# Synthesis of small PAMAM-dendrimers with Well-defined Structural Diversity.

Søren Leth Mejlsøe[a,c], Johannes Fabritius Petersen[b,c], Jørn Bolstad Christensen[c]*

[a]Present address: NCK A/S, Rugmarken 28, DK-3520 Farum, Denmark

[b]Present address: pK Chemicals A/S, Hårlev Mark 2, DK-4652 Hårlev, Denmark

[c]Department of Chemistry, University of Copenhagen, Thorvaldsensvej 40, DK-1871 Frederiksberg C, Denmark

Phone: (+45) 35332452 . E-mail: jbc@chem.ku.dk

**ABSTRACT:** In this paper, we present for the first time a general scalable, synthetic scheme that allows control over the position and number of different surface groups on PAMAM-dendrimers. The methodology is based on synthesis of small AB2-building blocks and cores having orthogonal protective groups allowing synthesis of PAMAM-dendrimers by convergent synthesis.

1. Introduction

Dendrimers are synthetic macromolecules with a tree-like structure based on repetitive branching from a core. This type of growth leads to macromolecules rapidly increasing in size and molecular weight making them well-defined, covalently bound nanoparticles. Dendrimers are also an example of a class of compounds, where the potential applications always have been way ahead of the synthetic chemistry needed to make them. This is probably because they were born in industrial laboratories as potential products for commercialization [1]. There are potential applications of dendrimers in a number of different areas ranging from diagnostics, nanomedicine, nanotechnology to cosmetics [2] due to their properties. The dendritic architecture provides a multivalent surface, which can be used for amplifying weak interactions between a ligand and a receptor as demonstrated with glycodendrimers [3, 4], for vaccines (MAPs) [5-8] or as artificial receptors [9-12]. The nanometer size of dendrimers allows targeting of cancer tumors using the enhanced permeation retention-effect (EPR) [13-16]. Amino-terminated dendrimers form complexes with DNA or siRNA that can be used for transfection as well as siRNA-therapy [17-19] and the interior cavities can be used as molds for synthesizing well-defined nanoparticles [20-22]. The interior may also be used to hold drug molecules for transport.

Most dendrimers reported have simple structures with one type of branch cell and one type of surface group or a statistical distribution of surface groups, while well-defined dendrimers with a well-defined heterogenous surface are mainly limited to peptide dendrimers made by solid phase peptide synthesis (SPPS) [23-26].

There are two different strategies that can be applied for synthesizing dendrimers with a well-defined surface chemistry; symmetry-breaking reactions on a preformed symmetrical dendrimer (which in essence is a protective group-free synthesis) or synthesis by convergent synthesis involving suitably protected building blocks. Symmetry-breaking reactions on preformed dendrimers such as amino-terminated dendrimers reflects the fact, that it is possible to achieve chemoselectivity in acylations on polyamines (see for example reference [27-29] and references therein). However due to the small differences in reactivity between the unmodified dendrimer and the partially acylated products mixtures are formed that require chromatographic separation of the products putting serious limitations to this approach [30].

In this paper we present a general synthetic methodology that allows synthesis of small generation, but well-defined structurally diverse PAMAM-dendrimers. Access to precisely functionalized dendrimers will make systematic studies of structure-activity relations between dendrimers and biological systems possible.

The only previous examples of unsymmetrical PAMAM-dendrimers are Janus-dendrimers [31, 32] and partially acylated G0 PAMAMs[30].

2. Results and Discussion

The ideal synthesis of structurally diverse dendrimers should be robust and simple with respect to purification of the intermediates and final products and it should be scalable allowing preparation of multigram amounts if necessary.

A convergent synthesis of PAMAM-dendrimers based on the coupling of structurally diverse dendrons to a core requires cores having up to four orthogonally addressable groups (figure 1).

The present methodology is based on the previously reported convergent synthesis of all-symmetrical PAMAM-dendrimers [10]. The methodology allows not only synthesis of PAMAM-dendrimers with a number of different surface groups but also analogs to the PAMAM-dendrimers built from different types of AB2-units (figures 2 - 5).

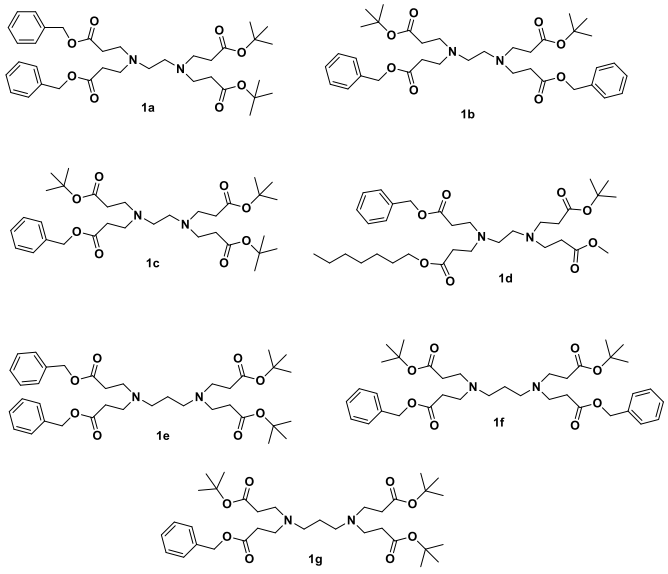



Figure 1: Cores synthesized. **1a** - **1d** are based on 1, 2-ethanediamine and **1e** – **1g** are based on 1,3-propanediamine.

The t-butyl esters are cleaved under acidic conditions, the benzyl esters by catalytic hydrogenation, the heptyl ester as an example of adding lipophilicity and potentially enzymatically cleavable and the methyl ester can be cleaved with nucleophiles or displaced by aminolysis. The cores were synthesized as shown in Schemes 1 and 2.

The A2B2-core **1a** was synthesized by a double Michael-addition between mono Z-protected Ethane-1,2-diamine (**5a**) [28,29] and t-butyl acrylate. The Z-group was removed by catalytic hydrogenation and a new double Michael-addition with benzyl acrylate [34] gave compound **1a**. The ABAB-core **1b** was synthesized from N,N'-dibenzyl-Ethane-1,2-diamine (**6b**) [33] and t-butyl acrylate to the N,N'-diben-

zylamine **7b** in quantitative yield. Catalytic hydrogenation using Pearlman's catalyst removed the benzyl-groups in quantitative yield giving compound **8b**, which gave the ABAB-core 4a in 90% yield after a double Michael-addition with benzyl acrylate [34]. The AB3-core **1c** was synthesized in a similar manner starting from N-benzyl-Ethane-1,2-diamine (**6a**) [35].

We found that the Michael-additions between primary amines and acrylates proceed in a stepwise manner with very good selectivity for mono-addition. Furthermore, the mono- and the bis-adducts are very simple to separate by column chromatography. This was utilized in the synthesis of the ABCD-core **1d** as shown in Scheme 2, where mono Z-protected Ethane-1,2-diamine (**5a**) [28,29] undergoes a mono Michael-addition with t-butyl acrylate to form compound **3g**, which undergoes a second Michael-addition with methyl acrylate to give dendron **3e**. Deprotection by catalytic hydrogenation gives the amine **9d** and a new sequence of mono Michael-additions gives the ABCD-core **1d**.

The protected dendrons are synthesized as shown in Scheme 1 (**3a**), Scheme 2 (**3e**) and Scheme 3 (**3b**, **3c**, **3d** and **3f**) starting either from carbamate protected (BOC or Z) or benzylated diamines.

The synthesis of dendrimers from the building blocks is exemplified in Scheme 4, which shows the synthesis of the unsymmetrical dendrimer **2g** by deprotection of the benzylester in core **1a** by catalytic hydrogenation and PYBOP-coupling of the dicarboxylic acid with dendron **4b**. Due to the flexibility of the synthetic scheme with respect to cores and dendrons, there is a need for a short hand notation for the structure of the dendrimers; the number of carbons between the amino-group and the esters in the dendrons is always three carbons in the present, but the ester groups vary as well as the number of carbons between the two amino groups in the dendron. In the case of dendrimer **2g** starting on the left side: There are two benzyl esters bound to a C2-dendron and one t-butyl ester bound to a C2-core with the same substituents on the other side of the core. This is expressed as $Bn_2C2Bu^t$-C2core-$Bu^tC2Bn_2$.

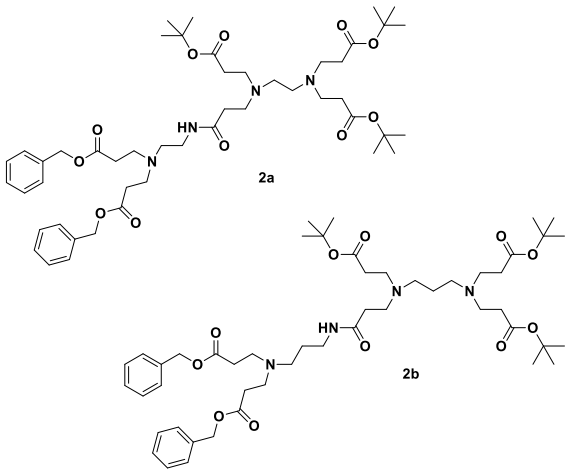



Figure 2: Unsymmetrical dendrimers with 5 surface groups.

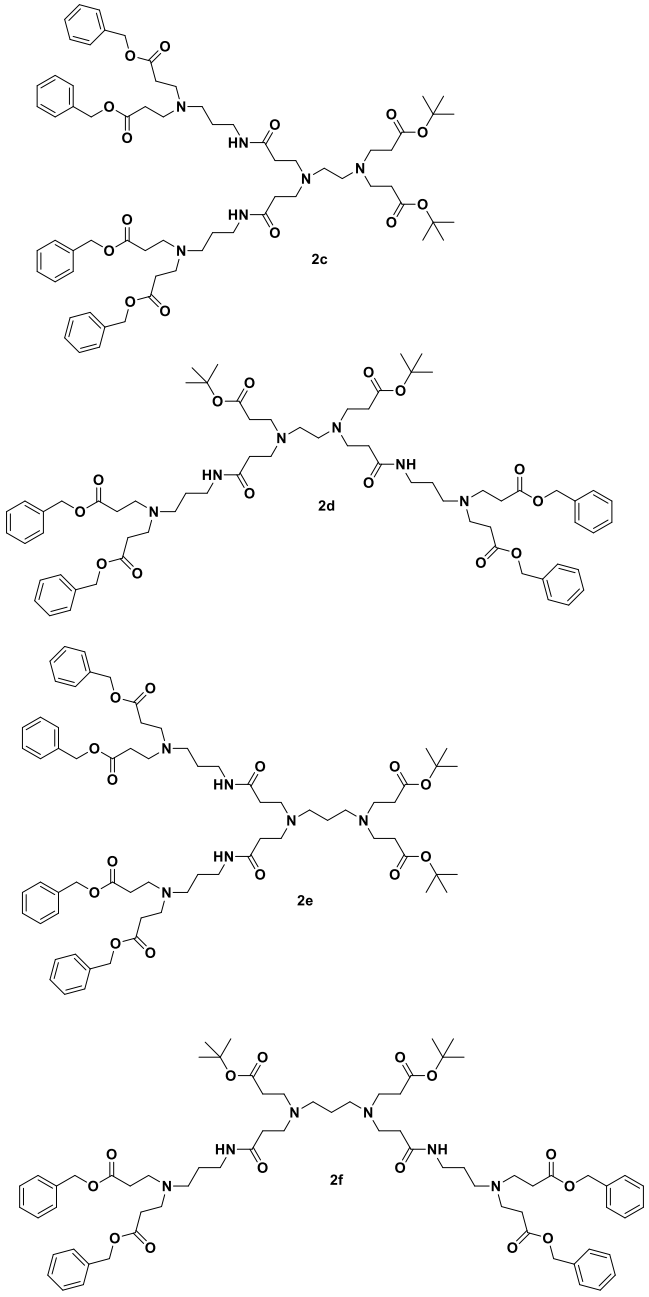



Figure 3: Unsymmetrical dendrimers with 6 surface groups.

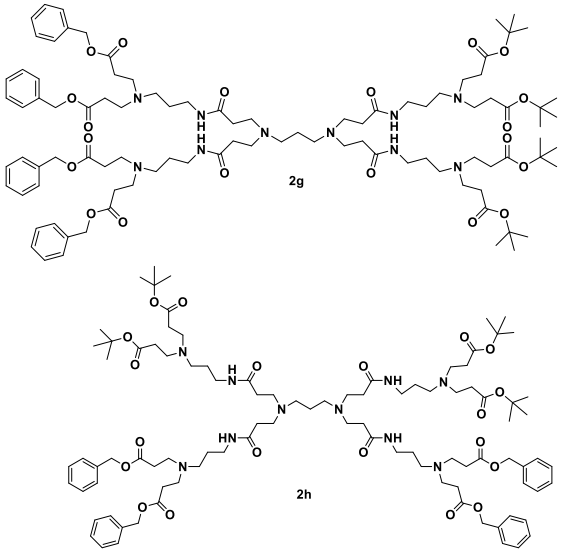



Figure 4: Unsymmetrical dendrimers with 8 surface groups and C2-symmetry.

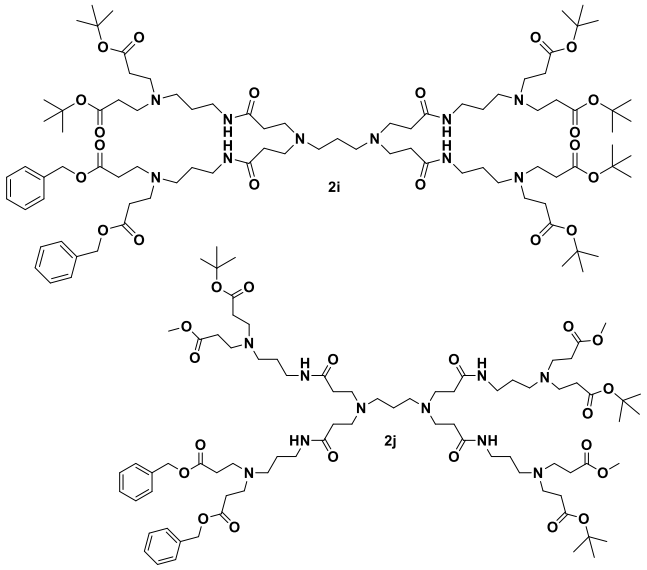



Figure 5: Unsymmetrical dendrimers with 8 surface groups.

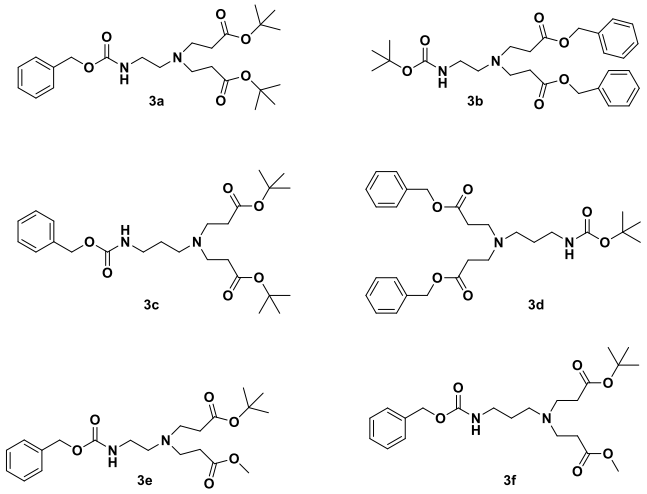
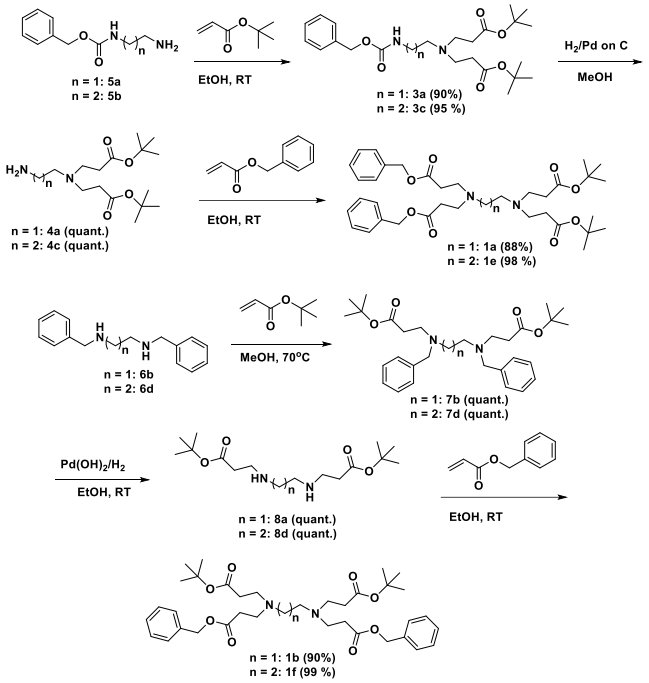
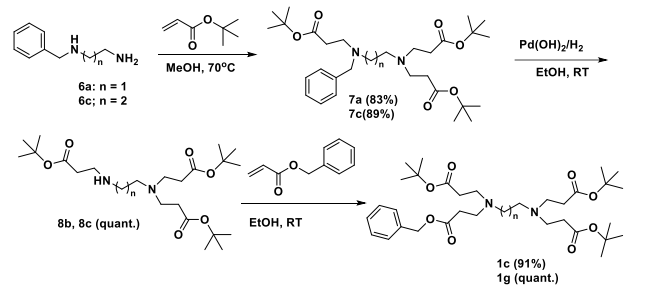
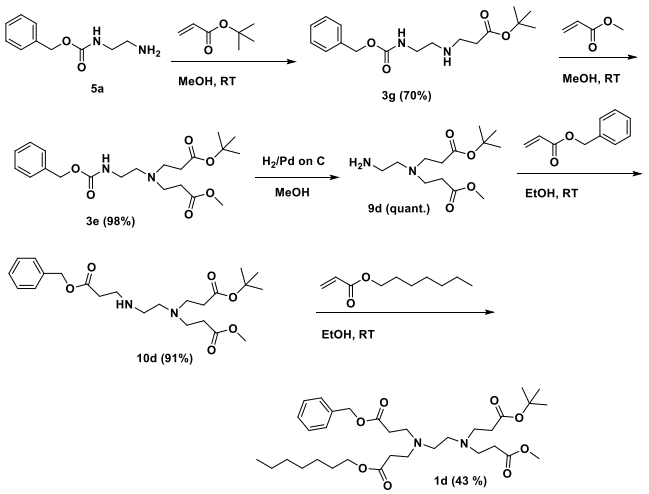



Figure 6: The protected dendron building blocks.

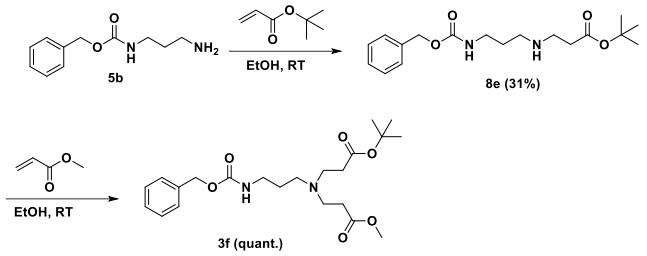



Scheme 1: Synthesis of the cores **1a, 1b**, **1e** and **1f**.

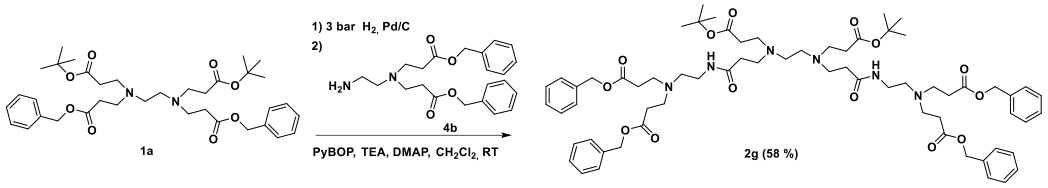



Scheme 2: Synthesis of the cores **1b, 1c** and **1d**.




Scheme 3: Synthesis of dendron **3f**




Scheme 4: The principles of the synthetic scheme for dendrimer synthesis illustrated by the synthesis of compound **2g** (**$Bn_2C3Bn_2C3$-C3core-$C3Bu^t_2C3Bu^t_2$**)

## 3 Conclusion

We have developed a methodology for the synthesis of PAMAM-dendrimers and dendrons that allows synthesis of PAMAM-dendrimers carrying different wedges. This is expected to have huge impact on areas such as the biomedical applications of dendrimers, where the studies reported up to now either have been carried out with all-symmetrically functionalized compounds or with dendrimers that have been modified in a purely statistical manner. Access to precisely functionalized dendrimers opens completely new areas ranging from programmable self-assembly through systematic studies of structure-activity relations between PAMAM-dendrimers and biological systems to truly well-defined targeted drug delivery systems based on dendrimers.

## 4 Experimental

### 4.1 Dibenzyl 3,3'-(2-(bis(3-tert-butoxy-3-oxopropyl)amino)ethylazanediyl)dipropanoate (1a)

A solution of **4a** (4.96 g, 15.67 mmol) and Benzyl Acrylate [34] (14.29 g, 88.09 mmol) in EtOH (abs., 50 mL) was stirred at RT for three days. Ethane-1,2-diamine (2.20 mL, 1.98 g, 32.94 mmol) was added and the reaction mixture stirred for additional two hours. This converts the excess of Benzyl Acrylate into mono- and bis-Michael adducts of Ethane-1,2-diamine that are retained on the column during purification. The solvent was removed *in vacuo* and the product purified on a dry column [36] (EtOAc/heptane, eluting 10% from heptane) to give the product **1a** as a light yellow oil. The yield for this reaction was 8.87 g (88%). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.27 (m, 10 H); 5.10 (s, 4 H); 2.79 (t, J = 7.2 Hz, 4 H); 2.69 (t, J = 7.3 Hz, 4 H); 2.47 (dt, J = 7.2 Hz, 8 H); 2.31 (t, J = 7.3 Hz, 4 H); 1.43 (s, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.54; 172.15; 136.20; 128.74; 128.49; 128.40; 80.45; 66.42; 52.68; 52.38; 50.11; 49.99; 34.08; 33.06; 28.34. MS (FAB) m/z (int. %): 641.7 $[MH]^+$ (18), 354.3 (66), 286.3 (57), 174.1 (99), 91.1 (100). Anal. Calcd for $C_{36}H_{52}N_2O_8$: C, 67.48; H, 8.18; N, 4.37. Found: C, 67.69; H, 8.24; N, 4.25.

### 4.2 Dibenzyl 3,3'-(2,2,15,15-tetramethyl-4,13-dioxo-3,14-dioxa-7,10-diazahexadecane-7,10-diyl)dipropionate (1b)

A solution of compound **8b** (3.61 g, 8.12 mmol) and benzyl acrylate [34] (2.68 g, 16.52 mmol) in EtOH (abs., 15 mL) was stirred at RT for two days.Ethane-1,2-diamine (0.50 g, 8.40 mmol) was added and the mixture stirred for additional two hours followed by concentration *in vacuo* and purification by dry column chromatography[36] (EtOAc/heptane, eluting 10% from heptane) to give 4.45 g (91%) of the product as a yellowish to colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.54 - 7.11 (m, 5 H); 5.11 (s, 2 H); 2.74 (dt, J = 7.3 Hz, 16.9, 2 H); 2.59 - 2.38 (m, 2 H); 2.31 (t, J = 7.3 Hz, 2 H); 1.43 (s, 27 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.61; 172.18; 172.13; 136.19; 128.75; 128.50; 128.41; 80.47; 66.43; 52.61; 52.46; 50.10; 49.95; 34.08; 34.03; 33.07; 28.35. MS (FAB) m/z (int. %): 607.8 $[MH]^+$ (36), 491.4 (13), 320.3 (58), 286.4 (90), 174.1 (100), 91.3 (41). Anal. Calcd for $C_{33}H_{54}N_2O_8$: C, 65.32; H, 8.97; N, 4.62. Found: C, 65.48; H, 9.05; N, 4.52.

### 4.3 Benzyl 3,3'-(2-(tris(3-tert-butoxy-3-oxopropyl)amino)ethylazanediyl)dipropanoate (1c)

A solution of compound **8c** (3.61 g, 8.12 mmol) and benzyl acrylate [34] (2.68 g, 16.52 mmol) in EtOH (abs., 15 mL) was stirred at RT for two days, Ethane-12-diamine (0.50 g, 8.40 mmol) was added and the mixture was stirred for additional two hours followed by up concentration in vacuo and purification on a dry column (EtOAc/heptane, eluting 10% from heptane) to give 4.45 g (91%) of the product as a yellowish to colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.54 - 7.11 (m, 5 H); 5.11 (s, 2 H); 2.74 (dt, J = 7.3 Hz, 16.9, 2 H); 2.59 - 2.38 (m, 2 H); 2.31 (t, J = 7.3 Hz, 2 H); 1.43 (s, 27 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.61; 172.18; 172.13; 136.19; 128.75; 128.50; 128.41; 80.47; 66.43; 52.61; 52.46; 50.10; 49.95; 34.08; 34.03; 33.07; 28.35.
MS (FAB) m/z (int. %): 607.8 $[MH]^+$ (36), 491.4 (13), 320.3 (58), 286.4 (90), 174.1 (100), 91.3 (41). Anal. Calcd for $C_{33}H_{54}N_2O_8$: C, 65.32; H, 8.97; N, 4.62. Found: C, 65.48; H, 9.05; N, 4.52.

### 4.4 Benzyl 3-((2-((3-tert-butoxy-3-oxopropyl)(3-methoxy-3-oxopropyl)amino)ethyl)(3-(heptyloxy)-3-oxopropyl)amino)propanoate (1d)

A solution of compound **8d** (3.55 g; 7.42 mmol) and heptyl acrylate (**9**) (2.55 g; 15 mmol) in EtOH (abs., 50 mL) was stirred at RT for seven days. The volatile components were removed under reduced pressure and the product purified on a dry column (eluting from heptane

with EtOAc) to give 4.5 g (43%) of **1d** as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 5 H); 5.11 (s, 2 H); 4.04 (t, J = 6.8 Hz, 2 H); 3.65 (s, 3 H); 2.75 – 2.66 (m, 8 H); 2.54 – 2.36 (m, 10 H); 2.31 (t, J = 7.2 Hz, 2 H); 1.66 – 1.56 (m, 2 H); 1.43 (s, 9 H); 1.39 – 1.22 (m, 8 H); 0.93 – 0.79 (m, 3 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.23; 172.85; 172.60; 172.12; 136.16; 128.75; 128.50; 128.43; 80.50; 66.45; 64.83; 52.55; 52.43; 51.77; 50.15; 49.97; 49.92; 34.01; 33.02; 32.95; 32.84; 31.95; 29.17; 28.84; 28.33; 26.10; 22.82; 14.32. MS (FAB) m/z (int. %): 607.3 $[MH]^+$ (28), 605.2 (26), 362.2 (100), 188.1 (67), 91.0 (44). Anal. calcd. for $C_{33}H_{54}N_2O_8$: C, 65.32; H, 8.97; N, 4.62. Found: C, 65.30; H, 8.53; N, 4.41.

**4.5 Di-tert-butyl 3,3'-((3-((3-(benzyloxy)-3-oxopropyl)(3-(tert-butoxy)-3-oxopropyl)amino)propyl)azanediyl)dipropionate (1e)**
A solution of (**4c**) (5.04 g, 15.27 mmol) and benzyl acrylate[34] (11.40 g, 68.97 mmol) in EtOH (abs., 60 mL) was stirred for six days, added EDA (2.00 mL, 1.50 g, 24.99 mmol) and stirred for additional 3 hours. The volatile compounds were removed under reduced pressure and the product purified on a dry column (eluting from heptane, 10% EtOAc) to give compound **1e** (9.81 g, 98%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 10 H); 5.10 (s, 4 H); 2.82 – 2.63 (m, 8 H); 2.48 (t, J = 7.5 Hz, 4 H); 2.43 – 2.24 (m, 8 H), 1.53 (p, J = 7.5 Hz, 2 H), 1.42 (s, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.62; 172.13; 136.15; 128.66; 128.38; 128.31; 80.37; 66.32; 51.78; 49.44; 49.29; 33.76; 32.74; 28.26; 25.10. MS (FAB) m/z (int. %): $[MH]^+$ 655.4 (100), 347.1 (72), 264.1 (79), 91.0 (89).
Anal. Calcd for $C_{37}H_{54}N_2O_8$: C, 67.86; H, 8.31; N, 4.28. Found: C, 67.87; H, 8.55; N, 4.25.

**4.6 Dibenzyl 3,3'-(2,2,16,16-tetramethyl-4,14-dioxo-3,15-dioxa-7,11-diazaheptadecane-7,11-diyl)dipropionate (1f)**
A solution of compound **8d** (8.79 g, 27.14 mmol) and benzyl acrylate [34] (14.24 g, 87.86 mmol) in EtOH (abs., 100 mL) was stirred for four days and treated with EDA (2.00 mL, 1.50 g, 24.99 mmol) and stirred for additional two hours. The volatile components were removed in vacuo and the product purified on a dry column (eluting from heptane, 10% EtOAc) to yield 17.26 g (99 %) of the product as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.19 (m, 10 H); 5.03 (s, 4 H), 2.66 (dt, J = 7.3 Hz, 8 H); 2.47 – 2.12 (m, 12 H); 1.56 – 1.41 (m, 2 H), 1.35 (s, 18 H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.62; 172.24; 136.00; 128.67; 128.43; 128.34; 80.37; 66.35; 51.72; 51.60; 49.24; 49.16; 33.61; 32.58; 28.21; 24.91. MS (FAB) m/z (int. %): 655.3 $[MH]^+$ (26), 354.0 (67), 286.1 (64), 206.0 (31), 174.0 (100), 91.0 (74). Anal. Calcd for $C_{37}H_{54}N_2O_8$: C, 67.86; H, 8.31; N, 4.28. Found: C, 67.39; H, 8.59; N, 4.16.

**4.7 Di-tert-butyl 3,3'-((3-((3-(benzyloxy)-3-oxopropyl)(3-(tert-butoxy)-3-oxopropyl)amino)propyl)azanediyl)dipropionate (1g)**
A solution of compound **8c** (6.27 g, 0.0137 mol) and benzyl acrylate [34] (4.25 g, 0.0262 mol) in EtOH (abs., 45 ml) was stirred for two days, added Ethane-1,2-diamine (1.00 mL, 0.75 g, 12,50 mmol) and stirred for additional three hours. The volatile components were removed under reduced pressure and the product purified on a dry column (eluting from heptane, 10% EtOAc) to give compound **1g** as a colorless oil (Yield: 8.45 g (quant.). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 5 H); 5.11 (s, 2 H); 2.77 (t, J = 7.3 Hz, 2 H), 2.74 – 2.67 (m, 6 H); 2.50 (t, J = 7.3 Hz, 2 H); 2.43 – 2.30 (m, 10 H); 1.59 – 1.46 (m, 2 H); 1.46 (s, 27 H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.67; 172.24; 172.17; 136.04; 128.67; 128.42; 128.34; 80.37; 66.34; 51.73; 51.68; 49.29; 49.17; 33.64; 33.61; 32.61; 28.23; 25.06. MS (FAB) m/z (int. %): 621.4 $[MH]^+$ (67), 453.2 (18), 264.1 (64), 174.0 (100), 91.1 (58). Anal. Calcd for $C_{34}H_{56}N_2O_8$: C, 65.78; H, 9.09; N, 4.51. Found: C, 65.70; H, 9.25; N, 4.24.

**4.8 Synthesis of the dendrimers:**
Typically, there were used 1.25 equivalents of dendron per carboxylic acid moiety. The deprotection reactions were confirmed using $^1$H-NMR and no further purification was done prior to coupling to the core unit.
The BOC groups and t-butyl esters were removed by dissolving the compound in $CH_2Cl_2$ (10 mL/g) followed by addition of Trifluoroacetic acid (5 mL/g). This was stirred for 2 – 3 hours followed by removal of the volatile compounds. The product was dried first in vacuo and then using a stream of $N_2$.
The Z groups and benzyl esters were removed using catalytic hydrogenation at 4 bar pressure ($H_2$) using Pd/C (10% on C, 0.10 g/g) and EtOH (96% or abs., about 15 mL/g) as solvent in a Parr shaker. The typical reaction time was about 15 h. The reaction mixture was filtered through a plug of celite on a glass filter funnel with suction and concentrated in vacuo. If the product was contaminated with residual Pd/C it was dissolved in $CH_2Cl_2$ (about 15 mL/g), filtered again using gravity filtration and concentrated in vacuo.
The PyBOP couplings were done by dissolving each of the deprotected compounds (dendron and core) in $CH_2Cl_2$ (10 mL/g) followed by adding Triethylamine to basic reaction on pH paper. The PyBOP (1.25 eq/acid moiety) was added the core followed by addition of the dendron solution. The resulting solution was added 4-N,N-Dimethylaminopyridine (10 mol%) and the reaction stirred for seven days. The volatile components were removed *in vacuo* and the product taken up in EtOAc (15 mL/g) and added water followed by vigorous stirring for several hours. The layers were separated and the organic phase washed with $K_2CO_3$ (aq) (10 %, 4 × 30 mL/g), $NaHCO_3$ (aq) (10%, 5 × 30 mL/g), water (5 × 30 mL/g) and finally brine (2 × 30 mL/g). The organic phase was dried ($Na_2SO_4$), filtered and the product concentrated in vacuo to give the product. The visual appearance of the product was light brown clear thick syrup.
If the product was contaminated with amino-terminated Dendron (checked with 1 % Ninhydrine in EtOH), it was dissolved in $CH_2Cl_2$ and treated with polystyrene carboxylic acid chloride (see supplementary material) followed by filtration and evaporation.

**4.8.1 Compound 2a ($Bn_2C2Bu^t$-C2core-$Bu^t_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from core **1c** (deprotection of benzyl-esters) and dendron **3b** (deprotection of BOC-group). Overall yield: 58%. $^1$NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 10 H); 7.09 (t, J = 5.2 Hz, 1 H); 5.10 (s, 4 H); 3.17 (dt, J = 3.5 Hz, 6.6 Hz, 2 H); 2.90 – 2.64 (m, 12 H); 2.62 – 2.23 (m, 18 H); 1.43 and 1.42 (s,s, 27 H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.48; 172.33; 172.05; 135.98; 128.71; 128.47; 128.42; 80.43; 66.49; 53.13; 52.07; 52.02; 50.54; 49.96; 49.78; 49.40; 46.45; 37.34; 34.04; 33.93; 33.52; 32.88; 28.26; 26.60. MS (FAB) m/z calcd. for $C_{48}H_{74}N_4O_{11}$ 882.54 Found: 883.9 $[MH]^+$.

**4.8.2 Compound 2b ($Bn_2C3Bu^t$-C3core-C3$Bu^t_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from core **1g** (deprotection of benzyl-ester) and dendron **3d** (deprotection of BOC-group). Overall yield: 71%. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 10 H); 5.09 (s, 4 H); 3.17 (q, J = 6.3 Hz, 2 H); 2.80 - 2.66 (m, 12 H); 2.52 – 2.27 (m, 18 H); 1.65 – 1.52 (m, 4 H); 1.43 (s, s, 27 H). $^{13}$C NMR (126 MHz,

$CDCl_3$) δ 172.55; 172.48; 172.16; 136.03; 128.69; 128.46; 128.38; 80.40; 66.43; 51.89; 51.41; 51.05; 50.24; 49.38; 49.32; 49.17; 37.24; 33.86; 33.78; 33.23; 32.76; 28.27; 27.04; 24.67. MS (FAB) m/z calcd. for $C_{50}H_{78}N_4O_{11}$ 910.57 Found: 911.6 $[MH]^+$.

**4.8.3 Compound 2c ($Bn_2C2Bn_2C2$-C2core-$Bu^t_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from core **1a** (deprotection of benzyl-ester) and dendron **3d** (deprotection of BOC-group). Overall yield: 54%. $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 20 H); 7.05 (br s, 2 H); 5.09 (s, 8 H); 3.32 – 3.19 (m, 4 H); 2.78 – 2.65 (m, 16 H); 2.51 – 2.41 (m, 16 H); 2.34 – 2.28 (m, 8 H); 1.42 (s, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 172.59; 172.46; 172.21; 136.05; 128.78; 128.50; 80.56; 66.56; 53.15; 51.93; 50.35; 50.01; 49.49; 39.98; 37.45; 33.93; 33.82; 33.00; 28.34. MS (MALDI-TOF) m/z cald. for $C_{66}H_{92}N_6O_{14}$, 1192.67. Found: 1193.075 $[MH]^+$.

**4.8.4 Compound 2d ($Bn_2C2Bu^t$-C2core-$Bu^tC2Bn_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from core **1a** (deprotection of benzyl-ester) and dendron **3d** (deprotection of BOC-group). Overall yield: 47%. $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.17 (m, 20 H); 6.98 (t, J = 5.4 Hz, 2 H); 5.02 (s, 8 H); 3.18 (q, J = 5.4 Hz, 4 H); 2.78 – 2.57 (m, 16 H); 2.52 – 2.33 (m, 16 H); 2.33 – 2.14 (m, 8 H); 1.33 (s, 18 H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 172.49; 172.30; 172.03; 135.97, 128.70; 128.45; 128.41; 80.47; 66.49; 53.09; 51.73; 50.46; 49.82; 49.40; 37.37; 34.07; 33.55; 32.90; 28.25. MS (FAB) m/z calcd. for $C_{66}H_{92}N_6O_{14}$ 1192.67.
Found: 1193.9 $[MH]^+$

**4.8.5 Compound 2e ($Bn_2C3Bn_2C3$-C3core-$Bu^t_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from core **1f** (deprotection of benzyl-ester) and dendron **3d** (deprotection of BOC-group). Overall yield: 66%. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 20 H); 5.08 (s, 8 H); 3.20 – 3.10 (m, 4 H); 2.81 – 2.64 (m, 16 H); 2.53 – 2.26 (m, 24 H); 1.71 – 1.54 (m, 6 H); 1.43 (s, 18 H). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 172.59; 172.39; 172.27; 135.99; 128.69; 128.44; 128.39; 80.47; 66.44; 51.97; 51.30; 51.00; 49.98; 49.29; 37.29; 33.81; 33.77; 32.73; 28.26; 26.94; 24.52. MS (FAB) m/z calcd. for $C_{69}H_{98}N_6O_{14}$ 1234.71 Found: 1235.55 $[MH]^+$

**4.8.6 Compound 2f ($Bn_2C3Bu^t$-C3core-$Bu^tC3Bn_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from core **1f** (deprotection of benzyl-ester) and dendron **3d** (deprotection of BOC-group). Overall yield: 78%.
$^1H$ NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 20 H); 7.19 (t, J = 5.6 Hz, 2 H); 5.09 (s, 8 H); 3.22 – 3.10 (m, 4 H); 2.80 – 2.63 (m, 16 H); 2.51 – 2.22 (m, 24 H); 1.66 – 1.50 (m, 6 H); 1.42 (s, 18 H). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 172.58; 172.38; 172.09; 136.01; 128.70; 128.46; 128.40; 80.52; 66.45; 51.52; 50.98; 50.11; 49.31; 37.30; 34.00; 33.34; 32.74; 28.26; 26.92; 24.19. MS (FAB) m/z calcd. for $C_{69}H_{98}N_6O_{14}$ 1234.71 Found: 1235.8 $[MH]^+$.

**4.8.7 Compound 2g ($Bn_2C3Bn_2C3$-C3core-$C3Bu^t_2C3Bu^t_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from dendrimer **2c** (deprotection of $Bu^t$-ester) and dendron **3c** (deprotection of Z-group). Overall yield: 51%. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.22 (m, 20 H); 5.09 (s, 8 H); 3.29 – 3.07 (m, 8 H); 2.81 – 2.61 (m, 24 H); 2.55 – 2.17 (m, 36 H); 1.76 – 1.49 (m, 10 H); 1.43 (s, 36 H). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 172.63; 172.35; 172.12; 135.99; 128.68; 128.42; 128.38; 80.59; 66.43; 52.48; 51.06; 50.68; 50.14; 50.02; 49.43; 49.27; 46.43; 46.40; 37.33; 34.01; 33.78; 33.57; 32.71; 28.24; 26.88; 26.59; 26.52; 25.77. MS (FAB) m/z calcd. for $C_{95}H_{146}N_{10}O_{20}$ 1747.07 Found 1748.52 $[MH]^+$.

**4.8.8 Compound 2h ($Bn_2C3Bu^t_2C3$-C3core-$C3Bu^t_2C3Bn_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from dendrimer **2f** (deprotection of t-Butyl-ester) and dendron **3c** (deprotection of Z-group). Overall yield: 61%. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 20 H); 5.09 (s, 8 H); 3.24 – 3.09 (m, 8 H); 2.80 – 2.61 (m, 24 H); 2.52 – 2.25 (m, 36 H); 1.73 – 1.50 (m, 10 H); 1.46 (s, 36 H). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 172.59; 172.31; 172.11; 136.00; 128.69; 128.43; 128.39; 80.56; 66.43; 52.49; 51.63; 51.06; 50.72; 50.03; 49.43; 49.28; 37.32; 34.03; 33.78; 33.57; 32.72; 28.25; 26.93; 25.77. MS (FAB) m/z calcd. for $C_{95}H_{146}N_{10}O_{20}$ 1747.07 Found: $[MH]^+$ 1748.00.

**4.8.9 Compound 2i ($Bn_2C3Bu^t_2C3$-C3core-$C3Bu^t_2C3Bu^t_2$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from dendrimer **2b** (deprotection of t-Butyl-ester) and dendron **3c** (deprotection of Z-group). Overall yield: 0.81 g (58%).
$^1H$ NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 10 H); 5.07 (s, 4 H), 3.25 – 3.11 (m, 8 H); 2.80 – 2.65 (m, 24 H); 2.53 – 2.25 (m, 36 H); 1.69 – 1.57 (m, 10 H); 1.45 (bs, ~54 H). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 172.61; 172.33; 172.12; 136.02; 128.70; 128.44; 128.39; 80.57; 66.44; 52.49; 50.75; 50.04; 49.44; 49.29; 46.41; 37.33; 34.03; 33.80; 33.58; 32.74; 28.26; 26.97; 26.60; 26.54; 25.78. MS (FAB) m/z calcd. for $C_{89}H_{150}N_{10}O_{20}$ 1679.10 Found 1680.25 $[MH]^+$.

**4.8.10 Compound 2j ($Bn_2C3Bu^tMeC3$-C3core-$C3Bu^tMeC3Bu^tMe$)**
This compound was synthesized according to the general procedure for PyBOP coupling reactions from dendrimer **2b** (deprotection of benzyl) and dendron **3e** (deprotection of Z-group). Overall yield: 0.71 g (42%).
$^1H$ NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 10 H); 5.02 (s, 4 H), 3.63 (s, 9 H); 3.25 – 3.12 (m, 8 H); 2.80 – 2.64 (m, 24 H); 2.50 – 2.27 (m, 36 H); 1.70 – 1.55 (m, 10 H); 1.44 (s, 27 H).
$^{13}C$ NMR (126 MHz, $CDCl_3$) δ 173.30; 172.65; 172.61; 172.25; 136.00; 129.10; 128.71; 128.44; 128.40; 80.61; 66.46; 51.77; 51.67; 51.03; 50.06; 49.49; 49.28; 37.42; 34.08; 33.82; 32.72; 32.52; 28.24; 26.93. MS(FAB) m/z calcd. for $C_{80}H_{132}N_{10}O_{20}$ 1552.96 Found: 1554.1 $[MH]^+$.

**4.9 Synthesis of the protected dendrons:**

Starting materials benzyl (2-aminoethyl)carbamate (**5a**), benzyl (3-aminopropyl)carbamate (**5b**), tert-butyl (2-aminoethyl)carbamate (**5c**), tert-butyl (3-aminopropyl)carbamate (**5d**), were synthesized as previously described [28, 29].

**4.9.1 Di-tert-butyl 3,3'-((2-(((benzyloxy)carbonyl)amino) ethyl) azanediyl) dipropionate (3a) [37]**
A solution of Benzyl (2-aminoethyl)carbamate (**5a**) (13.57 g, 70.00 mmol) and tert-Butyl acrylate (45.67 g, 356.31 mmol) in MeOH (100 mL) was stirred for six days followed by removal of the volatile component in vacuo. The product was purified on a dry column (eluting from heptane, with EtOAc, 10% fractions). The product was isolated as light yellow oil. Yield: 28.34 g (90%). $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 5.48 (s, 1H), 5.09 (s, 2H), 3.33 – 3.17 (m, 2H), 2.71 (t, J = 6.9, 4H), 2.59 – 2.46 (m, 2H), 2.33 (t, J = 6.9, 4H), 1.42 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.13, 156.65, 136.98, 128.50, 128.08, 127.99, 80.72, 66.52, 53.09, 49.19, 38.69, 33.77, 28.22. MS (FAB) m/z (int. %): 451.2 $[MH]^+$ (5), 339.0 (15), 286.1 (13), 174.0 (32), 57.0 (100).

**4.9.2 Dibenzyl 3,3'-((2-((tert-butoxycarbonyl)amino)ethyl)azanediyl)dipropionate (3b) [38]**
A solution of t-Butyl (2-aminoethyl)carbamate (**5c**) (11.36 g, 70.91 mmol) and benzyl acrylate (50.14 g, 309.15 mmol) in EtOH (100 mL) was stirred for five days. The mixture was added EDA (3 mL) and the reaction was stirred for additional three hours. The solvent was removed in vacuo and the product purified on a dry column (eluting from heptane with EtOAc, 10%) to give 30.45 g (89%) of compound **3b** as an oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 10H), 5.11 and 5.05 (s, bs, 5H), 3.15 (bs, 2H), 2.76 (t, 4H), 2.47 (dt, 6H), 1.43 (s, 9H). MS (FAB) m/z (int. %): 485.1 $[MH]^+$ (36), 354.2 (100), 279.1 (10), 91.2 (77). Data are consistent with literature except for the signal in the $^{1}$H-NMR at 1.43 (tert-butyl), which is not reported in the patent application.

**4.9.3 Di-tert-butyl 3,3'-((3-(((benzyloxy)carbonyl)amino)propyl) azanediyl)dipropionate (3c)**

A solution of Benzyl (3-aminopropyl)carbamate (**5b**) (32.53 g, 156.20 mmol) and tert-butyl acrylate (80.73 g, 629.87 mmol) in MeOH (150 mL) was stirred for six days. Ethane-1,2-diamine (15.00 mL, 11.27 g, 187.44 mmol) was added and the mixture stirred for additional 3 hours. The volatile components were removed in vacuo and the product purified on a dry column (eluting from heptane with EtOAc, 10%) to give 69.11 g (95%) of the product as a slightly yellow oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.19 (m, 5H), 5.55 (s, 1H), 5.03 (s, 2H), 3.15 (q, J = 6.2, 2H), 2.62 (t, J = 7.0, 4H), 2.38 (t, J = 6.2, 2H), 2.27 (t, J = 7.0, 4H), 1.66 – 1.50 (m, 2H), 1.36 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.20, 156.68, 137.09, 128.57, 128.11, 128.03, 80.65, 66.49, 51.00, 49.55, 39.37, 33.79, 28.24, 26.85. MS (FAB) m/z (int. %): 465.1 $[MH]^+$ (93), 286.2 (100), 174.0 (87), 91.2 (82). Anal. Calcd for $C_{25}H_{40}N_2O_6$: C, 64.63; H, 8.68; N, 6.03. Found: C, 65.08; H, 8.78; N, 5.95.

**4.9.4 Dibenzyl 3,3'-((3-((tert-butoxycarbonyl)amino)propyl) azanediyl)dipropionate (3d)**
A solution of t-Butyl (3-aminopropyl)carbamate (**5d**) (14.03 g, 80.52 mmol) and benzyl acrylate [34] (33.42 g, 206.05 mmol) in EtOH (abs., 100 mL) was stirred for five days and the solvent removed in vacuo. The product was purified on a dry column (eluting from heptane with EtOAc, 10%) to give compound **3d** (38.13 g (95%)) as a colorless oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.16 (m, 10 H); 5.04 (s, 4 H); 3.14 – 2.88 (m, 2 H*); 2*.67 (t, J = 7.0, 4 H); 2.50 – 2.27 (m, 6 H); 1.62 – 1.46 (m, 4 H); 1.35 (s, 9 H). MS (FAB) m/z (int. %): 499.2 $[MH]^+$ (49), 354.1 (73), 292.1 (36), 91.1 (100).

**4.9.5 t-Butyl 3-((2-(((benzyloxy)carbonyl)amino)ethyl)(3-methoxy-3-oxopropyl)amino)propanoate (3e)**
A solution of compound **3g** (2.52 g, 7.82 mmol) and methyl acrylate (2.29 g, 26.58 mmol) in MeOH (20 mL) was stirred for two days and the volatile components removed under reduced pressure. The product was purified on a dry column (eluting from heptane, EtOAc, 10% increase) to compound **3e** as a light yellow oil. Yield: 2.89 g (91%). $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.40 - 7.28 (m, 5 H); 5.47 (br s, 1 H); 5.10 (s, 2 H); 3.62 (s, 3H); 3.27 (m, 2 H); 2.72 (dt, J = 6.8, 4 H); 2.58 – 2.47 (m, 2 H); 2.42 (t, J = 6.8, 2 H); 2.32 (t, J = 6.7, 2 H); 1.41 (s, 9 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.13; 172.04; 156.63; 137.00; 128.51; 128.07; 128.00; 80.72; 66.52; 53.18; 51.72; 49.24; 49.20; 38.69; 33.80; 32.65; 28.18. MS (FAB) m/z (int. %): 409.0 $[MH]^+$ (18), 352.9 (32), 243.9 (47), 188.0 (100), 91.0 (98).

**4.9.6 t-Butyl 3-((3-(((benzyloxy)carbonyl)amino)propyl)(3-methoxy-3-oxopropyl)amino)propanoate (3f)**
A solution of compound **3h** (3.40 g, 10.11 mmol) and methyl acrylate (2.02 g, 23.46 mmol) in EtOH (abs., 5 mL) was stirred at RT for 28 hours. The volatile components were removed *in vacuo* and the product purified on a dry column (eluting from heptane, 10% EtOAc) and dried *in vacuo* to give 4.26 g (quant.) of the product as a colorless oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H); 5.57 (s, 1 H); 5.09 (s, 2 H); 3.64 (s, 3 H); 3.30 – 3.11 (m, 2 H); 2.70 (dt, J = 7.0, 4 H); 2.49 – 2.41 (m, 4 H); 2.33 (t, J = 7.0, 2H); 1.70 – 1.59 (m, 2 H); 1.43 (s, 9 H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.22; 172.12; 156.64; 137.06; 128.57; 128.14; 128.05; 80.67; 66.49; 51.77; 51.26; 49.56; 49.42; 39.44; 33.81; 32.54; 28.22; 26.79.
MS (FAB) m/z (int. %): $[MH]^+$ 423.3 (100), 367.2 (49), 244.2 (47), 188.1 (48), 91.3 (59). Anal. Calcd for $C_{22}H_{34}N_2O_6$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.30; H, 7.84; N, 6.36.

**4.9.7 t-Butyl 3-((2-(((benzyloxy)carbonyl)amino)ethyl)amino)propanoate (3g)**
A solution of Benzyl (2-aminoethyl)carbamate (**5a**) (3.00 g, 15.45 mmol) and tert-butyl acrylate (1.98 g, 15.45 mmol) in MeOH (20 mL) was stirred overnight, the volatile components removed under reduced pressure and the product purified on a dry column (eluting from heptane with EtOAc, 10%) to give the product as an oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H); 5.26 (bs, 1 H);

5.10 (s, 2 H); 3.28 (q, J = 6.0, 2 H); 2.82 and 2.74 (dt, J = 6.0, 6.3, 4 H); 2.39 (t, J = 6.3, 2 H); 1.44 (s, 9 H). $^{13}$C NMR (75 MHz, CDCl3) δ 172.27; 156.61; 136.78; 128.60; 128.20; 128.15; 80.74; 66.70; 48.65; 44.81; 40.67; 36.01; 28.24. MS (FAB) m/z (int. %): 323.1 $[MH]^+$ (62), 267.1 (100), 91.0 (64). Anal. Calcd. for $C_{17}H_{26}N_2O_4$: C, 63.33; H, 8.13; N, 8.69. Found: C, 63.02; H, 8.27; N, 8.69.

**4.9.8 t-Butyl 3-((3-(((benzyloxy)carbonyl)amino)propyl)amino)propanoate (3h)**
A solution of Benzyl (3-aminopropyl)carbamate (**5b**) (7.57 g, mmol) and *tert*-butyl acrylate (4.66 g, mmol) in EtOH (abs, 100 mL) was stirred overnight and the solvent was removed *in vacuo*. The product was purified on a dry column (eluting from heptane, 10% EtOAc) to give 3.82 g (31%) of the product as a colorless oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 5 H); 7.31 – 7.28 (m, 1 H); 5.09 (s, 2 H); 3.35– 3.20 (m, 2 H); 2.81 (t, J = 6.4, 2 H); 2.69 (t, J = 6.5, 2 H); 2.40 (t, J = 6.5, 2 H); 1.72 – 1.59 (m, 2 H); 1.44 (s, 9 H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.33; 156.61; 136.94; 128.63; 128.23; 128.15; 80.70; 66.62; 47.83; 45.35; 40.16; 35.94; 29.71; 28.26. MS (FAB) m/z (int. %): $[MH]^+$ 337.1 (100), 281.1 (44), 91.2 (27). Anal. Calcd for $C_{18}H_{28}N_2O_4$: C, 64.26; H, 8.39; N, 8.33. Found: C, 64.27; H, 8.32; N, 8.18.

**4.9.9 Di-t-butyl 3,3'-((2-aminoethyl)azanediyl)dipropionate (4a)**
A solution of compound **3a** (14.32 g, 31.78 mmol) in MeOH (100 mL) was treated with Pd/C (1.59 g, 10%) and $H_2$ at a pressure of 3 bar overnight. The mixture was filtered through a plug of celite on a glass filter funnel with suction and additional fractions of MeOH (3 × 10 mL) was added the filter to wash any residue of product out of the celite. The solvent was removed in vacuo to give 10.04 g (quant.) of the product as a light yellow oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 2.78 (m, 2 H); 2.71 (t, J = 7.0, 4 H); 2.64 (bs, 2 H), 2.54 – 2.47 (m, 2 H), 2.36 (t, J = 7.0, 4 H), 1.43 (s, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.19; 80.53; 56.39; 49.56; 39.58; 33.91; 28.24. MS (FAB) m/z (int. %): 316.9 $[MH]^+$ (64), 204.9 (68), 173.9 (61), 57.0 (100).

**4.9.10 N-Benzyl-ethane-1,2-diamine (6a)**
To a solution of ethane-1,2-diamine (13.70 g, 0.23 mol) in MeOH (75 mL) was drop wise added a solution of benzaldehyde (22.08 g, 0.21 mol) in MeOH (50 mL) over a period of 15 min. The reaction was allowed to stirrer for additional five hours and then slowly poured into a cooled (0 °C) mixture of $NaBH_4$ (8.60 g, 0.23 mol) in MeOH (100 mL) kept on ice. The resulting mixture/foam was allowed to stirrer for additional 30 minutes. The solid was collected on a glass filter funnel with suction. The filtrate was concentrated under reduced pressure and the product distilled (91°C at 8.5 × 10-1 mBar) to yield 20.35 g (65%) of the product as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.19 (m, 5H); 3.81 (s, 2 H); 2.82 (t, J = 5.7 Hz, 2 H); 2.70 (t, J = 5.7 Hz, 2 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 140.67; 128.49; 128.20; 127.00; 54.02; 52.18; 42.00. NMR data are consistent with the literature [35].

**4.9.11 $N^1$, $N^2$-Dibenzyl-Ethane-1,2-diamine (6b)**
To a solution of ethane-1,2-diamine (10.00 g, 166.39 mmol) in MeOH (200 ml) was added benzaldehyde (38.17 g, 359.69 mmol) and stirred at RT for five hours. This mixture was then added carefully to NaBH4 (16.00 g, 422.94 mmol) in MeOH (150 mL) with stirring and stirred for additional 30 minutes. HCl (aq) (5 M) was added to acid on pH paper. The volatile components were removed in vacuo and the product taken up in CH2Cl2 (150 mL) and NaOH (aq) (2 M) was added to basic on pH paper. The phases were separated and the aqueous phase was extracted with additional CH2Cl2 (3 × 30 mL). The collected organic phases were dried (Na2SO4), filtered and concentrated in vacuo. The product was further purified by adding Et2O (400 mL) and precipitation by drop wise addition of HCl (aq) (5 M) to acid reaction on pH paper. The salt was collected on a glass filter funnel with suction and the product washed with additional fractions of Et2O (3 × 50 mL) followed by drying in vacuo. The product was taken up in $CH_2Cl_2$ (150 mL) and NaOH (aq) (2 M) was added to basic on pH paper. The phases were separated and the aqueous phase extracted with additional $CH_2Cl_2$ (3 × 50 mL). The collected organic phases were dried ($Na_2SO_4$), filtered and concentrated in vacuo to give 22.39 g (56 %) of the product as a colorless oil. Boiling point: 127°C at 1.0 × 10-1 mBar. $^1$H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.12 (m, 10 H); 3.73 (s, 4 H); 2.72 (s, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 140.70; 128.50; 128.24; 127.01; 54.09; 48.98. MS (FAB) m/z (int. %): 241.3 $[MH]^+$ (100), 91.3 (42). Data are consistent with literature [33].

**4.9.12 N-Benzyl-propane-1,3-diamine (6c)**
To a solution of propane-1,3-diamine (16.38 g, 0.221 mol) in EtOH (abs., 150 mL) was drop wise added benzyl chloride (9.74 g, 0.077 mol) over a period of 3 hours and the mixture was allowed to stir for two days. To the milky mixture was added MeONa (25% wt in MeOH, 17.1 g, 18.1 mL, 79.0 mmol) and the volatile components were removed in vacuo. The white precipitate was taken up in $CH_2Cl_2$ (50 mL) and filtered through plug of celite on a glass filter funnel with suction and the plug was washed with additional fractions of CH2Cl2 (3 × 30 mL). The product was concentrated in vacuo and further purified by distillation (110°C, 1.5 mBar) to give 5.64 g (45%) of the product as a colorless oil. 1H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.12 (m, 5 H); 3.74 (s, 2 H); 2.69 (dt, J = 7.0, 4 H); 1.61 (p, J = 7.0, 2 H), 1.26 (s, 3 H). MS (FAB) m/z (int. %): $[MH]^+$ 165.1 (100), 91.1 (15). Data are consistent with literature [39].

**4.9.13 N,N'-Dibenzyl-propane-1,3-diamine (6d)**
Benzaldehyde (55.44 g, 0.52 mol) was added to a solution of propane-1,3-diamine (25.66 g, 0.35 mol) in MeOH (300 mL), stirred for four hours and then $NaBH_4$ (16.63 g, 0.44 mol) was added carefully. Stirring for additional 30 minuts. HCl (aq) (5 M) was added to acidic reaction on pH paper and the solvent was removed in vacuo. The precipitate was taken up in CH2Cl2 and NaOH(aq) (conc.) and the product extracted with $CH_2Cl_2$ (4 × 80 mL). The collected organic phases were washed with NaOH (aq) (5 M, 2 × 30 mL), $NaHCO_3$ (aq) (saturated, 2 × 20 mL) and concentrated in vacuo to give a colorless oil. This was purified by distillation (200 °C, 16 mbar) to yield 22.27 g (25%) of the product as a colorless oil.
$^1$H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.13 (m, 10 H), 3.74 (s, 4 H), 2.67 (t, J = 6.8, 4 H), 1.69 (p, J = 6.8, 2 H), 1.49 (s, 2 H).
MS (FAB) m/z (int. %): 255.2 $[MH]^+$ (100), 91.2 (23). Data are consistent with the literature [39].

**4.9.14 Di-tert-butyl 3,3'-((2-(benzyl(3-(tert-butoxy)-3-oxopropyl)amino)ethyl)azanediyl)dipropionate (7a)**

A solution of compound **6a** (4.68 g, 31.15 mmol) and tert-butyl acrylate (15.48 g, 120.78 mmol) in MeOH (50 ml) was stirred at 70°C (oil bath) for three days. The volatile components were removed in vacuo and the product purified on a dry column (EtOAc/heptane, eluting 10% from heptane). Yield: 83% of the product as a colorless oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.15 (m, 5 H); 3.58 (s, 2 H); 2.78 (t, J = 7.2, 2 H); 2.68 (t, J = 7.4, 4 H); 2.60 – 2.52 (m, 4 H); 2.38 (t, J = 7.2, 2 H); 2.29 (t, J = 7.4, 4 H); 1.43 (s, s, 27 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.26; 172.20; 139.77; 128.96; 128.38; 127.09; 80.43; 59.16; 52.30; 52.24; 50.48; 50.00; 34.14; 34.00; 28.33. MS (FAB) m/z (int. %): 535.1 $[MH]^+$ (64), 286.1 (89), 174.0 (100), 91.0 (94). Anal. Calcd for $C_{30}H_{50}N_2O_6$: C, 67.38; H, 9.42; N, 5.24. Found: C, 67.66; H, 9.57; N, 5.13.

**4.9.15 Di-tert-butyl 3,3'-(ethane-1,2-diylbis(benzylazanediyl))dipropionate (7b)**
A solution of compound **6b** (4.17 g, 17.35 mmol) and tert-butyl acrylate (7.19 g, 56.10 mmol) in MeOH (25 ml) was heated on 70°C (oil bath) for two days followed by removal of the solvent and the excess tert-butyl acrylate in vacuo. The product was purified on a dry column (EtOAc/heptane, eluting 10% from heptane), to give the product as a yellowish to colorless oil. Yield 8.63 g (quant.). $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.13 (m, 10 H); 3.52 (s, 4 H); 2.73 (t, J = 7.2, 4 H); 2.52 (s, 4 H); 2.34 (t, J = 7.2, 4 H); 1.42 (s, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.25; 139.72; 128.97; 128.34; 127.03; 80.38; 58.96; 51.84; 50.38; 34.11; 28.34. MS (FAB) m/z (int. %): 497.1 $[MH]^+$ (21), 248.0 (74), 192.0 (72), 91.0 (100). Anal. Calcd for $C_{30}H_{44}N_2O_4$: C, 72.55; H, 8.93; N, 5.64. Found: C, 72.14; H, 9.04; N, 5.58.

**4.9.16 Di-tert-butyl 3,3'-((3-(benzyl(3-(tert-butoxy)-3-oxopropyl)amino)propyl)azanediyl)dipropionate (7c)**
A solution of compound **6c** (5.33 g, 32.45 mmol), tert-butyl acrylate (18.82 g, 146.84 mmol) in MeOH (70 mL) was stirred for 7 days and then EDA (3.00 mL, 2.25 g, 37.44 mmol) was added and the mixture was allowed to stir for additional three hours. The solvent was removed in vacuo and the product was purified on a dry column (eluting from heptane with EtOAc, 10%) to give 15.90 g (89%) of the product as a colorless oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.13 (m, 5 H); 3.55 (s, 2 H); 2.80 – 2.62 (m, 6 H); 2.46– 2.25 (m, 10 H); 1.66 – 1.52 (m, 2 H); 1.43 (s, 27 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.24; 172.21; 139.79; 128.91; 128.26; 126.92; 80.32; 58.57; 51.89; 51.81; 49.75; 49.45; 33.83; 28.27; 25.04. MS (FAB) m/z (int. %): $[MH]^+$ 549.3 (72); 286.2 (83); 174.0 (98); 91.1 (100). Anal. Calcd for $C_{31}H_{52}N_2O_6$: C, 67.85; H, 9.55; N, 5.10. Found: C, 67.84; H, 9.72; N, 4.99.

**4.9.17 Di-tert-butyl 3,3'-(ethane-1,2-diylbis(azanediyl))dipropionate (8a)**
A mixture of compound **7b** (10.00 g, 20.10 mmol) and $Pd(OH)_2$ (1.00 g) in abs. EtOH (30 ml) was hydrogenated at 4 bar ($H_2$) for 14 hours. The reaction mixture was filtered through a plug of celite on a glass filter funnel with suction. The plug of celite was washed with additional fractions of abs. EtOH (4 × 10 ml) and the product concentrated in vacuo. This was dissolved in $CH_2Cl_2$ (15 ml) and filtered through a paper filter (gravity filtration) and concentrated *in vacuo* to give 6.37 g (quant.) of the product as a yellow oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 2.84 (t, J = 6.6, 4 H); 2.72 (s, 4 H); 2.42 (t, J = 6.6, 4 H); 1.45 (s, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.40; 80.65; 49.45; 45.47; 36.23; 28.34. MS (FAB) m/z (int. %): 317.4 $[MH]^+$ (100), 205.2 (28), 102.2 (10). Anal. Calcd for $C_{16}H_{32}N_2O_4$: C, 60.73; H, 10.19; N, 8.85. Found: C, 60.71; H, 10.37; N, 8.57.

**4.9.18 Di-tert-butyl 3,3'-((2-((3-(tert-butoxy)-3-oxopropyl)amino)ethyl)azanediyl)dipropionate (8b)**
Was synthesized by the procedure described for compound **8a.** $^{1}$H NMR (300 MHz, $CDCl_3$) δ 2.93 - 2.82 (m, 2 H); 2.76 - 2.63 (m, 6 H), 2.61 - 2.52 (m, 2 H), 2.50 - 2.41 (m, 2 H); 2.35 (t, J = 7.1, 4 H); 1.44 (ds, 27 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.32; 172.24; 80.51; 53.74; 49.57; 47.50; 45.63; 36.38; 33.81; 28.34. MS (FAB) m/z (int. %): 445.5 $[MH]^+$ (100), 286.4 (36), 277.3 (18), 174.1 (36). Anal. Calcd for $C_{23}H_{44}N_2O_6$: C, 62.13; H, 9.97; N, 6.30. Found: C, 62.48; H, 10.31; N, 6.15.

**4.9.19 Di-tert-butyl 3,3'-((3-((3-(tert-butoxy)-3-oxopropyl)amino)propyl)azanediyl)dipropionate (8c)**
Was synthesized by the procedure described for compound **8a**. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 2.81 (t, J = 6.6, 2 H), 2.71 (t, J = 7.3, 4 H); 2.60 (t, J = 7.1, 2 H); 2.50 – 2.28 (m, 8 H); 1.69 – 1.55 (m, 2 H); 1.44 (ds, 27 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 172.36; 172.20; 80.57; 80.38; 51.86; 49.50; 48.09; 45.45; 36.04; 33.84; 28.27; 27.84. MS (FAB) m/z (int. %): $[MH]^+$ 459.3 (100), 291.1 (20), 174.0 (20). Anal. Calcd for $C_{24}H_{46}N_2O_6$: C, 62.85; H, 10.11; N, 6.11. Found: C, 62.69; H, 10.29; N, 6.00.

**4.9.20 Benzyl 3-((2-((3-(tert-butoxy)-3-oxopropyl)(3-methoxy-3-oxopropyl)amino)ethyl)amino)propanoate (8d)**
A solution of **3g** (2.52 g, 7.82 mmol) and methyl acrylate (2.29 g, 26.58 mmol) in MeOH (20 mL) was stirred for two days and the volatile components removed under reduced pressure. The product was purified on a dry column (eluting from heptane, EtOAc, 10% increase) to give 2.89 g (91%) of the product as a light yellow oil. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.40 - 7.28 (m, 5 H), 5.47 (br s, 1 H); 5.10 (s, 2 H); 3.62 (s,3 H); 3.27 (m, 2 H); 2.72 (dt, J = 6.8, 4 H); 2.58 – 2.47 (m, 2 H); 2.42 (t, J = 6.8, 2 H); 2.32 (t, J = 6.7, 2 H); 1.41 (s, 9 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.13; 172.04; 156.63; 137.00; 128.51; 128.07; 128.00; 80.72; 66.52; 53.18; 51.72; 49.24; 49.20; 38.69; 33.80; 32.65; 28.18. MS (FAB) m/z (int. %): 409.0 $[MH]^+$ (18), 352.9 (32), 243.9 (47), 188.0 (100), 91.0 (98).

**4.6.8 t-Butyl 3-(3-(benzyloxycarbonylamino)propylamino)propanoate (8e)**
A solution of benzyl (3-aminopropyl)carbamate (7.57 g, mmol) and *tert*-butyl acrylate (4.66 g, mmol) in EtOH (abs, 100 mL) was stirred overnight and the solvent was removed *in vacuo*. The product was purified on a dry column (eluting from heptane, 10% EtOAc) to give 3.82 g (31%) of the product as a colorless oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 5H), 7.31 – 7.28 (m, 1H), 5.09 (s, 2H), 3.35 – 3.20 (m, 2H), 2.81 (t, J = 6.4, 2H), 2.69 (t, J = 6.5, 2H), 2.40 (t, J = 6.5, 2H), 1.72 – 1.59 (m, 2H), 1.44 (s, 9H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.33, 156.61, 136.94, 128.63, 128.23, 128.15, 80.70, 66.62, 47.83, 45.35, 40.16, 35.94, 29.71, 28.26. MS (FAB) m/z (int. %): $[MH]^+$ 337.1 (100), 281.1 (44), 91.2 (27). Anal. Calcd for $C_{18}H_{28}N_2O_4$: C, 64.26; H, 8.39; N, 8.33. Found: C, 64.27; H, 8.32; N, 8.18.

**Heptyl acrylate (9)**
To a solution of heptanol (10.15 g, 87.35 mmol) and triethylamine (26.12 g, 258.31 mmol) in THF (150 ml) at 0 °C was added a solution of acryloyl chloride (9.45 g, 104.41 mmol) in THF (50 ml) slowly over an hour. The reaction was stirred for an additional four hours at 0°C.

The reaction mixture was filtered through a glass filter funnel with suction, treated with $Na_2CO_3$, filtered again and concentrated in vacuo to give a brown liquid (13.44 g). This product was diluted in petroleum spirit (150 mL) and washed with HCl (aq) (1 M, 3 × 50 mL) and then NaOH (aq) (0.5 M, 3 × 50 mL) and finally brine. The organic phase was dried ($MgSO_4$), filtered to give 5.92 g (40%) of the acrylate as a colorless oil after concentration in vacuo. $^1$H NMR (300 MHz, $CDCl_3$) δ 6.40 (dd, J = 1.6 Hz, 17.3 Hz, 1 H); 6.12 (dd, J = 10.4 Hz, 17.3 Hz, 1 H); 5.81 (dd, J = 1.6 Hz, 10.4 Hz, 1 H); 4.15 (t, J = 6.7, 2 H); 1.74 – 1.52 (m, 2 H); 1.45 – 1.12 (m, 8 H); 0.88 (t, J = 6.7 Hz, 3 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.48; 130.54; 128.78; 64.85; 31.85; 29.05; 28.74; 26.02; 22.71; 14.19. Data are consistent with literature [40].

**Scavenger resin for removal of primary/secondary amines:**
Thionyl chloride (20 mL; 32.8 g; 0.28 mol) was added to dry Amberlite IR-50 (20 g) in a flask. DMF (10 drops) was added and the mixture left at room temperature overnight. Excess Thionyl chloride was removed in vacuo, the polymer was washed thoroughly with $CH_2Cl_2$ and dried and was used without further purification.

## References


[1] D.A. Tomalia, J.M.J. Frechet, Discovery of dendrimers and dendritic polymers: A brief historical perspective, Journal of Polymer Science Part a-Polymer Chemistry 40(16) (2002) 2719-2728.
[2] D.A. Tomalia, J.B. Christensen, U. Boas, Dendrimers, Dendrons, and Dendritic Polymers Discovery, Applications, Cambridge University Press 2012.
[3] A. Bernardi, J. Jimenez-Barbero, A. Casnati, C. De Castro, T. Darbre, F. Fieschi, J. Finne, H. Funken, K.E. Jaeger, M. Lahmann, T.K. Lindhorst, M. Marradi, P. Messner, A. Molinaro, P.V. Murphy, C. Nativi, S. Oscarson, S. Penades, F. Peri, R.J. Pieters, O. Renaudet, J.L. Reymond, B. Richichi, J. Rojo, F. Sansone, C. Schaffer, W.B. Turnbull, T. Velasco-Torrijos, S. Vidal, S. Vincent, T. Wennekes, H. Zuilhof, A. Imberty, Multivalent glycoconjugates as anti-pathogenic agents, Chemical Society Reviews 42(11) (2013) 4709-4727.
[4] L. Su, Y.L. Feng, K.C. Wei, X.Y. Xu, R.Y. Liu, G.S. Chen, Carbohydrate-Based Macromolecular Biomaterials, Chemical Reviews 121(18) (2021) 10950-11029.
[5] A. Abdoli, N. Radmehr, A. Bolhassani, A. Eidi, P. Mehrbod, F. Motevalli, Z. Kianmehr, M. Chiani, M. Mahdavi, S. Yazdani, M.S. Ardestani, M.R. Kandi, M.R. Aghasadeghi, Conjugated anionic PEG-citrate G2 dendrimer with multi-epitopic HIV-1 vaccine candidate enhance the cellular immune responses in mice, Artificial Cells Nanomedicine and Biotechnology 45(8) (2017) 1762-1768.
[6] H.H. Keah, E. Kecorius, M.T.W. Hearn, Direct synthesis and characterisation of multi-dendritic peptides for use as immunogens, Journal of Peptide Research 51(1) (1998), 2-8.
[7] M. Vanegas, A. Bermudez, Y.A. Guerrero, J.A. Cortes-Vecino, H. Curtidor, M.E. Patarroyo, J.M. Lozano, Protecting capacity against malaria of chemically defined tetramer forms based on the Plasmodium falciparum apical sushi protein as potential vaccine components, Biochemical and Biophysical Research Communications 451(1) (2014), 15-23.
[8] J. Villen, E. de Oliveira, J.I. Nunez, N. Molin, F. Sobrino, D. Andreu, Towards a multi-site synthetic vaccine to foot-and-mouth disease: addition of discontinuous site peptide mimic increases the neutralization response in immunized animals, Vaccine 22(27-28) (2004) 3523-3529.
[9] P.R. Alakshmi, D.N. Peter, S.J. Johnson, N. Ananthi, Structure-Activity Relationship of Supramolecular Compounds in Drug Delivery, Mini-Reviews in Organic Chemistry 18(7) (2021) 961-989.
[10] L. Cruz, J. Correa, N. Mateus, V. de Freitas, M.H. Tawara, E. Fernandez-Megia, Dendrimers as Color-Stabilizers of Pyranoanthocyanins: The Dye Concentration Governs the Host-Guest Interaction Mechanisms, Acs Applied Polymer Materials 3(3) (2021) 1457-1464.
[11] I. Hussain, N. Muhammad, Q. Subhani, D. Shou, M.C. Jin, L. Yu, G. Lu, X. Wen, A. Intisar, Z. Yan, A review on structural aspects and applications of PAMAM dendrimers in analytical chemistry: Frontiers from separation sciences to chemical sensor technologies, Trac-Trends in Analytical Chemistry 157 (2022), 116810.
[12] T. Tsukamoto, K. Tomozawa, T. Moriai, N. Yoshida, T. Kambe, K. Yamamoto, Highly Accurate Synthesis of Quasi-sub-nanoparticles by Dendron-assembled Supramolecular Templates, Angewandte Chemie-International Edition 61(8) (2022), e2021143.
[13] J.B. Christensen, Dendrimers-Based Nanoparticles for Cancer Therapy and Bioimaging, in: G. Goncalves, G. Tobias (Eds.), Nanooncology: Engineering Nanomaterials for Cancer Therapy and Diagnosis (2018), pp. 281-304.
[14] P. Garrigue, J. Tang, L. Ding, A. Bouhlel, A. Tintaru, E. Laurini, Y.Y. Huang, Z.B. Lyu, M.J. Zhang, S. Fernandez, L. Balasse, W.J. Lan, E. Mas, D. Marson, Y.H. Wen, X.X. Liu, S. Giorgi, J. Iovanna, S. Pricl, B. Guillet, L. Pen, Self-assembling supramolecular dendrimer nanosystem for PET imaging of tumors, Proceedings of the National Academy of Sciences of the United States of America 115(45) (2018) 11454-11459.
[15] D. Kalyane, N. Raval, R. Maheshwari, V. Tambe, K. Kalia, R.K. Tekade, Employment of enhanced permeability and retention effect (EPR): Nanoparticle-based precision tools for targeting of therapeutic and diagnostic agent in cancer, Materials Science and Engineering C-Materials for Biological Applications 98 (2019) 1252-1276.
[16] C. Song, Z.J. Ouyang, H.H. Guo, J. Qu, Y. Gao, J.D. Xia, M.W. Shen, X.Y. Shi, Core-Shell Tecto Dendrimers Enable Enhanced Tumor MR Imaging through an Amplified EPR Effect, Biomacromolecules 22(5) (2021) 2181-2188.
[17] J.P. Yang, Q. Zhang, H. Chang, Y.Y. Cheng, Surface-Engineered Dendrimers in Gene Delivery, Chemical Reviews 115(11) (2015) 5274-5300.
[18] L.P. Mendes, J.Y. Pan, V.P. Torchilin, Dendrimers as Nanocarriers for Nucleic Acid and Drug Delivery in Cancer Therapy, Molecules 22(9) (2017), 1301 - 1424.
[19] N. Sayed, P. Allawadhi, A. Khurana, V. Singh, U. Navik, S.K. Pasumarthi, I. Khurana, A.K. Banothu, R. Weiskirchen, K.K. Bharani, Gene therapy: Comprehensive overview and therapeutic applications, Life Sciences 294 (2022), 120375.

[20] K. Yamamoto, T. Imaoka, M. Tanabe, T. Kambe, New Horizon of Nanoparticle and Cluster Catalysis with Dendrimers, Chemical Reviews 120(2) (2020) 1397-1437.
[21] C.B. Gao, F.L. Lyu, Y.D. Yin, Encapsulated Metal Nanoparticles for Catalysis, Chemical Reviews 121(2) (2021) 834-881.
[22] T.Y. Chen, M.S. Qiu, Y. Peng, C.F. Yi, Z.S. Xu, Colloidal Polymer-Templated Formation of Inorganic Nanocrystals and their Emerging Applications, Small (2023).
[23] B.H. Gan, T.N. Siriwardena, S. Javor, T. Darbre, J.L. Reymond, Fluorescence Imaging of Bacterial Killing by Antimicrobial Peptide Dendrimer G3KL, Acs Infectious Diseases 5(12) (2019) 2164-2173.
[24] A. Giuliani, A.C. Rinaldi, Beyond natural antimicrobial peptides: multimeric peptides and other peptidomimetic approaches, Cellular and Molecular Life Sciences 68(13) (2011) 2255-2266.
[25] M. Morawiak, M. Stolarska, M. Cieslak, Z. Urbanczyk-Lipkowska, Interactions of rationally designed small peptide dendrons functionalized with valine or sinapic acid with alpha-helix and beta-sheet structures of poly-l-lysine and poly-l-glutamic acid, Peptide Science 112(3) (2020).
[26] W.Z. Zhang, D. Dhumal, X.L. Zhu, B. Ralahy, A. Ellert-Miklaszewska, J. Wu, E. Laurini, Y.W. Yao, C.L. Kao, J.L. Iovanna, S. Pricl, B. Kaminska, Y. Xia, L. Peng, Bola-Amphiphilic Glycodendrimers: New Carbohydrate-Mimicking Scaffolds to Target Carbohydrate-Binding Proteins, Chemistry-a European Journal 28(58) (2022).
[27] A.B. Sølvhoj, C. Tortzen, J.B. Christensen, Monoprotection of Triamines with Alkyl Phenyl Carbonates, Organic Preparations and Procedures International 44(4) (2012) 397-400.
[28] M. Pittelkow, R. Lewinsky, J.B. Christensen, Mono Carbamate Protection of Aliphatic Diamines Using Alkyl Phenyl Carbonates (2-Aminoethyl)carbamic acid tert-butyl ester, in: M.J. Miller (Ed.), Organic Syntheses 84, 2007, 209-214.
[29] M. Pittelkow, R. Lewinsky, J.B. Christensen, Selective synthesis of carbamate protected polyamines using alkyl phenyl carbonates, Synthesis-Stuttgart (15) (2002) 2195-2202.
[30] S.Z. Tang, D.A. Tomalia, B.G. Orr, J.R. Baker, B.H. Huang, Regio-specific size, shape and surface chemistry designed dendrimers based on differentiated dendroid templates, New Journal of Chemistry 37(3) (2013) 690-700.
[31] A.M. Caminade, R. Laurent, B. Delavaux-Nicot, J.P. Majoral, "Janus" dendrimers: syntheses and properties, New Journal of Chemistry 36(2) (2012) 217-226.
[32] I.K. Martin, L.J. Twyman, The synthesis of unsymmetrical PAMAM dendrimers using a divergent/divergent approach, Tetrahedron Letters 42 (2001) 1119-1121.
[33] J.Y. Hwang, H.Y. Kim, S. Jo, E. Park, J. Choi, S. Kong, D.S. Park, J.M. Heo, J.S. Lee, Y. Ko, I. Choi, J. Cechetto, J. Kim, J. Lee, Z. No, M.P. Windisch, Synthesis and evaluation of hexahydropyrimidines and diamines as novel hepatitis C virus inhibitors, European Journal of Medicinal Chemistry 70 (2013) 315-325.
[34] M. Pittelkow, J.B. Christensen, Convergent synthesis of internally branched PAMAM dendrimers, Organic Letters 7(7) (2005) 1295-1298.
[35] C.M. Micklitsch, Q. Yu, J.P. Schneider, Unnatural multidentate metal ligating alpha-amino acids, Tetrahedron Letters 47(35) (2006) 6277-6280.
[36] D.S. Pedersen, C. Rosenbohm, Dry column vacuum chromatography, Synthesis-Stuttgart (16) (2001) 2431-2434.
[37] D.F. King, R. A. Firestone; G. M. Dubowchik, Branched Peptide Linkers, WO1998019705A1 (1997).
[38] Z. Li, X. Chen, Radiolabeled bbn-rgd heterodimers for cancer targeting, US20100015058 (2009).

[39] M. V. de Almeida, A. P. S. Fontes, R. N. Berg, E. T. César, E. de C. A. Felício and J. D. de S. Filho, Synthesis of Platinum Complexes from N-Benzyl-1,3-Propanediamine Derivatives, Potential Antineoplastic Agents, Molecules, 2002, 7, 405 - 411.

[40] N. A. Porter;V. H.-T. Chang, Macrolide Formation by Free Radical Cyclization, J. Am. Chem. Soc. 109 (1987), 4976 - 4981.