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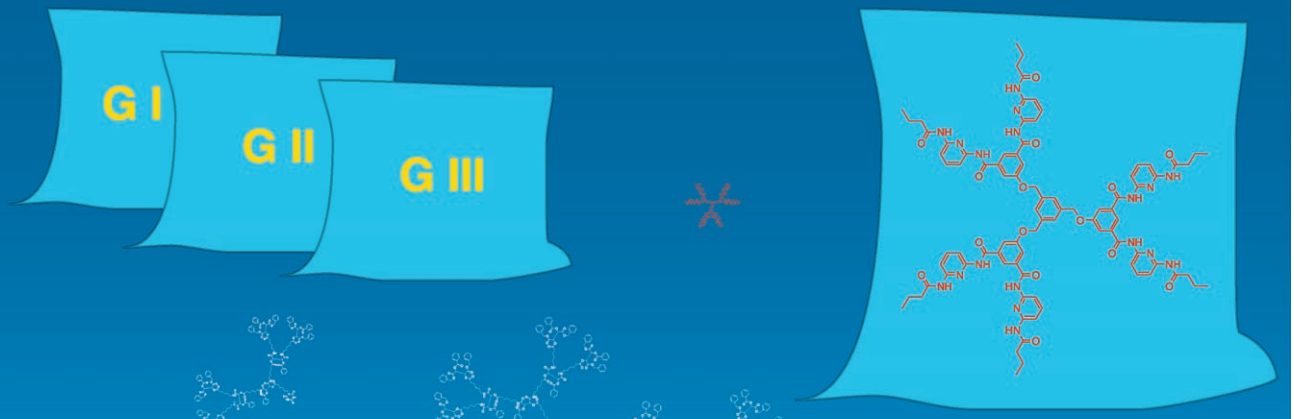

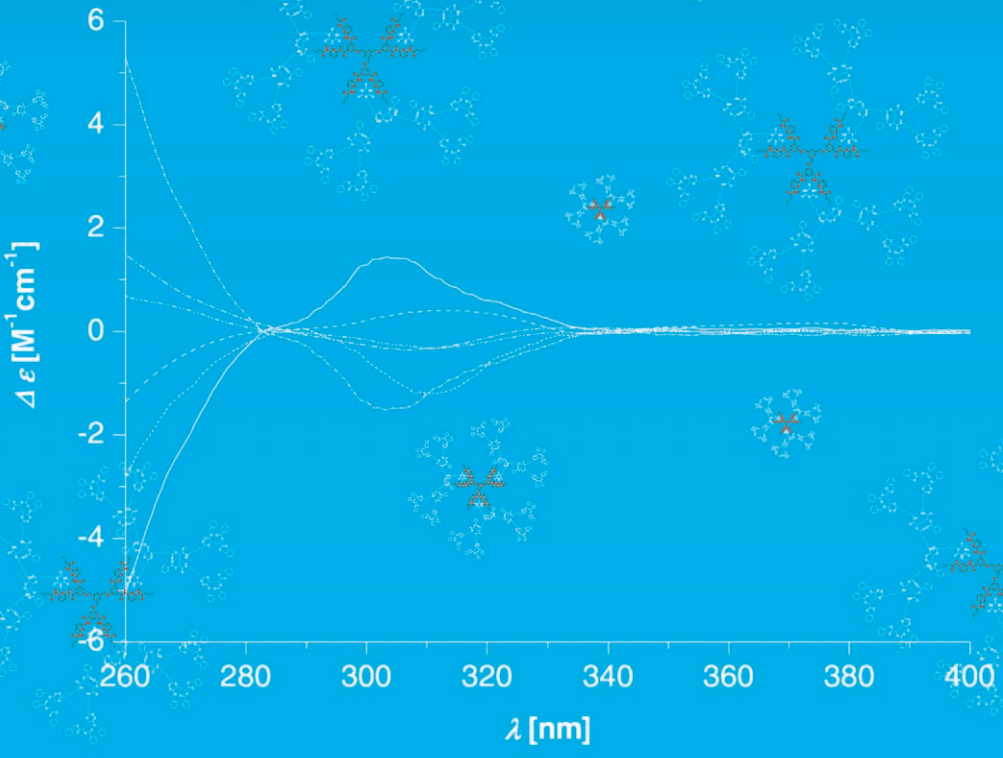

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Self-Assembly of Chiral Depsipeptide Dendrimers

Kristine Hager, Alexander Franz, and Andreas Hirsch*[a]

Abstract: The self-assembly of chiral depsipeptide dendrons **4**, which contain a cyanuric acid building block at their focal point, with the homotritopic Hamilton receptor **1** is reported. The 1:3 compositions of the resulting chiral supramolecular dendrimers, the association constants K_n, and the cooperativity of binding expressed by Scatchard plots and the Hill coefficients n_H was determined by NMR titration experiments. The most pronounced positive cooperativity was found for the complexes $\mathbf{1}L_3$ with L being the second-generation dendrons **4c–e**. The least stable complexes are formed with the bulky third-generation dendrons **4f–h**. Similar results are obtained by the corresponding complexation of the achiral Frechét-type first- to third-generation dendrons **3** with **1**. Chiroptical investigations of 1:3 complexes of **1** and **4** reveal chirality transfer from the dendron to the Hamilton receptor as demonstrated by the appearance of new CD absorption bands at 310 nm.

Keywords: chirality · cooperativity · dendrimers · depsipetides · hydrogen bonding

Introduction

We recently reported on the development of chiral depsipeptide dendrimers.[1–4] This new class of dendrimers closely resembles the natural depsipeptides, which consist of α-hydroxy and amino acids connected by ester and amide linkages. In this context we also reported the metal-induced chiral folding[3] and the diastereoselective assembly of chiral Ru^{II}-coordinated depsipeptide dendrimers[4] and investigated their chiroptical properties. The Ru^{II}-coordinated depsipeptide dendrimers consisted of three 2,2′-bipyridine ligands and involved two pairs of enantiomerically pure depsipeptide dendrons each, attached in a C_3-symmetrical Δ- or Λ-motif to a Ru^{II} metal center.[4] At the same time, these complexes represent examples of self-assembled dendrimers, which recently became a subject of increasing interest. The self-assembly of purely organic dendrimers has already been achieved by using hydrogen bonding,[5–9] electrostatic interactions,[10] or hydrophobic effects of amphiphilic building blocks.[11] Along these lines we developed a concept for the self-assembly of extended dendritic architectures based on the homotritopic Hamilton receptor **1**[12] as a core and the heterotritopic AB_2 unit **2** as branching element, which contains two Hamilton receptors as well as a complimentary cyanuric acid terminus. End-capping of the resulting dendritic structures was achieved by hydrogen bonding of various cyanuric acid derivatives **3**.[13] For comparison we investigated the formation of a series of $\mathbf{1{\cdot}3_3}$ aggregates, in which the termini R of **3** consist of first to third-generation Frechét-type dendrons. We now report on the self-assembly and the chiroptical properties of the first chiral supramolecular dendrimers $\mathbf{1{\cdot}4_3}$ involving three depsipetide dendrons **4** of generation 1–3 containing a cyanuric acid moiety at the focal point. The association properties of the complexes $\mathbf{1{\cdot}4_3}$, including the cooperativity of binding, is compared with those of the corresponding $\mathbf{1{\cdot}3_3}$ aggregates involving cyanuric acid units connected by C6 spacer units. On the basis of these results we also discuss the question of the compositional and structural diversity of supramolecular dendritic architectures formed by the self-assembly of **1**, **2**, and **3**,[13] which critically depends on the amount of cooperativity.

Results and Discussion

Syntheses: The synthesis of the homotritopic Hamilton receptor **1** was carried out according to the procedure of Lehn and co-workers.[12] As starting material for the synthesis of the chiral dendron **4** we used the tartaric acid derivatives **5** and **6** (see Scheme 2), and the depsipeptides **7–9**, whose synthesis was recently developed in our laboratory.[2–3] For the

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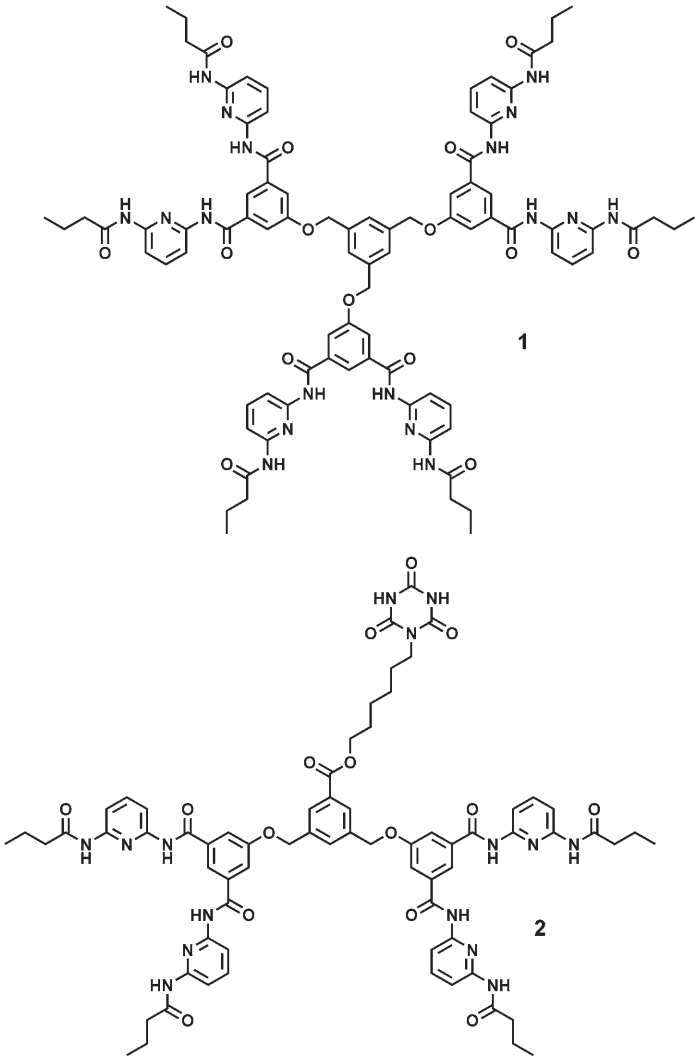
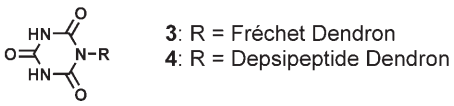
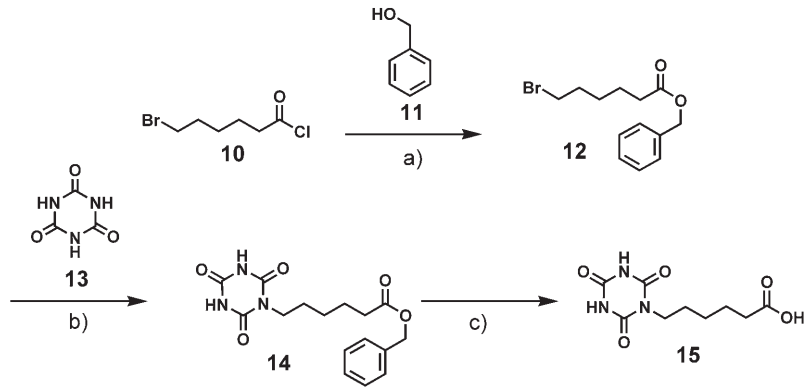






Scheme 1. Synthesis of the cyanuric acid derivate **15**. a) NEt_3, CH_2Cl_2, 0 °C, 3 h, 93 %; b) DBU, DMF, 70 °C, 24 h, 60 %; c) 10 % Pd/C, CH_3OH, room temperature, 24 h, 99 %.

synthesis of a cyanuric acid building block suitable to undergo binding with **1** we allowed ω-bromo hexanoyl chloride **10** to react with one equivalent of **11** to give the benzyl protected precursor **12** (Scheme 1). Reaction of **12** with cyanuric acid **13** afforded the substitution product **14**, which was finally deprotected to give the building block **15**. The yield of this reaction sequence is superior to the procedure described previously.[14]

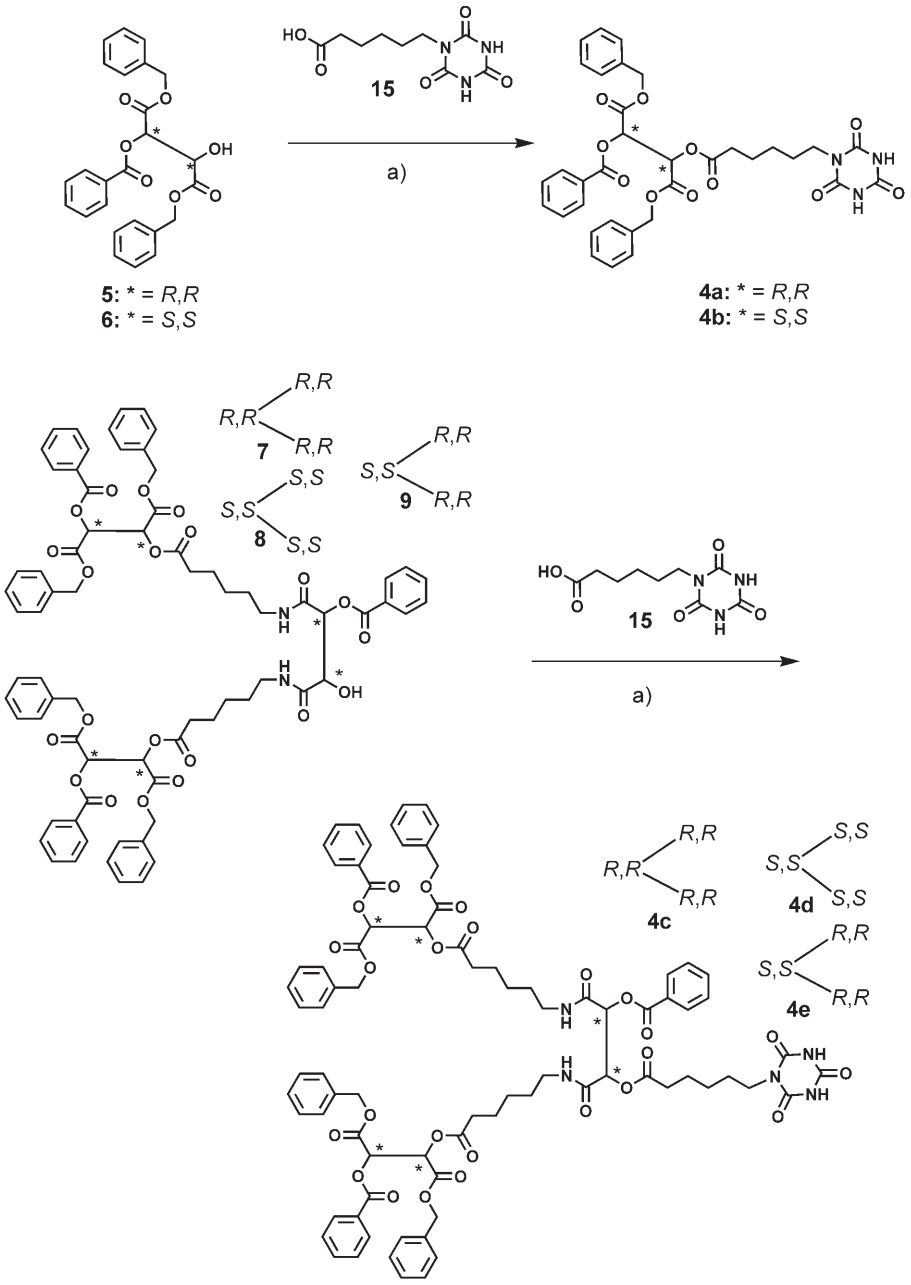
First- and second-generation dendrons **4a–e** were obtained using slightly modified standard ester coupling reactions (Scheme 2).[15,16] For these purposes 1-ethyl-3-(3-dimethylaminopropyl)carbodiimine hydrochloride (EDC·HCl) in the presence of 4-dimethylaminopyridine (DMAP) and 1-hydroxybenzoltriazole (HOBt) as the coupling reagent was used. Unfortunately, the cyanuric acid building block **15** is not soluble in the most common organic solvents and no coupling took place in *N*,*N*′-dimethylformamide (DMF). The reaction was therefore carried out in CH_2Cl_2 and proceeded heterogeneously so that a long reaction time (three days) was required to achieve complete conversion.

For the synthesis of the third-generation dendrons **4f–h,** the first-generation systems **4a**,**b** were first deprotected by hydrogenation, using 10 % Pd/C as a catalyst, to give the building blocks **16** and **17** (Scheme 3). Subsequent coupling of **16** and **17** with the amino-terminated depsipetide dendrons **18** and **19**[4] and purification by column chromatography afforded the dendrons **4f–h** in 26–32 % yield (Scheme 3).

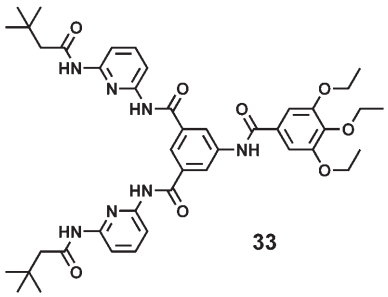
The synthesis of the Frechét-type dendrons **3**[17] required the introduction of the cyanuric acid building block **22**, which was obtained by the reaction of 1-nitrobiuret **20**[18] with 6-aminohexanol, followed by cyclization with diethyl carbonate (Scheme 4).

The dendronization of **22** was accomplished with the precursor dendrons **30–32** containing a carboxylic acid functionality at the focal point (Scheme 5). For this purpose, benzyl bromide derivatives **24**, **25** and **26**[19] were coupled with methyl-3,5-dihydroxybenzoate **23** using K_2CO_3 as base and [18]crown-6 as catalyst. Subsequent saponification of **27–29**[20] afforded the acids **30–32** in 78–95 % yield (Scheme 5). Finally, the dendrons **3** were obtained by Steglich coupling of **30–32** with **22** (Scheme 5).

To compare the complexation properties of the homotritopic receptor **1** with a monoreceptor, we also synthesized the model compound **33** by coupling of 3,4-diethoxy-5-propoxybenzoic acid with 5-amino-*N*,*N*′-bis[6-(3,3-dimethylbutyrylamino)pyridine-2-yl]isophtalamide.[21] To enhance solubility dimethylbutyrylamino groups were used as termini.



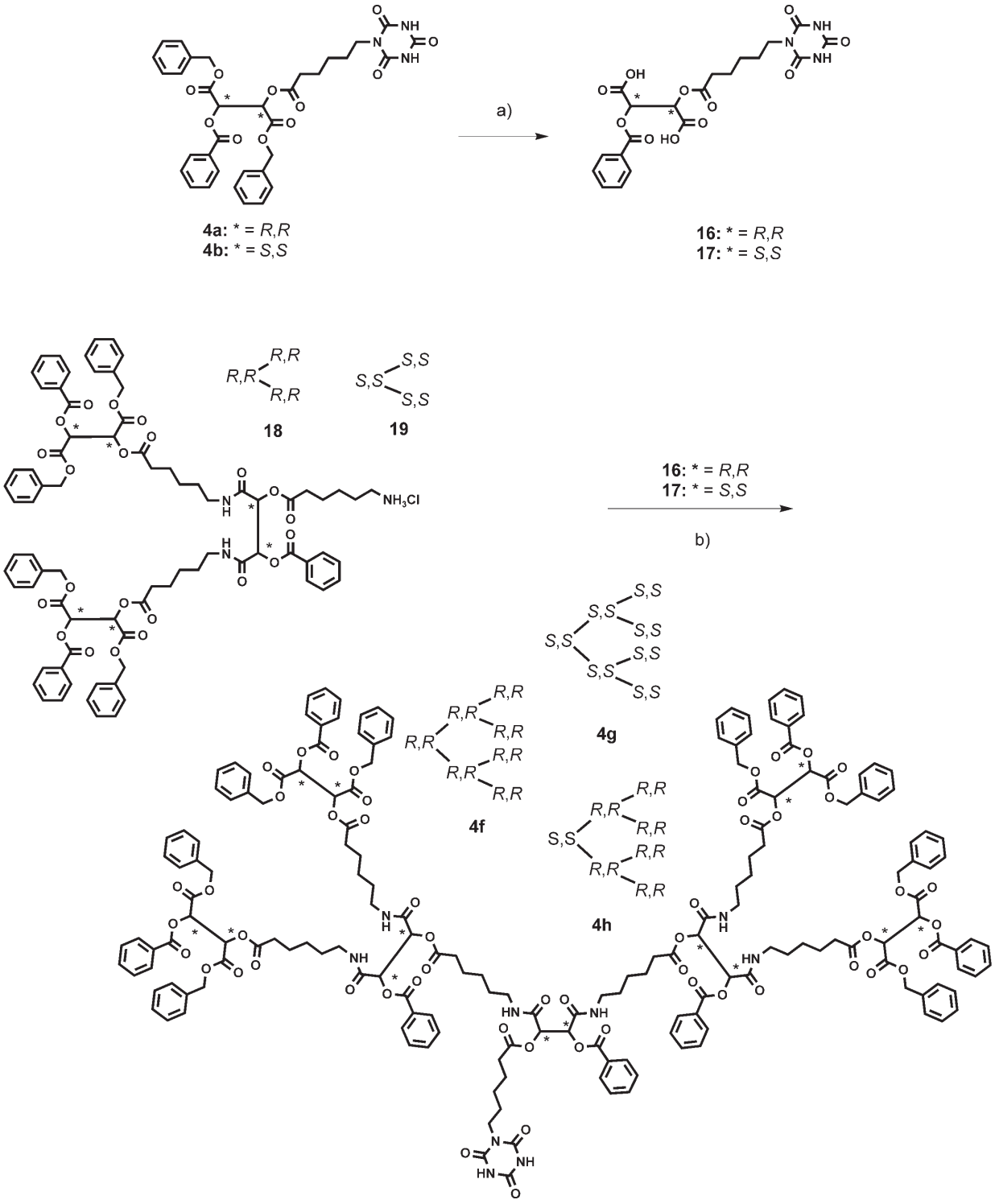
Scheme 2. Synthesis of the first- and second-generation depsipeptide dendrons **4a**–**e**. a) EDC, HOBt, DMAP, CH_2Cl_2, room temperature, 72 h.



Determination of association constants and cooperativity of binding: The ^{1}H NMR spectra of the Hamilton receptor **1** in $CDCl_3$ display rather broad and unresolved signals.[12] This is due to the presence of the large number of hydrogen-bond donors and acceptors causing the formation of intra- and intermolecular hydrogen bonds. Pronounced aggregation of **1** due to intermolecular hydrogen bonds is also the reason for the low solubility of **1** in chloroform. In DMSO, where intermolecular associations are not favored, the NMR spectra of **1** are well resolved. Remarkable sharpening of the signals in $CDCl_3$ occurs also upon successive addition of the dendritic cyanuric acid derivatives **3** and **4**. The sharpening of the signals is accompanied by a downfield shift of the amide proton NH^1 and NH^2 of **1** and indicates the formation of discrete $\mathbf{1{\cdot}4_3}$ and $\mathbf{1{\cdot}3_3}$ complexes (Figure 1).[12,13]

The 1:3 binding stoichiometry of the complexes $\mathbf{1{\cdot}4_3}$ (Scheme 6) was confirmed by applying Job's method of continuous variation to the NMR experiments.[12] The chemical shift variation of NH^1 ($\Delta(\delta)$) as a function of the mole fraction of **4d** $X(\mathbf{4d})$ was monitored, and the product of the mole fraction $X(\mathbf{4d})^{-1}$ and $\Delta(\delta)$ was plotted as a function of $X(\mathbf{1})$. As an example, the Job plot analysis of the system **1**:**4d** is shown in Figure 2.

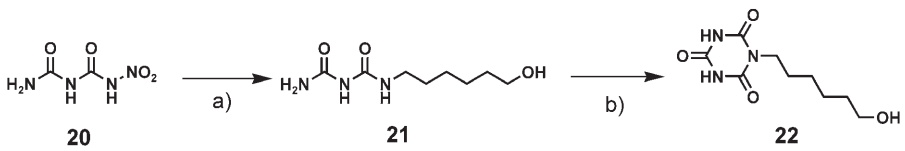
Temperature-dependent NMR spectroscopy reveals the dynamic character of the association of the complexes $\mathbf{1{\cdot}4_3}$ and $\mathbf{1{\cdot}3_3}$. As an example, the ^{1}H NMR spectra of a 1:10 mixture of **1** and **3c** are represented in Figure 3. At 30 °C no signal is found for the NH^3_{free} and NH^3_{bound} protons of the free and bound ligand, respectively. Lowering the temperature below 0 °C leads to the appearance of two signals for the NH^3_{free} and NH^3_{bound} protons, and indicates that the corresponding association–dissociation equilibrium is slow on the NMR time scale. The temperature range between 0–50 °C represents the coalescence regime, where the signals of NH^3 are very broad and cannot be detected anymore (Figure 4). Further increase of the temperature causes the NH^3_{free} and NH^3_{bound} protons to give rise to one averaged signal only,



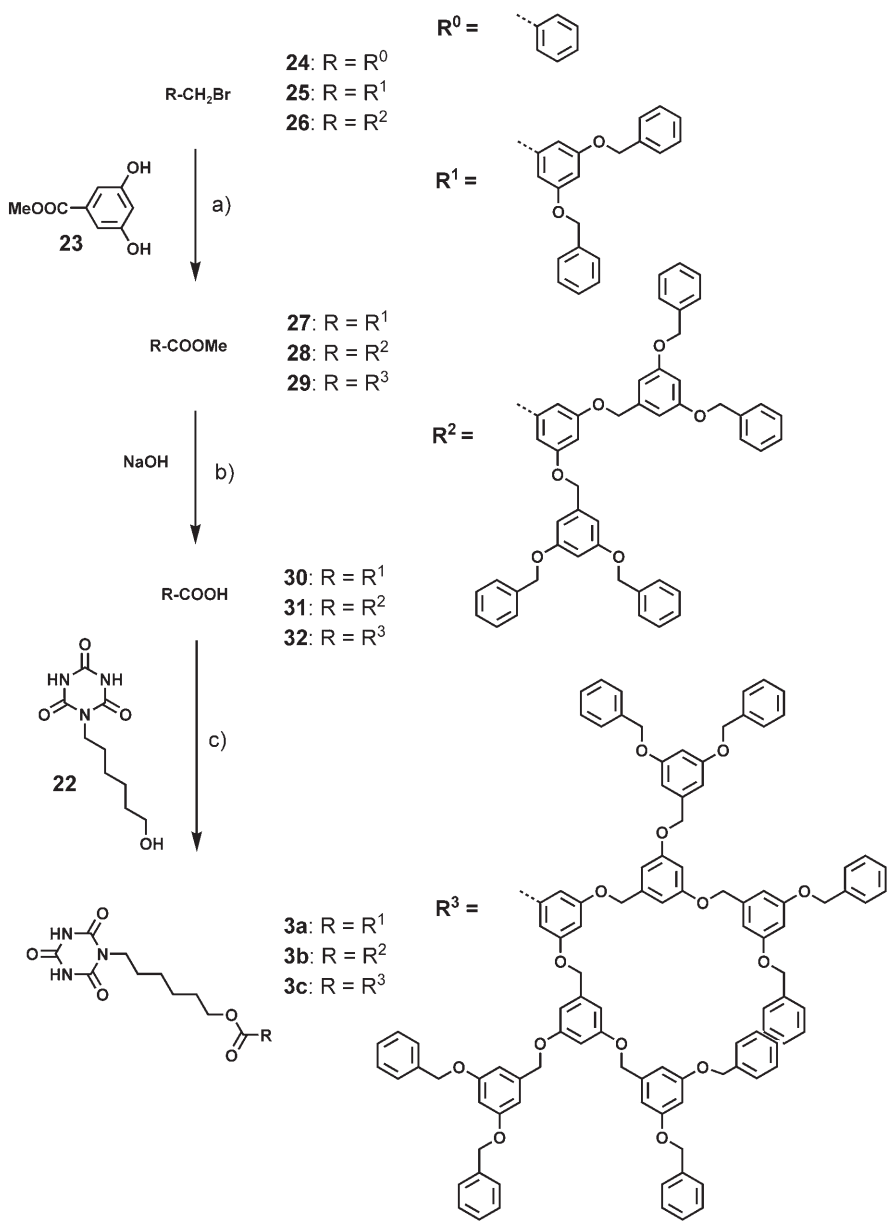
Scheme 3. Synthesis of the third-generation depsipeptide dendrons **4f–h**. a) 10% Pd/C, CH_3OH, room temperature, 24 h; b) EDC, HOBt, DMAP, CH_2Cl_2, room temperature, 72 h.

demonstrating fast exchange processes between free and bound ligands. The highfield shift of this signal upon increasing the temperature indicates the decreasing stability of the **1·3b$_3$** complex.

For the determination of the association constants and the analysis of the cooperativity phenomena, a series of ^{1}H NMR titration experiments in $CDCl_3$ was performed. Here the downfield shift of NH^1 and NH^2 of **1** was determined as a function of the dendron concentration. In a typical experiment, 0.5 mL of a 0.5 mM solution of **1** was titrated with 50 μL of a 2.5 mM solution of **3** and **4**. It is important to note that establishment of stable equilibria required some time



Scheme 4. Synthesis of cyanuric acid derivate **22.** a) 6-aminohexanol, H_2O, 115 °C, 1 h, 40 %; b) diethyl carbonate, NaOEt, EtOH, 105 °C, 2 h, 54 %.



Scheme 5. Synthesis of the Fréchet-type dendrons. a) K_2CO_3, [18]crown-6 acetone, 70 °C, 24 h; b) NaOH, H_2O, 70 °C, 24 h; c) DMAP, HOBt, DCC, DMF, room temperature, 72 h.

because the intermolecular interactions between free **1** needs to be overcome before the binding of the dendritic ligands can take place. As a consequence, the ^{1}H NMR spectra were taken not earlier than one hour after the components were mixed. It is interesting to note that especially the titration curves for the first- and second-generation systems **1**:**4**$_3$ exhibit a sigmoidal shape with an inflection point at about 1.5 equivalent of added **4** (Figure 5).

A similar trend is seen for the series of the **1**:**3** systems. A sigmoidal titration curve is a characteristic feature for a positive cooperative effect for the subsequent binding of guest molecules.[22,23] The association constants for the binding of the dendritic ligands **3** and **4** were determined using the program Chem-Equili[24,25] and are summarized in Table 1. The calculations were based on the assumptions of three equilibria (Equations (1–3)).

$$K_1: \ \mathbf{1} + \mathrm{L} \rightleftharpoons \mathbf{1}:\mathrm{L} \qquad (1)$$

$$K_2: \ \mathrm{L} + \mathbf{1}:\mathrm{L} \rightleftharpoons \mathbf{1}:\mathrm{L}_2 \qquad (2)$$

$$K_3: \ \mathrm{L} + \mathbf{1}:\mathrm{L}_2 \rightleftharpoons \mathbf{1}:\mathrm{L}_3 \qquad (3)$$

In general, the association constants K_n, especially those for the first and second-generation dendrons, are in good agreement with those reported by Lehn and co-workers for a $\mathbf{1}\mathrm{L}_3$ system, with L being a non-dendritic cyanuric acid derivative.[12] For the case of statistical binding, Equation (4) must be fulfilled,[22] for which t is the total number of binding sites (in this case $t=3$).

$$\frac{K_{n+1}}{K_n} = \frac{n(t-n)}{(n+1)(t-n+1)} \qquad (4)$$

However, the experimental values for K_{n+1}/K_n are much higher than those obtained from Equation (4), which clearly demonstrates the presence of pronounced positive cooperativity. In other words the free binding energy of the dendritic ligands increases by going from the monocomplex $\mathbf{1}\mathrm{L}$ to bis- and triscomplexes $\mathbf{1}\mathrm{L}_2$ and $\mathbf{1}\mathrm{L}_3$, respectively. This is also reflected by the sigmoidal shape of the corresponding titration curves (Figure 5). In the case of the first and second-

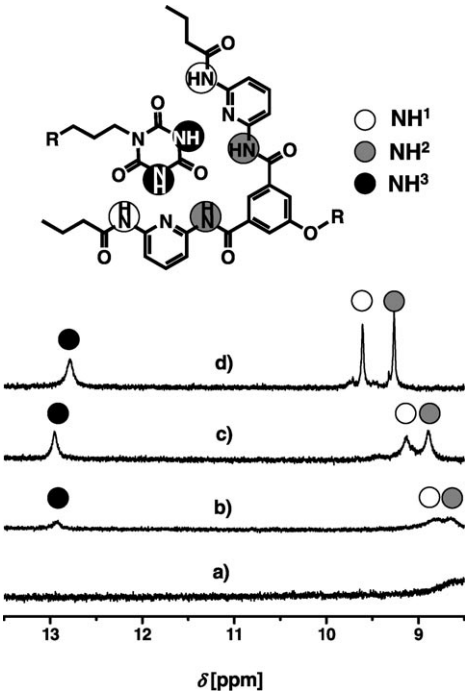


Figure 1. Binding motif between **1** and **3** or **4** with indication of the NH protons NH^1, NH^2 and NH^3 (top) and 300 MHz ^{1}H NMR spectra of **1** at a concentration of 0.5 mM in $CDCl_3$. a) 0 equivalents of **4a**; b) 1 equivalent of **4a**; c) 2 equivalents of **4a**; d) 3 equivalents of **4a** (bottom).

generation systems $\mathbf{1}L_3$ (L = **4a–e**), the third binding step (3) is accompanied by the largest cooperativity. Similar behavior is observed for the systems **1:3a** and **1:3b** (Table 1). In contrast, for the third-generation systems $\mathbf{1}L_3$ (L = **3c**, **4f–h**) the highest cooperativity is associated with the second binding step (2). Significantly, the binding cooperativities of the second-generation dendrons **4c–e** exhibit a pronounced diastereoselectivity. The subsequent binding of dendron **4e** with an all-*S* configuration of the inner and an all-*R* configuration of the outer tartrate layer shows a much higher cooperativity compared with the binding of **4c** and **4d**. A similar trend is observed for the corresponding third-generation systems involving the dendrons **4f**,**4g,** and **4h**, respectively. The $\mathbf{1}L_3$ complexes containing the third-generation dendrons **3c** and **4f–h** are less stable than their first- and second-generation analogues.

The preferred formation of $\mathbf{1}L_3$ (L = **4a–e**) complexes compared with the corresponding $\mathbf{1}L_2$ complexes also becomes apparent upon analysis of the distribution of **1** as free core and within the complexes **1:**L_n (n = 1–3), respectively, as a function of added dendron equivalents (Figure 6). Already at low concentrations of the added dendron, the amount of $\mathbf{1}L_3$ (L = **4a–e**) complexes prevails over the other species. After the addition of three equivalents of **4a–e,** the amount of $\mathbf{1}L_3$ complexes ranges between 88 and 94%. After the addition of four equivalents of **4a–e,** all of **1** is bound in the corresponding $\mathbf{1}L_3$ complex. On the other hand, the formation of $\mathbf{1}L_3$ complexes involving the third-generation dendrons **4f–4h** is much less pronounced (Figure 6). The $\mathbf{1}L_3$ fraction only becomes predominant when 2.5 or more equivalents of **4f–4h** are added. Even after the addition of 10 equivalents, only about 90% of **1** is bound as $\mathbf{1}L_3$ complex.

The most straightforward presentation of the cooperativity phenomena is based on the determination of the occupancy r, which is the average number of ligands bound to the receptor, and to write the results in terms of the stepwise equilibrium model (5).[22]

$$r = \frac{[1 \cdot L] + 2[1 \cdot L_2] + 3[1 \cdot L_3]}{[1] + [1 \cdot L] + [1 \cdot L_2] + [1 \cdot L_3]} \quad (5)$$

For statistical binding r can be described by the Scatchard equation (6), [22]

$$r = \frac{t \cdot Q \cdot \mathrm{x}}{1 + Q \cdot \mathrm{x}} \quad (6)$$

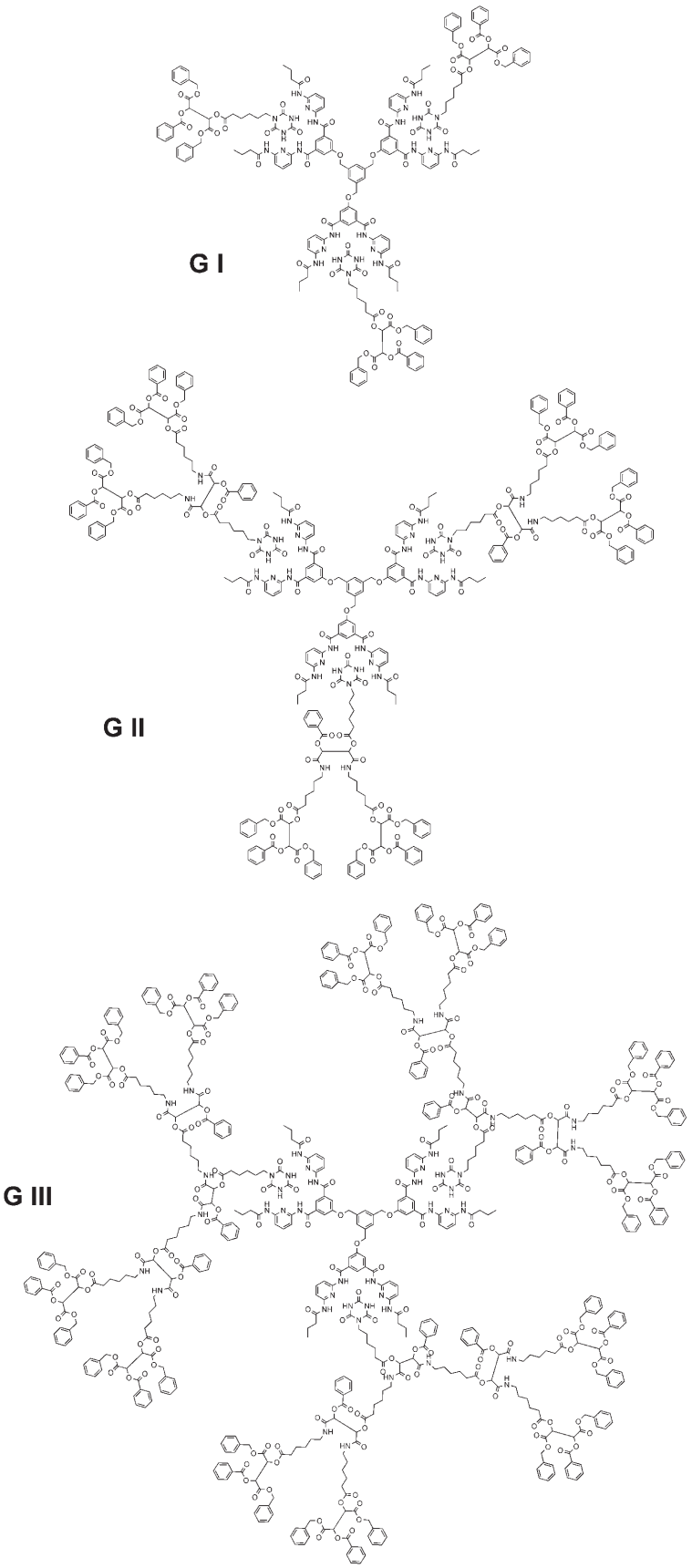
in which Q is the site binding constant and x the concentration of the added ligand. When the binding is statistical, the Scatchard plot r/x as a function of r is a straight line. However, when there is positive cooperativity, the plot is no longer a straight line but a concave curve. Especially the Scatchard plots of the first- and second-generation systems **1:4a–e** display very pronounced concave behavior (Figure 7). The deviation form linearity is less pronounced for the third-generation systems **1:4f–g** (Figure 7). This again shows that the cooperativity for the binding of the first- and second-generation dendrons is much higher than that for the third-generation analogues. Qualitatively the same behavior is found for the series **1:3**.

The quantification of the amount of cooperativity of a given system is usually expressed by the Hill coefficient n_H, which can be obtained from the maximum of the Scatchard plot according to Equation 7 .

$$n_H = \frac{r_{max}}{t - r_{max}} \quad (7)$$

The higher the value of n_H, the higher the degree of cooperativity; n_H becomes equal to t (here t = 3) for infinitely high cooperativity. However, this has never been observed in real systems. For both series **1:4** as well as **1:3,** the highest n_H values are found for the systems with the corresponding second-generation dendrons and the lowest n_H for their third-generation analogues (Table 1).

An open-chain Hamilton receptor, like that involved in **1,** can in principle adopt three distinct planar conformations, namely *cis–cis*, *cis–trans*, and *trans–trans* (Scheme 7). Upon binding of a barbiturate or cyanurate guest, the receptor is always forced into an in plane *cis–cis* configuration. A photophysical study by Vögtle and De Cola et al. performed on dendrimers containing Hamilton receptor moieties in their periphery revealed an increasing conformational restriction and preference of the *cis–cis* conformation with increasing



Scheme 6. Schematic representation of the chiral supramolecular dendrimers **1:4$_3$** (G I with **4a,b**; G II with **4c–e** and G III with **4f–h**).

generation number.[21] This can be explained by increasing sterical hindrance within the periphery of the dendrimer upon going to higher generation numbers.

These observations can be used to explain the association phenomena found for the systems **1**:**4** and **1**:**3**, namely, very pronounced cooperativity of the subsequent binding of G1 and G2 dendrons. The second-generation systems were more cooperative than the first-generation analogues, and weak cooperativity for the third-generation systems was found. Binding of the first and second dendron introduces additional sterical constraints and forces the remaining Hamilton receptor binding site to a preference for the *cis–cis* conformation, which, owing to its favorable preorganization, has the highest susceptibility for the binding of another cyanurate dendron. This effect is more pronounced in the second than in the first-generation dendrons because of the more extended sterical requirements of the ligands. In the third-generation systems, however, the dendritic ligands are so bulky that their threefold binding becomes less favorable again. The situation of the optimal balancing of the required sterical influence to cause the preference of the *cis–cis* conformation in the free sites of **1,** and self-hindrance as a consequence of the ligands' sterical demand, is best presented with the second-generation systems **3b** and **4c–e**.

On the basis of these results and considerations we wish to address, in the following paragraph, the question of structural diversity in dendritic architectures formed by the self-assembly of **1**, **2**, and **3**, as reported recently.[13] Interestingly, the size and sterical requirement of **3b** is very similar to that of the

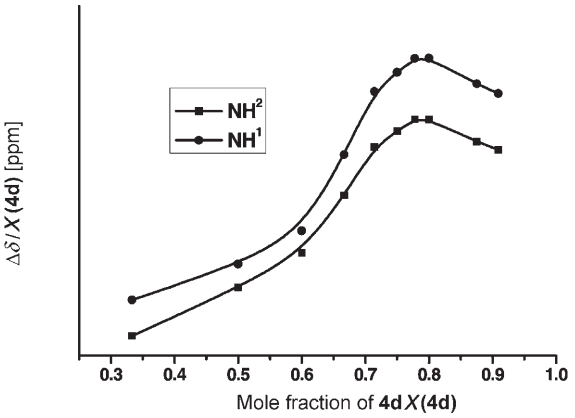


Figure 2. Determination of the 1:3 stoichiometry of the system **1:4d** at a total concentration of 2.75 mM by a Job plot analysis. The *y* axis has been normalized.

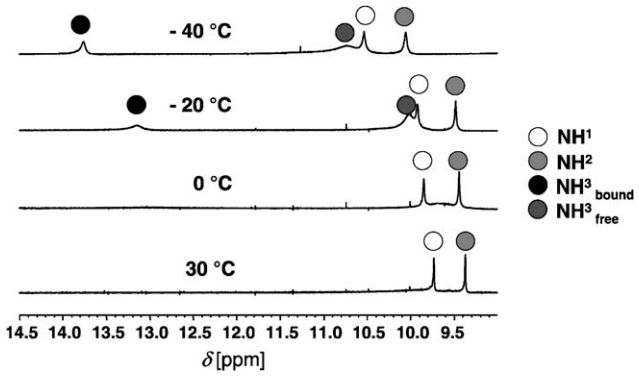


Figure 3. 400 MHz ^{1}H NMR spectra of a 1:10 mixture of **1** and **3b** at a concentration of 2.75 mM in $CDCl_3$ at −40 °C, −20 °C, 0 °C and 30 °C, respectively.

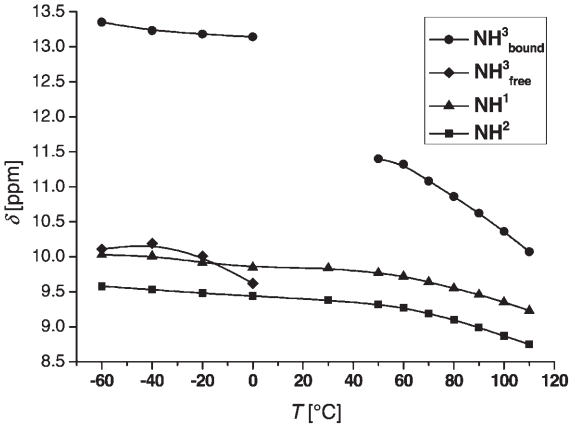


Figure 4. Chemical shifts of the NH^1-, NH^2-, NH^3_{free}- and NH^3_{bound} protons of a 1:10 mixture of **1** and **3b** in $C_2D_2Cl_4$ as a function of temperature.

AB_2 unit **2** that we used for the self-assembly of dendritic supramolecular structures. This concept was based on the idea that simple mixing of the components **1**, **2** and an end

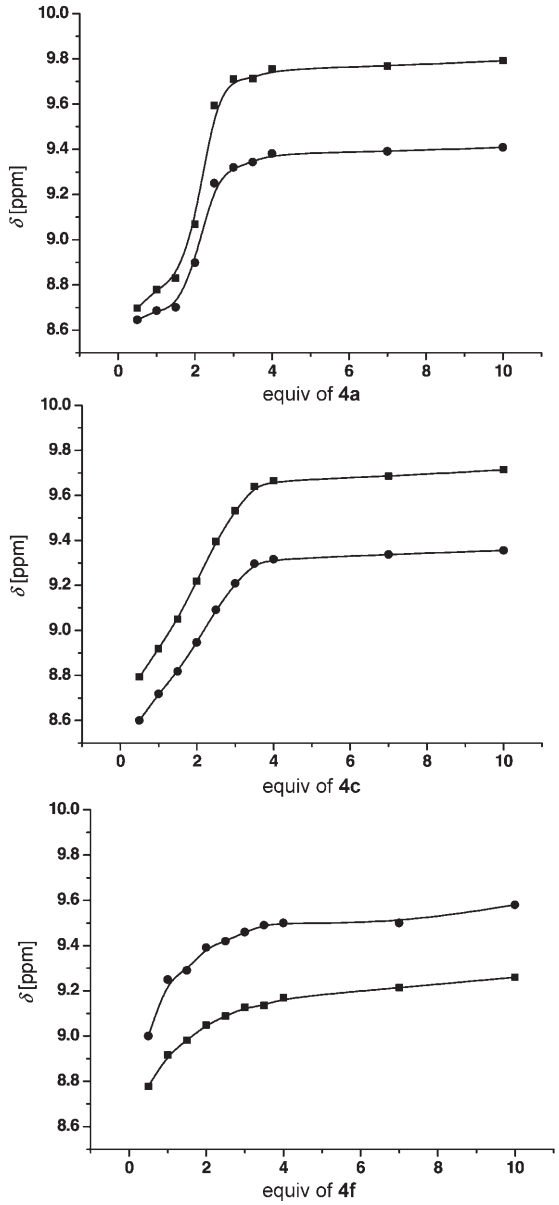


Figure 5. ^{1}H NMR titration plots of the chemical shifts of the NH^1 and NH^2 protons as a function of the amount of added dendrons **4a**, **4c**, **4f**.

Table 1. Association constants, *R* factor (*R*), r_{max}, and Hill coefficients for the systems **1**:**3** and **1**:**4**.

	$\log K_1$ [L mol^{-1}]	$\log K_2$ [L mol^{-1}]	$\log K_3$ [L mol^{-1}]	*R* [%]	r_{max}	n_H
1:3a	3.82	2.60	8.99	±0.25	1.92	1.78
1:3b	4.46	4.46	6.33	±0.17	1.98	1.94
1:3c	3.51	4.51	4.09	±0.23	1.40	0.88
1:4a	4.58	4.04	6.41	±0.36	1.82	1.54
1:4b	4.65	4.04	6.59	±0.23	1.84	1.58
1:4c	3.99	3.95	5.27	±0.19	1.85	1.61
1:4d	3.88	3.85	5.64	±0.22	1.86	1.63
1:4e	3.14	3.37	6.19	±0.26	1.93	1.80
1:4f	3.94	4.33	3.78	±0.32	1.08	0.56
1:4g	3.95	4.02	3.68	±0.32	1.02	0.52
1:4h	3.15	3.91	3.91	±0.22	1.29	0.75

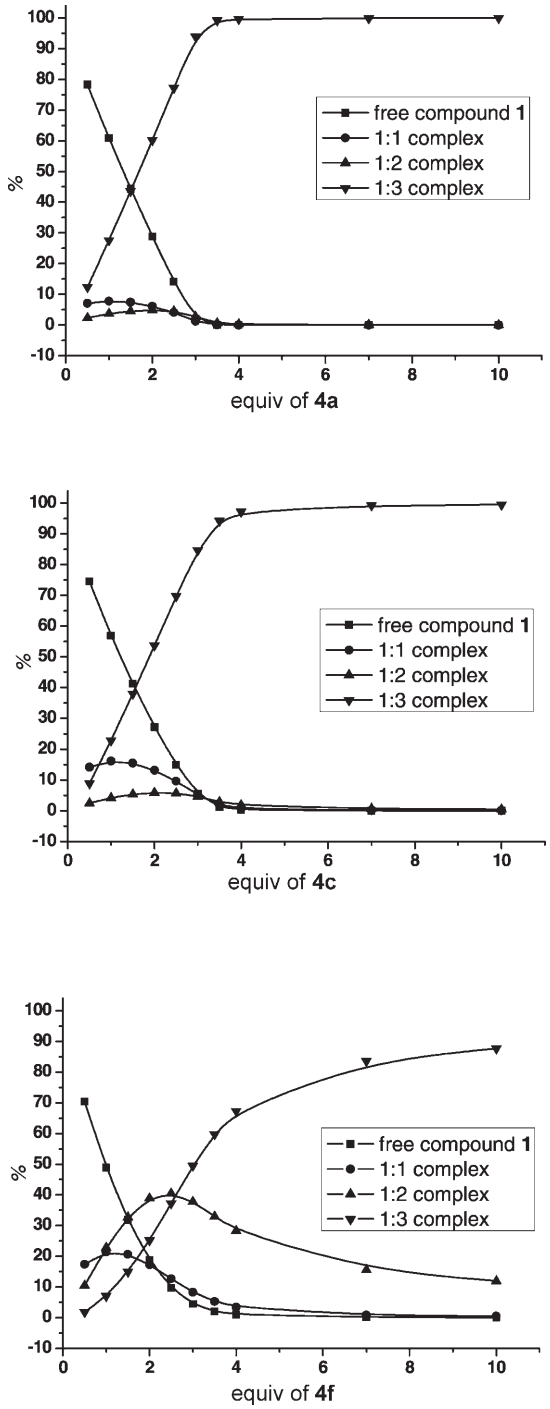


Figure 6. Distribution in percent of **1** as free core and within the complexes **1**:L_n ($n=1$–3) as a function of the amount of added dendrons **4a**, **4c**, **4f** obtained from analysis of the titration plots using the computer program Chem-Equili.[24,25] The total concentration of **1** within the mixtures is 0.5 mM.

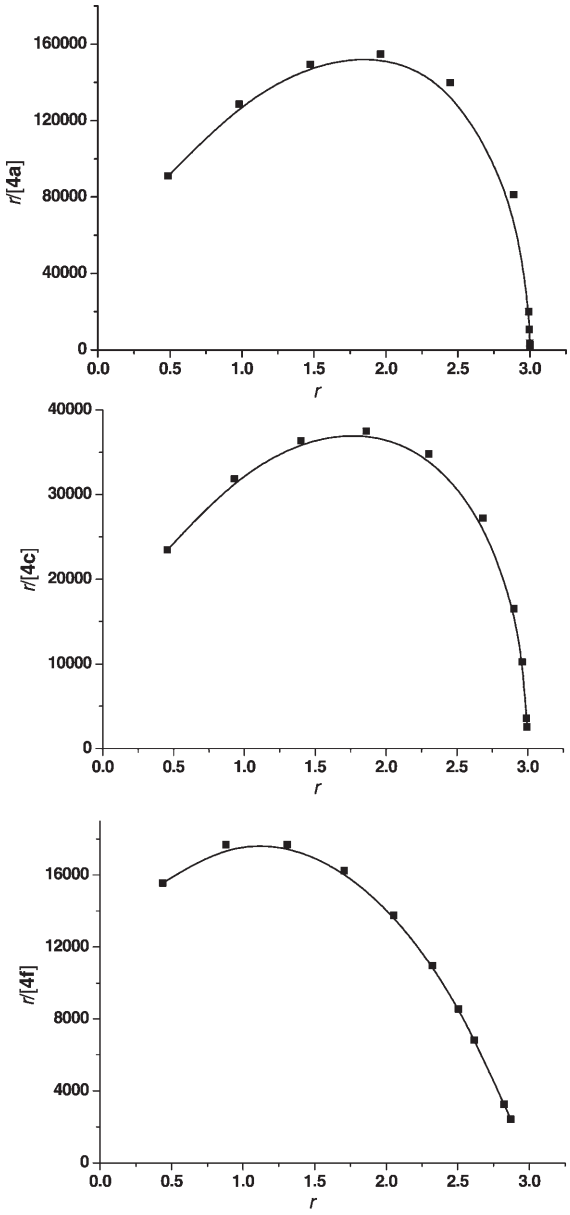
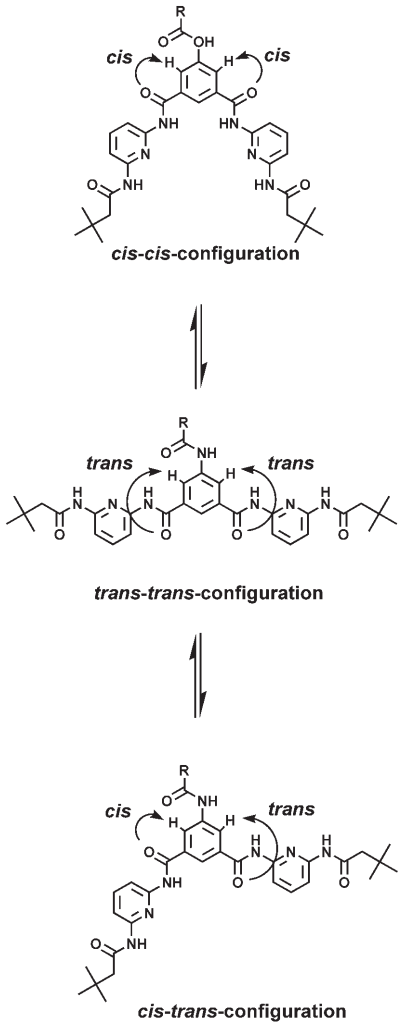


Figure 7. Scatchard plots for the systems **1** L (L = **4a**, **4c**, **4f**).

cap such as **3b** in the stoichiometric ratio of 1: $(3\times2^n-3)$: (3×2^n), with n = generation number, can lead to self-assembled dendrimers with a regular structure such as **I** ($n=3$) for a first-generation system (Figure 8). The driving force for the formation of **I** is the exhaustive use of all possible hydrogen bonds. That discrete dendritic and no ill-defined polymers are indeed formed was confirmed by a variety of methods such as thermal analysis, AFM and DOSY NMR spectroscopy.[13] Determination of the association properties of such structures using NMR titration experiments, like those carried out for the systems **1**:**3** and **1**:**4**, was hampered by the complexity of the huge number of equilibria involved. We already pointed out that in solution, especially in the case of stoichiometric mixtures of **1**, **2** and **3b** corresponding to higher generation numbers n, several objects of different sizes coexist in equilibrium.[13] This is due to the fact that a) based on the association constants, determined for **1**:**3** and **1**:**4**, serving as suitable models, it has to be assumed that rapid association–dissociation equilibria are present and b) at higher n the required ratio of **2** and the



Scheme 7. Planar rotamers of an open-chain Hamiliton receptor.

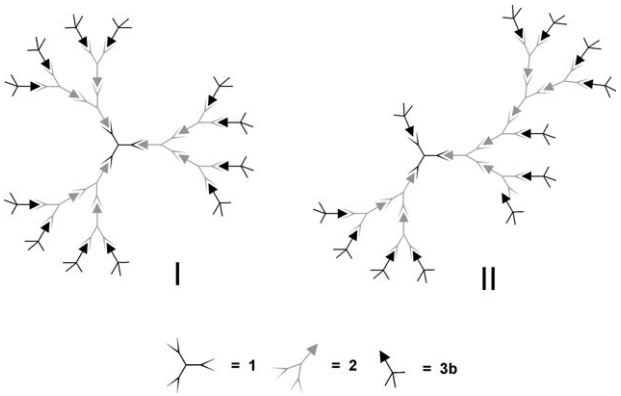


Figure 8. Schematic representation of supramolecular dendrimers composed of **1**, **2** and an end cap such as **3b** in a 1: $(3\times2^n-3)$: (3×2^n) stoichiometry. Left: **I** completely regular structure ($n=3$). Right: example for an irregular structure **II** ($n=3$).

end cap **3** differs only slightly and approaches a 1:1 limit. It has to be stated that not all objects, at least in solution, can be identical and cannot exhibit the perfect shape suggested by the schematic representation **I** in Figure 8. Moreover, it has to be pointed out that, for a given stoichiometry, not only a completely regular arrangement like that of **I,** but also irregular structures such as **II** ($n=3$) (Figure 8) are compatible with a 1:$(3\times2^n-3)$:(3×2^n) stoichiometry and with the exhaustive consumption of all possible hydrogen bonding sites. As a matter of fact, the number of possible isomers increases dramatically with increasing generation number. The key question is whether and how much the formation of **I** is favored over that of irregular structures such as **II** by a cumulating amount of cooperativity. A delicate balance exists between positive and negative cooperativity, as demonstrated for the model dendrimers **1**:**3** and **1**:**4**, namely, the most effective preorganization of the free Hamilton receptor binding sites and repulsive interaction between sterically overcrowded ligands. Although this question is difficult to address, the results presented here, as well as the fact that the structure of **3b** is very similar to that of **2**, suggest that the possibility of a cumulative cooperativity for the formation of completely regular dendrimers such as **I**, does exists. Regular structures could especially prevail in the solid state. Further work clarifying these critical questions is currently under way in our laboratory.

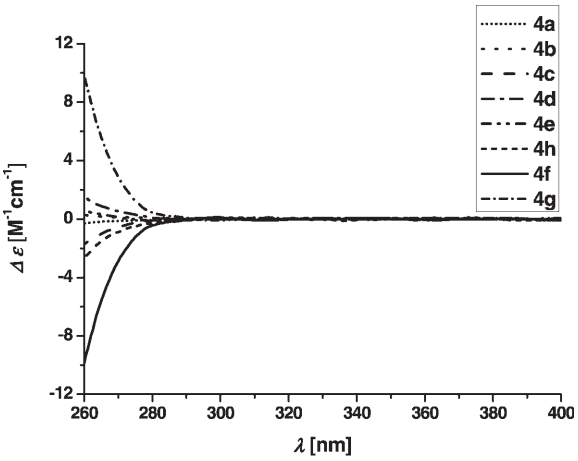


Figure 9. CD spectra of **4a**–**h** in $CHCl_3$ ($c=0.0002$ mol L^{-1}).

CD spectroscopy: The possibility to transmit chiral information over comparatively large distances represents an appealing opportunity for applications of dendritic macromolecules[26] in catalysis and molecular recognition. Chirality transfer is expected to occur from the chiral dendrons **4** to the achiral Hamilton receptor core **1** in the **1:4$_3$** dendrimers introduced here. The characteristic absorption bands of **1** at about 310 nm, which are distinct from the absorption of the aromatic groups of the chiral dendrons **4** at about 250 nm, should be highly diagnostic for the investigation of a chirality transfer process, since they should lead to new Cotton effects in the CD spectra of the supramolecular dendrimers **1:4$_3$**. The CD spectra of the free dendrons **4** recorded in $CHCl_3$ are shown in Figure 9. As expected, the Cotton effects increase with increasing generation number and conse-

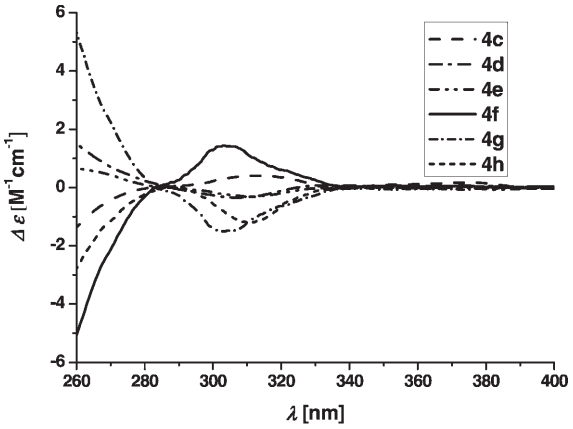


Figure 10. CD spectra of the 1:3 assemblies between **1** and **4c–h** in $CHCl_3$ ($c_1 = 0.00008$ mol L^{-1}).

quently with an increasing number of stereogenic centers and aromatic chromophores.[2] Pairs of enantiomers such as **4f** and **4g** give rise to CD spectra which represent perfect mirror images of each other.

The CD spectra of the chiral supramolecular dendrimers **1:4$_3$** are shown in Figure 10. Significantly, new Cotton effects were indeed observed in the region of the electronic absorption of the Hamilton receptor **1** at 310 nm for the case of the second- and third-generation systems **1** L_3 (L = **4c–h**). However, no Cotton effects in the absorption region of **1** were observed for the first-generation systems **1** L_3 (L = **4a,b**). This indicates that only a very weak chiral surrounding is provided by the two stereogenic centers of the first-generation dendrons **4a** and **4b**.

Complexes **1** L_3, involving second- and third-generation dendrons of opposite configuration such as **1:4c$_3$** and **1:4d$_3$**, lead to CD spectra with mirror-image behavior (Figure 10). On the other hand, the CD spectra of diastereoisomeric complexes such as **1:4e$_3$** or **1:4h$_3$** exhibit a different structure. For example, the CD spectrum of **1:4h$_3$** is characterized by two negative Cotton effects, below 280 nm and at 310 nm, whereas those of its diastereoisomers **1:4f$_3$** and **1:4g$_3$** display one positive and one negative Cotton effect each. The CD spectra of 1:1 complexes of **4** with the core **33** show similar characteristics as those of the corresponding **1:4$_3$** analogues (Figure 11). These characteristics include a) almost no Cotton effects at 310 nm for the first-generation dendrons, b) increasing Cotton effects with an increasing generation number, c) mirror image behavior for enantiomeric complexes, and d) the same characteristic shape of the diastereoisomeric complexes involving dendrons with mixed configurations. This demonstrates that the chiroptical properties of **1:4$_3$** are not due to the diastereoselective formation of chiral foldamers, such as the preferred C_3 symmetrical conformers of **1** within the 1:3 complexes, but are due to statistical chirality transfer from the chiral dendrons only.

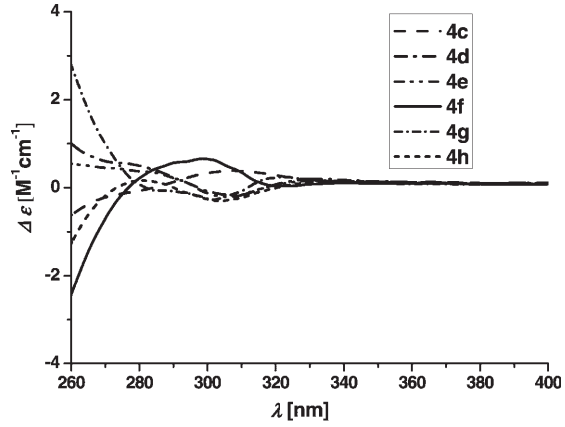


Figure 11. CD spectra of the 1:1 assemblies between **33** and **4c–h** in CH_2Cl_2 ($c_{33} = 0.0001$ mol L^{-1}).

Conclusion

The self-assembly of chiral depsipeptide dendrons **4**, which contain a cyanuric acid building block at their focal point, with the homotritopic Hamilton receptor **1** leads to the formation of the supramolecular complexes **1:4$_3$**. The subsequent binding of the dendrons to the core shows an overall positive cooperativity for all cases. The cooperativity is most pronounced for the binding of the second-generation dendrons **4c–e**. This is expressed, for example, by the magnitude of the association constants of the second and third complexation step and the high Hill coefficients n_H determined by NMR titration experiments. Significantly, the binding of the dendrons **4** to the receptor **1** is also diastereoselective. This is demonstrated, for example, by the fact that the subsequent binding of dendron **4e** with an all-*S* configuration of the inner and an all-*R* configuration of the outer tartrate layer shows a much higher cooperativity compared to the binding of **4c** and **4d** with all-*R* or all-S-configurations of all stereogenic centres. The formation of the **1:4$_3$** complexes with the third-generation dendrons **4f–h** shows the lowest cooperativity. This is due to the fact that these dendrons are very bulky, disfavoring the binding of the third dendron. In the case of the second-generation dendrons **4c–e,** the optimum balance between the preorganization of the Hamilton receptor into the favorable *cis–cis* conformation, caused by the subsequent binding of the first and second dendron and the steric overcrowding caused by their accumulation at receptor **1**, is guaranteed. Similar results are obtained by the corresponding complexation of the achiral Frechét-type dendrons **3** with **1**. Chiroptical investigations of 1:3 complexes of **1** and **4** reveal chirality transfer from the dendron to the Hamilton receptor, as demonstrated by the appearance of new CD absorptions at 310 nm. The complexes **1:4$_3$** represent the first examples of chiral supramolecular dendrimers whose construction is provided by complementary hydrogen bonding motifs.

Experimental Section

General remarks: All chemicals were obtained from Sigma-Aldrich and Acros Organics or were prepared according to known literature procedures. The preparation of **5–9**, **18**, and **19**[2–4] was described in previous communications. The solvents were purified by distillation. Reactions were monitored by thin-layer chromatography (TLC) using Riedel-de-Haën silica gel 60 F_{254} aluminium foils, detection by UV illumination. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Advance 300, JEOL JNM EX 400, JEOL JNM GX 400 and JEOL A 500 NMR spectrometers. The chemical shifts are given in ppm relative to TMS or the solvent peak as a standard reference. The resonance multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet), unresolved signals as brm. Mass spectra were measured with a Micromass Lab Spec (FAB) on a Finnigan MAT 900 spectrometer with 3-nitrobenzylalcohol as the matrix. IR spectra were recorded on React IR-1000 ASI Applied Systems (ATR-DiComp-Detector) on a diamond crystal. Circular dichroism (CD) measurements were carried out on a Jasco J 715 and Jasco J 810 machine using optical grade solvents and quartz glass cuvettes with a 2 mm path length. Optical rotations were measured on a Perkin Elmer 341 polarimeter. UV spectroscopy was performed using a Shimadzu UV-3102 spectrophotometer. Elemental analysis succeeded by combustion and gas chromatographical analysis was performed with an EA 1110 CHNS analyser (CEInstruments). Products were isolated by flash column chromatography (FC) (silica gel 60, particle size 0.04–0.063 mm, Merck).

Benzyl-6-bromohexanoate (12): Freshly distilled benzyl alcohol (2.32 mL, 18.92 mmol) was dissolved in CH_2Cl_2 and triethylamine (NEt_3, 2.63 mL, 18.92 mmol) was added. The mixture was cooled to 0 °C and 6-bromohexanoyl chloride (2.90 mL, 18.92 mmol) was added dropwise. After three hours the solution was washed with 10% aqueous HCl (1×100 mL) and with saturated aqueous $NaHCO_3$ (3×150 mL) and then dried over $MgSO_4$. The solvent was evaporated and the product dried in vacuo. Yield: 4.97 g (93%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (m, 2H; CH_2), 1.65 (m, 2H; CH_2), 1.83 (m, 2H; CH_2), 2.37 (t, ^3J = 7.7 Hz, 2H; CH_2CO), 3.39 (t, ^3J = 7.7 Hz, 2H; CH_2Br), 5.10 (s, 2H; CH_2–Bn), 7.37 ppm (m, 5H; Bn); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.9, 27.5, 32.2, 33.4, 33.9 (CH_2), 66.1 (CH_2–Bn), 128.1, 128.2, 128.5 (Ph), 135.9 (q-Ph), 173.1 ppm (C=O); MS (FAB): *m/z* (%): 285 $[M]^+$; IR (ATR): ν_{max} = 2941, 2868, 2362, 2343, 1733, 1455, 1382, 1355, 1254, 1212, 1162, 976, 737, 699 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{17}BrO_2$: C 54.75, H 6.01; found: C 54.63, H 6.2.

Benzyl-6-(2,4,6-trioxo-1,3,5-triazinan-1-yl)hexanoate (14): Compound **12** (2.84 g, 10 mmol) and cyanuric acid (6.50 g, 50 mmol) were dissolved in dry DMF (50 mL). 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 1.5 mL, 10 mmol) was added dropwise to the solution. The mixture was heated to 70 °C and stirred over night. The solvent was evaporated and the crude mixture purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 96:4). Yield: 2.00 g (60%) as a white solid; m.p. 149 °C; ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 1.24 (m, 2H; CH_2), 1.51 (m, 4H; CH_2), 2.33 (t, ^3J = 7.7 Hz, 2H; CH_2CO), 3.59 (t, ^3J = 7.7 Hz, 2H; CH_2N), 5.07 (s, 2H; CH_2–Bn), 7.34 (m, 5H; Bn), 11.39 ppm (brm, 2H; NH); ^{13}C NMR (100.6 MHz, [D_6]DMSO): δ = 24.1, 25.5, 27.0, 33.3, 38.9 (CH_2), 65.3 (CH_2–Bn), 127.9, 128.0, 128.5 (Ph), 136.3 (q-Ph), 148.7, 149.8, 172.7 ppm (C=O); IR (ATR): ν_{max} = 3030, 2949, 2837, 2362, 2343, 1779, 1729, 1664, 1490, 1428, 1243, 1173, 830, 760, 695 cm^{-1}; MS (FAB): *m/z* (%): 334 $[M]^+$; elemental analysis calcd (%) for $C_{16}H_{19}N_3O_5$: C 57.65, H 5.75, N 12.61; found: C 57.71, H 5.81, N 12.52.

1-(5-Carboxypentyl)-1,3,5-triazin-2,4,6-trion (15): Compound **14** (1500 mg, 4.5 mmol) was dissolved in CH_3OH (150 mL) and 10% Pd/C (150 mg) was added. This suspension was subjected to hydrogenation until no more hydrogen was consumed. The Pd-C was filtered over Celite and CH_3OH was evaporated. The product was dried in vacuo. Yield 1100 mg (99%) as a white solid; m.p. 213 °C; ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 1.33 (m, 2H; CH_2), 1.65 (m, 4H; CH_2), 2.30 (t, ^3J = 7.7 Hz, 2H; CH_2CO), 3.71 (t, ^3J = 7.7 Hz, 2H; CH_2N), 11.63 ppm (brm, 2H; NH); ^{13}C NMR (100.6 MHz, [D_6]DMSO): δ = 24.5, 25.9, 27.4, 33.8, 39.0 (CH_2), 149.0, 150.2, 174.8 ppm (C=O); IR (ATR): ν_{max} = 3476, 3214, 2938, 1730, 1690, 1632, 1466, 1417, 1381, 1319, 1262, 1213, 1058, 925, 790, 733, 551, 433 cm^{-1}; elemental analysis calcd (%) for $C_9H_{13}N_3O_5$: C 44.44, H 5.39, N 17.28; found: C 44.35, H 5.61, N 17.18.

General procedure for the preparation of the esters 4a–e: The carboxylic acid (1.6 mmol), 4-dimethylaminopyridine (DMAP, 1.6 mmol) and 1-hydroxybenzoltriazole (HOBt, 1.6 mmol) were added to a solution of the alcohol (1.6 mmol) in CH_2Cl_2 (100 mL). 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl) (1.6 mmol) was added all at once at room temperature and the suspension was stirred for 72 h. The solution was washed with 10% aqueous HCl (1×100 mL) and with saturated aqueous $NaHCO_3$ (3×150 mL) and then dried over $MgSO_4$. After evaporation of the solvent the crude product was purified by column chromatography.

Compound 4a: Compound **4a** was synthesized according to the general procedure from dendron **5** (720 mg, 1.66 mmol) and 1-(5-carboxypentyl)-1,3,5-triazin-2,4,6-trion (**15**) (400 mg, 1.66 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 15:1). Yield: 500 mg (46%) as a white solid; m.p. 80 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (m, 2H, CH_2), 1.53 (m, 4H, CH_2), 2.20 (m, 2H; CH_2), 3.73 (m, 2H; CH_2N), 5.03 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.09 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.16 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.20 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.75 (d, ^3J = 2.8 Hz, 1H; *CH), 5.85 (d, ^3J = 2.8 Hz, 1H; *CH), 7.09 (m, 3H; Bn), 7.10 (m, 2H; Bn), 7.29 (m, 5H; Bn), 7.33 (m, 2H; Bz), 7.57 (m, 1H; Bz), 7.89 (m, 2H; Bz), 8.85 ppm (brm, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.8, 25.5, 27.3 (CH_2), 33.6 (CH_2COO), 41.6 (CH_2N), 67.7, 67.8 (CH_2–Bn), 70.7, 71.2 (*CH), 128.2, 128.3, 128.4, 128.5, 128.6, 130.1 (Ph), 133.6, 134.5, 134.8 (q-Ph), 147.9, 149.1, 165.0, 165.6, 165.7, 172.1 ppm (C=O); IR (ATR): ν_{max} = 3227, 2972, 2362, 2339, 1737, 1455, 1374, 1231, 1092, 714, 695 cm^{-1}; MS (FAB): *m/z* (%): 660 $[M]^+$; UV/Vis (CH_3OH): $\lambda(\varepsilon)$ = 264 (1000), 231.5 nm (16000); elemental analysis calcd (%) for $C_{34}H_{33}N_3O_{11}$ (659.21): C 61.91, H 5.04, N 6.37; found: C 61.87, H 5.14, N 6.32; $[\alpha]_D^{20}$ = +30.0 (*c* = 0.0968, CH_2Cl_2).

Compound 4b: Compound **4b** was synthesized according to the general procedure from dendron **6** (720 mg, 1.66 mmol) and 1-(5-carboxypentyl)-1,3,5-triazin-2,4,6-trion (**15**) (400 mg, 1.66 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 15:1). Yield: 450 mg (41%) as a white solid; m.p. 79 C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (m, 2H; CH_2), 1.50 (m, 4H; CH_2), 2.20 (m, 2H; CH_2), 3.73 (m, 2H; CH_2N), 5.03 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.10 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.16 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.20 (d, ^2J = 12 Hz, 1H; CH_2–Bn), 5.75 (d, ^3J = 2.8 Hz, 1H; *CH), 5.85 (d, ^3J = 2.8 Hz, 1H; *CH), 7.09 (m, 3H; Bn), 7.10 (m, 2H; Bn), 7.29 (m, 5H; Bn), 7.33 (m, 2H; Bz), 7.57 (m, 1H; Bz), 7.89 (m, 2H; Bz), 8.93 ppm (brm, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.4, 25.1, 26.7 (CH_2), 32.8 (CH_2COO), 39.9 (CH_2N), 67.8, 68.1 (CH_2–Bn), 70.8, 71.1 (*CH), 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 129.9 (Ph), 133.8, 134.3, 134.7 (q-Ph), 165.0, 165.7, 165.8, 172.1 ppm (C=O); IR (ATR): ν_{max} = 3225, 2972, 2365, 2339, 1734, 1457, 1374, 1230, 1092, 718, 695 cm^{-1}; MS (FAB): *m/z* (%): 660 $[M]^+$; UV/Vis (CH_3OH): $\lambda(\varepsilon)$ = 264.5 (1000), 231.5 nm (13000); elemental analysis calcd (%) for $C_{34}H_{33}N_3O_{11}$: C 61.91, H 5.04, N 6.37; found: C 61.39, H 5.30, N 6.10; $[\alpha]_D^{20}$ = −31.0 (*c* = 1.2020, CH_2Cl_2).

Compound 4c: Compound **4c** was synthesized according to the general procedure from dendron **7** (755 mg, 0.57 mmol) and 1-(5-carboxypentyl)-1,3,5-triazin-2,4,6-trion (**15**) (140 mg, 0.57 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 15:1). Yield: 590 mg (65%) as a white solid; m.p. 75 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (m, 22H; CH_2), 2.14 (m, 6H; CH_2COO), 3.20 (m, 6H; CH_2N), 3.71 (brm, 1H; NH), 5.02 (d, ^2J = 5.5 Hz, 1H; CH_2–Bn), 5.05 (d, ^2J = 5.5 Hz, 1H; CH_2–Bn), 5.09 (d, ^2J = 6.5 Hz, 1H; CH_2–Bn), 5.12 (d, ^2J = 6.5 Hz, 1H; CH_2–Bn), 5.15 (d, ^2J = 6.0 Hz, 1H; CH_2–Bn), 5.18 (d, ^2J = 6.0 Hz, 1H; CH_2–Bn), 5.22 (d, ^2J = 4.0 Hz, 1H; CH_2–Bn), 5.24 (d, ^2J = 4.0 Hz, 1H; CH_2–Bn), 5.73 (d, ^3J = 3.0 Hz, 1H; *CH), 5.79 (d, ^3J = 3.0 Hz, 1H; *CH), 5.81 (d, ^3J = 3.0 Hz, 1H; *CH), 5.82 (d, ^3J = 3.0 Hz, 1H; *CH), 5.89 (d, ^3J = 3.0 Hz, 1H; *CH), 5.91 (d, ^3J = 3.0 Hz, 1H; *CH), 6.58 (brm, 1H; NH), 7.09 (m, 6H; Bn), 7.15 (m, 4H; Bn), 7.27 (m, 10H; Bn), 7.38 (m, 6H; Ph), 7.53 (m, 3H; Bz), 7.91 (m, 4H; Bz), 8.01 (m, 2H; Bz), 9.35 ppm (s, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.9, 24.0, 24.1, 25.2, 25.6, 25.82, 25.84, 27.1, 28.7, 28.8 (CH_2), 33.1, 33.2, 33.4

(CH_2COO), 39.2, 39.3, 41.2 (CH_2N), 67.7, 67.9 (CH_2–Bn), 70.7, 71.1, 71.2, 72.3 (*CH), 128.2, 128.3, 128.31, 128.42, 128.6, 128.7, 129.7, 129.9, 130.0, 133.6, 133.8, 134.4, 134.7, 134.8 (Ph), 147.9, 149.0, 164.9, 165.0, 165.6, 165.7, 166.2, 166.3, 171.8, 172.1, 172.2, 172.3 ppm (C=O); IR (ATR): ν_{max} = 3273, 2972, 2362, 2343, 1733, 1698, 1540, 1455, 1378, 1231, 1092, 953, 714 cm^{-1}; MS (FAB): *m/z* (%): 1539 $[M]^+$; UV/Vis (CH_3OH): λ (ε) = 264 (3000), 232 nm (39000); elemental analysis calcd (%) for $C_{84}H_{87}N_5O_{25}$: C 64.01, H 5.44, N 4.55; found: C 63.64, H 5.57, N 4.45; $[\alpha]_D^{20} = +20$ (*c* = 0.1106, CH_2Cl_2).

Compound 4d: Compound **4d** was synthesized according to the general procedure from dendron **8** (650 mg, 0.49 mmol) and 1-(5-carboxypentyl)-1,3,5-triazin-2,4,6-trion ((**15**) 120 mg, 0.49 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 15:1). Yield: 450 mg (59%) as a white solid; m.p. 75°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (m, 22H; CH_2), 2.14 (m, 6H; CH_2COO), 3.20 (m, 6H; CH_2N), 3.71 (br m, 1H; NH), 5.02 (d, ^2J = 5.5 Hz, 1H; CH_2–Bn), 5.05 (d, ^2J = 5.5 Hz, 1H; CH_2–Bn), 5.08 (d, ^2J = 6.5 Hz, 1H; CH_2–Bn), 5.12 (d, ^2J = 6.5 Hz, 1H; CH_2–Bn), 5.15 (d, ^2J = 6.0 Hz, 1H; CH_2–Bn), 5.18 (d, ^2J = 6.0 Hz, 1H; CH_2–Bn), 5.22 (d, ^2J = 4.0 Hz, 1H; CH_2–Bn), 5.24 (d, ^2J = 4.0 Hz, 1H; CH_2–Bn), 5.74 (d, ^3J = 3.0 Hz, 1H; *CH), 5.79 (d, ^3J = 3.0 Hz, 1H; *CH), 5.81 (d, ^3J = 3.0 Hz, 1H; *CH), 5.82 (d, ^3J = 3.0 Hz, 1H; *CH), 5.89 (d, ^3J = 3.0 Hz, 1H; *CH), 5.91 (d, ^3J = 3.0 Hz, 1H; *CH), 6.58 (br m, 1H; NH), 7.09 (m, 6H; Bn), 7.15 (m, 4H; Bn), 7.27 (m, 10H; Bn), 7.38 (m, 6H; Ph), 7.53 (m, 3H; Bz), 7.91 (m, 4H; Bz), 8.01 (m, 2H; Bz), 9.35 ppm (s, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.8, 24.0, 24.1, 25.2, 25.6, 25.82, 25.84, 27.1, 28.7, 28.8 (CH_2), 33.1, 33.2, 33.4 (CH_2COO), 39.2, 39.3, 41.2 (CH_2N), 67.7, 67.9 (CH_2–Bn), 70.7, 71.1, 71.2, 72.3 (*CH), 128.2, 128.3, 128.31, 128.42, 128.5, 128.7, 129.7, 129.9, 130.0, 133.6, 133.8, 134.4, 134.7, 134.8 (Ph), 147.9, 149.0, 164.9, 165.0, 165.6, 165.7, 166.2, 166.3, 171.8, 172.1, 172.2, 172.3 ppm (C=O); IR (ATR): ν_{max} = 3250, 2972, 2362, 2339, 1733, 1698, 1540, 1455, 1378, 1216, 1092, 958, 714 cm^{-1}; MS (FAB): *m/z* (%): 1539 $[M]^+$; UV/Vis (CH_3OH): λ (ε) = 264 (3000), 232 nm (39000); elemental analysis calcd (%) for $C_{84}H_{87}N_5O_{25}$: C 64.01, H 5.44, N 4.55; found: C 63.84, H 5.57, N 4.54; $[\alpha]_D^{20} = -20$ (*c* = 0.1098, CH_2Cl_2).

Compound 4e: Compound **4e** was synthesized according to the general procedure from dendron **9** (650 mg, 0.49 mmol) and 1-(5-carboxypentyl)-1,3,5-triazin-2,4,6-trion (**15**) (120 mg, 0.49 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 15:1). Yield: 560 mg (74%) as a white solid; m.p. 74°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (m, 22H; CH_2), 2.13 (m, 6H; CH_2COO), 3.20 (m, 6H; CH_2N), 3.73 (br m, 1H; NH), 5.02 (d, ^2J = 5.5 Hz, 1H; CH_2–Bn), 5.05 (d, ^2J = 5.5 Hz, 1H; CH_2–Bn), 5.09 (d, ^2J = 6.5 Hz, 1H; CH_2–Bn), 5.12 (d, ^2J = 6.5 Hz, 1H; CH_2–Bn), 5.15 (d, ^2J = 6.0 Hz, 1H; CH_2–Bn), 5.18 (d, ^2J = 6.0 Hz, 1H; CH_2–Bn), 5.22 (d, ^2J = 4.0 Hz, 1H; CH_2–Bn), 5.24 (d, ^2J = 4.0 Hz, 1H; CH_2–Bn), 5.73 (d, ^3J = 3.0 Hz, 1H; *CH), 5.79 (d, ^3J = 3.0 Hz, 1H; *CH), 5.81 (d, ^3J = 3.0 Hz, 1H; *CH), 5.82 (d, ^3J = 3.0 Hz, 1H; *CH), 5.89 (d, ^3J = 3.0 Hz, 1H; *CH), 5.91 (d, ^3J = 3.0 Hz, 1H; *CH), 6.48 (br m, 1H; NH), 7.09 (m, 6H; Bn), 7.14 (m, 4H; Bn), 7.28 (m, 10H; Bn), 7.38 (m, 6H; Ph), 7.54 (m, 3H; Bz), 7.90 (m, 4H; Bz), 8.01 (m, 2H; Bz), 9.05 ppm (s, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.9, 24.0, 24.1, 25.3, 25.6, 25.8, 27.1, 28.8, 28.9 (CH_2), 33.1, 33.2, 33.4 (CH_2COO), 39.2, 39.3, 41.3 (CH_2N), 67.7, 67.9 (CH_2–Bn), 70.7, 71.1, 72.3 (*CH), 127.0, 128.2, 128.3, 128.4, 128.6, 130.0, 133.6, 133.9, 134.4, 134.7 (Ph), 147.6, 149.0, 165.0, 165.6, 165.7, 166.2, 166.3, 171.8, 172.1, 172.3, 172.33 ppm (C=O); IR (ATR): ν_{max} = 3253, 2972, 2363, 2336, 1733, 1699, 1540, 1458, 1378, 1212, 1092, 954, 714 cm^{-1}; MS (FAB): *m/z* (%): 1539 $[M]^+$; UV/Vis (CH_3OH): $\lambda(\varepsilon)$ = 264 (3000), 232 nm (39000); elemental analysis calcd (%) for $C_{84}H_{87}N_5O_{25}$: C 64.01, H 5.44, N 4.55; found: C 63.84, H 5.49, N 4.43; $[\alpha]_D^{20} = +16$ (*c* = 0.1000, CH_2Cl_2).

General procedure for the preparation of compounds 16 and 17: The Bn ester was dissolved in CH_3OH (50 mL) and 30 mass percent of Pd/C (10% Pd) were added. This suspension was subjected to hydrogenation until no more hydrogen was consumed. The Pd/C was filtered over Celite and CH_3OH was evaporated. The product was dried in vacuo.

Compound 16: Compound **16** was synthesized according to the general procedure with compound **4a** (300 mg, 0.46 mmol) and 10% Pd/C (100 mg) in CH_3OH (70 mL). Yield: 217 mg (99%) as a white solid; m.p. 166 C; ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 1.27 (m, 2H; CH_2), 1.51 (m, 4H; CH_2), 2.33 (t, ^3J = 7.7 Hz, 2H; CH_2CO), 3.60 (t, ^3J = 7.7 Hz, 2H; CH_2N), 5.58 (br m, 1H; *CH), 5.70 (br m, 1H; *CH), 7.57 (m, 2H, Bz), 7.71 (m, 1H, Bz), 7.94 (m, 2H, Bz), 11.59 ppm (br m, 2H, NH); ^{13}C NMR (100.6 MHz, [D_6]DMSO): δ = 25.9, 27.5, 28.9, 35.0, 42.5 (CH_2), 129.9, 131.3, 131.4 (Ph), 135.0 (q-Ph), 150.9, 152.0, 167.6, 174.8 ppm (C=O); IR (ATR): ν_{max} = 3231, 2972, 2362, 2343, 1737, 1459, 1374, 1263, 1231, 1096, 764, 714 cm^{-1}.

Compound 17: Compound **17** was synthesized according to the general procedure with compound **4b** (400 mg, 0.46 mmol) and 10% Pd/C (130 mg) in CH_3OH (70 mL). Yield: 290 mg (99%) as a white solid; ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 1.27 (m, 2H; CH_2), 1.51 (m, 4H; CH_2), 2.33 (t, ^3J = 7.7 Hz, 2H; CH_2CO), 3.60 (t, ^3J = 7.7 Hz, 2H; CH_2N), 5.58 (br m, 1H, *CH), 5.70 (br m, 1H, *CH), 7.57 (m, 2H, Bz), 7.71 (m, 1H, Bz), 7.94 (m, 2H, Bz), 11.59 ppm (br m, 2H, NH); ^{13}C NMR (100.6 MHz, [D_6]DMSO): δ = 25.9, 27.5, 28.9, 35.0, 42.5 (CH_2), 129.9, 131.3, 131.4 (Ph), 135.0 (q-Ph), 150.9, 152.0, 167.6, 174.8 ppm (C=O); IR (ATR): ν_{max} = 3230, 2972, 2365, 2343, 1739, 1460, 1374, 1268, 1231, 1096, 768, 714 cm^{-1}.

General procedure for the preparation of compounds 4f–h: The diacid (0.35 mmol) was dissolved in CH_2Cl_2 (50 mL) and HOBt (0.70 mmol) was added. The solution was cooled to 0°C. In another vessel the amine (0.70 mmol) was dissolved in CH_2Cl_2 (50 mL) and after cooling the solution to 0°C NEt_3 (0.70 mmol) was added. Both solution were unified and EDC·HCl (0.70 mmol) was added. The mixture was stirred for 48 h. The solution was washed with 10% aqueous HCl (1×100 mL) and with saturated aqueous $NaHCO_3$ (3×150 mL) and then dried over $MgSO_4$. After evaporation of the solvent the crude product was purified by column chromatography.

Compound 4f: Compound **4f** was synthesized according to the general procedure from dendron **18** (1.00 g, 0.70 mmol) and compound **16** (177 mg, 0.35 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 30:1). Yield: 360 mg (32%) as a white solid; m.p. 78 C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (m, 42H; CH_2), 2.04 (m, 14H; CH_2COO), 3.20 (m, 14H; CH_2N), 3.71 (br m, 2H; NH), 5.05 (m, 8H; CH_2–Bn), 5.20 (m, 8H; CH_2–Bn), 5.74 (m, 10H; *CH), 5.89 (m, 4H; *CH), 6.61 (br m, 4H; NH), 7.09 (m, 12H; Ph), 7.14 (m, 8H; Bn), 7.27 (m, 20H; Bn), 7.38 (m, 14H; Bz), 7.53 (m, 7H; Bz), 7.91 (m, 8H; Bz), 8.01 (m, 6H; Bz), 9.53 ppm (s, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.8, 24.7, 25.3, 25.5, 25.7, 26.8,28.7, 28.8 (CH_2), 33.0, 33.2, 33.3, 33.7 (CH_2COO), 38.8, 39.0, 39.2, 41.0 (CH_2N), 67.7, 67.9 (CH_2–Bn), 70.7, 71.1, 71.2, 72.3, 72.9, 73.1 (*CH), 128.4, 128.5, 128.6, 128.7, 128.8, 129.0, 130.2, 133.8, 134.0, 134.2, 134.6, 134.9, (Ph), 148.2, 149.4, 165.31, 165.33, 165.36, 165.9, 166.0, 166.5, 166.6, 166.7, 172.0, 172.5, 172.6 ppm (C=O); IR (ATR): ν_{max} = 3277, 2941, 2343, 1729, 1687, 1540, 1455, 1254, 1212, 1092, 1027, 953, 714 cm^{-1}; MS (FAB): *m/z* (%): 3297 $[M]^+$; UV/Vis (CH_3OH): λ (ε) = 264 (8000), 232 nm (83000);elemental analysis calcd (%) for $C_{178}H_{183}N_9O_{53}\cdot CH_2Cl_2$: C 63.58, H 5.51, N 3.73; found: C 63.46, H 5.60, N 3.82; $[\alpha]_D^{20} = +18$ (*c* = 0.200, CH_2Cl_2).

Compound 4g: Compound **4g** was synthesized according to the general procedure from dendron **19** (370 mg, 0.26 mmol) and compound **17** (63 mg, 0.35 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 30:1). Yield: 110 mg (26%) as a white solid; m.p. 79 C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (m, 42H; CH_2), 2.04 (m, 14H; CH_2COO), 3.20 (m, 14H; CH_2N), 3.71 (br m, 2H; NH), 5.05 (m, 8H; CH_2–Bn), 5.20 (m, 8H; CH_2–Bn), 5.74 (m, 10H; *CH), 5.89 (m, 4H; *CH), 6.61 (br m, 4H; NH), 7.09 (m, 12H; Ph), 7.14 (m, 8H; Bn), 7.27 (m, 20H; Bn), 7.38 (m, 14H; Bz), 7.53 (m, 7H; Bz), 7.91 (m, 8H; Bz), 8.01 (m, 6H; Bz), 9.53 ppm (s, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 23.8, 24.7, 25.3, 25.5, 25.7, 26.8,28.7, 28.8 (CH_2), 33.0, 33.2, 33.3, 33.7 (CH_2COO), 38.8, 39.0, 39.2, 41.0 (CH_2N), 67.7, 67.9 (CH_2–Bn), 70.7, 71.1, 71.2, 72.3, 72.9, 73.1 (*CH), 128.4, 128.5, 128.6, 128.7, 128.8, 129.0, 130.2, 133.8, 134.0, 134.2, 134.6, 134.9, (Ph), 148.2, 149.4, 165.31, 165.33, 165.36, 165.9, 166.0, 166.5, 166.6, 166.7, 172.0, 172.5, 172.6 ppm (C=O); IR (ATR): ν_{max} = 3296, 2941, 2343, 1733, 1687, 1540, 1455, 1254, 1216, 1197, 1127, 957, 714 cm^{-1}; MS (FAB): *m/z* (%): 3297 $[M]^+$; UV/Vis (CH_3OH): $\lambda(\varepsilon)$ = 264.5 (8000), 231.5 nm (83000); elemen-

tal analysis calcd (%) for $C_{178}H_{183}N_9O_{53}{\cdot}CH_2Cl_2$: C 63.58, H 5.51, N 3.73; found: C 63.46, H 5.68, N 3.76; $[\alpha]_D^{20} = -18$ ($c = 0.500$, CH_2Cl_2).

Compound 4h: Compound **4h** was synthesized according to the general procedure from dendron **18** (800 mg, 0.56 mmol) and compound **17** (134 mg, 0.28 mmol). The crude product was purified by column chromatography (silica, CH_2Cl_2/CH_3OH, 30:1). Yield: 320 mg (32%) as a white solid; m.p. 78 C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.44$ (m, 42H; CH_2), 2.04 (m, 14H; CH_2COO), 3.20 (m, 14H; CH_2N), 3.71 (br m, 2H; NH), 5.05 (m, 8H; CH_2–Bn), 5.20 (m, 8H; CH_2–Bn), 5.74 (m, 10H; *CH), 5.89 (m, 4H; *CH), 6.61 (br m, 4H; NH), 7.09 (m, 12H; Ph), 7.14 (m, 8H; Bn), 7.27 (m, 20H; Bn), 7.38 (m, 14H; Bz), 7.53 (m, 7H; Bz), 7.91 (m, 8H; Bz), 8.01 (m, 6H; Bz), 9.53 ppm (s, 2H; NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 23.8$, 24.7, 25.3, 25.5, 25.7, 26.8,28.7, 28.8 (CH_2), 33.0, 33.2, 33.3, 33.7 (CH_2COO), 38.8, 39.0, 39.2, 41.0 (CH_2N), 67.7, 67.9 (CH_2Bn), 70.7, 71.1, 71.2, 72.3, 72.9, 73.1 (*CH), 128.4, 128.5, 128.6, 128.7, 128.8, 129.0, 130.2, 133.8, 134.0, 134.2, 134.6, 134.9, (Ph), 148.2, 149.4, 165.31, 165.33, 165.36, 165.9, 166.0, 166.5, 166.6, 166.7, 172.0, 172.5, 172.6 ppm (C=O); IR (ATR): $\nu_{max} = 3250$, 2941, 2343, 1735, 1687, 1540, 1458, 1254, 1213, 1197, 1125, 959, 714 cm^{-1}; MS (FAB): *m/z* (%): 3297 $[M]^+$; UV/Vis (CH_3OH): λ (ε) = 264 (8000), 232 nm (82000); elemental analysis calcd (%) for $C_{178}H_{183}N_9O_{53}{\cdot}CH_2Cl_2$: C 63.58, H 5.51, N 3.73; found: C 63.59, H 5.58, N 3.71; $[\alpha]_D^{20} = +26$ ($c = 0.200$, CH_2Cl_2).

Compound 28: The reaction was performed under nitrogen atmosphere. A mixture of compound **25** (4.89 g, 13.00 mmol), methyl-3,5-dihydroxybenzoate (1.09 g, 6.50 mmol), K_2CO_3 (2,25 g, 16.30 mmol) and [18]crown-6 (0.35 g, 1.30 mmol) was suspended in dry acetone (70 mL) and refluxed for 24 h. Water (100 mL) and Et_2O (100 mL) were added to the solution and the layers were separated. The water layer was extracted with Et_2O (3×150 mL) and the organic layer was dried over Na_2SO_4. After evaporation of the solvent the crude product was purified by column chromatography (SiO_2, CH_2Cl_2). Yield: 1.63 g (33%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.83$ (s, 3H; CH_3), 4.92 (s, 4H; CH_2Bn), 4.95 (s, 8H; CH_2Bn), 6.50 (t, $^4J = 2.2$ Hz, 2H; Ph), 6.60 (d, $^4J = 2.3$ Hz, 4H; Ph), 6.70 (t, $^4J = 2.3$ Hz, 1H; Ph), 7.20 (d, $^4J = 2.3$ Hz, 2H; Ph), 7.29 ppm (m, 20H; Ph); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 52.7$ (CH_3), 70.5 (CH_2Bn), 102.1, 106.8, 107.6, 108.9, 128.0, 128.4, 129.0, 132.5, 137.1, 139.3, 160.1, 160.6 (Ph), 167.1 ppm (C=O); IR (ATR): $\nu_{max} = 3246$, 3030, 2953, 2876, 1714, 1594, 1440, 1374, 1336, 1305, 1243, 1162, 1058, 1031, 834, 726, 695 cm^{-1}; MS (FAB): *m/z* (%): 773 $[M]^+$; elemental analysis calcd (%) for $C_{50}H_{44}O_8$: C 77.70, H 5.74; found: C 76.40, H 5.54.

Compound 29: The reaction was performed under a nitrogen atmosphere. A mixture of compound **26** (5.24 g, 6.49 mmol), methyl-3,5-dihydroxybenzoate (0.55 g, 3.24 mmol), K_2CO_3 (2.24 g, 16.21 mmol) and [18]crown-6 (0.35 g, 1.30 mmol) was suspended in dry acetone (120 mL) and refluxed for 24 h. Water (40 mL) and Et_2O (60 mL) were added to the solution and the layers were separated. The water layer was extracted with Et_2O (3×150 mL) and the organic layer was dried over Na_2SO_4. After evaporation of the solvent the crude product was purified by column chromatography (SiO_2, CH_2Cl_2). Yield: 3.73 g (71%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.83$ (s, 3H; CH_3), 4.95 (s, 8H; CH_2Bn), 4.97 (s, 4H; CH_2Bn), 5.00 (s, 16H), 6.53 (t, $^4J = 2.3$ Hz, 2H; Ph), 6.55 (t, $^4J = 2.2$ Hz, 4H; Ph), 6.65 (d, $^4J = 2.2$ Hz, 4H; Ph), 6.66 (d, $^4J = 2.3$ Hz, 8H; Ph), 6.78 (t, $^4J = 2.4$ Hz, 1H; Ph), 7.38 ppm (m, 42H; Ph); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 52.3$ (CH_3), 70.0, 70.1 (CH_2Bn), 101.54, 101.61, 106.3, 106.4, 107.6, 108.3, 127.4, 127.8, 128.4, 132.0, 137.1, 138.7, 139.0, 159.5, 160.1, 160.2 (Ph), 166.5 ppm (C=O); IR (ATR): $\nu_{max} =$ 3062, 3030, 2927, 2876, 1714, 1594, 1497, 1440, 1374, 1343, 1321, 1297, 1153, 1042, 834, 735, 695, 631 cm^{-1}; MS (FAB): *m/z* (%): 1622 $[M]^+$; elemental analysis calcd (%) for $C_{106}H_{92}O_{16}$: C 78.50, H 5.72; found: C 78.13, H 5.69.

Compound 30: A mixture of NaOH (24.00 g, 0.60 mol) and compound **27** (10.00 g, 28.70 mmol) was suspended in water (200 mL) and stirred for 24 h at 70°C. After evaporation of the solvent the residue was dissolved in EtOAc (80 mL) and filtrated. The solvent was evaporated and the product was dried in vacuum. Yield: 9.16 g (95%) as a white solid; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 5.19$ (br m, s, 4H; CH_2Bn) 6.97 (t, $^4J =$ 2.3 Hz, 1H; Ph), 7.21 (d, $^4J = 2.3$ Hz, 2H; Ph), 7.44 (m, 10H; Ph), 13.39 ppm (br m, s, 1H; COOH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): $\delta = 69.05$ (CH_2Bn) 106.11, 107.55, 127.23, 127.45, 128.00, 132.45, 136.30, 158.96 (Ph), 166.44 ppm (C=O); IR (ATR): $\nu_{max} = 3208$, 3110, 2945, 1687, 1594, 1444, 1420, 1378, 1343, 1301, 1274, 1216, 1162, 1058, 1027, 930, 903, 880, 849, 737, 695 cm^{-1}; MS (FAB): *m/z* (%): 335 $[M]^+$; elemental analysis calcd (%) for $C_{21}H_{18}O_4$ (334.37): C 75.43, H 5.43; found: C 75.19, H 5.55.

Compound 31: A solution of NaOH (6.00 g, 0.15 mmol) in water (40 mL) was added dropwise to a solution of compound **28** (1.55 g, 2.00 mmol) in THF (60.00 mL). The mixture was stirred for 24 h at 80°C and the pH of the solution was adjusted to 9 by the addition of conc. HCl. The solvent was evaporated and the residue was dissolved in $CHCl_3$ (200 mL) and water (200 mL). The two layers were separated and the organic layer was extracted with HCl (200 mL). The organic layer was dried with Na_2SO_4 and the solvent was evaporated. The crude product was purified by column chromatography (SiO_2, gradient CH_2Cl_2 → CH_2Cl_2/EtOAc 10:1 → EtOAc). Yield: 1.40 g (92%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.01$ (s, 4H; CH_2Bn), 5.02 (s, 8H; CH_2Bn), 6.55 (t, $^4J =$ 2.2 Hz, 2H; Ph), 6.66 (d, $^4J = 2.2$ Hz, 4H; Ph), 6.80 (t, $^4J = 2.3$ Hz, 1H; Ph), 7.14 (d, $^4J = 2.3$ Hz, 2H; Ph), 7.31 (m, 20H; Ph), 12.79 ppm (br m, 1H; COOH); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 69.2$ (CH_2Bn), 100.9, 106.1, 106.2, 107.9, 127.3, 127.5, 128.1, 132.7, 136.6, 138.8, 159.1, 159.4 (Ph), 166.8 ppm (C=O); IR (ATR): $\nu_{max} = 3235$, 3065, 3030, 2910, 2868, 1691, 1594, 1444, 1366, 1305, 1162, 1042, 845, 818, 753, 733, 695 cm^{-1}; MS (FAB): *m/z* (%): 759 $[M]^+$; elemental analysis calcd (%) for $C_{49}H_{42}O_8$ (758.85): C 77.55, H 5.58; found: C 77.46, H 5.58.

Compound 32: A solution of NaOH (12.00 g, 0.3 mmol) in water (100 mL) was added dropwise to a solution of compound **29** (3.50 g, 2.16 mmol) in THF (60.00 mL). The mixture was stirred for 24 h at 80°C. The obtained two layers were separated and the water layer was extracted with $CHCl_3$ (3x 100 mL). The organic layer was extracted with HCl (100 mL).and dried over Na_2SO_4. The solvent was evaporated and the crude mixture purified by column chromatography (SiO_2, EtOAc/CH_2Cl_2 1:20). Yield: 2.70 g (78%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.95$ (s, 8H; CH_2Bn), 4.97 (s, 4H; CH_2Bn), 4.99 (s, 16H; CH_2Bn), 6.54 (t, $^4J = 2.4$ Hz, 2H; Ph), 6.55 (t, $^4J = 2.1$ Hz, 4H; Ph), 6.66 (d, $^4J =$ 2.2 Hz, 12H; Ph), 6.82 (t, $^4J = 2.2$ Hz, 1H; Ph), 7.27 (d, $^4J = 3.0$ Hz, 2H; Ph), 7.34 (m, 40H; Ph), 11.59 ppm (br m, 1H; COOH); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 70.0$, 70.1, 70.2 (CH_2Bn), 101.5, 101.7, 106.3, 106.4, 107.9, 108.9, 127.4, 127.9, 128.4, 130.9, 136.6, 138.6, 139.0, 159.5, 159.9, 160.0 (Ph), 170.4 ppm (C=O); IR (ATR): $\nu_{max} = 3065$, 3030, 2872, 1691, 1594, 1444, 1370, 1328, 1305, 1162, 1042, 822, 733, 695, 681 cm^{-1}; MS (FAB): *m/z* (%): 1608 $[M]^+$; elemental analysis calcd (%) for $C_{100}H_{90}O_{16}$ (1607.83): C 78.44, H 5.64; found: C 77.20, H 5.98.

General procedure for the preparation of compounds 3a–c: The reaction was performed under nitrogen atmosphere. The carboxylic acid (1.5 mmol), DMAP (1.5 mmol) and HOBt (1.5 mmol) were added to a solution of the alcohol (1.5 mmol) in DMF (40 mL). A solution of DCC (1.5 mmol) in DMF (3 mL) was added slowly at room temperature and the mixture was stirred for 72 h. The solvent was evaporated and the remaining residue was dissolved in EtOAc (10 mL). The precipitate collected over night was filtered and the solvent evaporated. The crude mixture was further purified by column chromatography.

Compound 3a: Compound **3a** was synthesized according to the general procedure from dendron **30** (501 mg, 1.5 mmol) and compound **22** (344 mg, 1.5 mmol). The crude product was purified by column chromatography (SiO_2, gradient CH_2Cl_2 → CH_2Cl_2/EtOAc, 2:8). Yield: 279 mg (34%) as a white solid; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 1.34$ (m, 4H; CH_2), 1.51 (m, 2H; CH_2), 1.66 (m, 2H; CH_2), 3.64 (t, $^3J = 7.1$ Hz, 2H; CH_2), 4.23 ((t, $^3J = 6.5$ Hz, 2H; CH_2), 5.15 (s, 4H; CH_2Bn), 6.96 (s, 1H; Ph), 7.14 (s, 2H; Ph), 7.39 (m, 10H; Ph), 11.52 ppm (br m, 2H; NH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): $\delta = 26.0$, 26.6, 28.1, 28.9, 41.2, 65.7-(CH_2), 70.4(CH_2Bn), 107.7, 108.7, 128.6, 128.9, 129.3, 132.7, 137.5 (Ph), 149.5, 150.7(C=O), 160.4 (Ph), 166.2 ppm (C=O); IR (ATR): $\nu_{max} = 3204$, 3096, 1733, 1710, 1602, 1459, 1401, 1355, 1305, 1243, 1212, 1173, 1054, 760, 733 cm^{-1}; MS (FAB): *m/z* (%): 545 $[M]^+$; elemental analysis calcd (%) for $C_{30}H_{31}N_3O_7$ (545.58): C 66.04, H 5.73, N 7.70; found: C 65.94, H 5.91, N 7.52.

Compound 3b: Compound **3b** was synthesized according to the general procedure from dendron **31** (1.14 g, 1.5 mmol) and compound **22** (344 mg, 1.5 mmol). The crude product was purified by column chromatography (SiO_2, gradient CH_2Cl_2 → CH_2Cl_2/EtOAc, 6:4). Yield: 0.43 g (30%) as a pale yellow solid; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.32 (m, 4H; CH_2), 1.50 (m, 2H; CH_2), 1.67 (m, 2H; CH_2), 3.60 (t, ^3J = 7.3 Hz, 2H; CH_2), 4.22 ((t, ^3J = 6.6 Hz, 2H; CH_2), 5.06 (br m, 12H; CH_2Bn), 6.62 (d, ^4J = 2.2 Hz, 2H; Ph), 6.70 (d, ^4J = 2.1 Hz, 4H; Ph), 6.92 (t, ^4J = 2.2 Hz, 1H; Ph), 7.13 (s, 2H; Ph), 7.37 (m, 20H; Ph), 11.38 ppm (br m, 2H; NH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 25.0, 25.7, 27.2, 28.0, 40.1, 64.7-(CH_2), 69.34(CH_2Bn), 101.2, 106.4, 106.8, 107.9, 127.7, 127.8, 128.4, 131.8, 136.9, 139.1 (Ph), 148.6, 149.8 (C=O), 159.3, 159.6 (Ph), 165.3 ppm (C=O); IR (ATR): ν_{max} = 3235, 3069, 2937, 2860, 1718, 1687, 1594, 1451, 1374, 1301, 1239, 1150, 1046, 834, 753, 699 cm^{-1}; MS (FAB): *m/z* (%): 970 $[M]^+$; elemental analysis calcd (%) for $C_{58}H_{55}N_3O_{11}$ (970.07): C 71.81, H 5.71, N 4.33; found: C 71.33, H 5.91, N 4.13.

Compound 3c: Compound **3c** was synthesized according to the general procedure from dendron **32** (1.14 g, 1.5 mmol) and compound **22** (344 mg, 1.5 mmol). The crude product was purified by column chromatography (SiO_2, gradient CH_2Cl_2 → CH_2Cl_2/EtOAc, 6:4). Yield: 552 mg (46%) as a white solid; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.24 (m, 2H; CH_2), 1.31 (m, 2H; CH_2), 1.48 (m, 2H; CH_2), 1.63 (m, 2H; CH_2), 3.59 (t, ^3J = 7.3 Hz, 2H; CH_2), 4.18 ((t, ^3J = 6.5 Hz, 2H; CH_2), 4.99 (s, 8H; CH_2Bn), 5.04 (s, 20H; CH_2Bn), 6.60 (t, ^4J = 2.1 Hz, 6H; Ph), 6.67 (d, ^4J = 2.1 Hz, 8H; Ph), 6.68 (d, ^4J = 2.1 Hz, 4H; Ph), 6.94 (t, ^4J = 2.1 Hz, 1H; Ph), 7.14 (d, ^4J = 2.0 Hz, 2H; Ph), 7.34 (m, 40H, Ph), 11.38 ppm (br m, 2H; NH); ^{13}C NMR (100.6 MHz; [D$_6$]DMSO): δ = 25.0; 25.7; 27.2; 28.0; 40.1; 64.7(CH_2); 69.34(CH_2Bn); 107.7; 108.7; 128.6; 128.9; 129.3; 132.7; 137.5 (Ph); 149.5; 150.7(C=O); 160.4 (Ph); 166.2 ppm (C=O); IR (ATR): ν_{max} = 3235; 3088; 3065; 3034; 2934; 2868; 1698; 1594; 1447; 1374; 1297; 1146; 1042; 830; 733; 695 cm^{-1}; MS (FAB): *m/z* (%): 1816 $[M]^+$; elemental analysis calcd (%) for $C_{114}H_{103}N_3O_{19}$ (1819.05): C 75.27; H 5.71; N 2.31; found: C 73.82; H 5.72; N 2.25.

1-(6-Hydroxyhexyl)-biuret (21): 1-Nitrobiuret (4.44 g; 30.0 mmol) was dissolved in water (45 mL) and 6-aminohexanol (3.63 g; 30.0 mmol) was added. The mixture was stirred for one hour and then heated at reflux for 1 h. The solution was cooled one ice and filtered to remove a small amount of insoluble material before being concentrated to give the crude product. The product was purified by recrystalization from ethanol. Yield: 2.46 g (40%) as a white solid; ^{1}H NMR (400 MHz; [D$_6$]DMSO): δ = 1.27 (m; 4H; CH_2); 1.34 (m; 4H; CH_2); 3.06 (dt; $^3J_1$ = 6.7 Hz/$^3J_2$ = 6.0 Hz; 2H, CH_2OH), 3.37 (dt, $^3J_1$ = 11.8 Hz/$^3J_{2_}$5.6 Hz, 2H, CH_2NH), 4.33 (t, ^3J = 5.2 Hz, 1H, OH), 6.72 (br m, 2H, NH_2), 7.46 (br m, 1H, NH), 8.50 ppm (br m, 1H, NH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 25.5, 26.5, 29.7, 32.8 (CH_2), 39.0 (CH_2NH), 60.9 (CH_2OH), 154.7, 155.8 ppm (C=O); IR (ATR): ν_{max} = 3397, 3354, 3296, 2941, 2864, 1733, 1675, 1586, 1540, 1482, 1413, 1285, 1247, 1216, 1139, 1065, 1007, 984, 811, 764, 729, 633 cm^{-1}; elemental analysis calcd (%) for $C_8H_{17}N_3O_3$ (203.24): C 47.28, H 8.43, N 20.67; found: C 47.13, H 8.65, N 20.77.

1-(6-Hydroxyhexyl)-[1,3,5]-triazin-2,4,6-trion (22): The reaction was performed under nitrogen atmosphere. A solution of sodium ethoxide was prepared from sodium metal (517 mg, 22.50 mmol) and absolute ethanol (20 mL). Diethyl carbonate 1.82 mL, 15.0 mmol) was added with stirring followed by 1-(6-hydroxyhexyl)-biuret (**21**) (1.52 g, 7.50 mmol). The mixture was heated at reflux for 2 h, during which the sodium salt of the product precipitated from solution. The mixture was allowed to cool to room temperature, filtered and the precipitate was washed with cold ether/ethanol 1:1. The residue was dissolved in the minimum volume of water and the solution was carefully neutralized with 1 M sulfuric acid. The white product was filtered and dried in vacuum. Yield: 0.93 g (54%) as a white solid; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.25 (m, 4H, CH_2), 1.43 (m, 2H; CH_2), 1.51 (m, 2H; CH_2), 3.35 (t, ^3J = 6.2 Hz, 2H; CH_2N), 3.60 (t, ^3J = 7.3 Hz, 2H; CH_2OH), 4.32 (br m, 1H; OH), 11.63 ppm (br m, 2H; NH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 25.2, 26.0, 27.4, 32.4 (CH_2), 40.3 (CH_2N), 60.59 (CH_2OH), 148.6, 149.8 ppm (C=O); IR (ATR): ν_{max} = 3393, 3204, 3088, 2941, 2864, 1745, 1725, 1679, 1459, 1417, 1363, 1208, 1170, 1058, 1031, 1011, 914, 822, 791, 757, 683 cm^{-1}; elemental analysis calcd (%) for $C_9H_{15}N_3O_4$ (229.23): C 47.16, H 6.60, N 18.33; found: C 45.95, H 6.23, N 17.54.

Compound 33: 3,4-Diethoxy-5-propoxybenzoic acid (204 mg, 0.80 mmol) was dissolved in CH_2Cl_2 (50 mL) and cooled to 0 °C. DMAP (108 mg, 0.80 mmol), HOBt (98 mg, 0.80 mmol) and EDC·HCl (154 mg, 0.80 mmol) was added and the reaction was stirred for one hour at 0 °C. After the addition of 5-amino-*N*,*N*′-bis[6-(3,3-dimethylbutyrylamino)pyridine-2-yl]isophtalamide[21] (150 mg, 0.27 mmol) the mixture was stirred for 48 h at room temperature. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 30:1). Yield: 90 mg (42%) as a pale yellow solid; m.p. 134 C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.01 (s, 18H, $C(CH_3)_3$), 1.25 (t, ^3J = 7.2 Hz, 3H; CH_3), 1.36 (t, ^3J = 7.0 Hz, 6H; CH_3), 2.29 (s, 4H; CH_2), 4.04 (m, 2H; CH_2O), 4.12 (m, 4H; CH_2O), 7.32 (s, 2H; Ph) 7.81 (m, 6H; Py), 8.28 (s, 1H; Ph), 8.55(s, 2H; Ph), 10.02 (s, 2H; CONH), 10.42 (s, 2H; CONH), 10.44 (s, 1H; CONH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 14.7, 15.5 (CH_3), 29.6 ($C(CH_3)_3$), 30.1 (CH_2), 49.3 (C), 64.3, 68.1 (CH_2O), 106.3, 110.0, 110.4, 122.1, 123.2, 128.9, 134.7, 136.1, 139.7, 140.1, 140.2, 150.1, 150.6, 152.3 (Ph, Py), 165.1, 165.2, 170.9 ppm (C=O); IR (ATR): ν_{max} = 3277, 2957, 2343, 1671, 1583, 1502, 1444, 1328, 1297, 1227, 1123, 1027, 799, 753 cm^{-1}; MS (FAB): *m/z* (%): 797 $[M]^+$; elemental analysis calcd (%) for $C_{43}H_{53}N_7O_8$ (795.92): C 64.69, H 6.71, N 12.32; found: C 64.95, H 6.63, N 12.54.

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[1] J. Kress, A. Rosner, A. Hirsch, *Chem. Eur. J.* **2000**, *6*, 247.
[2] B. Buschhaus, W. Bauer, A. Hirsch, *Tetrahedron* **2003**, *59*, 3899.
[3] B. Buschhaus, F. Hampel, S. Grimme, A. Hirsch, *Chem. Eur. J.* **2005**, *11*, 3530.
[4] B. Buschhaus, A. Hirsch, *Eur. J. Org. Chem.* **2005**, 1148.
[5] D. A. Tomalia, H. Baker, J. Denwald, M. Hall, G. Kallos, S. Martin, J. Roeck, J. Ryder, P. Smith, *Macromolecules* **1986**, *19*, 2466.
[6] G. D. Mendanhall, S. X. Liang, E. H. T. Chen, *J. Org. Chem.* **1990**, *55*, 3697.
[7] D. A. Tomalia, H. D. Durst, *Top. Curr. Chem.* **1993**, *195*, 193.
[8] H. Ihre, O. L. Padilla de Jesús, J. M. J. Fréchet, *J. Am. Chem. Soc.* **2001**, *123*, 5908.
[9] C. J. Hawker, J. M. J. Fréchet, *J. Am. Chem. Soc.* **1990**, *112*, 7638.
[10] T. M. Miller, T. X. Neenan, *Chem. Mater.* **1990**, *2*, 346.
[11] Z. F. Xu, J. S. Moore, *Macromolecules* **1991**, *24*, 5893.
[12] V. Berl, M. Schmutz, M. J. Krische, R. G. Khoury, J. M. Lehn, *Chem. Eur. J.* **2002**, *8*, 1227.
[13] A. Franz, W. Bauer, A. Hirsch, *Angew. Chem.* **2005**, *117*, 1588; *Angew. Chem. Int. Ed.* **2005**, *44*, 1564.
[14] M. Mascal, J. Hansen, P. S. Fallon, A. J. Blake, B. R. Heywood, M. H. Moore, J. P. Turkenburg, *Chem. Eur. J.* **1999**, *5*, 381.
[15] G. Höfle, W. Steglich, *Synthesis*, **1972**, 619.
[16] B. Neiss, W. Steglich, *Angew. Chem.* **1978**, *90*, 556; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 522.
[17] We recently reported in a short communication on first NMR titration experiments of **3** with **1**.[13] Here we present full experimental details on the synthesis of **3** and its association with **1.**
[18] J. Thiele, E. Uhlfelder, *Liebigs Ann. Chem.* **1898**, *303*, 93.
[19] C. J. Hawker, J. M. J. Fréchet, *J. Am. Chem. Soc.* **1990**, *112*, 7638.
[20] T. Kametami, S. Kano, *J. Pharmac. Soc. Japan* **1962**, *82*, 1059.
[21] A. Dirksen, U. Hahn, F. Schwanke, M. Nieger, J. N. H. Reek, F. Vögtle, L. De Cola, *Chem. Eur. J.* **2004**, *10*, 2036.
[22] B. Perlmutter-Hayman, *Acc. Chem. Res.* **1986**, *19*, 90.

[23] H.-J. Schneider, A. Yatsimirsky, *Principles and Methods in Surpramolecular Chemistry*, Wiley, Chichester, **2000**.
[24] V. P. Solov′ev, E. A. Vnuk, N. N. Strakhova, O. A. Reavsky, VINITI, Moscow, **1991**.
[25] V. P. Solov′ev, V. E. Baulin, N. N. Strahova, V. P. Kazachenko, V. K. Belsky, A. A. Varnek, T. A. Volkova, G. Wipff, *J. Chem. Soc. Perkin Trans. 1* **1998**, *2*, 1489.
[26] P. Ghandi, B. Huang, J. C. Gallucci, J. R. Parquette, *Org. Lett.* **2001**, *3*, 3129.

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