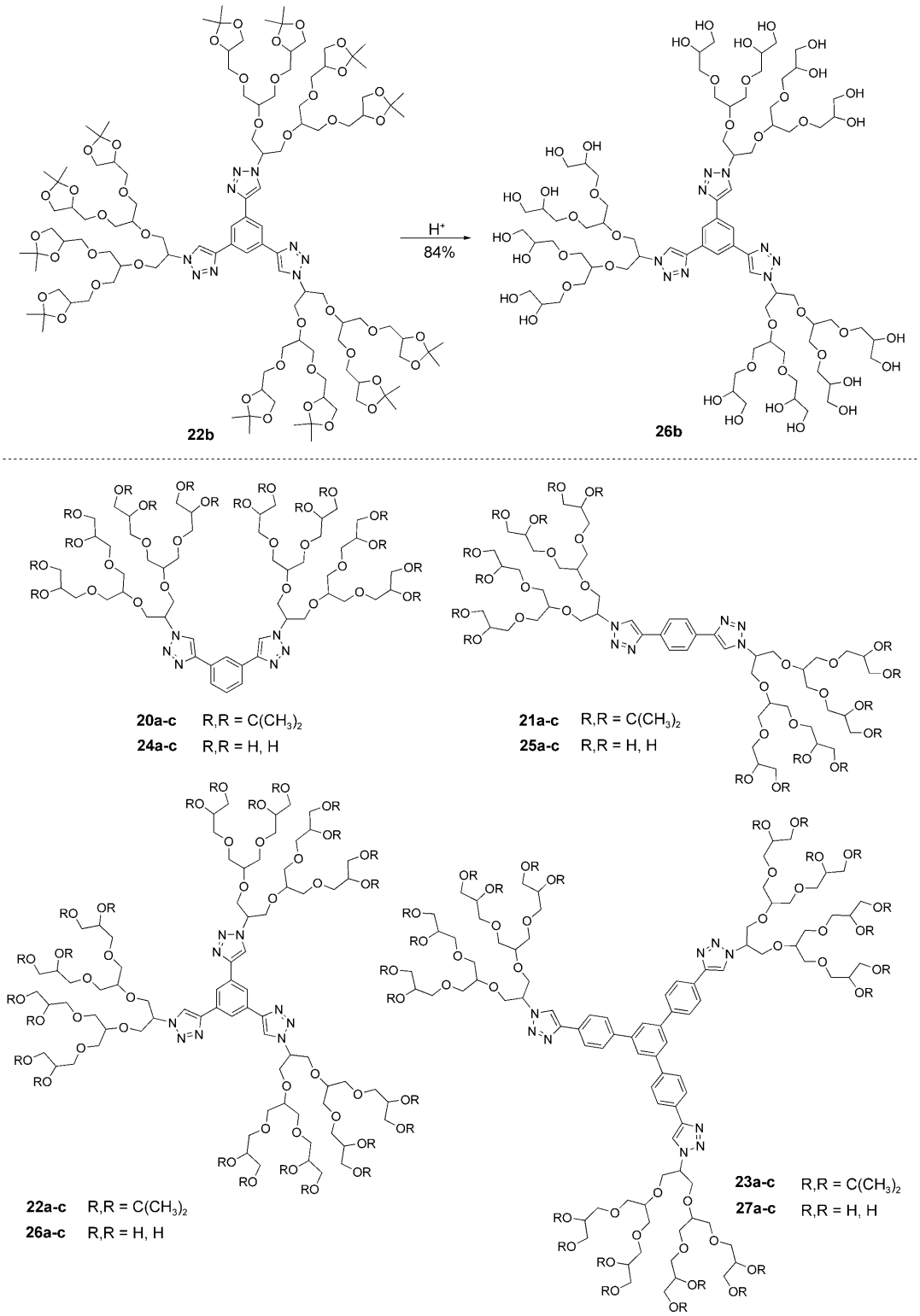
## Structure–transport relationship

*Complex formation with Nile red*: We investigated the transport properties of **24–27** by using Nile red, a neutral, poorly water soluble, and environmentally sensitive fluorescent dye (Figures 2 and 3). The fluorescence of Nile red strongly depends on the polarity of the environment; it is redshifted in polar solvents and reaches its maximum blueshift and intensity in nonpolar solvents/environment.[31] The remarkable sensitivity of Nile red was beneficial in studying the local polarity of bolaamphihiles,[32] micelles,[33] and interactions with cyclodextrins.[34] Small changes in the organization of the surfactants in the solvent system could be monitored




Scheme 5. Functionalization of the oligoacetylene core by glycerol dendrons: 5–15 mol% $CuSO_4$, 10–30 mol% sodium ascorbate, and 10–30 mol% DIPEA, THF/$H_2O$ (1/1).




Scheme 6. Removal of the acetal groups: Dowex 50W, MeOH, reflux. Core–shell architectures based on polyglycerol dendrons (coupling with [G2.0] is shown).

with Nile red,[33c] and the specific properties of this hydrophobic dye can also be used to characterize new amphiphilic molecules and their self-assembly processes.

For the dye solubilization measurements, 2.5 mL of an aqueous solution of the respective compound at a concentration of 1.0 g $L^{-1}$ and 3 mg of Nile was stirred at room temperature for 24 h. These saturated solutions were filtered

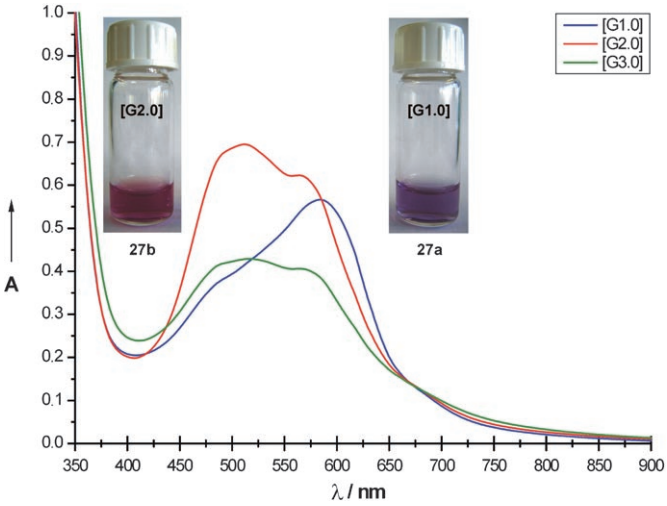



Figure 2. UV spectra of the complexes of **27a–c** ($c = 1\ mg\,mL^{-1}$) with Nile red.

to remove all solids. Then UV spectroscopy was carried out at 25 °C. Calibration curves for Nile red in toluene, acetone, methanol, and ethanol were recorded by using known concentrations of dye in the respective solvent. Assuming that the extinction coefficients of dye in the solvents are almost the same as in water, the amount of solubilized Nile red in the polymer solution can be calculated (see Figure 3). All saturated aqueous solutions of compounds **24–27** show good long-term stability (several months).

*Characterization of polymer–dye complexes*: Figure 3a summarizes the Nile red transport efficiency as a function of dendrimer generation and the structure of the hydrophobic core.

Even through Nile red is solubilized by each type of structure, the highest transport efficiency (w/w) is obtained for the compounds with the largest hydrophobic core. The highest value (6.1 mg Nile red) for this class of substance was obtained for [G2.0] (Scheme 6, Figures 2 and 3). Nevertheless, a clear dependence on the size of the core and the dendrimer generation can be seen in Figure 3b. As expected, the transport capacity (mmol dye/mol polymer) of the dye improved significantly with increasing core size, especially for [G3.0]. The transport capacity also increases with higher dendron generation. In contrast to a previous report on polyglycerol dendrons coupled to a biphenyl core by amide bonds,[16a] here we find a clear and systematic dependence of complex formation with Nile red on dendrimer generation.

The adsorption spectrum of Nile red is strongly dependent on solvent/environment and shows a large redshift with increasing solvent/environment polarity.[31a,c] The absorption spectra (Figure 2) revealed a strong red shift of the absorption band of Nile red in the [G1.0] dendron complex, with $\lambda_{max} = 585$ nm, and a blueshift for [G2.0] and [G3.0] dendron complexes, with $\lambda_{max} = 515$ nm. The first shift suggests that a very polar environment, such as glycerol groups, surrounds the Nile red molecules. Probably, the hydrophobic cores

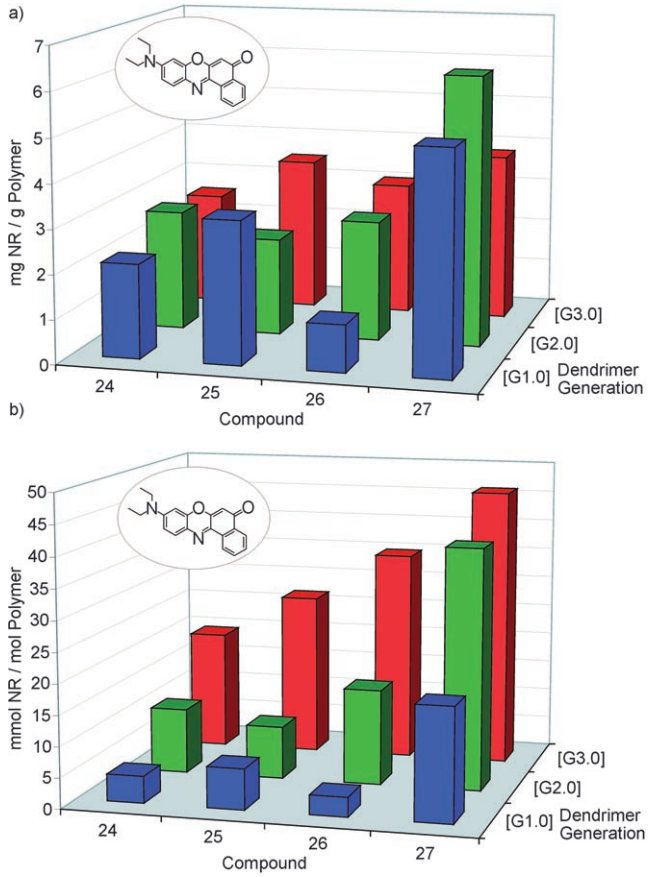



Figure 3. Structure–transport relationship of core–shell architectures 24–27 with Nile red (NR). a) mg NR/g polymer. b) mmol NR/mol polymer. For reasons of clarity the error bars of the UV measurements are not shown; these deviations are typically in the range of ±15%.

coupled with the smallest dendron [G1.0] tend to form aggregates by π–π interactions, and therefore the dye was not accommodated into the core. In the case of higher generations, for which the maximum absorption is shifted to lower wavelengths, Nile red is located more in the hydrophobic core. The observable band splitting in UV absorbance (nicely visible for compound **27b**) is a typical behavior of Nile red in nonpolar solvents/environments.[31c] This leads to the conclusion that an extended aromatic core is required for efficient encapsulation and transport of hydrophobic compounds such as Nile red. Especially in comparison to our previous work[16a] in which polyglycerol dendrons were attached to a biphenyl core by amide bonds, we significantly improved the encapsulation of Nile red by a factor of about 200 by increasing both core and dendrimer size, as shown in Figure 3.

## Conclusion

In conclusion, we have demonstrated a new, osmium-free convergent approach to monoazido polyglycerol dendrons, as opposed to the traditional divergent pathway. Glycerol

dendrimers are readily accessible on multigram scale up to the fourth generation, which is an important advantage over the conventional divergent pathway. Additionally, with this environment friendly synthetic pathway (less toxic reagents used in only small excess) we achieved higher structural purity and could apply simple separation protocols, such as column filtration.

Furthermore, a library of core–shell architectures **24–27**, based on a variety of aromatic cores and different generations of highly biocompatible click dendrons, were prepared by using a click chemistry concept. The unprecedented characteristic properties of the click dendrons, such as easy accessibility and solubility in water, make them a powerful tool for the modification of different hydrophobic cores with highly biocompatible and water-soluble shells. In addition these new architectures were used as solubilizing agents for the hydrophobic dye Nile red. The structure–transport relationship showed a clear dependence on core size and generation of the polyglycerol dendrons. These new dendritic polyglycerol architectures with extended aromatic cores show much higher transport efficiency than the previously reported biphenyl-based structures.

## Experimental Section

**General remarks**: Reactions requiring dry conditions were carried out in Schlenk glassware under argon. Dry, analytical-grade solvents were purchased from Acros or Aldrich and used as received. Triglycerol was obtained as a gift from Solvay Chemicals GmbH and used as received. $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker AB 250 (250 and 67.5 MHz for $^1$H and $^{13}$C, respectively), Bruker ECX 400 (400 and 100 MHz for $^1$H and $^{13}$C, respectively), and Delta JEOL Eclipse 500 (500 and 125 MHz for $^1$H and $^{13}$C, respectively) spectrometers at 25 °C. AMX 500 and ECX 400 spectrometers were used to record high-resolution $^{13}$C NMR spectra. The spectra were calibrated on the solvent peak ($CDCl_3$: $\delta = 7.26$ ppm for $^1$H and $\delta = 77.0$ ppm for $^{13}$C; $CD_3OD$: $\delta = 4.84$ ppm for $^1$H and $\delta = 49.05$ ppm for $^{13}$C; [D$_6$]acetone: $\delta = 2.05$ ppm for $^1$H and $\delta = 30.83$ ppm for $^{13}$C). Flash chromatography was performed on silica gel 60 (230–400 mesh) with head pressure developed by means of compressed air. IR spectra were recorded on KBr pellets on a Nicolet 5SXC FTIR Interferometer. Elemental analyses were performed on a Perkin-Elmer EA 240. For ESI-TOF measurements an Agilent 6210 ESI-TOF (Agilent Technologies, Santa Clara, USA) and for electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry (ESI-FTICRMS) measurements an Ionspec QFT-7 (Varian Inc., Lake Forest, USA) were used. HPLC was carried out on a Knauer HPLC (pump K-1800) using a Knauer RI-detector K-2401 and a Nucleosil 50-5 (32×240) column. UV measurements were carried out on a S-3100 System UV/Vis spectrometer (SCINCO) at 25 °C.

**Typical encapsulation procedure and determination of transport capacity**: Compounds **24–27** were dissolved in Milli-Q water (2.5 mL) at a concentration of 1.0 g L$^{-1}$, and Nile red (3 mg) as a fine powder was added. The obtained suspension was stirred vigorously for 24 h with a magnetic stirrer at 1000 rpm. Next the insoluble solid residue of the dye was removed by filtration through a 0.2 μm cellulose acetate filter (Whatman), and the obtained clear solution was analyzed by UV/Vis spectroscopy. Obtained adsorptions were compared with a calibration curve of the Nile red to determine the concentration of the guest molecule in the solution. The UV/Vis spectra were recorded from 220 to 1000 nm with water as reference.

**Acetal protection of triglycerol (1) to give (2)**: Triglycerol (**1**; 300 g, 1.25 mol) was gently heated with a heat gun (max. 120 °C) until it took on a liquid consistency. 2,2-dimethoxypropane (0.608 L, 4.995 mol) was added followed by slow addition of *p*-toluenesulfonic acid (PTSA; 15.12 g, 0.125 mol). The reaction was carried out overnight at 30–40 °C. After the mixture had been stirred for 0.5 h, a homogeneous solution was obtained. The resulting yellow-orange solution was neutralized by addition of triethylamine (0.125 mol) and subsequent stirring for 30 min at room temperature. Then the solvent was evaporated in vacuo and the remaining crude liquid was purified by filtration over silica gel (ethyl acetate/*n*-hexane 1/2, 2/1, 6/1) or by HPLC (15% 2-propanol in *n*-hexane) to give **2** as a pale yellow oil (70–78%; triglycerol contains ca. 20–30% other oligomers). $^1$H NMR (500 MHz, [D$_6$]acetone, 25 °C): $\delta = 4.19$ (q, $J = 11.9$, 6.3 Hz, 2H), 4.00 (dd, $J = 8.2$, 6.4 Hz, 2H), 3.84 (m, 1H), 3.75 (td, $J = 4.9$, 1.5 Hz, 1H), 3.69 (dd, $J = 8.2$, 6.3 Hz, 2H), 3.50 (ddd, $J = 31.8$, 10.1, 5.5 Hz; ddd, $J = 17.4$, 11.9, 6.3 Hz, 8H), 2.83 (s, 1H, OH), 1.33 (s, 6H; $CH_3$), 1.28 ppm (s, 6H; $CH_3$); $^{13}$C NMR (125 MHz, [D$_6$]acetone, 25 °C): $\delta = 109.4$, 75.6, 73.9, 73.8, 73.14, 73.12, 70.17, 67.4, 27.1, 25.7 ppm; FABMS (*m*-nitrbenzyl alcohol (mNBA) matrix) found for $C_{15}H_{28}O_7$ (calcd 320.18): *m*/*z* (%): 343.2 $[M+Na]^+$, 321.3 $[M+H]^+$; elemental analysis calcd (%) for $C_{15}H_{28}O_7$ (calcd 320.38): C 56.23, H 8.81; found: C 55.88, H 8.65.

**General procedure for synthesis of [G*n*]-ene**: [G*n*]-OH (1.05 equiv per Cl), 60% NaH (2.5–5.0 equiv per OH) in mineral oil, cat. [15]crown-5, and freshly distilled dry THF were placed in a dry two-necked round-bottomed flask under an Ar atmosphere. After the mixture had been stirred for 2–3 h at 40 °C, 1.0 equiv of methallyl dichloride and cat. KI and [18]crown-6 were added to the solution. The mixture was stirred under reflux for 12–24 h. After the mixture was cooled to room temperature, the reaction was quenched with distilled water and extracted with dichloromethane. The organic layer then was dried over $Na_2SO_4$ and the solvent was removed under vacuum. The residue was purified by HPLC with 2-propanol/*n*-hexane as eluent.

**[G1.0]-ene (3)**: Reaction conditions and workup were as described above, with solketal **4** (15.0 g, 0.113 mol, 2.1 equiv), NaH (60% in mineral oil, 11.18 g, 0.284 mol, 2.5 equiv per OH), MDC (6.25 mL, 54.05 mmol, 1.0 equiv), and cat. KI, [15]crown-5, and [18]crown-6 in THF (150 mL). Purification of the residue by silica-gel column chromatography (ethyl acetate/*n*-hexane 1/4) provided **3** (16.93 g, 99%) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 5.17$ (s, 2H), 4.23–4.27 (q, $J = 6.0$ Hz, 2H), 4.02–4.05 (dd, $J = 6.4$, 8.3 Hz, 2H), 4.0–4.01 (m, 4H), 3.70–3.73 (dd, $J = 6.4$, 8.2 Hz, 2H), 3.40–3.50 (ddd, $J = 5.6$, 9.9, 34.5 Hz, 4H), 1.39 (s, 6H; $CH_3$), 1.33 ppm (s, 6H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 142.1$, 114.6, 109.4, 74.7, 72.1, 71.2, 66.9, 26.8, 25.5 ppm; IR: $\tilde{\nu} = 2986$, 2869, 1455, 1371, 1256, 1214, 1089, 845 cm$^{-1}$; EIMS (40 °C) found for $C_{16}H_{28}O_6$ (calcd 316.1886): *m*/*z* (%): 316.2 (0.6) $[M^+]$, 301.2 (24.5) $[M^+-CH_3]$, 43 (100) $[C_2H_3O^+]$; elemental analysis calcd (%) for $C_{16}H_{28}O_6$ (316.39): C 60.74, H 8.92; found: C 60.85, H 8.47.

**[G2.0]-ene (6)**: Reaction conditions and workup were as described above, with alcohol **2** (90.0 g, 0.281 mol, 2.1 equiv), NaH (60% in mineral oil, 28.09 g, 0.702 mol, 2.5 equiv per OH), MDC (15.48 mL, 16.72 g, 133.8 mmol, 1.0 equiv), cat. KI, [15]crown-5, and [18]crown-6 in THF (650 mL). Purification of the residue by by HPLC (25% 2-propanol in *n*-hexane) gave **6** (87.1 g, 94%) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 5.15$ (dd, $J = 4.7$, 13.2 Hz, 2H), 4.23–4.27 (2×q, $J = 6.1$, 5.7 Hz, 4H), 4.09 (d, $J = 10.2$ Hz, 3H), 4.02–4.05 (dd, $J = 6.6$, 8.1 Hz, 4H), 3.96 (d, $J = 11.6$ Hz, 1H), 3.72–3.70 (m, $J = 8.2$ Hz, 4H), 3.65–3.51 (br m, 14H), 3.45 (dt, $J = 5.7$, 9.6 Hz, 4H), 1.37 (s, 12H; $CH_3$), 1.33 ppm (s, 12H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 143.0$, 114.1, 109.3, 78.62, 78.60, 74.71, 74.69, 74.55, 74.54, 72.43, 72.41, 71.5, 71.3, 70.7, 70.1, 66.9, 66.7, 26.7, 25.3 ppm; IR: $\tilde{\nu} = 2986$, 2875, 1456, 1371, 1256, 1214, 1082, 975, 918, 885 cm$^{-1}$; EIMS (120 °C) found for $C_{34}H_{60}O_{14}$ (calcd 692.3983): *m*/*z* (%): 692.3 (1.5) $[M^+]$, 677.2 (34.9) $[M^+-CH_3]$, 114.9 (100) $[C_6H_{11}O_2^+]$, 101.0 (90.1) $[C_5H_9O_2^+]$, 55 (33.3) $[C_3H_3O^+]$, 42.9 (37.8) $[C_2H_3O^+]$.

**[G3.0]-ene (8)**: Reaction conditions and workup were as described above, with alcohol **7** (50.0 g, 71.75 mmol, 2.1 equiv), NaH (60% in mineral oil, 14.35 g, 0.36 mol, 5 equiv per OH), MDC (3.95 mL, 4.27 g, 34.17 mmol, 1.0 equiv), cat. KI, [15]crown-5, and [18]crown-6 in THF (400 mL). Purification of the residue by HPLC (50% 2-propanol in *n*-hexane) gave **8** (45.4 g, 92%) as a colorless oil. $^1$H NMR (250 MHz,

$CDCl_3$, 25 °C): $\delta = 5.15$ (s, 2H), 4.22 (q, $J = 5.8$ Hz, 8H), 4.03 (dd, $J = 6.9$, 13.6 Hz, 8H), 4.01 (s, 4H), 3.70 (dd, $J = 6.6$, 7.9 Hz, 8H), 3.77–3.41 (br m, 46H; $CH_2CH$ backbone), 1.39 (s, 24H; $CH_3$), 1.33 ppm (s, 24H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 143.1$, 113.6, 109.3, 78.4, 74.71, 74.6, 74.55, 74.54, 72.4, 72.41, 71.5, 71.3, 70.7, 70.1, 66.9, 66.7, 26.7, 25.4 ppm; IR: $\tilde{\nu} = 2985$, 2874, 1456, 1371, 1256, 1214, 1083, 845 $cm^{-1}$; ESI-TOF-MS found for $C_{70}H_{124}O_{30}$ (calcd 1444.8177): $m/z$ (%): 1445.8227 $[M+H]^+$, 1467.8045 $[M+Na]^+$; elemental analysis calcd (%) for $C_{70}H_{124}O_{30}$ (1445.72): C 58.15, H 8.65; found: C 58.08, H 8.24.

**[G4.0]-ene (10)**: Reaction conditions and workup were as described above, with alcohol **9** (25.0 g, 17.25 mmol, 2.1 equiv), NaH (60% in mineral oil, 3.45 g, 86.25 mmol, 5 equiv per OH), MDC (0.95 mL, 1.03 g, 8.21 mmol, 1.0 equiv), cat. KI, [15]crown-5, and [18]crown-6 in THF (220 mL). Purification of the residue by by HPLC (50% 2-propanol in *n*-hexane) gave **10** (15.9 g, 66%) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 5.15$ (s, 2H), 4.21 (m, 16H), 4.02 (m, 20H), 3.70 (m, 16H), 3.63–3.42 (br m, 102H; $CH_2CH$ backbone), 1.37 (s, 48H; $CH_3$), 1.33 ppm (s, 48H; $CH_3$); $^{13}$C NMR (67.5 MHz, $CDCl_3$, 25 °C): $\delta = 143.2$, 112.73, 109.23, 78.78, 78.60, 78.35, 78.28, 74.70, 74.54, 72.44, 71.97, 71.68, 71.55, 71.42, 71.30, 71.14, 70.58, 70.15, 69.93 66.88, 66.75, 26.76, 25.38 ppm; IR: $\tilde{\nu} = 2985$, 2874, 1456, 1371, 1256, 1214, 1083, 844 $cm^{-1}$; ESI-TOF-MS found for $C_{142}H_{252}O_{62}$ (calcd 2949.6566): $m/z$ (%): 2950.6563 $[M+H]^+$, 2972.6260 $[M+Na]^+$; elemental analysis calcd (%) for $C_{142}H_{252}O_{62}$ (2951.48): C 57.79, H 8.61; found: C 57.52, H 8.92.

**General procedure for the synthesis of [G*n*]-OH**: [G*n*]-ene (1.0 equiv) was dissolved in dry MeOH/$CH_2Cl_2$ (1/1, $c = 0.13$ mol $L^{-1}$) and cooled to −78 °C. Ozone was bubbled through the solution until it turned blue. After the removal of excess ozone with a vigorous stream of oxygen, sodium borohydride (10.0 equiv) was added. While stirring for 12–15 h the mixture was allowed to slowly warm to room temperature. The reaction mixture was quenched by addition of saturated $NH_4Cl$ solution followed by stirring for 1–2 h. The phases were separated and the aqueous layer was extracted with dichloromethane. The combined organic phases were washed with water, dried over anhydrous $Na_2SO_4$, and filtered. Evaporation of the solvent yielded the target compound in pure form.

**[G1.0]-OH (2)**: Reaction conditions and workup were as described above, with **3** (10.0 g, 31.61 mmol, 1.0 equiv) and $NaBH_4$ (11.96 g, 0.316 mol, 10.0 equiv) in $CH_2Cl_2$/MeOH (30 mL). Extraction with $CH_2Cl_2$ yielded **2** (10.0 g, 99.0%) as a colorless oil.

**[G2.0]-OH (7)**: Reaction conditions and workup were as described above, with **6** (64.64 g, 93.3 mmol, 1.0 equiv) and $NaBH_4$ (35.3 g, 0.933 mol, 10.0 equiv) in $CH_2Cl_2$/MeOH (720 mL). Extraction with $CH_2Cl_2$ yielded **7** (64.9 g, 99.9%) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 4.22$ (2 × q, $J = 6.2$ Hz, 4H), 4.01 (dd, $J = 6.9$, 7.7 Hz, 4H), 3.86 (tt, $J = 5.5$, 10.9 Hz, 1H), 3.69 (m, 4H), 3.65 (m, 4H), 3.57–3.44 (br m, 18H), 3.18 (br s, 1H; OH), 1.39 (s, 12H; $CH_3$), 1.32 ppm (s, 12H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 109.3$ (4C), 78.6, 74.5, 72.4, 71.9 71.7, 71.6, 69.7, 66.7, 26.7, 25.3 ppm; IR: $\tilde{\nu} = 3490$, 2986, 2876, 1456, 1371, 1257, 1214, 1081, 975, 844, 515 $cm^{-1}$; FABMS found for $C_{33}H_{60}O_{15}$ (calcd 696.3932): $m/z$ (%): 719.4 $[M+Na]^+$; elemental analysis calcd (%) for $C_{33}H_{60}O_{15}$ (696.8205): C 56.88, H 8.68; found: C 56.73, H 8.81.

**[G3.0]-OH (9)**: Reaction conditions and workup were as described above, with **8** (35.0 g, 24.21 mmol, 1.0 equiv) and $NaBH_4$ (9.16 g, 0.242 mol, 10.0 equiv) in $CH_2Cl_2$/MeOH (200 mL). Extraction with $CH_2Cl_2$ yielded **9** (34.8 g, 99.1%) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 4.2$ (m, 8H), 4.01 (m, 8H), 3.82 (m, 1H), 3.72–3.41 (br m, 59H; $CH_2CH$ backbone, OH), 1.37 (s, 24H; $CH_3$), 1.32 ppm (s, 24H; $CH_3$); $^{13}$C NMR (67.5 MHz, $CDCl_3$, 25 °C): $\delta = 109.3$, 78.4, 74.7, 74.6, 72.4, 71.5, 71.2, 70.4, 66.7, 26.7, 25.4 ppm; IR: $\tilde{\nu} = 3460$, 2986, 2878, 1727, 1456, 1372, 1257, 1215, 1082, 975, 844 $cm^{-1}$; ESI-TOF-MS found for $C_{69}H_{124}O_{31}$ (calcd 1448.8127): $m/z$ (%): 1449.8207 $[M+H]^+$, 1466.8479 $[M+NH_4]^+$, 1471.8041 $[M+Na]^+$; elemental analysis calcd (%) for $C_{69}H_{124}O_{31}$ (1449.7043): C 57.17, H 8.62; found: C 56.87, H 8.60.

**[G4.0]-OH (11)**: Reaction conditions and workup were as described above, with **10** (10.0 g, 3.39 mmol, 1.0 equiv) and $NaBH_4$ (1.28 g, 33.88 mmol, 10.0 equiv) in $CH_2Cl_2$/MeOH (30 mL). Extraction with $CH_2Cl_2$ yielded **11** (10.0 g, 99.9%) as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 4.20$ (p, $J = 5.8$ Hz, 16H), 4.00 (m, 16H), 3.80 (m, 1H), 3.68 (m, 20H), 3.64–3.41 (br m, 102H; $CH_2CH$ backbone), 2.97 (br s, 1H; OH), 1.36 (s, 48H; $CH_3$), 1.30 ppm (s, 48H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 109.2$, 78.51, 78.29, 78.22, 74.62, 74.49, 72.38, 71.50, 71.35, 71.24, 71.05, 70.23, 69.85, 69.57, 66.79, 66.68, 26.72, 25.35 ppm; IR: $\tilde{\nu} = 3501$, 2985, 2875, 1456, 1371, 1256, 1214, 1106, 975, 844, 515 $cm^{-1}$; ESI-TOF-MS found for $C_{141}H_{252}O_{63}$ (calcd 2953.6515): $m/z$ (%): 2954.6738 $[M+H]^+$, 2976.6684 $[M+Na]^+$; 2992.6075 $[M+K]^+$; elemental analysis calcd (%) for $C_{141}H_{252}O_{63}$ (2955.4718): C 57.30, H 8.59; found: C 56.98, H 8.62.

**General procedure for the synthesis of azide dendrons [G*n*]-$N_3$**: Methanesulfonyl chloride (MsCl, 1.1–3.0 equiv) was added to a solution of [G*n*]-OH (1.0 equiv) and triethylamine (1.1–3.0 equiv) in toluene cooled to 0 °C in an ice bath. Progress of the reaction was monitored by TLC. After completion, the precipitate was removed by filtration and the mixture concentrated under vacuum to give the final product (100%). The crude product was used for next reaction step. $NaN_3$ (2.5–5.0 equiv) was added to a solution of [G*n*]-OMs (1.0 equiv) in dry DMF. After the mixture had been stirred at 120 °C under argon for 3 h, excess $NaN_3$ was filtered off and DMF was removed under high vacuum by cryodistillation. The crude product was purified by filtration over a thin layer of silica gel (ethyl acetate/*n*-hexane). [G*n*]-$N_3$ was obtained as a light yellow, viscous oil.

**[G1.0]-$N_3$ (12)**: Reaction conditions and workup were as described above, with **2** (20.0 g, 62.43 mmol, 1.0 equiv), $Et_3N$ (9.21 mL, 65.55 mmol, 1.1 equiv), MsCl (5.06 mL, 65.55 mmol, 1.1 equiv) in toluene (160 mL). The crude product [G1.0]-OMs (62.43 mmol, 1.0 equiv) was treated with $NaN_3$ (10.2 g, 0.157 mol, 2.5 equiv) in dry DMF (150 mL). Filtration through a thin layer of silica gel (ethyl acetate/*n*-hexane 2/1) gave **12** (20.7 g, 96%) as a light yellow, viscous oil. $^1$H NMR (500 MHz, [D$_6$]acetone, 25 °C): $\delta = 4.21$ (q, $J = 11.7$, 6.2, 5.6 Hz, 2H), 4.03 (ddd, $J = 8.2$, 6.4, 1.0 Hz, 2H), 3.76 (m, 1H), 3.72 (dd, $J = 8.2$, 6.3 Hz, 2H), 3.67 (tdd, $J = 9.6$, 7.8, 4.5 Hz, 2H), 3.61 (ddd, $J = 5.5$, 5.0, 2.2 Hz, 2H), 3.54 (ddd, $J = 17.9$, 10.3, 5.1 Hz, 4H), 1.34 (s, 6H; $CH_3$), 1.28 ppm (s, 6H; $CH_3$); $^{13}$C NMR (125 MHz, [D$_6$]acetone, 25 °C): $\delta = 109.6$, 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 $cm^{-1}$; FABMS (mNBA) found for $C_{15}H_{27}N_3O_6$ (calcd 345.39): $m/z$ (%): 346.3 $[M+H]^+$, 368.2 $[M+Na]^+$; elemental analysis calcd (%) for $C_{15}H_{27}N_3O_6$ (345.39): C 52.16, H 7.88, N 12.17; found: C 52.03, H 7.46, N 11.84.

**[G2.0]-$N_3$ (13)**: Reaction conditions and workup were as described above, with **7** (25.0 g, 35.88 mmol, 1.0 equiv), $Et_3N$ (5.45 mL, 39.46 mmol, 1.1 equiv), and MsCl (3.04 mL, 39.46 mmol, 1.1 equiv) in toluene (150 mL). The crude product [G2.0]-OMs (35.88 mmol, 1.0 equiv) was treated with $NaN_3$ (11.68 g, 0.179 mol, 5.0 equiv) in dry DMF (150 mL). Filtration through a thin layer of silica gel (ethyl acetate/*n*-hexane 6/1) gave **13** (25.6 g, 99%) as a light yellow, viscous oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 4.22$ (qtd, $J = 3.0$, 5.9, 8.7 Hz, 4H), 4.02 (dd, $J = 6.6$, 8.1 Hz, 4H), 3.71 (dd, $J = 7.3$ Hz, 5H), 3.67–3.51 (m, 18H), 3.47 (dt, $J = 5.3$, 10.3 Hz, 4H), 1.36 (s, 12H; $CH_3$), 1.39 ppm (s, 12H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 109.3$, 78.4, 74.6, 74.5, 72.4, 71.6, 71.4, 71.1, 66.7, 66.6, 60.5, 26.7, 25.3 ppm; IR (KBr): $\tilde{\nu} = 2986$, 2934, 2874, 2100, 1456, 1380, 1371, 1258, 1214, 1082, 1055, 975, 844, 515 $cm^{-1}$; ESI-TOF-MS found for $C_{33}H_{59}O_{14}N_3$ (calcd 721.3997): $m/z$ (%): 722.4001 $[M+H]^+$, 744.3880 $[M+Na]^+$, 760.3622 $[M+K]^+$.

**[G3.0]-$N_3$ (14)**: Reaction conditions and workup were as described above, with **9** (7.0 g, 4.83 mmol, 1.0 equiv), $Et_3N$ (1.34 mL, 9.66 mmol, 2.0 equiv), and MsCl (0.75 mL, 9.66 mmol, 2.0 equiv) in toluene (60 mL). The crude product [G3.0]-OMs (4.83 mmol, 1.0 equiv) was treated with $NaN_3$ (1.57 g, 24.14 mmol, 5.0 equiv) in dry DMF (60 mL). Filtration through a thin layer of silica gel (ethyl acetate/*n*-hexane 10/1) gave **14** (6.5 g, 91%) as a light yellow, viscous oil. $^1$H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 4.22$ (m, 8H), 4.02 (dd, $J = 6.5$, 8.2 Hz, 8H), 3.70 (dd, $J = 6.3$, 8.3 Hz, 8H), 3.77–3.42 (br m, 51H; $CHCH_2$ backbone), 1.39 (s, 24H; $CH_3$), 1.33 ppm (s, 24H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 109.3$, 79.0, 78.8, 78.4, 78.3, 74.7, 74.5, 72.4, 71.5, 71.4, 71.2, 70.3, 66.7, 66.6, 60.4, 26.8, 25.4 ppm; IR: $\tilde{\nu} = 2986$, 2934, 2874, 2100, 1456, 1380, 1371, 1258, 1214, 1082, 1055, 975, 844, 515 $cm^{-1}$; ESI-TOF-MS found for $C_{69}H_{123}O_{30}N_3$ (calcd 1473.8191): $m/z$ (%): 759.9144 $[M+2Na]^{2+}$,

1496.8243 $[M+Na]^+$; elemental analysis calcd (%) for $C_{69}H_{123}N_3O_{30}$ (1474.72): C 56.20, H 8.41, N 2.85; found: C 56.10, H 8.61, N 3.03.

**[G4.0]-$N_3$ (15)**: Reaction conditions and workup were as described above, with **11** (6.0 g, 2.03 mmol, 1.0 equiv), $Et_3N$ (0.86 mL, 6.09 mmol, 3.0 equiv), and MsCl (0.47 mL, 6.09 mmol, 3.0 equiv) in toluene (40 mL). The crude product [G4.0]-OMs (2.03 mmol, 1.0 equiv) was treated with $NaN_3$ (0.66 g, 10.15 mmol, 5.0 equiv) in dry DMF (50 mL). Filtration through a thin layer of silica gel (2-propanol/*n*-hexane 1/1) gave **15** (6.02 g, 99.5%) as a light yellow, viscous oil. $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=4.21$ (m, 16H), 4.01 (m, 16H), 3.80 (m, 1H), 3.69 (m, 20H), 3.64–3.42 (br m, 102H; $CH_2CH$ backbone), 1.38 (s, 48H; $CH_3$), 1.32 ppm (s, 48H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta=109.25$, 79.08, 78.78, 78.58, 78.29, 74.70, 74.56, 72.46, 71.31, 71.14, 69.91, 66.92, 66.77, 61.68, 26.78, 25.41 ppm; IR: $\tilde{\nu}=2985$, 2875; 2101, 1456, 1371, 1257, 1214, 1108, 975, 844, 515 cm$^{-1}$; ESI-TOF-MS found for $C_{141}H_{251}N_3O_{62}$ (calcd 2978.6580): 1015.8753 $[M+3Na]^{3+}$, 1490.3352 $[M+2H]^{2+}$, 1512.3181 $[M+2Na]^{2+}$, 3001.6304 $[M+Na]^+$.

**General procedure for the coupling of azide dendrons to the aromatic core**: DIPEA (10–30 mol% per triple bond) was added to 1.0 equiv of oligoacetylene core (**16**–**19**) and 1.1 equiv of [Gn]-$N_3$ per triple bond dissolved in THF. After the mixture had been stirred for 5 min, 10–30 mol% per triple bond of sodium ascorbate was added, followed by 5–15 mol% of $CuSO_4{\cdot}5H_2O$ per triple bond. (A stock solution of sodium ascorbate and $CuSO_4{\cdot}5H_2O$ in water was prepared in concentration 100 mg/mL) The THF/$H_2O$ ratio must be 1/1 (v/v). The heterogeneous mixture was stirred vigorously until TLC analysis indicated complete consumption of the starting material. The reaction mixture was diluted with water and extracted with dichloromethane. The combined organic layers were washed with a small amount of saturated solution of EDTA, dried with $Na_2SO_4$, and concentrated in vacuo. Purification by column chromatography or HPLC gave the desired product.

**Ph-1,3-click-[G1.0] (20a)**: Reaction conditions and workup were as described above, with **16** (0. 498 g, 3.948 mmol, 1.0 equiv), **12** (3.0 g, 8.686 mmol, 2.2 equiv), DIPEA (65.2 μL, 0.395 mmol, 0.1 equiv), sodium ascorbate (156.4 mg, 0.79 mmol, 0.2 equiv), and copper(II) sulfate pentahydrate (98.6 mg, 0.395 mmol, 0.1 equiv) in THF/$H_2O$ (16 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6/1) and 5% MeOH in $CH_2Cl_2$) gave **20a** (3.021 g, 95.6%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=8.26$ (s, 1H), 8.10–8.0 (m, 2H), 7.77 (m, 2H,), 7.42 (t, 1H, $J=7.7$ Hz), 4.90 (m, 2H), 4.93 (q, 1H, $J=5.6$ Hz), 4.63 (m, 1H), 4.45 (m, 1H), 4.18 (m, 4H), 3.96 (m, 10H), 3.72–3.41 (m, 13H), 1.39–1.29 ppm (m, 24H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta=147.15$, 146.93, 131.17, 129.15, 125.09, 122.66, 121.60, 121.46, 120.25, 120.17, 109.39, 109.36, 98.10, 77.68, 74.55, 74.42, 74.36, 72.62, 72.40, 72.31, 72.10, 71.56, 70.34, 70.07, 70.0, 66.31, 66.14, 60.54, 60.46, 60.39, 51.25, 51.10, 26.57, 25.17 ppm; IR: $\tilde{\nu}=3567$, 3135, 2985, 2877,1618, 1456, 1371, 1215, 1054, 974, 841, 798, 698, 516 cm$^{-1}$; ESI-TOF-MS found for $C_{40}H_{60}N_6O_{12}$ (calcd 816.4269): *m*/*z* (%): 817.4346 $[M+H]^+$, 839.4167 $[M+Na]^+$, 855.3911 $[M+K]^+$; elemental analysis calcd (%) for $C_{40}H_{60}N_6O_{12}$ (816.94): C 58.81, H 7.40, N 10.29; found: C 58.36, H 7.19, N 10.21.

**Ph-1,3-click-[G2.0] (20b)**: Reaction conditions and workup were as described above, with **16** (0.25 g, 1.982 mmol, 1.0 equiv), **13** (3.15 g, 4.36 mmol, 2.2 equiv), DIPEA (32.7 μL, 0.198 mmol, 0.1 equiv), sodium ascorbate (78.5 mg, 0.396 mmol, 0.2 equiv), and copper(II) sulfate pentahydrate (49.5 mg, 0.198 mmol, 0.1 equiv) in THF/$H_2O$ (16 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6/1) and 5% MeOH in $CH_2Cl_2$) gave **20b** (3.01 g, 97%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=8.31$ (s, 1H), 8.11, 8,07, 8,02 (m, 2H), 7.76 (br s, 2H,), 7.43 (t, 1H, $J=7.7$ Hz), 4.90 (m, 2H), 4.17 (m, 8H), 4.05 (m, 5H), 3.95 (m, 11H), 3.62 (m, 12H), 3.57–3.36 (br m, 32H), 1.34 (s, 24H; $CH_3$), 1.28 ppm (s, 24H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta=146.70$, 146.60, 131.39, 131.31, 129.19, 125.02, 122.51, 120.48, 120.29, 109.25, 109.18, 78.65, 78.33, 74.69, 74.64, 74.51, 72.40, 71.64, 71.46, 71.30, 70.18, 69.27, 66.58, 66.43, 61.18, 60.93, 26.65, 25.26 ppm; ESI-TOF-MS found for $C_{76}H_{124}N_6O_{28}$ (calcd 1568.8464): *m*/*z* (%): 1569.8499 $[M+H]^+$, 1591.8315 $[M+Na]^+$, 1607.8075 $[M+K]^+$.

**Ph-1,3-click-[G3.0] (20c)**: Reaction conditions and workup were as described above, with **16** (77.8 mg, 0.616 mmol, 1.0 equiv), **14** (2.0 g, 1.356 mmol, 2.2 equiv), DIPEA (10.2 μL, 0.062 mmol, 0.1 equiv), sodium ascorbate (24.4 mg, 0.123 mmol, 0.2 equiv), and copper(II) sulfate pentahydrate (15.4 mg, 0.062 mmol, 0.1 equiv) in THF/$H_2O$ (10 mL). Purification by HPLC (2% MeOH in $CH_2Cl_2$) gave **20c** (0.6 g, 32%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=8.40$–8.34 (m, 1H), 8.13 (m, 2H), 7.74, 7.73 (2s, 2H), 7.43 (t, 1H, $J=7.6$ Hz), 4.88 (m, 2H), 4.17 (m, 16H), 4.04 (m, 8H), 3.98 (m, 16H), 3.62 (m, 20H), 3.57–3.36 (br m, 86H), 1.34 (s, 24H; $CH_3$), 1.28 ppm (s, 24H; $CH_3$); $^{13}$C NMR (67.5 MHz, $CDCl_3$, 25°C): $\delta=$ 146.47, 131.57, 130.78, 129.10 (C-2), 125.05, 122.53, 122.51, 120.74, 109.22, 79.06, 78.80, 78.51, 78.31, 74.67, 74.53, 72.39, 71.48, 71.40, 71.24, 71.18, 70.29, 69.28, 66.80, 66.75, 66.62, 61.26, 26.71, 25.34 ppm; ESI-TOF-MS found for $C_{148}H_{252}N_6O_{60}$ (calcd 3073.6852): *m*/*z* (%): 1537.8480 $[M+2H]^{2+}$, 1559.8312 $[M+2Na]^{2+}$; elemental analysis calcd (%) for $C_{148}H_{252}N_6O_{60}$ (3075.5887): C 57.80, H 8.26, N 2.73; found: C 57.54, H 7.88, N 2.99.

**Ph-1,4-click-[G1.0] (21a)**: Reaction conditions and workup were as described above, with **17** (0. 498 g, 3.948 mmol, 1.0 equiv), **12** (3.0 g, 8.686 mmol, 2.2 equiv), DIPEA (65.2 μL, 0.395 mmol, 0.1 equiv), sodium ascorbate (156.4 mg, 0.79 mmol, 0.2 equiv), and copper(II) sulfate pentahydrate (98.6 mg, 0.395 mmol, 0.1 equiv) in THF/$H_2O$ (16 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6:1) and 5% MeOH in $CH_2Cl_2$) gave **21a** (3.071 g, 97%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=8.11$–8.0 (m, 2H), 7.87 (m, 4H), 4.94 (q, 1H, $J=5.4$ Hz), 4.62 (m, 1H), 4.47 (m, 1H), 4.20 (m, 4H), 3.97 (m, 10H), 3.74–3.43 (br m, 13H), 1.39–1.29 ppm (m, 24H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta=147.0$, 130.32, 125.90, 121.48, 121.34, 120.17, 109.48, 109.43, 77.74, 74.68, 74.60, 74.50, 74.41, 72.47, 72.13, 71.26, 71.21, 70.35, 70.18, 70.11, 70.06, 70.0, 66.34, 66.16, 60.45, 51.15, 26.64, 25.22 ppm; IR: $\tilde{\nu}=3567$, 3137, 2985, 2878, 1772, 1482, 1456, 1371, 1214, 1054, 973, 841, 735, 698, 516 cm$^{-1}$; QFTESIMS found for $C_{40}H_{60}N_6O_{12}$ (calcd 816.4269): *m*/*z* (%): 817.4342 $[M+H]^+$, 839.4152 $[M+Na]^+$, 855.3858 $[M+K]^+$; elemental analysis calcd (%) for $C_{40}H_{60}N_6O_{12}$ (816.94): C 58.81, H 7.40, N 10.29; found: C 58.71, H 7.29, N 10.10.

**Ph-1,4-click-[G2.0] (21b)**: Reaction conditions and workup were as described above, with **16** (0.25 g, 1.982 mmol, 1.0 equiv), **13** (3.15 g, 4.36 mmol, 2.2 equiv), DIPEA (32.7 μL, 0.198 mmol, 0.1 equiv), sodium ascorbate (78.5 mg, 0.396 mmol, 0.2 equiv), and copper(II) sulfate pentahydrate (49.5 mg, 0.198 mmol, 0.1 equiv) in THF/$H_2O$ (16 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6/1) and 5% MeOH in $CH_2Cl_2$) gave **21b** (2.42 g, 78%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=8.05$, 8,01, 7.97, 7.96 (m, 2H), 7.86 (s, 4H), 4.90 (m, 2H), 4.17 (m, 8H), 4.06 (m, 5H), 3.95 (m, 11H), 3.62 (m, 12H), 3.57–3.36 (br m, 32H), 1.34 (s, 24H; $CH_3$), 1.26 ppm (s, 24H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta=146.63$, 130.35, 125.85, 120.10, 109.26, 78.63, 78.31, 74.67, 74.62, 74.50, 72.38, 71.60, 71.47, 71.29, 71.16, 70.18, 69.27, 66.56, 66.41, 61.20, 60.92, 26.64, 25.24 ppm; ESI-TOF-MS found for $C_{76}H_{124}N_6O_{28}$ (calcd 1568.8464): *m*/*z* (%): 1569.8650 $[M+H]^+$, 1591.8483 $[M+Na]^+$.

**Ph-1,4-click-[G3.0] (21c)**: Reaction conditions and workup were as described above, with **16** (77.8 mg, 0.616 mmol, 1.0 equiv), **14** (2.0 g, 1.356 mmol, 2.2 equiv), DIPEA (10.2 μL, 0.062 mmol, 0.1 equiv), sodium ascorbate (24.4 mg, 0.123 mmol, 0.2 equiv), and copper(II) sulfate pentahydrate (15.4 mg, 0.062 mmol, 0.1 equiv) in THF/$H_2O$ (10 mL). Purification by HPLC (2% MeOH in $CH_2Cl_2$) gave **21c** (0.56 g, 30%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta=8.09$ (m, 2H), 7.88 (s, 4H), 4.83 (m, 2H), 4.18 (m, 16H), 4.04 (m, 7H), 3.98 (m, 17H), 3.66 (m, 20H), 3.57–3.38 (br m, 86H), 1.36 (s, 48H; $CH_3$), 1.30 ppm (s, 48H; $CH_3$); $^{13}$C NMR (67.5 MHz, $CDCl_3$, 25°C): $\delta=146.36$, 130.50, 125.85, 120.10, 109.22, 79.05, 78.81, 78.50, 78.31, 74.66, 74.52, 72.39, 71.49, 71.38, 71.19, 70.13, 69.27, 66.78, 66.60, 61.24, 26.69, 25.32 ppm; ESI-TOF-MS found for $C_{148}H_{252}N_6O_{60}$ (calcd 3073.6852): *m*/*z* (%): 1537.8454 $[M+2H]^{2+}$, 1548.8356 $[M+H+Na]^{2+}$, 1559.8268 $[M+2Na]^{2+}$, 1567.8268 $[M+Na+K]^{2+}$; elemental analysis calcd (%) for $C_{148}H_{252}N_6O_{60}$ (3075.5887): C 57.80, H 8.26, N 2.73; found: C 57.76, H 8.31, N 3.08.

**Ph-1,3,5-click-[G1.0] (22a)**: Reaction conditions and workup were as described above, with **18** (0.2 g, 1.332 mmol, 1.0 equiv), **12** (1.518 g, 4.395 mmol, 3.3 equiv), DIPEA (33.0 μL, 0.1998 mmol, 0.15 equiv), sodium ascorbate (79.2 mg, 0.3996 mmol, 0.3 equiv), and copper(II) sul-

fate pentahydrate (50.0 mg, 0.1998 mmol, 0.15 equiv) in THF/$H_2O$ (14 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6/1) and 5% MeOH in $CH_2Cl_2$) gave **22a** (1.55 g, 98.3%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta$ = 8.31 (s, 3H), 8.15 (m, 3H), 4.98 (q, 3H, $J$ = 5.6 Hz), 4.22 (m, 6H), 3.99 (m, 18H), 3.64 (m, 6H), 3.55–3.47 (m, 12H), 1.37 (s, 18H; $CH_3$), 1.31 ppm (s, 18H; $CH_3$); $C^{13}$ NMR (125 MHz, $CDCl_3$, 25°C): $\delta$ = 146.9, 131.9, 122.4, 120.7, 109.7, 74.7, 72.7, 72.4, 70.4, 70.3, 66.4, 60.9, 26.8, 25.4 ppm; ESI-TOF-MS found for $C_{57}H_{87}N_9O_{18}$ (calcd 1185.6169): $m/z$ (%): 1186.6277 $[M+H]^+$, 1208.6104 $[M+Na]^+$, 1224.5849 $[M+K]^+$.

**Ph-1,3,5-click-[G2.0] (22b)**: Reaction conditions and workup were as described above, with **18** (0.2 g, 1.332 mmol, 1.0 equiv), **13** (3.172 g, 4.395 mmol, 3.3 equiv), DIPEA (33.0 µL, 0.1998 mmol, 0.15 equiv), sodium ascorbate (79.2 mg, 0.3996 mmol, 0.3 equiv), and copper(II) sulfate pentahydrate (50.0 mg, 0.1998 mmol, 0.15 equiv) in THF/$H_2O$ (14 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6/1) and 5% MeOH in $CH_2Cl_2$) gave **22b** (2.79 g, 91%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta$ = 8.27 (s, 3H), 8.23–8.12 (m, 3H), 4.92 (m, 3H), 4.17 (m, 12H), 4.05 (m, 8H), 3.95 (m, 16H), 3.64 (m, 20H), 3.54–3.47 (m, 46H), 1.33 (s, 36H; $CH_3$), 1.26 ppm (s, 36H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta$ = 146.53, 132.1, 122.0, 120.73, 109.4, 78.85, 78.51, 74.75, 74.70, 72.55, 71.65, 70.36, 69.42, 69.38, 66.4, 66.61, 61.08, 26.83, 25.45 ppm; ESI-TOF-MS found for $C_{111}H_{183}N_9O_{42}$ (calcd 2314.2461): $m/z$ (%): 2315.2548 $[M+H]^+$, 2337.2186 $[M+Na]^+$, 2353.2322 $[M+K]^+$.

**Ph-1,3,5-click-[G3.0] (22c)**: Reaction conditions and workup were as described above, with **18** (77.3 mg, 0.514 mmol, 1.0 equiv), **14** (2.5 g, 1.695 mmol, 3.3 equiv), DIPEA (25.4 µL, 0.154 mmol, 0.3 equiv), sodium ascorbate (61.1 mg, 0.308 mmol, 0.6 equiv), and copper(II) sulfate pentahydrate (38.5 mg, 0.154 mmol, 0.3 equiv) in THF/$H_2O$ (14 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (10/1) and 5% MeOH in $CH_2Cl_2$) gave **22c** (1.02 g, 44%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta$ = 8.43–4.83 (br m, 6H), 4.88 (m, 3H), 4.17 (m, 24H), 4.03–3.97 (br m, 34H), 3.68–3.46 (br m, 164H), 1.36 (s, 72H; $CH_3$), 1.26 ppm (s, 72H; $CH_3$); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta$ = 146.6, 129.30, 128.31, 123.14, 120.47, 109.25, 78.82, 78.50, 78.31, 74.64, 74.51, 72.37, 71.38, 70.28, 69.20, 69.16, 66.60 66.61, 26.69, 25.32 ppm; ESI-TOF-MS found for $C_{219}H_{375}N_9O_{90}$ (calcd 4571.5044): $m/z$ (%): 2286.2651 $[M+2H]^{2+}$, 2337.2186 $[M+Na]^+$, 2353.2322 $[M+K]^+$.

**Ph-Ph-1,3,5-click-[G1.0] (23a)**: Reaction conditions and workup were as described above, with **19** (0.2 g, 0.528 mmol, 1.0 equiv), **12** (0.602 g, 1.744 mmol, 3.3 equiv), DIPEA (39.2 µL, 0.238 mmol, 0.45 equiv), sodium ascorbate (94.2 mg, 0.476 mmol, 0.9 equiv), and copper(II) sulfate pentahydrate (59.4 mg, 0.238 mmol, 0.45 equiv) in THF/$H_2O$ (8 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (3/1) and 5% MeOH in $CH_2Cl_2$) gave **23a** (0.74 g, 99%). $^1$H NMR 500 MHz, $CDCl_3$, 25°C): $\delta$ = 8.09 (t, 3H, $J$ = 9.8 Hz), 7.95 (d, 6H, $J$ = 8.2 Hz), 7.83 (s, 3H), 7.76 (d, 6H, $J$ = 8.3 Hz), 4.96 (m, 3H), 4.12 (m, 6H), 4.98 (m, 18H), 3.64 (m, 6H), 3.51 (m, 12H), 1.37 (s, 18H), 1.31 ppm (s, 18H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta$ = 146.86, 141.75, 140.41, 129.98, 127.57, 125.98, 124.74, 120.22, 109.43, 109.40, 74.45, 74.37, 72.39, 72.07, 70.03, 69.97, 66.12, 60.45, 26.59, 25.19 ppm; ESI-TOF-MS found for $C_{75}H_{99}N_9O_{18}$ (calcd 1413.7108): $m/z$ (%): 1414.7170 $[M+H]^+$, 1436.6993 $[M+Na]^+$, 1452.6667 $[M+K]^+$.

**Ph-Ph-1,3,5-click-[G2.0] (23b)**: Reaction conditions and workup were as described above, with **19** (0.14 g, 0.37 mmol, 1.0 equiv), **13** (0.881 g, 1.221 mmol, 3.3 equiv), DIPEA (27.4 µL, 0.166 mmol, 0.45 equiv), sodium ascorbate (65.9 mg, 0.333 mmol, 0.9 equiv), and copper(II) sulfate pentahydrate (41.5 mg, 0.166 mmol, 0.45 equiv) in THF/$H_2O$ (8 mL). Purification by column chromatography (ethyl acetate/*n*-hexane (6/1) and 10% MeOH in $CH_2Cl_2$) gave **23b** (0.80 g, 87%). $^1$H NMR (400 MHz, $CDCl_3$, 25°C): $\delta$ = 8.096–8.05 (br m, 3H), 7.95 (d, 6H, $J$ = 7.8 Hz), 7.82 (s, 3H), 7.76 (d, 6H, $J$ = 8.0 Hz), 4.92 (m, 3H), 4.18 (m, 12H), 4.07 (m, 6H), 3.98 (m, 16H), 3.64–3.34 (br m, 68H), 1.35 (s, 36H), 1.29 ppm (s, 36H); $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C): $\delta$ = 146.75, 146.64, 146.54, 141.80, 140.45, 130.17, 130.07, 129.97, 127.62, 125.97, 124.76, 120.38, 120.22, 109.28, 78.65, 78.34, 74.67, 74.50, 72.41, 71.62, 71.50, 70.21, 69.32, 66.60, 66.45, 61.24, 60.98, 26.66, 25.26 ppm; QFT-ESI MS found for $C_{129}H_{195}N_9O_{42}$ (calcd 2542.3400): $m/z$ (%): 1272.1793 $[M+2H]^{2+}$.

**Ph-Ph-1,3,5-click-[G3.0] (23c)**: Reaction conditions and workup were as described above, with **19** (0.19 g, 0.502 mmol, 1.0 equiv), **14** (2.443 g, 1.657 mmol, 3.3 equiv), DIPEA (74.5 µL, 0.226 mmol, 0.9 equiv), sodium ascorbate (89.5 mg, 0.452 mmol, 0.9 equiv), and copper(II) sulfate pentahydrate (56.4 mg, 0.226 mmol, 0.45 equiv) in THF/$H_2O$ (8 mL). Purification by column chromatography (35% 2-propanol in *n*-hexane and 10% MeOH in $CH_2Cl_2$) gave **23c** (1.73 g, 72%). $^1$H NMR (500 MHz, $CDCl_3$, 25°C): $\delta$ = 8.11 (br s, 3H), 7.95 (d, 6H, $J$ = 7.7 Hz), 7.83 (s, 3H), 7.76 (d, 6H, $J$ = 7.9 Hz), 4.89 (m, 3H), 4.17 (m, 24H), 4.07 (m, 9H), 3.98 (m, 24H), 3.64–3.41 (br m, 165H), 1.37 (s, 72H), 1.31 ppm (s, 72H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C): $\delta$ = 146.33, 141.74, 140.34, 130.28, 127.60, 125.97, 124.72, 120.62, 109.21 78.81, 78.46, 78.25, 74.61, 74.48, 74.45, 72.35, 71.48, 71.35, 71.14, 70.31, 70.14, 69.34, 66.75, 66.56, 66.37, 61.32, 26.67, 25.29 ppm; ESI-TOF-MS found for $C_{237}H_{387}N_9O_{90}$ (calcd 4799.5983): $m/z$ (%): 1600.8726 $[M+3H]^{3+}$, 2400.8223 $[M+2H]^{2+}$, 2422.7902 $[M+2Na]^{2+}$.

**General procedure for the deprotection of the alcohol functionality**: Ion-exchange resin Dowex 50W was added to 1.0 equiv of acetal-protected compound (**20**–**23**) dissolved in MeOH, and the mixture heated to reflux for 12–24 h. After cooling, Dowex 50W was filtered off and washed with a 5% solution of $Et_3N$ in MeOH, and concentration of the residue under vacuum yielded **24**–**27**.

**Ph-1,3-click-[G1.0]-OH (24a)**: Reaction conditions and workup were as described above, with **20a** (1.06 g, 1.31 mmol) in MeOH (25 mL). Evaporation of the solvent gave **24a** (0.743 g, 1.13 mmol, 86.4%). $^1$H NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.53, 8.49, 8.45, 8.42 (br m, 2H), 8.22 (s, 1H), 7.76 (d, 2H, $J$ = 7.8 Hz), 7.44 (t, 1H, $J$ = 7.8 Hz), 5.01 (m, 2H) 4.77–4.66 (m, 2H), 3.94 (m, 6H), 3.68 (m, 4H), 3.45 ppm (br m, 16H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 148.25, 148.08, 132.52, 132.45, 130.69, 126.38, 124.12, 124.08, 123.91, 122.65, 78.89, 78.81, 73.96, 73.83, 73.72, 72.69, 72.63, 72.31, 72.13, 72.04, 71.27, 64.27, 64.20, 62.49, 52.18 ppm; ESI-TOF-MS found for $C_{28}H_{44}N_6O_{12}$ (calcd 656.3017): $m/z$ (%): 657.3074 $[M+H]^+$, 679.2891 $[M+Na]^+$, 695.2601 $[M+K]^+$.

**Ph-1,3-click-[G2.0]-OH (24b)**: Reaction conditions and workup were as described above, with **20b** (1.77 g, 1.764 mmol) in MeOH (30 mL). Evaporation of the solvent gave **24b** (1.395 g, 1.12 mmol, 99%). $^1$H NMR (500 MHz, $CD_3OD$, 25°C): $\delta$ = 8.60, 8.58, 8.56 (m, 2H), 8.37 (s, 1H), 7.87 (d, 2H, $J$ = 8.0 Hz), 7.55 (t, 1H, $J$ = 7.8 Hz), 5.08 (m, 2H), 4.20–4.01 (br m, 8H), 3.74 (m, 12H), 3.65–3.40 ppm (br m, 48H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 147.96, 147.90, 132.54, 130.80, 126.48, 123.84, 122.93, 122.83, 80.03, 79.67, 73.89, 72.83, 72.75, 72.47, 72.40, 72.13, 71.41, 70.47, 64.39, 63.26, 62.94 ppm; ESI-TOF-MS found for $C_{52H92}N_6O_{28}$ (calcd 1248.5960): $m/z$ (%): 1249.6002 $[M+H]^+$, 1271.5827 $[M+Na]^+$, 1287.5562 $[M+K]^+$.

**Ph-1,3-click-[G3.0]-OH (24c)**: Reaction conditions and workup were as described above, with **20c** (0.483 g, 0.157 mmol) in MeOH (10 mL). Evaporation of the solvent gave **24c** (0.378 g, 0.155 mmol, 99%). $^1$H NMR (400 MHz, $CD_3OD$, 25°C): $\delta$ = 8.59 (m, 1H), 8.41 (m, 1H), 7.86 (d, 1H, $J$ = 7.3 Hz), 7.57 (t, 1H, $J$ = 7.7 Hz), 4.07 (m, 2H), 4.16 (m, 8H), 3.70–3.40 ppm (br m, 140H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 147.78, 131.77, 129.10, 127.46, 123.09, 120.74, 80.56, 80.31, 79.83, 76.13, 73.97, 72.95, 72.43, 72.30, 72.20, 71.28, 71.07, 70.51, 67.56, 64.52, 63.43 ppm; ESI-TOF-MS found for $C_{100}H_{188}N_6O_{60}$ (calcd 2433.1844): $m/z$ (%): 1217.5989 $[M+2H]^{2+}$, 1239.5814 $[M+2Na]^{2+}$, 2434.1578 $[M+H]^+$, 2456.1628 $[M+Na]^+$.

**Ph-1,4-click-[G1.0]-OH (25a)**: Reaction conditions and workup were as described above, with **21b** (1.1 g, 1.35 mmol) in MeOH (25 mL). Evaporation of the solvent gave **25b** (0.774 g, 1.19 mmol, 88%). H$^1$ NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.66, 8.61, 8.56, 8.54 (m, 2H), 7.98 (s, 4H), 5.14 (m, 2H), 4.77–4.66 (m, 2H), 4.07 (m, 6H), 3.81 (m, 4H), 3.58 ppm (br m, 16H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 148.20, 148.04, 131.64, 127.19, 123.98, 123.94, 122.53, 83.47, 78.92, 78.84, 73.85, 73.73, 72.15, 71.29, 64.26, 62.51, 52.19 ppm; ESI-TOF-MS found for $C_{28}H_{44}N_6O_{12}$ (calcd 656.3017): $m/z$ (%): 657.3094 $[M+H]^+$, 679.2906 $[M+Na]^+$.

**Ph-1,4-click-[G2.0]-OH (25b)**: Reaction conditions and workup were as described above, with **21b** (1.5 g, 0.955 mmol) in MeOH (25 mL). Evaporation of the solvent gave **25b** (1.13 g, 0.91 mmol, 95%). $^1$H NMR (400 MHz, $CD_3OD$, 25°C): $\delta$ = 8.54, 8.53, 8.52, 8.50 (m, 2H), 7.95 (s, 4H), 5.04 (m, 2H), 4.18, 4.12 (m, 5H), 4.02, 3.98 (m, 3H), 3.71 (m, 10H), 3.63–3.38 ppm (br m, 50H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 147.90, 131.66, 122.70, 80.09, 79.74, 73.92, 72.88, 72.79, 72.53, 72.46, 72.37, 72.19, 71.35, 70.52, 64.43, 63.29, 62.98 ppm; ESI-TOF-MS found for $C_{52}H_{92}N_6O_{28}$ (calcd 1248.5960): *m*/*z* (%): 1249.6003 $[M+H]^+$, 1271.5822 $[M+Na]^+$, 1287.5535 $[M+K]^+$.

**Ph-1,4-click-[G3.0]-OH (25c)**: Reaction conditions and workup were as described above, with **21c** (0.526 g, 0.171 mmol) in MeOH (10 mL). Evaporation of the solvent gave **25c** (0.406 g, 0.167 mmol, 98%). $^1$H NMR (400 MHz, $CD_3OD$, 25°C): $\delta$ = 8.57 (s, 2H), 7.98 (s, 4H), 5.06 (m, 2H), 3.74 (m, 8H), 3.66–3.41 ppm (br m, 140H); $^{13}$C NMR (67.5 MHz, $CD_3OD$, 25°C): $\delta$ = 147.85, 132.77, 130.97, 126.64, 123.89, 123.20, 80.56, 80.31, 80.08, 79.83, 73.96, 72.95, 72.43, 72.30, 72.19, 71.28, 71.07, 70.53, 64.52, 63.40 ppm; ESI-TOF-MS found for $C_{100}H_{188}N_6O_{60}$ (calcd 2433.1844): *m*/*z* (%): 1217.6011 $[M+2H]^{2+}$, 1228.5929 $[M+H+Na]^{2+}$, 2434.2160 $[M+H]^+$.

**Ph-1,3,5-click-[G1.0]-OH (26a)**: Reaction conditions and workup were as described above, with **22a** (1.38 g, 1.16 mmol) in MeOH (25 mL). Evaporation of the solvent gave **26a** (1.05 g, 1.1 mmol, 95.3%). $^1$H NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.66, 8.61, 8.56, 8.54 (m, 3H), 8.28, 8.27 (m, 3H), 5.10 (m, 3H), 4.76–4.58 (br m, 2H), 4.06 (m, 5H), 4.00 (m, 4H), 3.78 (m, 7H), 3.62–3.48 ppm (m, 24H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 147.77, 133.34, 123.38, 122.98, 83.49, 78.93, 78.85, 74.02, 73.89, 73.79, 72.75, 72.68, 72.35, 72.17, 72.08, 71.30, 64.34 62.56 ppm; ESI-TOF-MS found for $C_{39}H_{63}N_9O_{18}$ (calcd 945.4291): *m*/*z* (%): 946.4364 $[M+H]^+$, 968.4183 $[M+Na]^+$, 984.3923 $[M+K]^+$.

**Ph-1,3,5-click-[G2.0]-OH (26b)**: Reaction conditions and workup were as described above, with **22b** (1.62 g, 0.955 mmol) in MeOH (25 mL). Evaporation of the solvent gave **26b** (1.07 g, 84%). $^1$H NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.65, 8.64 (m, 3H), 8.33 (m, 3H), 5.06 (m, 3H), 4.15 (m, 6H), 3.97 (m, 6H), 3.70 (m, 16H) 3.61–3.47 ppm (m, 74H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 147.71, 147.65, 133.44, 123.53, 123.30, 123.21, 80.12, 79.72, 79.66, 73.95, 72.88, 72.80, 72.55, 72.47, 72.37, 72.20, 71.49, 64.43, 63.43, 63.11 ppm; ESI-TOF-MS found for $C_{75}H_{135}N_9O_{42}$ (calcd 1833.8705): *m*/*z* (%): 1834.8782 $[M+H]^+$, 1856.8598 $[M+Na]^+$.

**Ph-1,3,5-click-[G3.0]-OH (26c)**: Reaction conditions and workup were as described above, with **22c** (0.8 g, 0.175 mmol) in MeOH (25 mL). Evaporation of the solvent gave **26c** (0.589 g, 0.16 mmol, 92%). $^1$H NMR (400 MHz, $CD_3OD$, 25°C): $\delta$ = 8.68 (br s, 3H), 8.02, 7.99 (m, 3H), 5.10 (m, 3H), 4.20 (m, 12H), 3.77–3.54 ppm (br m, 214H); $^{13}$C NMR (125 MHz, $CD_3OD$, 25°C): $\delta$ = 146.89, 133.27, 130.15, 129.61, 125.24, 124.98 123.97, 123.57, 83.89, 83.09, 80.53, 80.28, 79.82, 76.10, 73.95, 72.93, 72.41, 72.29, 72.17, 71.24, 71.05, 70.45, 64.50, 63.39 ppm; ESI-TOF-MS found for $C_{150}H_{283}N_9O_{90}$ (calcd 3650.7845): *m*/*z* (%): 1826.3985 $[M+2H]^{2+}$.

**Ph-Ph-1,3,5-click-[G1.0]-OH (27a)**: Reaction conditions and workup were as described above, with **23a** (0.62 g, 0.438 mmol) in MeOH (15 mL). Evaporation of the solvent gave **27a** (0.446 g, 0.38 mmol, 87%). $^1$H NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.45 (s, 3H), 7.86 (d, 6H, *J* = 8.2 Hz), 7.84 (s, 3H), 7.67 (d, 6H, *J* = 8.3 Hz), 5.01 (m, 3H), 3.96 (m, 12H), 3.72 (m, 8H), 3.58–3.40 ppm (m, 22H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 148.18, 142.93, 141.79, 131.08, 128.79, 127.24, 125.59, 122.53, 73.90, 73.77, 72.20, 72.11, 71.33, 64.31, 62.50 ppm; ESI-TOF-MS found for $C_{57}H_{75}N_9O_{18}$ (calcd 1173.5230): *m*/*z* (%): 1174.5330 $[M+H]^+$, 1196.5147 $[M+Na]^+$, 1212,4864 $[M+K]^+$.

**Ph-Ph-1,3,5-click-[G2.0]-OH (27b)**: Reaction conditions and workup were as described above, with **23b** (0.773 g, 0.304 mmol) in MeOH (20 mL). Evaporation of the solvent gave **27b** (0.548 g, 0.265 mmol, 87.4%). $^1$H NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.46 (br m, 3H), 7.90 (m, 6H), 7.83 (m, 9H), 4.96 (m, 3H), 4.06 (m, 6H), 3.91 (m, 6H), 3.64 (m, 16H), 3.44 ppm (br m, 74H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 148.01, 143.13, 141.87, 131.20, 128.94, 127.35, 125.73, 122.68, 80.10, 79.77, 73.96, 72.92, 72.84, 72.49, 72.21, 71.43, 70.52, 64.47, 63.26, 62.94, 62.49 ppm; ESI-TOF-MS found for $C_{93}H_{147}N_9O_{42}$ (calcd 2061.9644): *m*/*z* (%): 2062.9786 $[M+H]^+$, 1031.9927 $[M+2H]^{2+}$.

**Ph-Ph-1,3,5-click-[G3.0]-OH (27c)**: Reaction conditions and workup were as described above, with **23c** (1.2 g, 0.25 mmol) in MeOH (25 mL). Evaporation of the solvent gave **27c** (0.89 g, 0.227 mmol, 91%). $^1$H NMR (250 MHz, $CD_3OD$, 25°C): $\delta$ = 8.55 (s, 3H), 7.94 (m, 15H), 5.03 (m, 3H), 4.11 (m, 12H), 3.70–3.46 ppm (br m, 205H); $^{13}$C NMR (100 MHz, $CD_3OD$, 25°C): $\delta$ = 1147.89, 143.21, 142.01, 131.31, 129.08, 127.45, 125.81, 123.07, 79.83, 73.97, 72.96, 72.21, 71.54, 71.28, 71.08, 64.53 ppm; ESI-TOF-MS found for $C_{165}H_{291}N_9O_{90}$ (calcd 3838.8471): *m*/*z* (%): 1942.4156 $[M+2Na]^{2+}$.

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