Synthesis of carbosilane dendritic wedges and their use for the construction of dendritic receptors

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A divergent route for the synthesis of carbosilane wedges that contain either a bromine or amine as focal point has been developed. These new building blocks enable the construction of various core-functionalized carbosilane dendrimers. As a typical example carbosilane dendrimers up to the third generation containing a *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core (**G1**–**G3**) have been synthesized. This new class of molecules has been studied as host molecules and they have been found to bind protected amino acids as guest molecules *via* hydrogen bonding interactions. A decrease in the association constants was observed for the higher generation dendritic hosts, which is attributed to the increased steric hindrance around the core where the binding site is located. The binding properties of the dendritic host molecules can be tuned by modifying the binding motif at the core of the carbosilane dendrimers. A higher association constant for *N*-CBZ-protected glutamic acid 1-methyl ester (**5**) was observed when the third generation *N*,*N*′,*N*″-1,3,5-tris(L-alaninyl)benzenetricarboxamide core-functionalized carbosilane dendrimer (**G3**′) was used as the host molecule compared to **G3**. Different association constants for the formation of the diastereomeric **G3**′·L-**5** ($K = 295$ M^{-1}) and **G3**′·D-**5** ($K = 236$ M^{-1}) host–guest complexes were observed, pointing to a small enantioselective recognition effect. The difference between the association constants for the formation of the **G3**′·(L-**5**)$_2$ and **G3**′·(D-**5**)$_2$ host–guest complexes was much more pronounced, $K = 37$ M^{-1} *versus* $K = 10$ M^{-1}, respectively.

Introduction

Dendrimers are interesting macromolecules owing to their well-defined, highly branched structures and physical properties, and they have drawn the attention of chemical, biological and materials scientists for more than two decades.[1] The propensity of dendrimers to enclose guest molecules and their potential application in drug delivery and gene therapy[2] has been studied since the early developments in dendrimer chemistry. Dendrimers specifically designed for the molecular recognition of substrates,[3] including chiral ones,[4] are generally synthesized by connecting wedges (dendrons) to receptors.

Within the different dendrimer families known, the carbosilane dendrimers form a special class. The physical properties of the carbosilane dendrimers, such as their viscosity, core-accessibility, the size of the internal voids and the generation at which surface congestion occurs, can be tuned easily by choosing the appropriate building blocks for the dendrimer growth sequence.[5,6] Furthermore, carbosilane dendrimers are robust, highly apolar macromolecules with low glass transition temperatures. The synthesis of carbosilane dendrimers consists of a repetitive sequence of ω-alkenylations, using either Grignard or lithium reagents, and platinum-catalyzed hydrosilylations with chlorosilanes.[7] The degree of branching can be varied between 1–3 by performing the hydrosilylation with either mono-, di- or trichlorosilanes. The distance between the branching points depends on the choice of the ω-alkenylation reagent. In principle, it is possible to alter the degree of branching as well as the branch-length at every generation. The presence of either silicon-chloride or allyl end-groups can be used for the introduction of a functionality at the periphery of the dendrimer. This versatility offered by carbosilane dendrimers, has led to the extensive use of carbosilane dendrimers as scaffolds with various functional groups. Functional materials such as liquid crystals,[8] catalysts,[9] sensors[10] and unimolecular micelles[11] have been synthesized by functionalization of carbosilane dendrimers with mesogens, catalysts, metal-complexes[12] and water-soluble groups, respectively.

Surprisingly, little attention has been devoted to *core*-functionalized carbosilane dendrimers. The reaction conditions applied during the carbosilane synthesis impose strong limitations to the functional groups that can be present in the core during the synthesis. Polar groups such as amides and esters are neither compatible with the Grignard nor with the hydrosilylation reactions. Therefore the number of core-functionalized carbosilane dendrimers directly obtained through divergent carbosilane dendrimer synthesis starting from a core-functionality is scarce.[13]

Convergent dendrimer synthesis, pioneered by Hawker and Fréchet,[14] follows a strategy in which dendritic wedges are first prepared, which subsequently can be connected to functional building blocks leading to core-functionalized dendrimers. This synthetic route has led to the synthesis of a large number of core-functionalized dendrimers.[15] The availability of carbosilane

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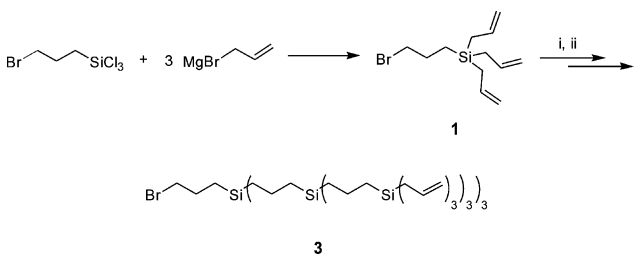
wedges would greatly facilitate the synthesis of core-functionalized carbosilane dendrimers. A first example of a core-functionalized hyper-branched carbosilane polymer—obtained through a convergent approach—has been reported by Lach *et al*.[16] They synthesized an oxazoline core-functionalized hyper-branched carbosilane polymer, which subsequently was condensed to 1,3,5-benzenetricarboxylic acid yielding a *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core-functionalized hyper-branched carbosilane polymer. Gossage *et al*. reported the divergent synthesis of phenol core-functionalized carbosilane dendritic wedges up to the third generation.[17] The first generation wedge was condensed successfully with 1,3,5-benzenetricarbonyl trichloride. Oosterom *et al*. synthesized *p*-bromophenyl core-functionalized wedges starting from *p*-bromostyrene. These dendritic building blocks were used for the synthesis of core-functionalized dendritic phosphines.[18] Müller *et al*. synthesized an *o*-diphenylphosphinophenol core-functionalized carbosilane wedge and applied this wedge as a ligand in the nickel-catalyzed Shell Higher Olefin Process.[19]

This article describes the synthesis of three generations of 3-bromopropyl core-functionalized carbosilane dendritic wedges (**1–3**) as useful building blocks for the synthesis of core-functionalized dendrimers. Bromine was selected as a focal point of the carbosilane wedges because it is inert towards the conditions applied in the dendrimer growth sequence and can readily be modified *via* simple substitution reactions.[20] These wedges have been used previously to synthesize a number of core-functionalized dendrimers in collaboration with the groups of Nolte,[21] Jerôme[22] and van Maarseveen.[23] In this article we illustrate the versatility of the building blocks by the facile synthesis of three generation *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core-functionalized carbosilane dendrimers (**G1**–**G3**). The dendrimers **G1**–**G3** have been used as hosts for the binding of (amino) acid guests. The effect of the introduction of an L-alanine spacer, between the core and the wedge of **G3**, on the binding of chiral guest molecules is evaluated.

Results and discussion

Synthesis of carbosilane wedges and core-functionalized dendrimers

(3-Bromopropyl)triallylsilane **1** was prepared as the smallest wedge and starting compound for the synthesis of the higher generations (Scheme 1). A platinum-catalyzed hydrosilylation of allyl bromide with trichlorosilane yielded (3-bromopropyl)-trichlorosilane in 70% yield after vacuum distillation, which gave **1** after a Grignard reaction with allylmagnesium bromide. The catalyst used in the hydrosilylation reaction was bis(tetrabutylammonium)platinum hexachloride (Lukevics catalyst, 0.002 mol%).[24] The side-product of the hydrosilylation of allyl bromide is propyltrichlorosilane, which is also observed in the synthesis of (3-chloropropyl)trichlorosilane,[25] and originates from the hydrosilylation of propene that is generated *via* a platinum-catalyzed H/Br exchange of allyl bromide (yielding propene and $SiBrCl_3$). Wedge **1** could be grown in the same way as described for the synthesis of carbosilane dendrimers by Van der Made and Van Leeuwen,[7] *i.e*. *via* a repetitive sequence of hydrosilylation with trichlorosilane followed by a Grignard reaction with allylmagnesium bromide. No cross-coupling of the bromine functionalized wedges with the Grignard reagent was observed within the duration of the experiment (5–6 hours). Wedges up to the third generation were prepared in quantitative conversion, 73–89% isolated yield.



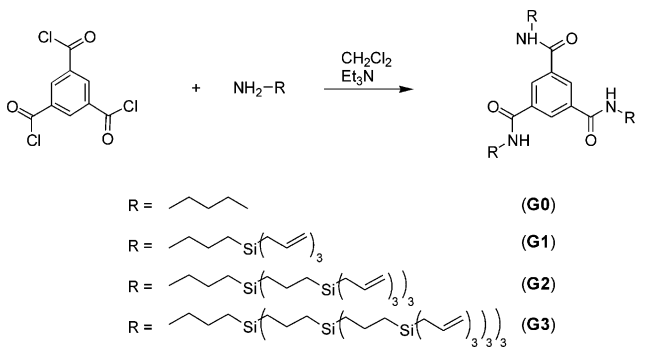
Scheme 1 Synthesis of higher generation carbosilane wedges from **1** (third generation wedge **3** is shown). Reaction conditions: (i) $HSiCl_3$, $(Bu_4N)_2PtCl_6$, rt; (ii) (allyl)MgBr, Et_2O, rt, 5–6 h.

The use of the Lukevics catalyst in the hydrosilylation reactions gave 100% selectivity for the linear hydrosilylated products. It is well-established that hydrosilylation reactions might suffer from induction periods of variable length and the need for small amounts of oxygen to activate the catalyst, depending on the alkene and hydrosilane reagents.[26] In the current reaction the activity of the hydrosilylation catalyst was rather unpredictable, but it was proven that it required the presence of oxygen in the reaction mixture.[27] Although the selectivity in all cases remained the same (100% linear product), the reaction could take over one week to run to completion and sometimes required additional catalyst. The poor reproducibility of the activity is most likely related to the oxygen sensitivity of the catalyst. Stein *et al*. showed that, for poorly coordinating olefins (1-hexene), oxygen is required to prevent the formation of inactive, multi-nuclear Pt species.[26] Furthermore Kleyer *et al*. showed that the hydrosilylation rate can be controlled by the amount of oxygen present in the reaction mixture (introduced as a 1–5 weight percent mixture with an inert gas such as nitrogen or argon).[28] The addition of either an insufficient amount or an excess of oxygen can lead to lower reaction rates or the formation of inactive species. The hydrosilylation reactions were performed as follows: the wedges were dissolved together with 0.01 mol% Lukevics catalyst (with respect to the allyl groups) under an inert atmosphere of nitrogen in a mixture of dichloromethane (in order to dissolve the catalyst) and diethyl ether (good solvent for the dendritic wedges), after which trichlorosilane was added to the reaction mixture. Oxygen was allowed to diffuse into the reaction mixture *via* a calcium chloride tube on the reaction vessel after closing the nitrogen inlet.[29] By performing the hydrosilylation in this fashion sufficient time is offered for the platinum complex to be reduced, after which diffusion of air from the head space into the reaction mixture slowly increases the oxygen content, thereby passing through the optimal oxygen concentration.

Substitution of the bromine focal point by an amine could be achieved by stirring the different generations of bromine functionalized wedges in a large excess of liquid ammonia at 70 °C under 15 bar of pressure, resulting in a new series of functionalized wedges. Importantly, the reactions should be performed at sufficiently high dilution ($\leq$0.11 M) since otherwise secondary and tertiary amines are formed as a result of the

higher nucleophilicity of the product compared to ammonia. The dendritic wedges **2** and **3** are immiscible with liquid ammonia and require the addition of diethyl ether as a co-solvent. In the absence of co-solvent the reaction with liquid ammonia gave a mixture of the starting compound and the primary, secondary and tertiary amine products. For example, the reaction of 2.50 g of **2** in 50 mL liquid ammonia (0.07 M) at 70 °C yielded a mixture of 20% **2**, 50% of the desired primary amine product, 30% of the secondary and traces of tertiary amine products after 20 hours, indicating that the reaction is taking place in a dispersion rather than in a homogeneous solution. When performed under the optimized conditions, the amine wedges could be isolated as colorless oils in 90–96% yield.

The amine functionalized wedges were condensed with 1,3,5-benzenetricarbonyl trichloride in dry CH_2Cl_2 in the presence of triethylamine yielding carbosilane dendrimers containing an *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core (**G1**–**G3**) in 85–94% yield after column chromatography (Scheme 2). *N*,*N*′,*N*″-1,3,5-Tributylbenzenetricarboxamide **G0** was prepared using similar conditions. The quality of the silica gel used for the column chromatography is of great influence on the isolated yields obtained. The silica gel should not be too acidic since this leads to lower yields as a result of the de-allylation of the carbosilane dendrimer. The Si–OH groups present on the silica gel surface lead to immobilization of the dendrimer *via* Si–O–Si bond formation. In fact Shimada *et al*. used this hydrolytic procedure with functionalized allylsilanes for the covalent linking of functional groups to silica gel.[30]



Scheme 2 Synthesis of different generations of carbosilane dendrimers containing an *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core.

Both **G0** and **G1** are white solids, whereas **G2** and **G3** are colorless oils. All dendrimers were characterized by IR spectroscopy, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis. GPC analysis (Fig. 1) revealed that the dendrimers obtained are monodisperse. The plot of the logarithm of the calculated molecular weight of the dendrimers as function of their GPC retention times shows a linear correlation, as is commonly observed for molecules of different molecular weights that have similar shapes.

The carbosilane dendrimers were subjected to MALDI-TOF MS analysis and satisfactory mass spectra were obtained after Ag^+ labeling of the dendrimers with silver trifluoroacetate[31] and using dithranol (1,8,9-anthracenetriol) as the matrix (Fig. 2a–c). In all cases the peak corresponding to the $[M + Ag]^+$ ion was the most abundant one and arises from the cation–π interaction between Ag^+ and the allylic end groups or the aromatic core.

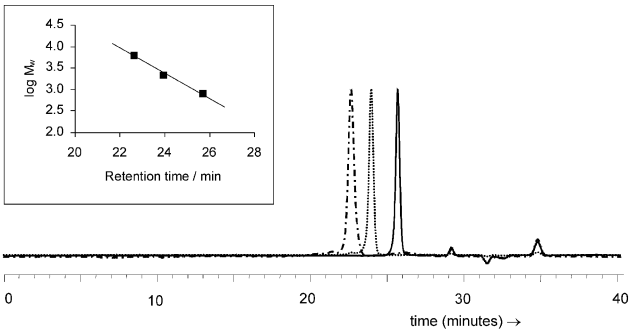


Fig. 1 GPC traces of carbosilane dendrimers **G1** (—), **G2** (···) and **G3** (-·-). Inset: calculated logM_w of **G1**–**G3** as function of the GPC retention times of **G1**–**G3**.

The mass spectrum of **G1** (Fig. 2a) displays a peak at m/z = 890 with the isotope pattern corresponding to $[M + Ag]^+$ and a peak at m/z = 769 corresponding to $[M - (3 \times \text{allyl}) + Ag]^+$. In the case of **G2** the mass spectrum (Fig. 2b) displays peaks at m/z = 2259 with an isotope pattern corresponding to $[M + Ag]^+$, and at m/z = 2368 corresponding to the $[M + 2Ag]^+$ ion. For **G3** three peaks are observed in the mass spectrum (Fig. 2c), corresponding to $[M]^+$ (m/z = 6267), $[M + Ag]^+$ (m/z = 6375) and $[M + 2Ag]^+$ (m/z = 6484) respectively. The resolution of the mass spectrum of **G3** is insufficient for identification of a clear isotope pattern, which indicates that at higher generations the ionization becomes increasingly more difficult. This effect has been observed previously for carbosilane dendrimers.[32]

Synthesis of a carbosilane dendrimer with an extended core

Focal point manipulation of the amine core-functionalized dendritic wedges can be used to introduce different binding motifs in the core of the carbosilane dendrimers, for example by introducing amino acid spacers using standard peptide chemistry. This provides easy access to new dendritic receptors, which are expected to have different affinities for guest molecules since the introduction of an amino acid spacer increases the number of H-bond donors/acceptors present in the core and enlarges the volume of the void inside the dendrimer. Furthermore, the introduction of a chiral amino acid generates a chiral binding site that might be able to discriminate between two enantiomeric guest molecules. Therefore, an analogue of carbosilane dendrimer **G3** containing an L-alanine spacer between the aromatic core and the carbosilane wedges (**G3′**, Scheme 3) was synthesized, applying the convergent strategy.

To this end a third generation carbosilane wedge, with saturated peripheral groups and an amine focal point was functionalized with L-alanine and a subsequent condensation reaction with 1,3,5-benzenetricarboxylic acid yielded **G3′** (Scheme 4). The Gabriel synthesis[33] was used to introduce the primary amine as the focal point. The bromine focal point was substituted by a phthaloyl group by reacting dendritic wedge **3** with potassium phthalimide in DMF at 80 °C. The substituted product (**7**) was obtained in 56% yield after column chromatography. The allylic peripheral groups were fully hydrogenated using palladium on carbon under an atmospheric pressure of hydrogen. Hydrazinolysis of the saturated wedge **8** and an alkaline work-up afforded the amine focal point

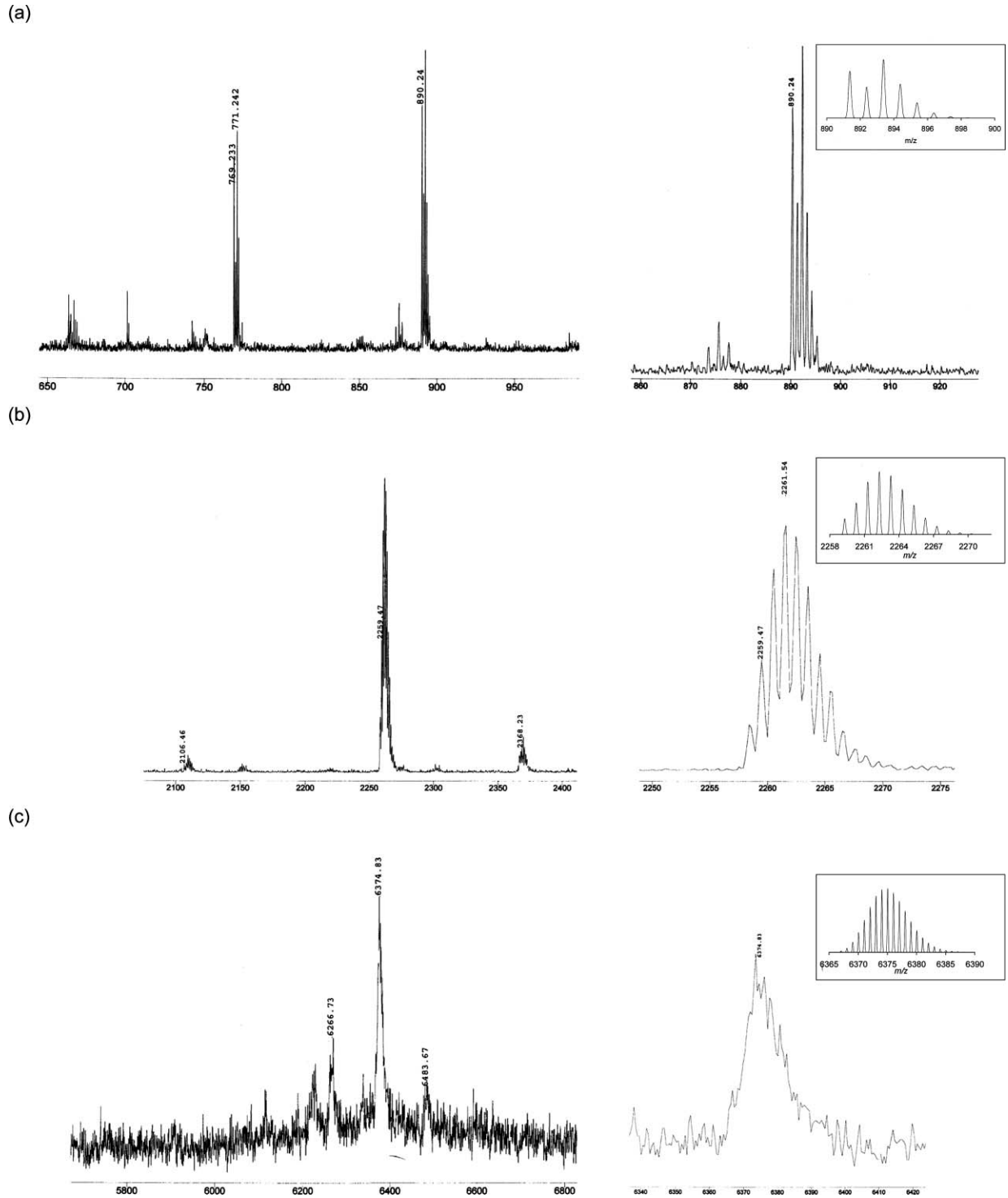
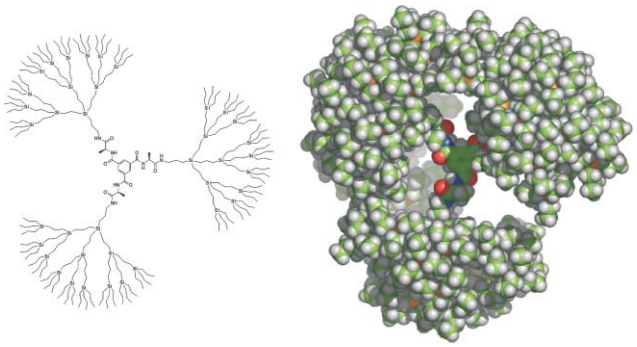
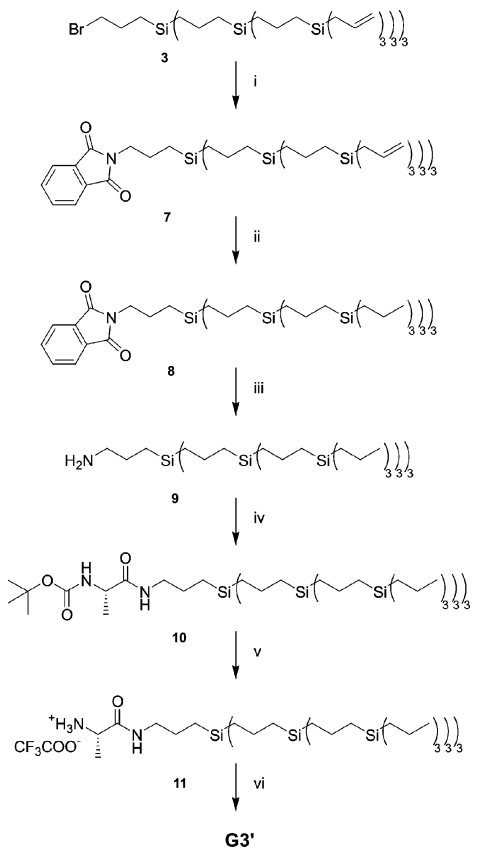


Fig. 2 MALDI-TOF MS spectra recorded after Ag^+ labeling with silver trifluoroacetate using dithranol as the matrix: (a) **G1**; (b) **G2**; (c) **G3**. Insets: calculated and observed isotope patterns.

functionalized wedge **9** in quantitative conversion, 94% isolated yield. Next BOC-protected L-alanine was coupled to the wedge *via* a DCC coupling, affording wedge **10** in 82% yield. The BOC-group was removed by stirring the wedge in a 50% (v/v) TFA solution in dichloromethane, affording wedge **11** in quantitative yield. Condensation of the amine functionalized wedge **11** with 1,3,5-benzenetricarboxylic acid (trimesic acid) using benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP) as the carboxylic acid activating reagent yielded dendrimer **G3′** in 93% yield after column chromatography. NMR and IR dilution experiments show that **G3′** does not self-associate in apolar solvents, in contrast to its lower generation analogues.[34]



Scheme 3 Schematic representation and CPK-representation of a computed structure of *N*,*N*′,*N*″-tris(L-alaninyl)-1,3,5-benzenetricarboxamide core-functionalized carbosilane dendrimer **G3**′.



Scheme 4 Synthesis of *N*,*N*′,*N*″-1,3,5-tris(L-alaninyl)benzenetricarboxamide core-functionalized dendrimer **G3**′. Reagents: (i) potassium phthalimide, DMF, 80 °C; (ii) H_2, Pd/C (10%), EtOAc; (iii) $H_2NNH_2{\cdot}H_2O$, EtOH, reflux followed by HCl (aq), reflux, alkaline work-up; (iv) BOC-L-alanine, DCC, DMAP, CH_2Cl_2; (v) TFA–CH_2Cl_2 (1:1); (vi) trimesic acid, PyBOP, DiPEA, THF.

Binding studies

The *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core can be used as a binding site for guest molecules.[35] CPK models of the dendrimers **G1**–**G3** show that the cores in the higher generation dendrimers are more shielded from the environment by the dendritic carbosilane wedges (Fig. 3). In order to study the ability of these dendrimers to accommodate guest molecules, the binding of three different guest molecules was studied by IR and ^{1}H NMR spectroscopy.

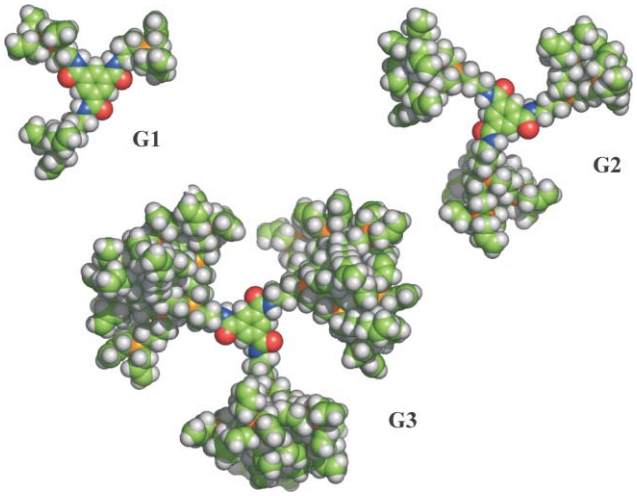
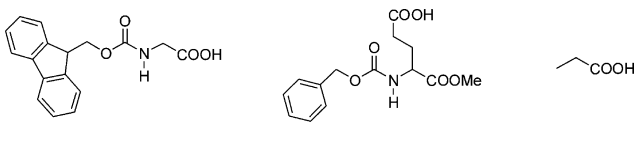


Fig. 3 CPK-representations of computed structures of the carbosilane dendrimers **G1**–**G3**.

Binding studies were performed in dry chloroform-*d* with **G0**–**G3** at a concentration of 5 mM using FMOC-glycine **4**, *N*-CBZ-L-glutamic acid 1-methyl ester (L-**5**) and propionic acid (**6**) as the guest molecules. The IR spectra of 5 mM solutions of **G0** and **G1** in chloroform-*d* showed N–H stretching vibrations at 3455 and 3451 cm^{-1}, respectively, characteristic of non-hydrogen bonded amides, indicating that these molecules do not self-associate in this solvent at this concentration.[36] The IR spectra of the guest molecules **4** (13 mM)[37] and **5** (25 mM) in chloroform-*d* also showed only non-hydrogen bonded amide stretching vibrations at 3454 and 3430 cm^{-1}, respectively, indicating that these molecules do not aggregate under the conditions applied in the NMR titration experiments. ^{1}H NMR titration experiments were employed to determine the association constants K_a (M^{-1}) and complexation induced shifts $\Delta\delta_{CIS}$ (Hz), defined as the chemical shift difference of a proton of the host–guest complex and that of the free host. The shifts of the aromatic and amide proton resonances of the dendrimers were monitored during the titration experiments (Table 1). The titration curves were fitted assuming the formation of 1:1 complexes, using a non-linear least-squares fitting procedure, and satisfactory fits were obtained.



4 **5** **6**

The observed shifts of the NMR resonances belonging to the amide protons present in the dendrimers clearly indicate that binding of the guest molecules is based on H-bonding. This is substantiated by IR measurements on **G2** (ν_{NH} = 3448 cm^{-1}) showing a new amide N–H stretching vibration at 3385 cm^{-1} upon complexation with **6**. The low association constant found for **6** suggests that the amide bonds in **4** and L-**5** contribute to the binding with the dendrimer core.

The association constants of **G0** to **G2** reveal that the binding of guests **4** and L-**5** is slightly weaker in higher generation dendrimers, while for **G3** hardly any binding is observed. These observations reflect the increase in steric hindrance imposed by the dendritic

Table 1 Association constants K_a and complexation induced shifts $\Delta\delta_{CIS}$ of the dendrimer–guest complexes in chloroform-*d* calculated from the shifts of the aromatic and amide proton resonances of the dendrimer

Dendrimer	Guest	K_a (M^{-1})[a]	$\Delta\delta_{CIS,ArH}$ (ppm)	$\Delta\delta_{CIS,NH}$ (ppm)
G0	**4**	87	0.31	1.17
G1	**4**	69	0.26	0.99
G2	**4**	65	0.19	0.63
G3	**4**	5[b]		
G0	L-**5**	40	0.33	1.05
G1	L-**5**	38	0.29	0.94
G2	L-**5**	10	0.32	1.14
G3	L-**5**	5[b]		
G2	**6**	24	0.47	1.39

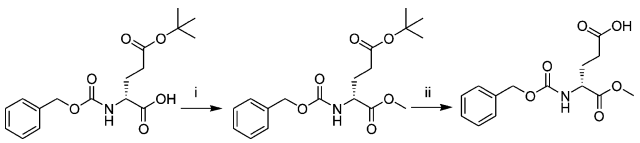
[a] Estimated error 5%. [b] Estimated *K* values. The small shifts prohibited accurate determination of the association constant.

wedges in the higher generation dendrimers, shielding the binding site located at the core of the dendrimer. In **G3** the carbosilane wedges almost fully encapsulate the binding site, as can be seen from the CPK model (Fig. 3), hampering the binding of the guest molecules.

The calculated changes in the free energy of formation of the host–guest complexes ($\Delta G°$) range from −2.6 (**G0**) to −0.95 kcal mol^{-1} (**G3**), indicating that the binding is based on one H-bonding interaction (the energy of a hydrogen bond typically varies between 2–5 kcal mol^{-1} depending on the distance between the donor and acceptor atom). Amino acid L-**5** is bound weaker than **4**, which might be explained by a difference in the binding geometry. Complexation induced shift values provide some structural information about the binding geometry and a different trend in $\Delta\delta_{CIS}$ within the dendrimer series **G0**–**G2** is observed for **4** compared to L-**5**. A drop in the $\Delta\delta_{CIS}$ value (upon complexation with **4**) is observed for the higher generation hosts, indicating that the geometry of the host–guest complex of **G2** differs from that of **G0** and **G1**. Most likely this change in binding geometry is induced by steric hindrance of the dendritic wedges. The different binding geometry, however, reduces the association constant within the dendrimer series to a smaller extent compared to L-**5**. No drop in $\Delta\delta_{CIS}$ is observed for L-**5** within the dendrimer series **G0**–**G2**, suggesting that the host–guest complexes have a similar geometry. The inability to adopt a different binding geometry might explain the relatively large drop in association constant observed for L-**5** within the dendrimer series compared to **4** and might be attributed to the steric bulk around the amide bond in L-**5**. The increased steric hindrance in the higher generation dendrimer might hamper, for example, the formation of the hydrogen bond between the dendritic host and the amide bond of L-**5** leading to a lower association constant.

Binding studies on a carbosilane dendrimer with an extended core

The binding behavior of dendrimer **G3′** with both L- and D-**5** was studied using ^{1}H NMR spectroscopy. D-**5** was synthesized starting from commercially available *N*-CBZ-D-glutamic acid γ-*tert*-butyl ester by subsequent esterification with methanol, *via* a DCC coupling, and de-esterification of the *tert*-butyl ester using TFA (Scheme 5). Partial racemization was observed, which is probably the result of direct abstraction of the αH by 4-dimethylaminopyridine (DMAP).[38] Optically enriched D-**5** was



Scheme 5 Synthesis of optically enriched D-**5**. Reaction conditions: (i) DCC, DMAP (11%), MeOH, CH_2Cl_2; (ii) TFA, CH_2Cl_2.

obtained in 87% overall yield and 61% optical purity (determined from the specific optical rotation by comparison with optically pure L-**5**).

A Job plot analysis of **G3′** with L-**5** was performed to determine the binding stoichiometry of the host–guest complex formed (Fig. 4).[39] The shift of the resonance of the αH of L-**5** was monitored as a probe in solutions containing different [**G3′**]:[L-**5**] ratios while keeping [**G3′**] + [L-**5**] constant. The maximum of the Job plot is found at a mole fraction L-**5** of 0.50, indicating the formation of a 1:1 host–guest complex.

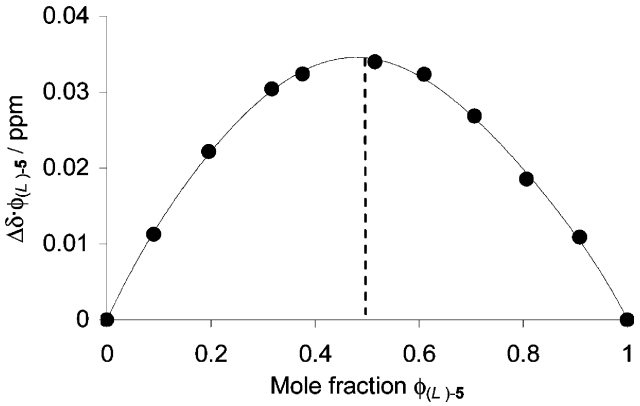


Fig. 4 Job plot analysis of a titration of **G3′** with L-**5**.

^{1}H NMR titration experiments (300 MHz) were employed to determine the association constants of **G3′** with both enantiomers of **5** (Table 2). The shifts of the resonances belonging to the aromatic protons, the αH of the alaninyl spacer and the amide proton adjacent to the wedge of **G3′** were monitored during the titration experiment. Although the Job plot analysis revealed a 1:1 binding stoichiometry, the best results in the non-linear least-squares fitting procedure were obtained when the formation of a 1:2 host–guest complex was assumed. This discrepancy can be explained by the fact that the binding of the second guest is relatively weak, and consequently the shift is too small to be detected in the Job plot titration experiment.

The association constant for the formation of the **G3′**·L-**5** host–guest complex (K_1 = 295 M^{-1}) is considerable higher than the formation of the **G3**·L-**5** host–guest complex (estimated K_a = 5 M^{-1}), which clearly indicates that extending the core leads to a better accessibility of guest molecules. Compared to the hosts **G0** and **G1**, the association constant for the binding of L-**5** in the dendritic host **G3′** is a factor of 7 higher, which can be attributed to the number of H-bonds involved in the complexation. IR spectra of **G3′** containing guest **5** showed N–H stretching vibrations at 3333 and 3306 cm^{-1}, confirming that the binding is based on H-bonding interactions involving the amide bonds (a non-hydrogen bonded N–H stretching vibration belonging to free **5** was found at 3437 cm^{-1}).

Table 2 Association constants K_1 and K_2 and complexation induced shifts $\Delta\delta_{CIS\,1,2}$ of the dendritic host **G3′**–guest **5** complexes in chloroform-*d* calculated from ^{1}H NMR titration experiments

			$\Delta\delta_{ArH}$ (ppm)		$\Delta\delta_{NH}$ (ppm)[b]		$\Delta\delta_{CH}$ (ppm)[c]	
Guest	K_1 (M^{-1})[a]	K_2 (M^{-1})[a]	CIS_1	CIS_2	CIS_1	CIS_2	CIS_1	CIS_2
L-**5**	295	37	0.045	0.47	0.27	3.5	−0.076	−0.95
D-**5**	236 (221)[d]	10 (3.3)[d]	0.038	1.2	0.21	4.9	−0.048	−1.4

[a] Estimated error 5%. [b] Complexation induced shifts of the amide protons adjacent to the aromatic core. [c] Complexation induced shifts of the αH of the alaninyl spacer. [d] Value corrected for optically pure D-**5**.

The two enantiomers of **5** are bound in the dendritic host **G3′** with different association constants, demonstrating that the chiral core can discriminate between the two enantiomers through diastereomeric interactions. The calculated ΔG^0 for the formation of the **G3′**·L-**5** and **G3′**·D-**5** host–guest complexes are −3.34 kcal mol^{-1-} and −3.17 kcal mol^{-1}, respectively, corresponding to $\Delta\Delta G$ ($\Delta G_L - \Delta G_D$) = −0.17 kcal mol^{-1}. In a racemic mixture of **5**, 57% of the bound guest is the L-**5** enantiomer, indicating that the enantioselective recognition of the first guest molecule is small. Interestingly, the binding of the first guest molecule enhances the enantioselective binding of the second guest molecule, which is expressed by a larger $\Delta\Delta G$ of 1.4 kcal mol^{-1} calculated for the formation of the 1:2 host–guest complexes (ΔG_L = −2.1 kcal mol^{-1}; ΔG_D = −0.70 kcal mol^{-1}). Consequently, in a racemic mixture of **5**, 92% of the L-**5** would be bound as the second guest molecule, which can be considered significant.[40] This enhanced enantioselective recognition in the binding of the second guest molecule might be attributed to the presence of the first guest molecule preorganizing the binding site for the binding of the second guest molecule, leading to a higher energy barrier between the 'match' and 'mismatch' diastereomeric interactions.

Conclusions

Carbosilane dendritic wedges both with a bromine or amine focal point have been prepared and shown to be useful building blocks for the construction of core-functionalized carbosilane dendrimers that are otherwise difficult to obtain. Substitution of the bromide focal point or using standard peptide chemistry with the amine focal point can be used to synthesize carbosilane dendrimers in a convergent manner. We have synthesized two types of core-functionalized carbosilane dendrimers, which can be used for the (enantioselective) molecular recognition of guest molecules. The modular approach used enables the construction of carbosilane dendrimers containing a variety of binding sites, based on various amino acids, which might result in systems that can bind guest molecules with higher enantioselectivities and binding constants. These carbosilane dendrimers containing amino acids may be used as novel recyclable organocatalysts by binding and converting substrate molecules[41] or as new materials for the resolution of amino acid derivatives.

Experimental section

General remarks

All reactions were carried out in flame-dried glassware and under a dry nitrogen atmosphere using standard Schlenk techniques unless mentioned otherwise. Solvents were dried and distilled under nitrogen; Et_2O from sodium–benzophenone and CH_2Cl_2 from CaH_2. Bis(tetrabutylammonium)platinum hexachloride [$(Bu_4N)_2PtCl_6$] was synthesized according to a literature procedure.[24] Benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP) and *N*-(benzyloxycarbonyl)-D-glutamic acid 5-*tert*-butyl ester were purchased from NovaBiochem. Other chemicals were purchased from Acros Organics or the Aldrich Chemical Company. Allyl bromide was distilled prior to use. Allylmagnesium bromide was prepared in Et_2O according to modified literature procedures.[42] The molarity of the Grignard was determined prior to use *via* a titration with a 0.50 M isopropanol solution in xylenes using 1,10-phenanthroline as an indicator. Silica 60 (SDS Chromagel, 70–200 μm) was used for column chromatography. Melting points were determined on a Gallenkamp apparatus. Optical rotations were measured with a Perkin Elmer 241 Polarimeter. $[a]_D$ values are given in 10^{-1}deg cm^2 g^{-1}. IR spectra were measured on a BioRad FT-IR (FTS-7) spectrophotometer. ^{1}H and ^{13}C NMR spectra were collected on a Bruker AMX 300 spectrometer, a Varian Mercury 300 or a Varian Inova 500 spectrophotometer. The chemical shift values δ are given in ppm, the values of the coupling constants J in Hz. GC/MS spectra were recorded on a Hewlett Packard 5890/5971-GC/MS (split/splitless injector, ZB-5 15 m column, film thickness 0.25 μm, carrier gas: 0.2 bar He). FAB mass spectra were recorded on a JOEL JMS SX/SX102A four sector mass spectrometer coupled to a JOEL MS-MP7000 data system using 3-nitrobenzyl alcohol as a matrix. MALDI-TOF mass spectra were collected on a Voyager-DE Biospectrometry Workstation (PerSeptive Biosystems Inc., Framingham, MA, USA) mass spectrometer equipped with a nitrogen laser emitting at 337 nm (3 ns pulses). The samples were labeled using silver trifluoroacetate[31] and analyzed using dithranol as the matrix. Gel permeation chromatography (GPC) was performed on a Shimadzu apparatus equipped with three Waters Styragel Columns (HR-1, HR-2 and HR-4) connected in series and with a RID-10A refractive index detector and a SPD-10A VP UV/Vis detector.

CAUTION: Hydrosilylation reactions are highly exothermic and good care should be taken. It is our experience that the occurrence of a vigorous reaction seems to be completely unpredictable (if this happened, it was always between 10 and 90 minutes) and a dry ice–acetone bath should be kept at hand when adding the trichlorosilane as a precaution.

(3-Bromopropyl)trichlorosilane. A 250 mL flame-dried three-necked round bottom flask equipped with a nitrogen inlet was charged with allyl bromide (25.0 mL, 0.288 mol), dry CH_2Cl_2 (250 mL) and dry Et_2O (12.5 mL). To this solution was added

0.55 mL of a freshly prepared 0.050 M solution of $(Bu_4N)_2PtCl_6$ (0.60×10^{-5} mol) in dry CH_2Cl_2. Subsequently trichlorosilane (36.5 mL, 0.362 mol) was added to the solution. A calcium chloride-tube was installed and the nitrogen inlet was closed. After 10 minutes an exothermic reaction occurred and the reaction vessel was cooled using a dry ice–acetone bath if it became too vigorous. After the exothermic reaction had subsided the reaction mixture was stirred overnight after which it was concentrated *in vacuo*. The crude product was purified by vacuum distillation, affording the title compound as a colorless liquid (52.4, 70%). δ_H (300 MHz, $CDCl_3$) 3.47 (2H, t, *J* 6.6, $BrCH_2$), 2.13 (2H, m, $BrCH_2CH_2$) and 1.58 (2H, m, CH_2Si). δ_C (75 MHz, $CDCl_3$) 35.7, 27.1 and 24.6.

(3-Bromopropyl)triallylsilane 1. (3-Bromopropyl)trichlorosilane (52.4 g, 0.204 mol) was added dropwise over a period of $1\frac{1}{2}$ hours to a 1.1 M allylmagnesium bromide solution in Et_2O (612 mL, 0.673 mol). The reaction mixture was stirred for 5 hours at room temperature after which it was hydrolyzed by carefully pouring it into an ice-cold 10% ammonium chloride solution in water (400 mL). The layers were separated and the water layer was washed with Et_2O (3×200 mL). The combined ethereal layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash chromatography over silica using hexanes as an eluent gave **1** (40.6 g, 73%) as a colorless liquid. (Found: C, 52.80; H, 7.67. Calc. for $C_{12}H_{21}SiBr$; C, 52.74; H, 7.75%). δ_H (300 MHz, $CDCl_3$) 5.77 (3H, m, $SiCH_2CH{=}CH_2$), 4.88 (6H, m, $SiCH_2CH{=}CH_2$), 3.37 (2H, t, *J* 6.9, $BrCH_2$), 1.89 (2H, m, $BrCH_2CH_2$), 1.61 (6H, d, *J* 8.1, $SiCH_2CH{=}CH_2$) and 0.71 (2H, m, $BrCH_2CH_2CH_2Si$). δ_C (75 MHz, $CDCl_3$) 135.3, 115.4, 38.2, 28.8, 20.9 and 12.2. *m/z* (GC/MS) 231 (M^+ − allyl).

Carbosilane wedge Br[G2](allyl)$_9$ 2. Compound **1** (10.0 g, 0.0366 mol) was dissolved in dry CH_2Cl_2 (17.5 mL) and dry Et_2O (10.5 mL). To the solution was added 0.22 mL of a freshly prepared 0.05 M solution of $(Bu_4N)_2PtCl_6$ (1.1×10^{-5} mol) in dry CH_2Cl_2, followed by trichlorosilane (14.0 mL, 0.139 mol). The flask was equipped with a calcium chloride tube and the nitrogen inlet was closed. The reaction mixture was stirred overnight after which a ^{1}H NMR spectrum showed complete conversion of all the allylic end groups. The reaction mixture was concentrated *in vacuo* and dissolved in dry Et_2O (14.0 mL). The solution was added dropwise to a 2.9 M solution of allylmagnesium bromide solution in Et_2O (140 mL, 0.406 mol) over a period of 1 hour. The reaction mixture was stirred for 5 hours after which it was poured slowly into an ice-cold 10% ammonium chloride solution in water (300 mL). The organic layer was separated and the water layer was extracted with Et_2O (3×150 mL). The combined organic layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash chromatography over silica using hexanes–Et_2O (9:1) as an eluent gave **2** (23.7 g, 89%) as a colorless oil. (Found: C, 63.85; H, 9.43. Calc. for $C_{39}H_{69}Si_4Br$; C, 64.15; H, 9.52%). δ_H (300 MHz, $CDCl_3$) 5.82 (9H, m, $SiCH_2CH{=}CH_2$), 4.91 (18H, m, $SiCH_2CH{=}CH_2$), 3.38 (2H, t, *J* 6.9, $BrCH_2$), 1.83 (2H, m, $BrCH_2CH_2$), 1.61 (18H, d, *J* 8.2, $SiCH_2CH{=}CH_2$), 1.38 (6H, m, $CH_2Si(allyl)_3$), 0.69 (6H, $SiCH_2CH_2CH_2Si$) and 0.61 (8H, m, $CH_2Si(CH_2)_3$). δ_C (75 MHz, $CDCl_3$) 134.5, 113.7, 37.2, 28.2, 19.9, 18.4, 17.5, 16.8 and 11.9. *m/z* (MALDI-TOF) 795 (M^+ + Ag − allyl).

Carbosilane wedge Br[G3](allyl)$_{27}$ 3. To a solution of **2** (4.00 g, 5.48 mmol) in dry CH_2Cl_2 (7.8 mL) and dry Et_2O (4.75 mL) was added 0.099 mL of a freshly prepared 0.050 M solution of $(Bu_4N)_2PtCl_6$ (5.0×10^{-6} mol) in dry CH_2Cl_2. Subsequently trichlorosilane (6.5 mL, 64.4 mmol) was added to the solution, a calcium chloride tube was introduced and the nitrogen inlet was closed. The reaction mixture was stirred for one week after which a ^{1}H NMR spectrum showed complete conversion of all the allylic end groups. The solvents were evaporated and the residue was dissolved in dry Et_2O (10 mL). The silane solution was added dropwise to a 1.1 M solution of allylmagnesium bromide in Et_2O (150 mL, 0.165 mol) over a period of 30 minutes and subsequently stirred for 6 hours. The reaction mixture was poured slowly into an ice-cold 10% ammonium chloride solution in water (250 mL), the layers were separated and the water layer was extracted with Et_2O (3×50 mL). The combined organic layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash chromatography over silica using hexanes–Et_2O (9:1) as an eluent gave **3** (9.1 g, 79%) as a viscous, colorless oil (Found: C, 68.63; H, 10.17. Calc. for $C_{120}H_{213}Si_{13}Br$; C, 68.60; H, 10.22%). δ_H (300 MHz, $CDCl_3$) 5.78 (27H, m, $SiCH_2CH{=}CH_2$), 4.86 (54H, m, $SiCH_2CH{=}CH_2$), 3.38 (2H, t, *J* 6.9, $BrCH_2$), 1.82 (2H, m, $BrCH_2CH_2$), 1.59 (54H, d, *J* 8.1, $SiCH_2CH{=}CH_2$), 1.35 (24H, m, (3-bromopropyl)$Si(CH_2)_3$ and $CH_2Si(allyl)_3$), 0.66 (24H, m, $SiCH_2CH_2CH_2Si$) and 0.57 (26H, m, $BrCH_2CH_2CH_2$ and $\{CH_2Si(CH_2)_3\}_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 134.5, 113.7, 37.4, 28.3, 19.9, 18.8, 18.5, 18.0, 17.9, 17.7, 16.8 and 11.8. *m/z* (MALDI-TOF) 2164 (M^+ + Ag − allyl).

(3-Aminopropyl)triallylsilane. A stainless steel autoclave was charged with **1** (1.50 g, 5.49 mmol) and liquid ammonia (50 mL). The solution was heated to 75 °C and stirred overnight ($p \approx 15$ bar). The reaction mixture was cooled to room temperature and the ammonia was evaporated. Water (15.0 mL) was added to the residue and the water layer was extracted with Et_2O (4×10 mL). The combined ethereal layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*, affording the title compound (1.15 g, quantitative) as a slightly yellow liquid. δ_H (300 MHz, $CDCl_3$) 5.68 (3H, m, $SiCH_2CH{=}CH_2$), 4.78 (6H, m, $SiCH_2CH{=}CH_2$), 2.59 (2H, t, *J* 7.0, NH_2CH_2), 2.57 (2H, broad s, NH_2), 1.51 (6H, d, *J* 8.2, $SiCH_2CH{=}CH_2$), 1.41 (2H, m, $NH_2CH_2CH_2$) and 0.50 (2H, m, CH_2Si). δ_C (75 MHz, $CDCl_3$) 134.2, 113.8, 45.1, 27.0, 19.6 and 8.6. *m/z* (GC/MS) 168 (M^+ − allyl).

Second generation carbosilane wedge H$_2$N[G2](allyl)$_9$. A stainless steel autoclave was charged with **2** (0.60 g, 0.82 mmol), Et_2O (5 mL) and liquid ammonia (50 mL). The solution was heated to 75 °C and stirred overnight ($p \approx 15$ bar). The reaction mixture was cooled to room temperature and the ammonia was evaporated. To the residue was added water (5.0 mL) and the water layer was extracted with Et_2O (4×3 mL). The combined ethereal layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*, affording the title compound (0.46 g, 96%) as a colorless oil. δ_H (300 MHz, $CDCl_3$) 5.67 (9H, m, $SiCH_2CH{=}CH_2$), 4.87 (18H, m, $SiCH_2CH{=}CH_2$), 2.65 (2H, t, *J* 7.0, NH_2CH_2), 1.57 (18H, d, *J* 8.0, $SiCH_2CH{=}CH_2$), 1.34 (10H, m, $NH_2CH_2CH_2$, NH_2 and $SiCH_2CH_2CH_2Si$), 0.65 (8H, m, $CH_2Si(allyl)_3$), 0.56 (6H, m, $Si(CH_2)_3$) and 0.46 (2H, m, $NH_2CH_2CH_2CH_2$). δ_C (75 MHz,

$CDCl_3$) 134.5, 113.7, 45.9, 28.4, 19.8, 18.4, 17.6, 16.7 and 9.65. *m/z* (FAB) 666.472 ($M^+ + H$. Calc. for $C_{39}H_{72}NSi_4$ 666.474).

Third generation carbosilane wedge $H_2N[G3](allyl)_{27}$. A stainless steel autoclave was charged with **3** (1.10 g, 0.524 mmol), Et_2O (5 mL) and liquid ammonia (50 mL). The solution was heated to 75 °C and stirred overnight ($p \approx 15$ bar). The reaction mixture was cooled to room temperature and the ammonia was evaporated. To the residue was added water (5.0 mL) and the water layer was extracted with Et_2O (4 × 3 mL). The combined ethereal layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*, affording the title compound (1.06 g, 99%) as a colorless oil (Found: C, 70.52; H, 10.22; N, 0.68. Calc. for $C_{120}H_{215}Si_{13}N$; C, 70.75; H, 10.64; N, 0.69%). δ_H (300 MHz, $CDCl_3$) 5.78 (27H, m, $SiCH_2CH{=}CH_2$), 4.89 (54H, m, $SiCH_2CH{=}CH_2$), 2.66 (2H, t, *J* 7.0, NH_2CH_2), 1.59 (54H, d, *J* 8.2, $SiCH_2CH{=}CH_2$), 1.35 (28H, m, $NH_2CH_2CH_2$ and (3-aminopropyl)$Si(CH_2)_3$, NH_2 and $CH_2Si(allyl)_3$), 0.66 (24H, m, $SiCH_2CH_2CH_2Si$), 0.56 (24H, m, $\{CH_2Si(CH_2)_3\}_3$) and 0.50 (2H, $NH_2CH_2CH_2CH_2$). δ_C (75 MHz, $CDCl_3$) 134.5, 113.7, 45.8, 28.5, 19.9, 18.8, 18.5, 18.1, 18.0, 17.7, 16.8 and 9.5.

***N*,*N*′,*N*″-1,3,5-Tributylbenzenetricarboxamide G0.** To a solution of 1,3,5-benzenetricarbonyl trichloride (0.250 g, 0.942 mmol) and Et_3N (0.475 mL, 3.41 mmol) in THF (5.0 mL) was added dropwise a solution of 1-aminobutane (0.279 mL, 2.83 mmol) in THF (10 mL). The reaction mixture was stirred overnight after which a white suspension had formed. The reaction mixture was poured into water (30 mL). The water layer was extracted with Et_2O (4 × 10 mL). The combined ethereal layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*, affording **G0** (0.332 g, 94%) as a white solid. (Found: C, 66.86; H, 8.76; N, 11.22. Calc. for $C_{21}H_{33}N_3O_3$; C, 67.17; H, 8.86; N, 11.19%). Mp 197.5–197.9 °C. ν_{max}(KBr)/cm^{-1} 3241 (broad), 3076, 2961, 2932, 2873, 1642 and 1561. δ_H (300 MHz, $CDCl_3$) 7.65 (3H, s, Ar*H*), 7.33 (3H, broad t, N*H*), 3.38 (6H, q, *J* 6.4, $NHCH_2$), 1.57 (6H, quintet, *J* 7.3, $NHCH_2CH_2$), 1.38 (6H, sextet, *J* 7.4, $NHCH_2CH_2CH_2$) and 0.95 (9H, t, *J* 7.3, CH_3). δ_C (75 MHz, $CDCl_3$) 165.9, 135.6, 128.1, 40.3, 31.8, 20.3 and 14.0. *m/z* (FAB) 376.260 ($M^+ + H$. Calc. for $C_{21}H_{34}N_3O_3$ 376.260).

First generation *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core-functionalized dendrimer G1. A solution of **4** (0.590 g, 2.82 mmol) and Et_3N (0.404 mL, 2.90 mmol) in CH_2Cl_2 (1.0 mL) was cooled to 0 °C. To the solution was added dropwise 1,3,5-benzenetricarbonyl trichloride (0.224 g, 0.845 mmol) in CH_2Cl_2 (1.0 mL). The reaction mixture was warmed to room temperature and stirred overnight after which the reaction mixture was poured into water (5 mL). The layer were separated and the water layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography over silica using CH_2Cl_2–Et_2O (4:1) as an eluent gave **G1** (0.600 g, 91%) as a white solid. (Found: C, 68.34; H, 8.59; N, 5.51. Calc. for $C_{45}H_{69}N_3O_3Si_3$; C, 68.91; H, 8.87, N, 5.36%). ν_{max}(KBr)/cm^{-1} 3247 (broad), 3085, 2995, 2972, 2920, 2883, 1634 and 1560. δ_H (300 MHz, $CDCl_3$) 8.37 (3H, s, Ar*H*), 6.54 (3H, t, *J* 5.6, N*H*), 5.78 (9H, m, $SiCH_2CH{=}CH_2$), 4.90 (18H, m, $SiCH_2CH{=}CH_2$), 3.45 (6H, *J* 6.7, $NHCH_2$), 1.63 (6H, m, $NHCH_2CH_2$), 1.62 (18H, d, *J* 8.0, $SiCH_2CH{=}CH_2$) and 0.66 (6H, m, CH_2Si). δ_C (75 MHz, $CDCl_3$) 165.8, 135.4, 134.3, 128.3, 114.2, 43.7, 24.0, 19.7 and 9.0. *m/z* (MALDI-TOF) 890 ($M^+ + Ag$). *m/z* (FAB) 784.476 ($M^+ + H$. Calc. for $C_{45}H_{70}N_3O_3Si_3$ 784.472).

Second generation *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core-functionalized dendrimer G2. A solution of **5** (0.200 g, 0.300 mmol) and Et_3N (0.070 mL, 0.50 mmol) in CH_2Cl_2 (1.0 mL) was cooled to 0 °C. To the solution was added dropwise 1,3,5-benzenetricarbonyl trichloride (0.0241 g, 0.0909 mmol) in CH_2Cl_2 (1.0 mL). The reaction mixture was warmed to room temperature and stirred overnight. The resulting white suspension was poured into water (5.0 mL) and the layers were separated. The water layer was extracted with CH_2Cl_2 (3 × 3.0 mL). The combined organic layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by column chromatography over silica using hexanes–Et_2O (2:1) as an eluent gave **G2** (0.148 g, 94%) as a colorless oil. (Found: C, 69.99, H, 10.01, N, 1.91. Calc. for $C_{126}H_{213}N_3O_3Si_{12}$: C, 70.22, H, 9.96, N, 1.95%). ν_{max}(KBr)/cm^{-1} 3354 (broad), 3075, 2994, 2970, 2914, 2876, 2795, 1790, 1667, 1629 and 1519. δ_H (300 MHz, $CDCl_3$) 8.35 (3H, s, Ar*H*), 6.44 (3H, t, *J* 5.6, N*H*), 5.77 (27H, m, $SiCH_2CH{=}CH_2$), 4.88 (54H, m, $SiCH_2CH{=}CH_2$), 3.44 (6H, q, *J* 6.7, $NHCH_2$), 1.58 (6H, m, $NHCH_2CH_2$), 1.58 (54H, d, *J* 8.0, $SiCH_2CH{=}CH_2$), 1.36 (18H, m, $CH_2Si(allyl)_3$), 0.67 (18H, m, $SiCH_2CH_2CH_2Si$), 0.59 (18H, m, $CH_2Si(CH_2)_3$) and 0.54 (6H, m, $NHCH_2CH_2CH_2$). δ_C (75 MHz, $CDCl_3$) 165.4, 135.3, 134.6, 128.0, 113.7, 43.9, 24.6, 19.9, 18.4, 17.5, 16.8 and 10.1. *m/z* (MALDI-TOF) 2261 ($M^+ + Ag$).

Third generation *N*,*N*′,*N*″-1,3,5-benzenetricarboxamide core-functionalized dendrimer G3. A solution of **6** (0.137 g, 0.0673 mmol) and Et_3N (0.030 mL, 0.21 mmol) in CH_2Cl_2 (1.0 mL) was cooled to 0 °C. To the solution was added dropwise 1,3,5-benzenetricarbonyl trichloride (5.4 mg, 0.020 mmol) in CH_2Cl_2 (1.0 mL). The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was poured into water (5.0 mL) and the layers were separated. The water layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by column chromatography over silica using hexanes–Et_2O (19:1) as an eluent gave **G3** (0.106 g, 85%) as a colorless oil. (Found: C, 70.52, H, 10.22, N, 0.68. Calc. for $C_{369}H_{645}N_3O_3Si_{39}$; C, 70.71, H, 10.37, N, 0.67%). ν_{max}(KBr)/cm^{-1} 3431, 3076, 3059, 2996, 2971, 2913, 2877, 2795, 1793, 1674, 1629 and 1517. δ_H (300 MHz, $CDCl_3$) 8.35 (3H, s, Ar*H*), 6.43 (3H, broad t, N*H*), 5.77 (81H, m, $SiCH_2CH{=}CH_2$), 4.89 (162H, m, $SiCH_2CH{=}CH_2$), 3.42 (6H, q, *J* 5.8, $NHCH_2$), 1.59 (168H, d, *J* 8.1, $NHCH_2CH_2CH_2$ and $SiCH_2CH{=}CH_2$), 1.36 (72H, m, $NHCH_2CH_2CH_2Si(CH_2)_3$ and $CH_2Si(allyl)_3$), 0.66 (72H, m, $SiCH_2CH_2CH_2Si$) and 0.61 ppm (78H, m, $NHCH_2CH_2CH_2$ and $\{CH_2Si(CH_2)_3\}_3$). δ_C (75 MHz, $CDCl_3$) 165.2, 135.2, 134.9, 134.6, 113.8, 44.2, 24.7, 19.6, 18.5, 18.3, 17.9, 17.7, 16.8 and 10.2. *m/z* (MALDI-TOF) 6375 ($M^+ + Ag$).

Carbosilane wedge $Pht[G3](allyl)_{27}$ 7. Compound **3** (5.03 g, 2.39 mmol) and potassium phthalimide (0.58 g, 3.13 mmol) were suspended in DMF (25 mL) and heated to 80 °C for a period of 1 hour. The reaction mixture was poured into water

(200 mL) and extracted with Et_2O (3 × 80 mL). The combined ethereal layers were washed with water (2 × 60 mL), dried on $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude product by flash column chromatography using hexanes–Et_2O (9:1) as an eluent gave **7** (2.90 g, 56%) as a colorless oil. (Found: C, 70.90; H, 10.15; N, 0.72. Calc. for $C_{128}H_{217}NO_2Si_{13}$; C, 70.94; H, 10.09; N, 0.65%). δ_H (500 MHz, $CDCl_3$) 7.81 (2H, m, Ar*H*), 7.68 (2H, m, Ar*H*), 5.73 (27H, m, $SiCH_2CH{=}CH_2$), 4.86 (54H, m, $SiCH_2CH{=}CH_2$), 3.62 (2H, t, *J* 7.5, NCH_2), 1.57 (56H, d, *J* 8.1, $SiCH_2CH{=}CH_2$ and NCH_2CH_2), 1.33 (24H, m, {3-(Pht)propyl}$SiCH_2$ and $CH_2Si(allyl)_3$), 0.64 (24H, m, $SiCH_2CH_2CH_2Si$) and 0.56 (26H, m, $PhtCH_2CH_2CH_2$ and $\{CH_2Si(CH_2)_3\}_3$). δ_C (125.8 MHz, $CDCl_3$) 168.4, 134.7, 134.0, 132.5, 123.3, 113.8, 41.4, 23.6, 19.9, 18.8, 18.5, 18.1, 17.9, 17.7, 16.9 and 9.9. *m/z* (MALDI-TOF) 2126.4 ($M^+ - C_3H_6$).

Carbosilane wedge Pht[G3](propyl)$_{27}$ 8. To **7** (3.91 g, 1.80 mmol) and Pd on C (10%, 0.26 g) was added EtOAc (90 mL). The mixture was placed under an atmospheric pressure of H_2 and stirred overnight. The reaction mixture was filtered over Celite and concentrated *in vacuo*, affording **8** (3.61, 90%) as a colorless oil. (Found: C, 69.34; H, 12.45; N, 0.62. Calc. for $C_{128}H_{271}NO_2Si_{13}$; C, 69.20; H, 12.30; N, 0.63%). δ_H (500 MHz, $CDCl_3$) 7.82 (2H, m, Ar*H*), 7.68 (2H, m, Ar*H*), 3.63 (2H, t, *J* 7.5, NCH_2), 1.64 (2H, m, NCH_2CH_2), 1.29 (78H, m, $SiCH_2CH_2CH_3$ and $SiCH_2CH_2CH_2Si$), 0.94 (81H, t, *J* 7.1, CH_3), 0.55 (48H, m, CH_2SiCH_2) and 0.48 (56H, m, $SiCH_2CH_2CH_3$ and $Pht–CH_2CH_2CH_2$). δ_C (125.8 MHz, $CDCl_3$) 168.2, 133.7, 132.3, 123.1, 41.2, 23.4, 18.7 (2C), 18.5, 18.2, 17.9, 17.8, 17.7, 17.5, 15.5 and 9.8. *m/z* (MALDI-TOF) 2179 ($M^+ - C_3H_6$).

Carbosilane wedge H_2N[G3](propyl)$_{27}$ 9. Compound **8** (3.50 g, 1.58 mmol) was dissolved in EtOH (85 mL) and hydrazine monohydrate (0.79 mL, 16 mmol) was added. The solution was heated to 90 °C and the resulting white dispersion was stirred overnight. The reaction mixture was cooled to room temperature after which a concentrated HCl solution (15 mL) was added to the dispersion. The resulting mixture was heated at 90 °C for 5 hours after which a white, crystalline precipitate had formed. The mixture was cooled and poured into an ice-cold NaOH solution (1.5 M, 125 mL). The mixture was partially concentrated and subsequently extracted with Et_2O (3 × 40 mL). The organic layer was washed with water (2 × 40 mL), dried on $MgSO_4$, filtered and concentrated *in vacuo*, affording **9** (3.10 g, 94%) as a colorless oil. (Found: C, 68.40; H, 13.04; N, 0.61. Calc. for $C_{120}H_{269}NSi_{13}$; C, 68.91; H, 12.96; N, 0.67%). δ_H (500 MHz, $CDCl_3$) 2.66 (2H, t, *J* 6.8, NH_2CH_2), 1.41 (2H, m, $NH_2CH_2CH_2$), 1.31 (80H, m, $SiCH_2CH_2CH_3$, $SiCH_2CH_2CH_2Si$ and NH_2), 0.96 (81H, t, *J* 7.3, CH_3), 0.56 (48H, m, CH_2SiCH_2) and 0.50 (56H, m, $SiCH_2CH_2CH_3$ and $NH_2CH_2CH_2CH_2$). δ_C (125.8 MHz, $CDCl_3$) 45.9, 28.7, 18.7, 18.6, 18.1, 17.9, 17.8, 17.5, 15.4 and 9.5. *m/z* (MALDI-TOF) 2093 ($M^+ + H$).

Carbosilane wedge BOC-L-alaninyl[G3](propyl)$_{27}$ 10. Compound **9** (0.796 g, 0.381 mmol), BOC-L-Ala (0.0720 g, 0.381 mmol), DCC (0.0785 g, 0.381 mmol) and DMAP (4.65 mg, 0.0381 mmol) were dissolved in CH_2Cl_2 (10 mL) and stirred for 2 hours. The solution was concentrated *in vacuo*. Purification of the crude product by column chromatography over silica using hexanes–EtOAc (9:1) as an eluent gave **10** (0.707 g, 82%) as a colorless oil. (Found: C, 68.11; H, 12.47; N, 1.20. Calc. for $C_{128}H_{282}N_2O_3Si_{13}$; C, 67.94; H, 12.56; N, 1.24%). $[\alpha]_D^{20}$ −3.7° (*c* 1.0 in $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3442, 2956, 2919, 2869, 2795, 1700 and 1676. δ_H (500 MHz, $CDCl_3$) 6.03 (1H, broad t, N*H*), 5.02 (1H, broad s, N*H*), 4.13 (1H, broad m, C*H*), 3.28 (1H, dt, *J* 13.5 and 6.6, $NHCHH'$), 3.20 (1H, dt, *J* 13.5 and 6.6, $NHCHH'$), 1.47 (12H, s, CH_3 (BOC and Ala)), 1.34 (80H, m, $NHCH_2CH_2$, $SiCH_2CH_2CH_3$ and $SiCH_2CH_2CH_2Si$), 0.98 (81H, t, *J* 7.0, $SiCH_2CH_2CH_3$), 0.59 (48H, m, CH_2SiCH_2) and 0.52 (56H, m, $SiCH_2CH_2CH_3$ and $NHCH_2CH_2CH_2$). δ_C (125.8 MHz, $CDCl_3$) 179.8, 172.4, 43.1, 31.2, 28.6, 24.6, 18.9, 18.8, 18.5, 18.1, 18.0, 17.9, 17.8, 15.7 and 10.0.

Carbosilane wedge L-alaninyl[G3](propyl)$_{27}$ ammonium trifluoroacetate salt 11. A solution of **10** (0.668 g, 0.295 mmol) in CH_2Cl_2 (10.0 mL) was cooled under dry, aerobic conditions ($CaCl_2$ tube) to 0 °C using an ice–water bath. To this solution was added TFA (5.0 mL) in 1.0 mL portions. The reaction was stirred for 10 minutes at 0 °C, followed by stirring for 1 hour at room temperature. To the reaction mixture was added toluene (15 mL) and the solvents were removed *in vacuo*. The residue was re-dissolved and evaporated to dryness twice using toluene (15 mL) and once using diethyl ether (20 mL), affording **10** (0.671 g, quantitative) as a colorless oil. (Found: C, 63.88; H, 12.42; N, 0.96. Calc. for $C_{125}H_{275}F_3N_2O_3Si_{13}$; C, 65.95; H, 12.18; N, 1.23%). $[\alpha]_D^{20}$ −0.9° (*c* 1.0 in $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3280, 2956, 2918, 2869, 2795 and 1676. δ_H (500 MHz, $CDCl_3$) 6.35 (1H, broad s, N*H*), 4.09 (1H, broad s, C*H*), 3.38 (1H, broad m, $NHCHH'$), 3.14 (1H, broad m, $NHCHH'$), 1.57 (83H, m, $NH_3^+CH_2CH_2$, $SiCH_2CH_2CH_3$ and $SiCH_2CH_2CH_2Si$), 0.98 (81H, t, *J* 7.3, $SiCH_2CH_2CH_3$), 0.59 (48H, m, CH_2SiCH_2) and 0.52 (56H, m, $SiCH_2CH_2CH_3$ and $NHCH_2CH_2CH_2$). δ_C (125.8 MHz, $CDCl_3$) 179.7, 169.2, 134.5, 49.7, 43.8, 24.2, 18.9, 18.1, 18.0, 17.8, 15.7 and 10.2. *m/z* (FAB) 2162.9 ($M^+ - CF_3COO$).

***N*,*N*′,*N*″-1,3,5-Tris(L-alaninyl)benzenetricarboxamide core-functionalized dendrimer G3′.** 1,3,5-Benzenetricarboxylic acid (0.0192 g, 0.0914 mmol), **11** (0.635 g, 0.279 mmol) and PyBOP (0.145 g, 0.279 mmol) were suspended in THF (10.0 mL). To the suspension was added DiPEA (0.107 mL, 0.614 mmol) after which a clear solution was obtained. The reaction mixture was stirred overnight. The solvent was removed *in vacuo*. Purification of the residue by column chromatography over silica using hexanes–EtOAc (4:1) as an eluent gave **G3′** (0566 g, 93%), as a colorless oil. (Found: C, 68.39; H, 12.72; N, 1.42. Calc. for $C_{378}H_{822}N_6O_6Si_{39}$; C, 68.33; H, 12.47; N, 1.26%). $[\alpha]_D^{20}$ −2.5° (*c* 1.0 in $CHCl_3$). δ_H (500 MHz, $CDCl_3$) 8.40 (3H, s, Ar*H*), 7.12 (3H, d, *J* 7.0, $ArC(O)NH$), 5.72 (3H, broad s, $C(O)NHCH_2$), 4.62 (3H, quintet, *J* 7.0, C*H*), 3.45 (3H, dt, *J* 11.7 and 3.8, $NHCHH'$), 3.08 (3H, dt, *J* 9.6 and 3.5, $NHCHH'$), 1.50 (15H, d, *J* 7.0, CH_3(Ala) and $NHCH_2CH_2$), 1.31 (234H, m, $SiCH_2CH_2CH_3$ and $SiCH_2CH_2CH_2Si$), 0.95 (243, t, *J* 7.3, $SiCH_2CH_2CH_3$), 0.56 (144H, m, CH_2SiCH_2) and 0.50 (168H, m, $SiCH_2CH_2CH_3$ and $NHCH_2CH_2CH_2$). δ_C (125.8 MHz, $CDCl_3$) 171.8, 165.2, 135.1, 128.9, 49.7, 43.4, 24.5, 19.5, 18.9, 18.8, 18.5, 18.1, 18.0, 17.9, 17.8, 15.7 and 10.2. *m/z* (MALDI-TOF) 6669 ($M^+ + Na$).

***N*-(Benzyloxycarbonyl)-D-glutamic acid 5-*tert*-butyl ester 1-methyl ester.** To a solution of *N*-(benzyloxycarbonyl)-D-glutamic acid 5-*tert*-butyl ester (0.25 g, 0.742 mmol), DCC (0.135 g,

0.741 mmol) and DMAP (9.6 mg, 79 μmol) in CH_2Cl_2 (4.0 mL) was added MeOH (50.0 μL, 1.23 mmol). The reaction mixture was stirred for 2 hours after which the solvent was removed *in vacuo*. Purification of the crude product by column chromatography over silica using EtOAc–hexanes (99:1) as an eluent gave the title compound (0.246 g, 95%) as a colorless oil. $[\alpha]_D^{20}$ −3.7° (*c* 1.0 in $CHCl_3$). $\nu_{max}(CDCl_3)/cm^{-1}$ 3431, 3008, 2982, 2961, 2937 and 1723. δ_H (300 MHz, $CDCl_3$) 7.31 (5H, m, Ar*H*), 5.49 (1H, d, *J* 8.1, N*H*), 5.07 (2H, s, PhCH_2), 4.36 (1H, q, *J* 8.1, C*H*), 3.71 (3H, s, C(O)OCH_3), 2.29 (2H, q, *J* 6.9, CH_2C(O)O*t*Bu), 2.11 (1H, m, CHC*H*H′), 1.92 (1H, m, CHCH*H*′) and 1.40 (9H, s, CH_3 (BOC)). δ_C (75 MHz, $CDCl_3$) 172.7, 172.2, 156.2, 136.4, 128.7, 128.4, 128.3, 81.0, 67.2, 53.7, 52.7, 31.6, 28.2 and 27.8. *m*/*z* (GC/MS) 295 ($M^+ - t$Bu).

***N*-(Benzyloxycarbonyl)-D-glutamic acid 1-methyl ester D-5.** *N*-(Benzyloxycarbonyl)-D-glutamic acid 5-*tert*-butyl ester 1-methyl ester (0.161 g, 0.457 mmol) was dissolved under a dry atmosphere ($CaCl_2$ tube) in CH_2Cl_2 (6.0 mL). The solution was cooled with an ice–water bath and TFA (1.0 mL) was added to the solution. The reaction mixture was stirred for 10 minutes at 0 °C and subsequently 1 hour at room temperature. To the reaction mixture was added toluene (10 mL) after which the solvents were removed *in vacuo*. Purification of the crude product by column chromatography over silica using EtOAc–hexanes (19:1) as an eluent gave D-**5** (0.124 g, 92%) as a white solid. $[\alpha]_D^{20}$ −4.8° (*c* 1.0 in $CHCl_3$), 61% optical purity.[43] $\nu_{max}(CDCl_3)/cm^{-1}$ 3511, 3430, 3036, 2951, 2856 and 1716. δ_H (300 MHz, $CDCl_3$) 7.34 (5H, m, Ar*H*), 5.43 (1H, d, *J* 7.8, N*H*), 5.10 (2H, s, PhCH_2), 4.43 (1H, q, *J* 7.2, C*H*), 3.74 (3H, s, C(O)OCH_3), 2.44 (2H, q, *J* 7.0, CH_2COOH), 2.20 (1H, m, CHC*H*H′) and 1.97 (1H, m, CHCH*H*′). δ_C (75 MHz, $CDCl_3$) 177.5, 172.5, 156.2, 136.3, 128.8, 128.5, 128.3, 67.4, 53.4, 52.9, 30.0 and 27.8.

NMR titration experiments[39]. The NMR titration experiments (300 MHz, 24 °C) were performed in $CDCl_3$ that was previously distilled from calcium hydride and stored on molecular sieves (4 Å). The dendrimer concentration in the prepared solutions was *ca*. 5 mM and contained up to 5 equivalents of guest, except for the titration with propionic acid in which the dendrimer concentration was 14 mM and solutions containing up to 10 equivalents of acid were measured. The association constants and complexation induced shifts were obtained by non-linear least-squares fitting using the GraFit 4.0 software package.[44] The uncertainties are the standard deviations determined by the error analysis of the program.

The binding constants K_1 and K_2 of host **G3**′ with both enantiomers of guest *N*-CBZ-glutamic acid 1-methyl ester (**5**) in $CDCl_3$ ($T = 24$ °C) were determined by varying the guest concentration between 0.76–14 mM while keeping the host concentration constant at approximately 3.4 mM. The downfield shifts of the **G3**′ aromatic, Ala-C*H* and C(O)N*H*CH$_2$ proton resonances were followed. The association constants were calculated from the data using a non-linear least-squares fitting program.[45] The best fits were obtained assuming a 1:2 host–guest binding stoichiometry. The titration experiments were performed in duplo.

Job plot analysis[39]. Two stock solutions of 9.34 mM L-**5** and 9.07 mM **G3**′ in $CDCl_3$ were prepared. Nine solutions with varying [H]:[G] while keeping [H] + [G] constant were prepared in NMR tubes by mixing the stock solution in different proportions (total volume: 500 μL). ^{1}H NMR spectra were recorded for each NMR tube. The $\Delta\delta$ values were calculated by subtracting the chemical shift of the αH resonance of L-**5** in the spectrum (δ_x) from the same resonance of the pure L-**5** solution (δ_0). A graph of the $\Delta\delta$ value as function of the mole fraction L-**5** was plotted. The maximum corresponds to 0.5 mole fraction, corresponding to a 1:1 binding stoichiometry.

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