Radially Layered Poly(amidoamine−organosilicon) Dendrimers

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ABSTRACT: A versatile approach to a new family of radially layered copolymeric poly(amidoamine−organosilicon) (PAMAMOS) dendrimers containing hydrophilic polyamidoamine (PAMAM) interiors and hydrophobic organosilicon (OS) exteriors is described. The synthesis involves either Michael addition of organosilicon acrylates or methacrylates to amine-terminated PAMAM dendrimer precursors or their haloalkylation by chloroalkyl- or iodoalkylsilanes. Convenient NMR techniques were developed to monitor the course of these reactions and to enable preparation of products with precisely controlled degree of OS coverage. Compositional variety of the resulting dendrimers is achieved by variation of the generation of PAMAM precursor and the type and functionality of the organosilicon reagent. A range of different PAMAMOS dendrimers was prepared having (a) different number of PAMAM branch cell layers in their interiors, (b) one or two layers of OS branch cells in their exteriors, (c) a variety of inert (e.g., trimethylsilyl or trimethylsiloxy) or reactive (e.g., alkoxysilyl, vinylsilyl, or vinylsiloxy) end groups, and (d) different relative amounts of these end groups. NMR, electrospray−ionization mass spectroscopy, and gel permeation chromatography confirmed the expected structures. Evaluation of selected physical properties of these PAMAMOS dendrimers showed that while solubility and glass transition temperatures were compositionally and architecturally dependent, their thermal and thermooxidative stability were limited by the presence of the less stable PAMAM component.

Introduction

During the past two decades, dendritic macromolecules in general, and among them dendrimers in particular, have become one of the fastest growing areas of polymer science.[1,2] The “eruption” of publications and patents on these unique polymers, from barely a dozen or so in the 1980s to over 2500 by the end of 1999, is undoubtedly due to their unprecedented architecture.[2] In essence, dendrimers are globular macromolecules which consist of two or more treelike dendrons, emanating from either a single central atom or an atomic group, called the core (see Figure 1).[3] The main building blocks of dendrimer architecture are the branch cells (depicted in Figure 1 as shaded or clear circles with Arabic numerals inside), which represent dendritic repeat units and always contain at least one branch juncture (small filled or unfilled circles in the center of each branch cell). In an idealized case of complete and perfect connectivity (i.e., in an ideal dendrimer), these branch cells are organized in a series of regular, radially concentric layers (called generations) around the core. Each of these layers contains a mathematically precise number of branch cells which increases in a geometrically progressive manner from the core to the outer dendrimer surface (see structures of Figure 1).

Exceptional regularity and geometrical control of dendrimer structure[4] exerts a major influence on a variety of their properties.[5] In fact, some of these properties are so architecturally specific that they are not found in any other type of macromolecular organization.[5] Consequently, architecture and architecture-related characteristics have become the main focus of research interest in dendritic polymers,[1−4] with their compositional features receiving only secondary attention. However, it is intrinsically clear that practical utilization of these unique polymers necessarily also depends on their composition and that optimal products for specific potential applications will only be obtained if both architecturally and compositionally driven properties are maximized in synergistic interaction(s).

To date, over 50 different dendrimer families with a variety of different end group modifications have been reported.[1] Of these, a large majority are “fully organic” dendrimers (i.e., those built exclusively of carbon, hydrogen, nitrogen, and oxygen), although a number of different silicon-, phosphorus-, sulfur-, or other element-containing counterparts have also been described.[1] However, with the notable exception of poly(benzyl ether−benzyl ester)s,[6] all reported dendrimers are inherently homopolymeric in character (see Figure 1A), and their copolymeric derivatives containing more than one type of compositional building block (i.e., branch cells)[3] have been seriously neglected. This clearly contrasts with traditional macromolecular chemistry (of linear, cross-linked, and randomly branched architectures),[2] where a combination of different repeat units in different types of copolymeric arrangements has resulted in practically unlimited compositional versatility of synthetic polymers. Accordingly, a similar ability to combine different dendritic building blocks in different orders of placement and/or relative amounts in dendrimer organization should give rise to a variety of new materials with either completely new properties or further diversification of those already specific for this unique type of macromolecular architecture.[7] Among others, these properties may include solubility, chemical reactivity, surface characteristics, glass temperatures, thermal and thermooxidative stability, rheological be-

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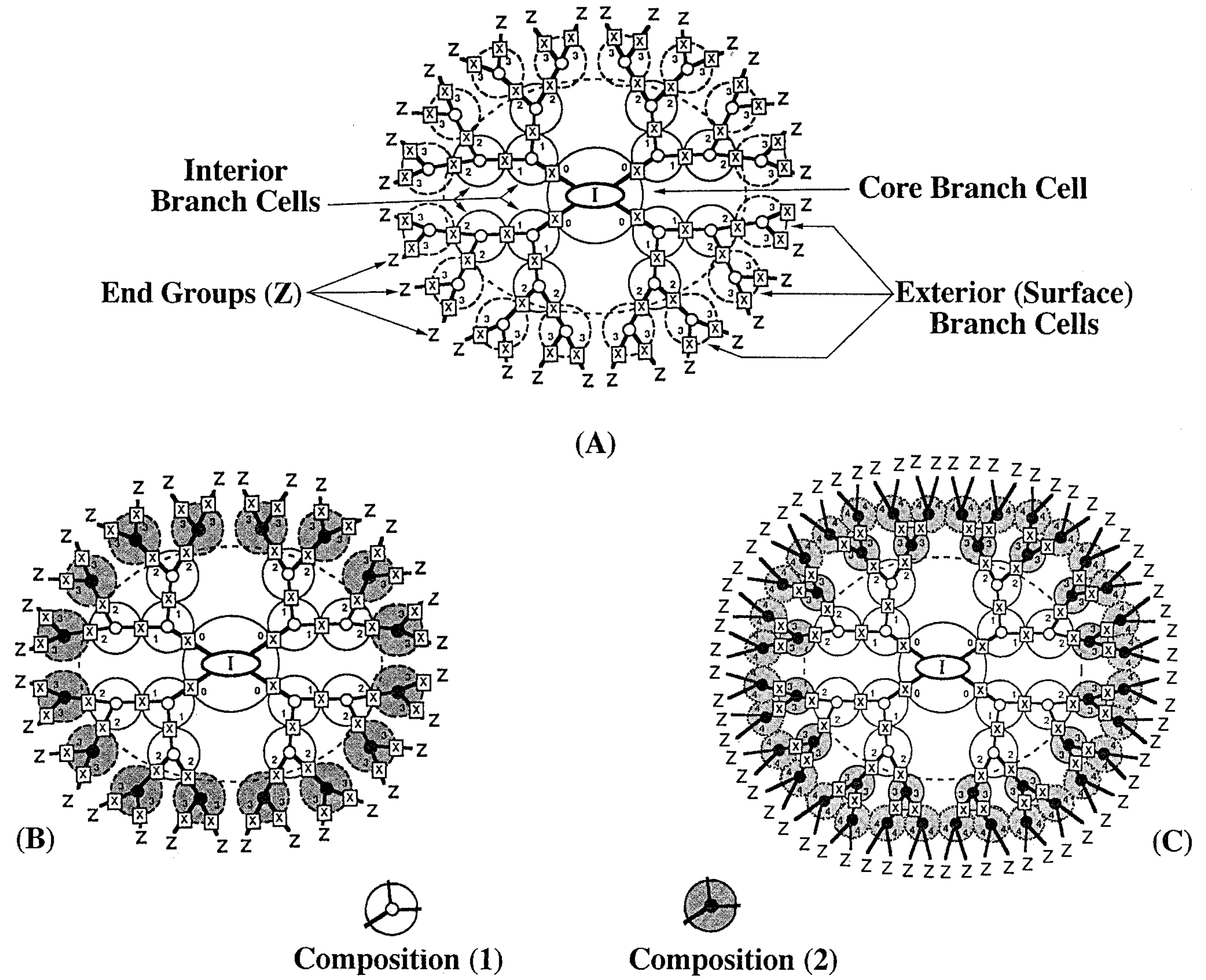


Figure 1. Schematic representation of homopolymeric (A) and two types of radially layered copolymeric tetradendron dendrimers (B and C). Note three basic building blocks of dendrimer architecture in each of these structures: core cells (I), interior branch cells, and exterior branch cells. Also note that copolymeric dendrimers contain two compositionally different types of branch cells represented by blank (composition 1) and shaded (composition 2) circles. Structure B is the simplest type of radially layered copolymeric dendrimers with only one layer of branch cells 2, while structure C is higher homologue with two layers of branch cells 2. Of PAMAMOS dendrimers described in this report, derivatives **1**, **5**, **14**, and **15** belong to type B, while derivatives **2**, **3**, and **4** belong to type C. Arabic numerals in the circles representing branch cells denote generations.

havior, compatibility, diffusion, electrical and optical responses, etc.[5]

Toward this end, we report here on a new family of radially layered dendrimers which contain hydrophilic polyamidoamine (PAMAM) interiors and oleophilic (i.e., hydrophobic) organosilicon (OS) exteriors.[8] These poly(amidoamine−organosilicon) (PAMAMOS) dendrimers may be represented by general structures B and C of Figure 1, because they consist of two different types of branch cells, and not merely of different end groups (Z of Figure 1) attached to a homopolymeric scaffold.[7] They may also be viewed as inverted-micelle-type, covalently bonded, highly branched amphiphiles or as globular, nanoscaled, organo-inorganic precursors that can be further used for preparation of other structures with higher order of organizational complexity.[9] Which of these roles a particular PAMAMOS dendrimer type may play will depend on the nature of its end groups and whether they are inert or reactive. In this report, we describe two types of PAMAMOS dendrimers with inert end groups (i.e., those containing trimethylsilyl and trimethylsiloxysilyl units) and three types of their reactive derivatives (i.e., those having vinylsilyl, vinylsiloxysilyl, and alkoxysilyl ones).

Experimental Section

General Procedures. ^{1}H, ^{13}C, and ^{29}Si NMR spectra were recorded on a 300 MHz Varian Unity 300 spectrometer equipped with a 5 mm four-nuclei probe. The solvent signals were used as standards, and chemical shifts are reported relative to tetramethylsilane. Mass spectra were obtained from methanol solutions of the samples on a Finnigan MAT TSQ 700 electrospray−ionization spectrometer (ESI-MS). Gel-permeation chromatography (GPC) was carried out on a Waters model 510 pump system equipped with WISP 710A control unit and a model 410 differential refractometer detection unit. Two in series connected PLgel 10 μm mixed columns were used with NMP/0.1% (w/v) LiBr mobile phase preheated to 80 °C. Polymer Lab PL Caliber version 6 software was used for data analysis. Differential scanning calorimetry (DSC) measurements were performed on a DuPont Instruments model 912 unit. Samples were dried to crisp solids under reduced pressure overnight and transferred into the DSC pans in a dry bag under nitrogen. Measurements were performed between −100 and 60 °C, with 1−10 mg samples at a heating rate of 10 °C/min. Thermal gravimetric analysis (TGA) was performed on a DuPont Instruments model 951 in air and in nitrogen. The temperature interval from 25 to 700 °C was scanned at a heating rate of 20 °C/min.

(3-Acryloxypropyl)methylbis(vinyldimethylsiloxy)silane (10). A 100 mL three-necked round-bottomed flask was equipped with a nitrogen inlet, a vertical condenser connected with a bubbler containing 1 N NaOH solution, and a rubber septum. Inside this reactor, the nitrogen inlet was submerged just below the surface level of the reaction mixture so that the gas could be bubbled directly into it. (3-Acryloxypropyl)dimethoxymethylsilane **7** (2 mL, 2 g, 8.47 mmol) was charged into the reactor, followed by THF (25 mL) and freshly distilled chlorodimethylvinylsilane (**12**) (6.9 mL, 6.13 g, 50.82 mmol), and the mixture was homogenized by stirring under nitrogen for several minutes. When this was completed, water (0.94 mL, 52 mmol) was added dropwise through the septum from a syringe at room temperature for 16.5 h. Methylene chloride was then added and the mixture washed several times with water until neutral pH. The organic phase was dried over Na_2SO_4 and filtered, and the solvent was evaporated. The obtained product (60.4% yield) was subsequently used for PAMAMOS synthesis without further purification. ^1H NMR ($CDCl_3$): δ 0.01 (s, $-CH_2-SiCH_3(-O-Si\equiv...)_2$); 0.12 (s; $-O-Si(CH_3)_2Vi$); 0.48 (m; $CH_2-CH_2-Si\equiv$); 1.64 (m; $-CH_2-CH_2-CH_2-$); 4.06 (t; $-COO-CH_2-$); 5.64−6.38 (dxd + d; $\equiv Si-CH{=}CH_2$). ^{13}C NMR ($CDCl_3$): δ −0.43 and 0.19 ($\equiv Si-CH_3$); 13.43 ($-CH_2-CH_2-Si\equiv$); 22.35 ($-COO-CH_2-CH_2-CH_2-Si\equiv$); 66.74 ($-COO\text{-}CH_2-$); 128.62 and 130.20 ($CH_2{=}CH-COO-$); 131.73 and 139.08 ($CH_2{=}CH-Si\equiv$); 166.12 ($-COO-$).

Dendrimer Synthesis. The following examples describe typical procedures. In each case, other generational homologues can be prepared using identical reaction conditions and appropriately recalculated quantities of the reagents.

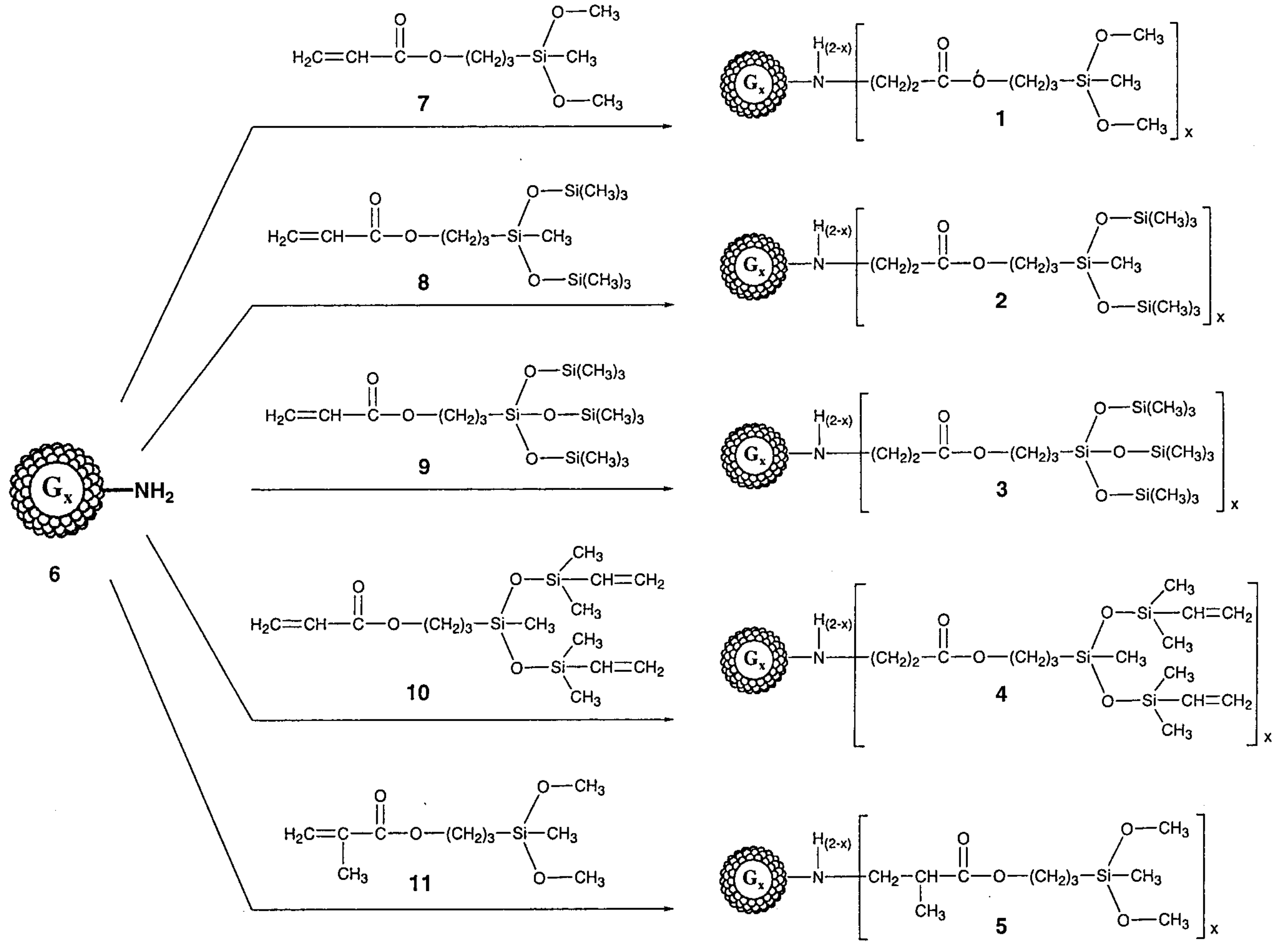
Dimethoxymethylsilyl (DMOMS)-Functionalized PAMAMOS Dendrimers 1 and General Procedure for the Synthesis of PAMAMOS Dendrimers via Michael Addition of Organosilicon Acrylates. A two-necked, round-bottomed flask was equipped with a Teflon-coated magnetic stirring bar, stopper, and a condenser with a nitrogen inlet at its top. The reactor was charged with 1.56 g (0.23 mmol) of generation 3 PAMAM dendrimer (corresponding to 14.45 mmol of −NH groups assuming ideal structure) in the form of 10% (w/w) methanol solution and (3-acryloxypropyl)dimethoxymethylsilane (**7**) (4.2 mL, 4.2 g, 17.79 mmol), and the mixture was stirred under nitrogen at room temperature for 3 days. The extent of NH groups substitution determined by ^1H NMR was 80%, and the resulting PAMAMOS dendrimer was stable as long as it was kept in the reaction mixture solution and under anhydrous conditions. ^1H NMR ($CDCl_3$): δ 0.02 (s; $\equiv Si-CH_3$); 0.52 (m; $-CH_2-Si\equiv$); 1.61 (m; $-COO-CH_2-CH_2-CH_2-Si\equiv$); 2.4−3.6 (PAMAM dendrimer protons); 3.40 (s; $\equiv Si-O-CH_3$); 3.94 (t; PAMAM$-COO-CH_2-$); 4.02 (t, $CH_2{=}CH-COO-CH_2-$); 5.68−6.32 (d + dxd + d; $CH_2{=}CH-COO-$). ^{13}C NMR ($CDCl_3$): δ −6.18 ($\equiv Si-CH_3$); 8.89 ($-CH_2-Si\equiv$); 21.82 ($-COO-CH_2-CH_2-CH_2-Si\equiv$); 32.37 ($=N-CH_2-CH_2-COO-(CH_2)_3-Si\equiv$); 33.54 ($-CH_2-CO-NH-$); 34.75 ($-NH-CH_2-CH_2-COO-(CH_2)_3-Si\equiv$); 37.10 and 37.29 ($-CO-NH-CH_2-$); 38.76 ($-CO-NH-CH_2-CH_2-NH-(CH_2)_2-COO-$); 44.43($-CO-NH-CH_2-CH_2-NH-(CH_2)_2-COO-$);48.37($-NH-CH_2-CH_2-COO-(CH_2)_3-Si\equiv$); 48.92 ($-CO-NH-CH_2-CH_2-N-((CH_2)_2-COO-...)_2$); 49.54 ($-CO-NH-CH_2-CH_2-N=$); 49.89 ($\equiv Si-O-CH_3$); 51.33 ($=N-CH_2-CH_2-COO-$); 52.20 and 52.60 ($=N-CH_2-CH_2-CONH-$); 66.31 ($=N-(CH_2)_2-COO-CH_2-$); 128.32 and 130.18 ($CH_2{=}CH-$); 172.21 and 172.31 ($-CH_2-CH_2-COO-$ and $-CO-NH-$) and unreacted acrylate reagent **7** δ −6.18 ($\equiv Si-CH_3$); 8.89 ($-CH_2-Si\equiv$); 21.82 ($-COO-CH_2-CH_2-CH_2-Si\equiv$); 49.89 ($\equiv Si-O-CH_3$); 66.36 ($CH_2{=}CH-COO-CH_2-$); 128.32 and 130.18 ($CH_2{=}CH-$); 165.92 ($CH_2{=}CH-COO-$).

Trimethylsiloxysilyl (TMS)-Functionalized PAMAMOS Dendrimers 3. The procedure for this preparation is analogous to that described for dendrimer **1**. Generation 3, EDA-core PAMAM dendrimer (0.32 g, 0.47×10^{-4} mol, equivalent of 3 mmol of −NH groups) and (3-acryloxypropyl)tris(trimethylsiloxy)methylsilane (**9**) (1.47 g, 3.6 mmol) were reacted in methanol at room temperature for 3 days. The obtained product was purified by dialysis (MWCO: 3500, Spectra/Por 7) in methanol, yielding 0.80 g of the recovered sample. The extent of −NH groups substitution determined by ^1H NMR was 45%. ^1H NMR ($CDCl_3$): δ 0.05 (s, $\equiv SiCH_3$); 0.40 (m; $-CH_2-Si\equiv$); 1.59 (m; $-COO-CH_2-CH_2-CH_2-Si\equiv$); 2.1−3.6 (PAMAM dendrimer protons); 3.96 (t; PAMAM$-COO-CH_2-$). ^{13}C NMR ($CDCl_3$): δ 1.68 ($\equiv Si-CH_3$); 10.33 ($-CH_2-Si\equiv$); 22.66 ($-CH_2-CH_2-CH_2-$); 32.45 ($=N-CH_2-CH_2-COO-(CH_2)_3-Si\equiv$); 34.34 ($-CH_2-CO-NH-$ and $-NH-CH_2-CH_2-COO-$); 37.58 ($-CO-NH-CH_2-CH_2-N=$); 39.03 ppm ($-CONH-CH_2-CH_2-NH-$); 44.63 ppm ($-CONH-CH_2-CH_2-NH-$); 48.56 ppm ($-CH_2-NH-CH_2-CH_2-COO-$); 49.04 ppm ($-CO-NH-CH_2-CH_2-N-((CH_2)_2-COO-...)_2$); 50.24 ($-CO-NH-CH_2-CH_2-N=$); 51.58 ($=N-CH_2-CH_2-COO-$); 52.48 ($=N-CH_2-CH_2-CONH-$); 66.78 ($=N-(CH_2)_2-COO-CH_2-$); 172.56 and 173.02 ($-CO-NH-$ and CH_2-CH_2-COO-).

Dimethylvinylsiloxysilyl (DMVSOS)-Functionalized PAMAMOS Dendrimers 4. The procedure is analogous to that described for preparation of dendrimers **1** and **3** above. Generation 3 EDA-core PAMAM dendrimer lyophilized under vacuum overnight (0.63 g, 9.12×10^{-5} mol, equivalent of 5.83 mmol of −NH groups) and freshly prepared (3-acryloxypropyl)bis(vinyldimethylsiloxy)methylsilane (**10**) (1.93 g, 5.12 mmol) were mixed in methanol (5 mL) and stirred at room temperature for 24 h. The obtained product was purified by dialysis (MWCO: 3500, Spectra/Por 7) in methanol, after evaporation of which 0.79 g of the sample was recovered. The extent of −NH group substitution found by ^1H NMR was 51%. ^1H NMR ($CDCl_3$): δ 0.01 and 0.03 (s, $-CH_2-SiCH_3(-O-Si\equiv...)_2$); 0.12 (s; $-O-Si(CH_3)_2-CH{=}CH_2$); 0.45 (m; $-CH_2-Si\equiv$); 1.60 (m; $-COO-CH_2-CH_2-CH_2-Si\equiv$); 2.1−3.6 (PAMAM dendrimer protons); 3.96 (t; PAMAM$-COO-CH_2-$); 5.65−6.14 (d + d + dxd; $\equiv Si-CH{=}CH_2$). ^{13}C NMR ($CDCl_3$): δ −0.37 and 0.29 ($\equiv Si-CH_3$); 13.43 ($-CH_2-Si\equiv$); 22.33 ($-CH_2-CH_2-CH_2-$); 32.56 ($=N-CH_2-CH_2-COO-(CH_2)_3-Si\equiv$); 33.77 ($-CH_2-CO-NH-$); 37.35 ($-CO-NH-CH_2-$); 49.13 ($-CO-NH-CH_2-CH_2-N-((CH_2)_2-COO-...)_2$); 49.83 ($-CO-NH-CH_2-CH_2-N=$); 51.58 ($=N-CH_2-CH_2-COO$); 52.50 and 52.90 ($=N-CH_2-CH_2-CONH-$); 66.82 ($=N-(CH_2)_2-COO-CH_2-$); 128.62 and 130.32 ($CH_2{=}CH-COO-$); 131.79 and 139.10 ($CH_2{=}CH-Si\equiv$); 172.50 ($-CO-NH-$ and $-CH_2-CH_2-COO-$).

Trimethylsilyl (TMS)-Functionalized PAMAMOS Dendrimers 14 (with 50% =NH Substitution). A. Chloroalkylation of PAMAM Dendrimers 6 with Chloromethyltrimethylsilane (16). Generation 3 EDA-core PAMAM dendrimer was lyophilized in methanol in a round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and kept under partial vacuum overnight. 1.30 g (0.18 mmol; equivalent of 12.00 mmol −NH groups) of the obtained crispy solid was dissolved in NMP (6 mL), following which 0.83 mL (0.73 g, 5.96 mmol) of chloromethyltrimethylsilane (**16**) was added to the obtained solution, and a condenser was mounted on the flask. The resulting mixture was stirred, heated to 80 °C, and kept under nitrogen for the total of 161 h. After the heating was stopped, an aliquot of the reaction mixture was dissolved in CD_3OD and analyzed by ^1H NMR to determine the extent of dendrimer conversion (44.5% of the original −NH groups had reacted). Following this, Na_2CO_3 (0.65 g, 6.13 mmol) and methanol were added, and the reaction mixture was stirred overnight. Insoluble salts were filtered out, and the filtrate was dialyzed first in a 50/50: methanol/water mixture and then in pure methanol. Methanol was evaporated and the obtained dendrimer was dried under partial vacuum.^1H NMR (CD_3OD): δ 0.07 (s, $\equiv Si-CH_3$); 2.08−3.35 (PAMAM dendrimer protons). ^{13}C NMR (CD_3OD): δ −2.23 ($\equiv Si-CH_3$); 34.82 ($-CH_2-CO-NH-$); 38.68 ($-CO-NH-CH_2-CH_2-N=$); 39.33 and 40.53 ($-CO-NH-CH_2-CH_2-NH-CH_2-Si\equiv$ and $-CO-NH-CH_2-CH_2-NH-CH_2-Si\equiv$); 42.09 ($-CO-NH-CH_2-CH_2-NH_2$); 42.93 ($-CO-NH-CH_2-CH_2-NH_2$); 51.18 ($-CO-NH-CH_2-CH_2-N=$ and $=N\text{-}CH_2-CH_2-CONH-(CH_2)_2-NH_2$); 53.55 ($=N-CH_2-CH_2-CONH-(CH_2)_2-N=$); 54.19 ($-NH-CH_2-Si\equiv$); 174.64, 175.00, and 175.10 ($-CO-NH-$).

Scheme 1



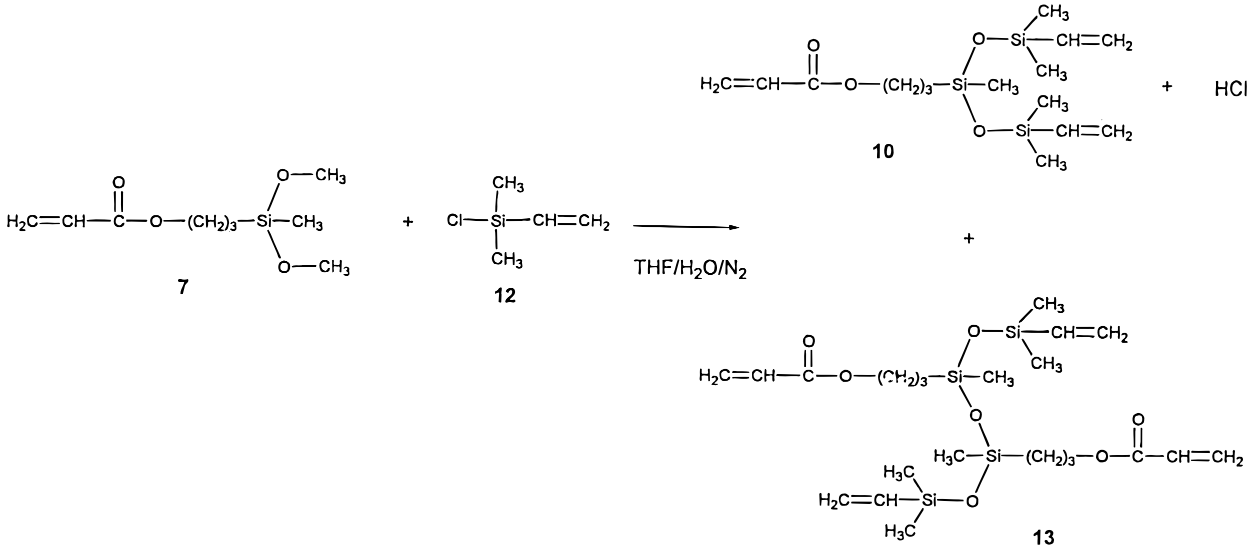
B. Iodoalkylation of PAMAM Dendrimers 6 with Iodomethyltrimethylsilane (17). Chloromethyltrimethylsilane (**16**) (2.00 mL, 1.77 g, 14.44 mmol), sodium iodide (2.4 g, 16.0 mmol, [NaI]/[ClR] = 1.1), 15-C-5 crown ether (0.24 g, 0.89 mmol, 6.2%/ [-Cl]), and NMP (5 mL) were placed in a round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and a condenser. The apparatus was filled with nitrogen, and the reaction mixture was stirred at 60 °C overnight. Generation 3 EDA-core PAMAM dendrimer was lyophilized in methanol in a round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and kept under partial vacuum overnight. The obtained crispy solid (1.63 g, 0.23 mmol; equivalent of 15.06 mmol of −NH groups) was dissolved in 15 mL of NMP and added to the previous reaction mixture followed by sodium bicarbonate (1.26 g, 15.00 mmol). The reaction mixture was stirred at 80 °C, and samples were periodically taken for ^{1}H NMR analysis which was used to follow the course of the reaction. Stirring and heating were stopped after 92 h of the reaction time when complete modification of =NH groups was achieved. The resulting mixture was filtered and the filtrate was dialyzed, first in a 50/50 water/methanol mixture and then in pure methanol (Spectra/Por 7; MWCO 3500). ^{1}H NMR (CD$_3$OD): δ 0.08 (s, ≡Si−*CH$_3$*); 2.03−3.33 (PAMAM dendrimer protons). ^{13}C NMR (CD$_3$OD): δ −0.90 (≡Si−*CH$_3$*); 34.81 (−*CH$_2$*−CO−NH−); 38.05 (−CO−NH−*CH$_2$*−CH$_2$−N−(CH$_2$−Si(CH$_3$)$_3$)$_2$); 38.62 (−CO−NH−*CH$_2$*−CH$_2$−N=); 50.74 (−CO−NH−CH$_2$−*CH$_2$*−N−(CH$_2$−Si−(CH$_3$)$_3$)$_2$); 51.16 (−CO−NH−CH$_2$−*CH$_2$*−N=); 51.56 (=N−*CH$_2$*−CH$_2$−CONH−(CH$_2$)$_2$−N−(CH$_2$SiMe$_3$)$_2$); 53.51 (=N−*CH$_2$*−CH$_2$−CONH−(CH$_2$)$_2$−N=); 61.31 (=N−*CH$_2$*−Si≡); 174.53 and 174.67 (−*C*O−NH−).

Dimethylvinylsilyl (DMVS)-Functionalized PAMAMOS Dendrimers 15. The procedure is analogous to that described for the preparation of trimethylsilylated (TMS) PAMAMOS dendrimers **14** with the following exceptions. The reactor was a three-necked, round-bottomed flask, equipped with a stopper, mechanical stirrer, and vertical condenser with a nitrogen inlet at its top. Chloromethyldimethylvinylsilane (**18**) (8.1 mL, 7.22 g, 53.64 mmol), sodium iodide (8.87 g, 59.18 mmol, [NaI]/[ClR] = 1.1), 15-C-5 crown ether (0.72 g, 2.72 mmol, 5.1% [-Cl]), and NMP (20 + 30 mL) yielded 100% modification of =NH PAMAM groups. ^{1}H NMR (CD$_3$OD): δ 0.14 (s, ≡Si−*CH$_3$*); 2.11−3.34 (PAMAM dendrimer protons); 5.71−6.26 (≡Si−*CH*=*CH$_2$*). ^{13}C NMR (CD$_3$OD): δ −2.80 (≡Si−*CH$_3$*); 34.77 (−*CH$_2$*−CO−NH−); 38.25 (−CO−NH−*CH$_2$*−CH$_2$−N−(CH$_2$−Si(CH$_3$)$_2$Vi)$_2$); 38.58 (−CO−NH−*CH$_2$*−CH$_2$−N=); 50.50 (−CO−NH−CH$_2$−*CH$_2$*−N−(CH$_2$−Si(CH$_3$)$_2$Vi)$_2$); 51.09 (−CO−NH−CH$_2$−*CH$_2$*−N= and N−*CH$_2$*−CH$_2$−CONH−(CH$_2$)$_2$−Si≡); 53.48 (=N−*CH$_2$*−CH$_2$−CONH−(CH$_2$)$_2$−N=); 61.14 (=N−*CH$_2$*−Si≡); 133.16 and 139.67 (≡Si−*CH*=*CH$_2$*); 174.16 and 174.45 (-*C*O−NH−). ^{29}Si NMR (CD$_3$OD): δ −8.74 (=N−CH$_2$−*Si*(CH$_3$)$_2$Vi).

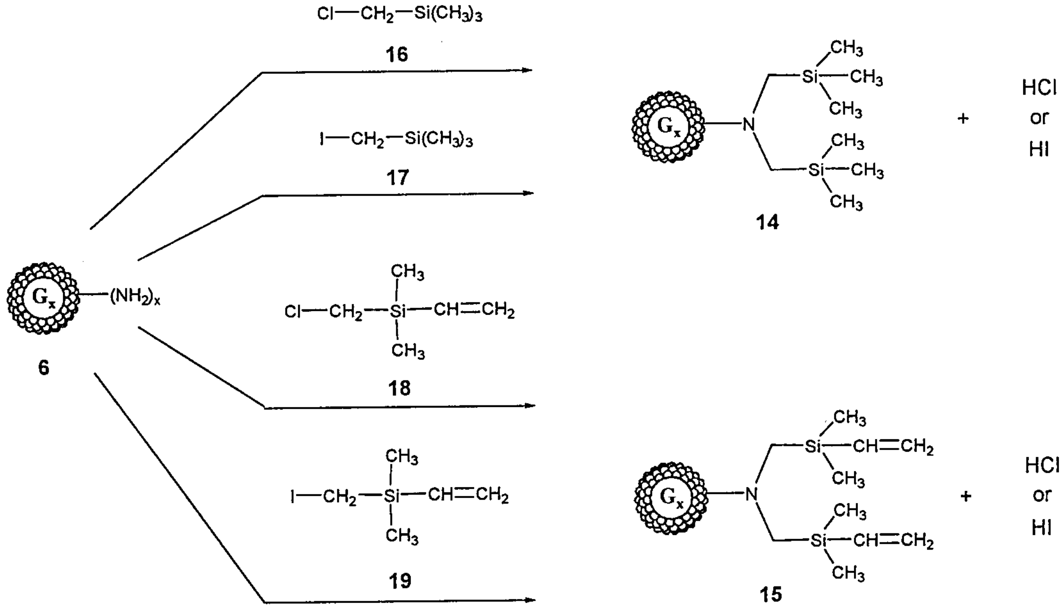
Results and Discussion

Seven different types of radially layered poly(amidoamine−organosilicon) (PAMAMOS) dendrimers were prepared from amine-terminated polyamidoamine (PAMAM) precursors by either (a) Michael addition of silicon-containing acrylates and/or methacrylates or (b) haloalkylation with chloro- or iodoalkylsilanes (see Schemes 1 and 3, respectively).[8] Depending on the choice of PAMAM dendrimer generation, silicon-containing reagent, and the synthetic route, the resulting PAMAMOS dendrimers differed in (a) the relative content (i.e., number) of PAMAM and/or OS branch cell layers, (b)

Scheme 2



Scheme 3



the type of OS branch cells involved, (c) the type and relative content of reactive or nonreactive end groups, and (d) the degree of "coverage" of the PAMAM interior by the OS exterior.

Synthesis of PAMAMOS Dendrimers by Michael Addition of Amine-Terminated PAMAM Dendrimers and Silicon-Containing Acrylates and/or Methacrylates. A series of PAMAMOS dendrimers (**1**−**5**) were prepared from ethylenediamine (EDA) core, amine-terminated PAMAM tetradendron dendrimers (**6**), and silicon-containing acrylates (**7**−**10**) and/or methacrylates (such as **11**), as shown in Scheme 1. Depending on the generation of PAMAM dendrimer selected (G_x), the resulting PAMAMOS dendrimers (**1**−**5**) contained a predetermined number (G_{x+1}) of layers of polyamidoamine branch cells, $-[CH_2-CH_2-C(O)-N(H)-CH_2-CH_2-N]<$, in their interiors and one or two layers of organosilicon (OS) branch cells in their exteriors (compare with structures B and C of Figure 1). The OS branch cells varied in composition from $-Si(CH_3)(OCH_3)_2$ in dendrimers **1** and **5**, to $-Si(CH_3)[O-Si(CH_3)_3]_2$ in dendrimers **2**, $-Si[O-Si(CH_3)_3]_3$ in dendrimers **3**, and $-Si(CH_3)[O-Si(CH_3)_2CH=CH_2]_2$ in dendrimers **4**. While dendrimers **1** and **5** contained only a single layer of OS branch cells around the PAMAM interior, dendrimers **2**−**4** contained two such layers. In dendrimers **1**−**4**, the PAMAM and OS branch cell layers were connected with $-[CH_2-CH_2-C(O)-O-(CH_2)_3]-$ bridging segments, while in dendrimers **5**, this connection was through $-[CH_2-CH(CH_3)-C(O)-O-(CH_2)_3]-$ units. Of the silicon-containing reagents of Scheme 1, compounds **7**−**9** and **11** were commercially available, while (3-acryloxypropyl)bis(vinyldimethylsiloxy)methylsilane (**10**) was prepared as shown in Scheme 2. Of the PAMAM dendrimers available, generations 1−4 EDA-core tetradendron derivatives, having nominal molecular characteristics listed in Table 1, were employed.

The PAMAMOS dendrimer structures **1**−**5** were verified by ^1H, ^{13}C, and ^{29}Si NMR. For example, PAMAMOS dendrimer **3**, prepared from generation 3 PAMAM **6** after 83% of its NH groups reacted with OS acrylate

Table 1. Selected Molecular Characteristics of EDA-Core Tetradendron Polyamidoamine (PAMAM) Dendrimers

generation	no. of end groups[a]	mol wt[a]	hydrodynamic diameter,[b] Å
0	4	517	
1	8	1430	20.2
2	16	3256	28.8
3	32	6909	35.0
4	64	14215	50.0
5	128	28826	65.8

[a] Nominal values calculated for ideal PAMAM dendrimer structure. [b] By dilute solution viscometry in water−citric acid buffer at 25 °C.

9, should contain four layers of 60 (4 + 8 + 16 + 32) PAMAM branch cells, $-[(CH_2)_2-C(O)-N(H)-(CH_2)_2-N]<$, surrounded by two layers of OS branch cells, with the inner one containing 53 (0.83 × 64) $-[(CH_2)_2-C(O)O-(CH_2)_3-Si]<$ units and the outer one containing 160 (0.83 × 192) $-O-Si(CH_3)_3$ groups, respectively. ^{1}H NMR of the product obtained after isolation and purification by dialysis in methanol and taken in $CDCl_3$ confirmed the expected structure by showing a strong $Si-CH_3$ singlet at 0.09 ppm, three triplets at 0.46, 1.65, and 4.00 ppm for three CH_2 groups extending between $-Si[O-Si(CH_3)_3]$ and ester $-C(O)O-$ units, respectively, and a not too well resolved multiplet between 2.3 and 3.6 ppm. This multiplet contained signals from both PAMAM interior and $-(CH_2)_2-$ bridging groups connecting PAMAM and OS dendrimer domains in structure **3**.

^{13}C NMR of the same dendrimer was even more specific. Not only that all relevant carbon atoms could be identified and assigned in this spectrum, but it was also possible to distinguish between fully and partially reacted amino groups. Thus, while tertiary amines resulting from PAMAM dendrimer amino end groups in which both NH units reacted with OS reagent gave methylene signals at 37.56, 49.1, 51.56, and 32.48 ppm, the secondary ones obtained from PAMAM amino end groups where only one NH was used up in silylation reaction gave corresponding signals at 39.03, 44.71, 48.66, and 34.4 ppm, respectively. Further spectroscopic confirmation of the expected structure of this dendrimer was obtained from ^{29}Si NMR, which (taken in $CDCl_3$) showed two intense singlets at 7.29 ppm (for $-O-\boldsymbol{Si}(CH_3)_3$) and at −66.36 ppm (for $-CH_2-\boldsymbol{Si}-[O-Si-(CH_3)_3]_3$), with the ratio of their intensities 1.51/0.49 = 3.08, in excellent agreement with expectations for ideal structure **3** (see Scheme 1).

All syntheses of Scheme 1 were performed under nitrogen, at room temperature and with 10−20 mol % excess of the silicon reagent over the nominal number of NH groups expected for the ideal structure of the PAMAM dendrimer used. Concentrations of the reaction mixtures ranged from 0.8 to 1.5 mol NH groups/L, with methanol as the reaction medium in all cases. This choice of solvent was based on several reasons. First, in addition to being a good solvent for hydrophilic PAMAM dendrimers (**6**), methanol was also effective in dissolving hydrophobic PAMAMOS (**1**−**5**) products (see Table 2). This provided homogeneous, one-phase reaction mixtures for all syntheses of Scheme 1, enabling easy handling of preparations, including efficient stirring of reaction mixtures and facile sampling for monitoring purposes. Second, it appears that methanol acts not only as a solvent in these reaction systems but also as a reaction catalyst accounting for the high degrees of conversion routinely obtained. Consequently, all PAMAMOS syntheses shown in Scheme 1 were performed in methanol, with only two exceptions where acrylate **7** was reacted with generation 3 PAMAM dendrimer in *N,N′*-dimethylformamide (DMF). However, while the methanol reactions normally resulted in about 80−90 mol % conversion of PAMAM NH groups, in the two DMF cases only about 50 mol % conversion was attained.

Table 2. Solubility of PAMAMOS Dendrimers as a Function of the Degree of NH Substitution by Trimethylsilylmethylene (TMS) Groups[a]

	dendrimer			
solvent	PAMAM[b]	TMS 57[c]	TMS 68[c]	TMS 100[c]
water	soluble	soluble	nonsoluble	nonsoluble
methanol	soluble	soluble	soluble	soluble
chloroform, THF	nonsoluble	nonsoluble	soluble	soluble
toluene	nonsoluble	nonsoluble	nonsoluble	soluble

[a] Data for PAMAMOS dendrimers **14** prepared from generation 4 PAMAM precursor. [b] Data for generation 4 PAMAM dendrimer. [c] Numbers denote mole % of NH groups substituted by $-CH_2-Si(CH_3)_3$ (TMS) units.

To gain better control over these reactions, ^{1}H NMR was used to monitor their progress. One method involved following the increase of the ratio of intensities of signals originating from $-O-C\boldsymbol{H}_2-$ methylene units in ester groups of PAMAMOS dendrimer products (E in Figure 2) and of those same groups in yet unreacted silicon-containing acrylate reagents (**7**−**11**) (e in Figure 2). As shown in Figure 2, in the case of synthesis with acrylate **7**, for example, these signals were at 3.89 and 3.96 ppm, respectively. Alternatively, the reaction progress could be followed by the decrease of relative intensities of signals from $-CH{=}CH_2$ or $-(CH_3)C{=}CH_2$ protons of the acrylate or methacrylate reagents as these groups converted into ethylene or propylene bridges during the addition. As also shown in Figure 2, the signals for $=C\boldsymbol{H}-$ and two $C\boldsymbol{H}_2=$ protons were at 5.65, 5.97, and 6.24 ppm, respectively. Therefore, they could be conveniently compared with the signals from methyl or methylene group protons near the silicon atoms since $-(CH_2)_2-$ units forming between the outmost PAMAM nitrogens and ester carbonyls were practically indistinguishable from other methylene units inside the PAMAM structure. Although both methods should give identical results, the former was preferred because of its higher accuracy, probably due to relatively long relaxation times expected for the protons located near the silicon atoms.

Application of ^{1}H NMR monitoring to the synthesis of PAMAMOS dendrimers by Scheme 1 revealed several interesting features of these reaction systems. First, all silicon-containing acrylates **7**−**10** reacted with amine-terminated PAMAM dendrimers much faster than methacrylate **11**. For example, while reagent **7** routinely gave 80−90% conversion within 5−10 h, the same reaction(s) with reagent **11** required more than 14 days for less than 50 mol % conversion. Second, while temperature had little effect on the rate of these reactions, they were considerably dependent on the generation of PAMAM dendrimer used (see Figure 3) and on the degree of solvent dryness. As shown in Figure 3, the order of reactivity of various PAMAM dendrimers with acrylate **7** was $G_1 > G_2 \sim G_3 > G_4$, which was identical to the order of reactivity of the same dendrimers with methyl acrylate, while the presence of

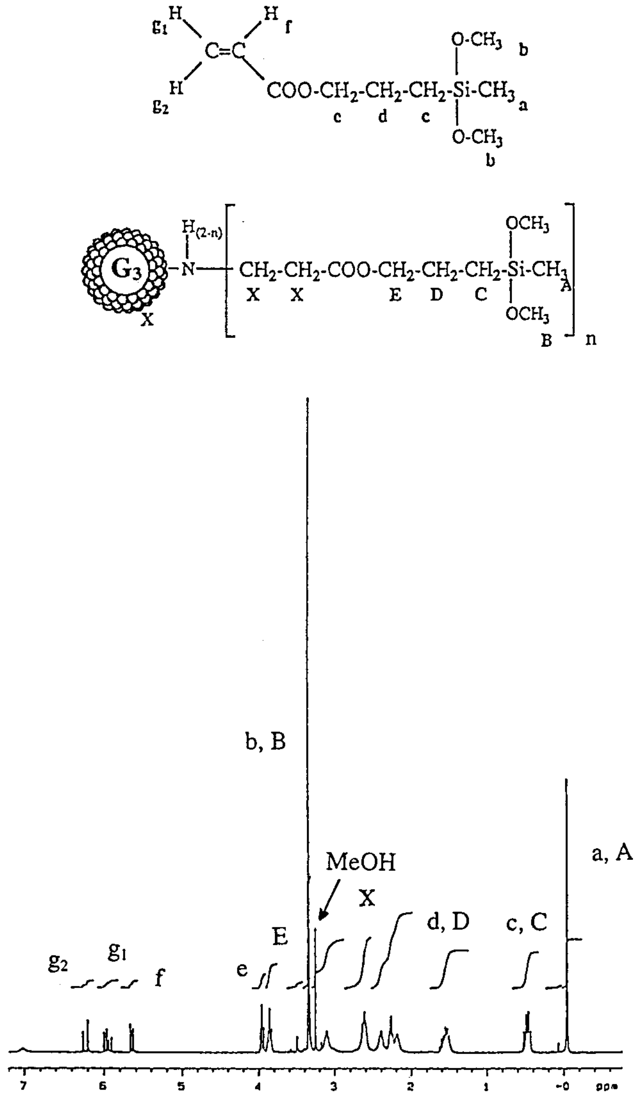


Figure 2. Monitoring of the synthesis of PAMAMOS dendrimer **1** by Michael addition reaction of Scheme 1 by ^{1}H NMR. Note distinctly separated signals from protons e and E and easily distinguished signals from protons f, g_1, and g_2.

small amounts of water led to about 10−15% increase in the degree of NH conversion relative to the same reaction performed in rigorously dried solvent and under otherwise identical conditions.

Synthesis of PAMAMOS Dendrimers by Alkylation of Amine-Terminated PAMAM Dendrimers with Haloalkylsilanes. Another facile route to PAMAMOS dendrimers (such as **14** and **15**) was alkylation of amine-terminated PAMAMs (**6**) with haloalkylsilanes (such as **16**−**19**), as shown in Scheme 3.

In contrast to PAMAMOS **1**−**5** of Scheme 1, dendrimers **14** and **15** had simple methylene connectors between their outmost PAMAM nitrogens and the silicon atoms, but they could also contain either inert ($-CH_3$) or reactive ($-OCH_3$ or $-CH{=}CH_2$) end groups (compare with dendrimers **2**−**3** and **1**, **4**, and **5**, respectively). At first, this synthetic approach was examined using chloromethyltrimethylsilane (**16**) and chloromethyldimethylvinylsilane (**18**) in DMF as solvent, and a series of preparations were performed under different reaction conditions with either 50 mol % deficit or 20 mol % excess of the silane reagent relative to the nominal number of PAMAM dendrimer NH groups. In the latter case, $NaHCO_3$ was added to the reaction mixtures as acid acceptor. Both reaction rate and degree of NH conversion were found to be dependent on temperature, as shown in Figure 4.

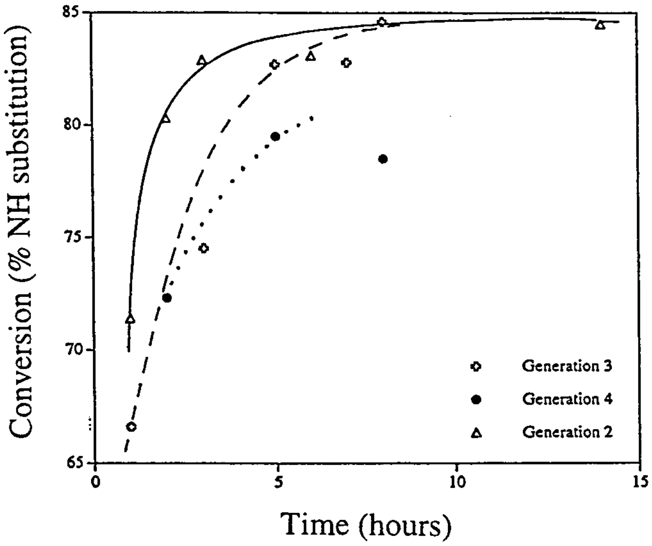


Figure 3. Effect of the generation of PAMAM dendrimer precursor on the rate of formation of PAMAMOS dendrimers **1** by Michael addition reaction of PAMAM dendrimer (**6**) and (3-acryloxypropyl)dimethoxymethylsilane (**7**) in methanol at room temperature.

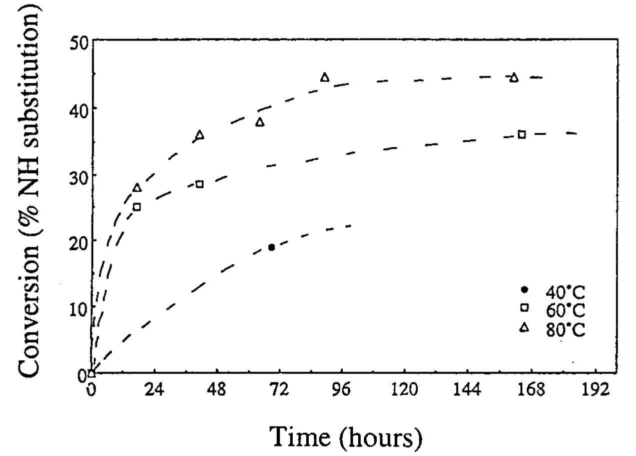
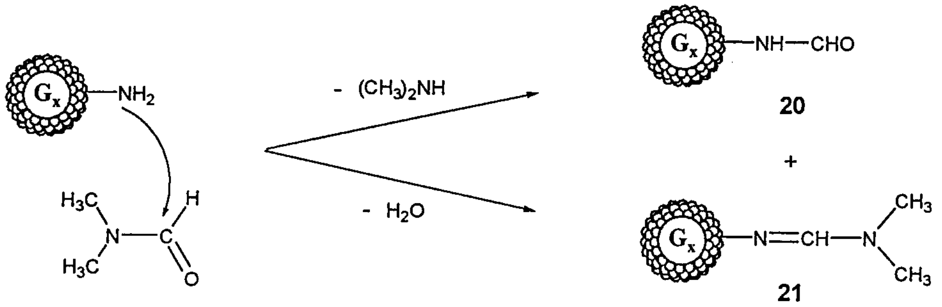


Figure 4. Effect of temperature on the rate of chloroalkylation of generation 3 PAMAM dendrimer (**6**) by chloromethyldimethylvinylsilane (**18**) in DMF.

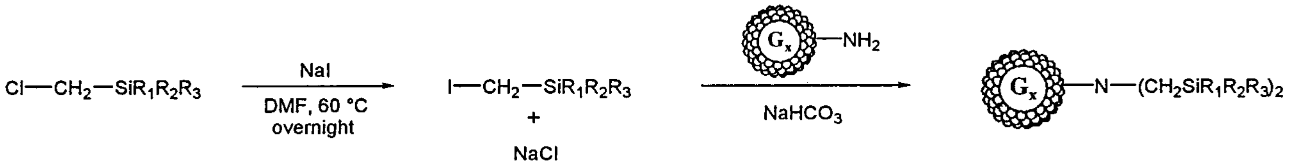
Although chloroalkylation routinely yielded about 90% conversion of PAMAM NH groups in 120−160 h, depending on exact reaction conditions used, repeated attempts to achieve complete silylation failed, indicating that at temperatures around 80 °C DMF may become reactive toward PAMAM amino groups,[10] inducing undesired side reactions, such as those shown in Scheme 4.

Clearly, if such reactions occurred, they would convert reactive dendrimer end groups into nonreactive $-N(H)-C(O)H$, **20**, and/or, $-N{=}C(H)-N(CH_3)_2$, **21**, units, and the overall degree of PAMAM silylation would be smaller than quantitative by a factor corresponding to the relative extent of their occurrence (i.e., to the relative amount of these new end groups formed, which was about 10−15% in most cases). However, this amount should also depend on the relative rates of reaction(s) of Scheme 4 and chloroalkylations of Scheme 3, so that in order to increase the content of OS units

Scheme 4



Scheme 5



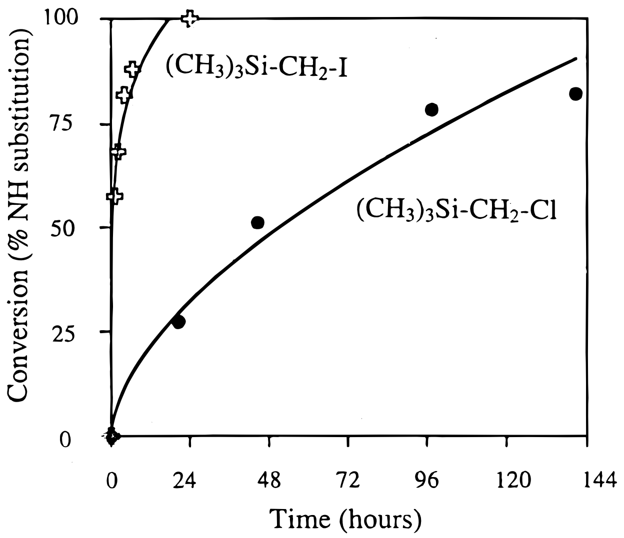


Figure 5. Effect of the type of silylating reagent on the rate of formation of PAMAMOS dendrimer **14** by haloalkylation of generation 4 PAMAM dendrimer (**6**) in DMF at 80 °C.

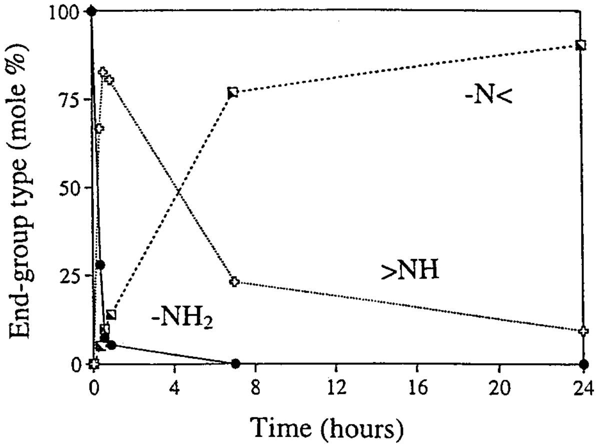


Figure 6. Progress of chloroalkylation of generation 2 PAMAM dendrimer (**6**) with chloromethyltrimethylsilane (**16**) in DMF at 80 °C: disappearance (i.e., consumption) of primary amino groups (−NH_2; black circles); formation and subsequent consumption of secondary amino groups (>NH; crosses); formation of tertiary amino groups (−N<; half-black squares).

in desired PAMAMOS dendrimers **14** and **15**, either the former process had to be suppressed or the latter enhanced. Consequently, two different approaches were examined for this purpose. In the first, chloroalkylsilanes (**16** and **18**) were replaced by their more reactive iodo derivatives (**17** and **19**), prepared in situ as shown in Scheme 5, while in the second, a series of polar aprotic solvents, consisting of *N*-methylpyrolidone (NMP), *N*,*N*′-dimethylacetamide (DMAc), and dimethyl sulfoxide (DMSO), were tried in place of DMF.

As expected, replacement of chloro- by iodomethyltrichlorosilanes resulted in considerably faster and, more importantly, practically complete conversions in reactions of Scheme 3. For example, according to both ^1H and ^{13}C NMR data, using **17** (obtained from **16** and sodium iodide in the presence of 15-C-5 crown ether in DMF; see Scheme 5) in place of **16** in the reaction with generation 4 EDA-core PAMAM dendrimer (containing nominal number of 64 NH_2 end groups per molecule) resulted in 58% NH conversion after only 0.5 h, 68% after 1.5 h, 82% after 6 h, and 100% after 24 h. Eventually, this gave about 20% higher conversion and about 120 h shorter reaction time than when the same generation 4 PAMAM was reacted under comparable conditions with chloromethylsilane **16** (see Figure 5). The reason for this difference was considerably slower chloromethylation of secondary amines in the late stages of the reaction (i.e., at high degrees of NH conversion). Namely, while (as shown in Figure 6) primary PAMAM amines reacted with chloroalkylsilane **16** almost completely in less than 1 h, and a major portion of the secondary ones reacted between the first and the eighth hour of the reaction time, almost 10−15% of the latter remained unreacted even after 24 h.

To evaluate stability of amine-terminated PAMAM dendrimers **6** in selected solvents, samples of generation 1 EDA-core PAMAM were heated in each of these solvents (at concentrations of about 1 mol NH groups/L, in nitrogen, for 24 h, at 80 °C) and examined by ^{13}C NMR and electrospray−ionization mass spectroscopy (ESI-MS) before and after the treatment. As shown in Figure 7, the results obtained clearly confirmed that under these conditions DMF was reactive toward PAMAMs and that NMP was a much better (i.e., inert) solvent.

It was also found that haloalkylation reactions of Scheme 3 could be easily and very effectively monitored by ^1H, ^{13}C, or ^{29}Si NMR. When ^1H NMR was used for

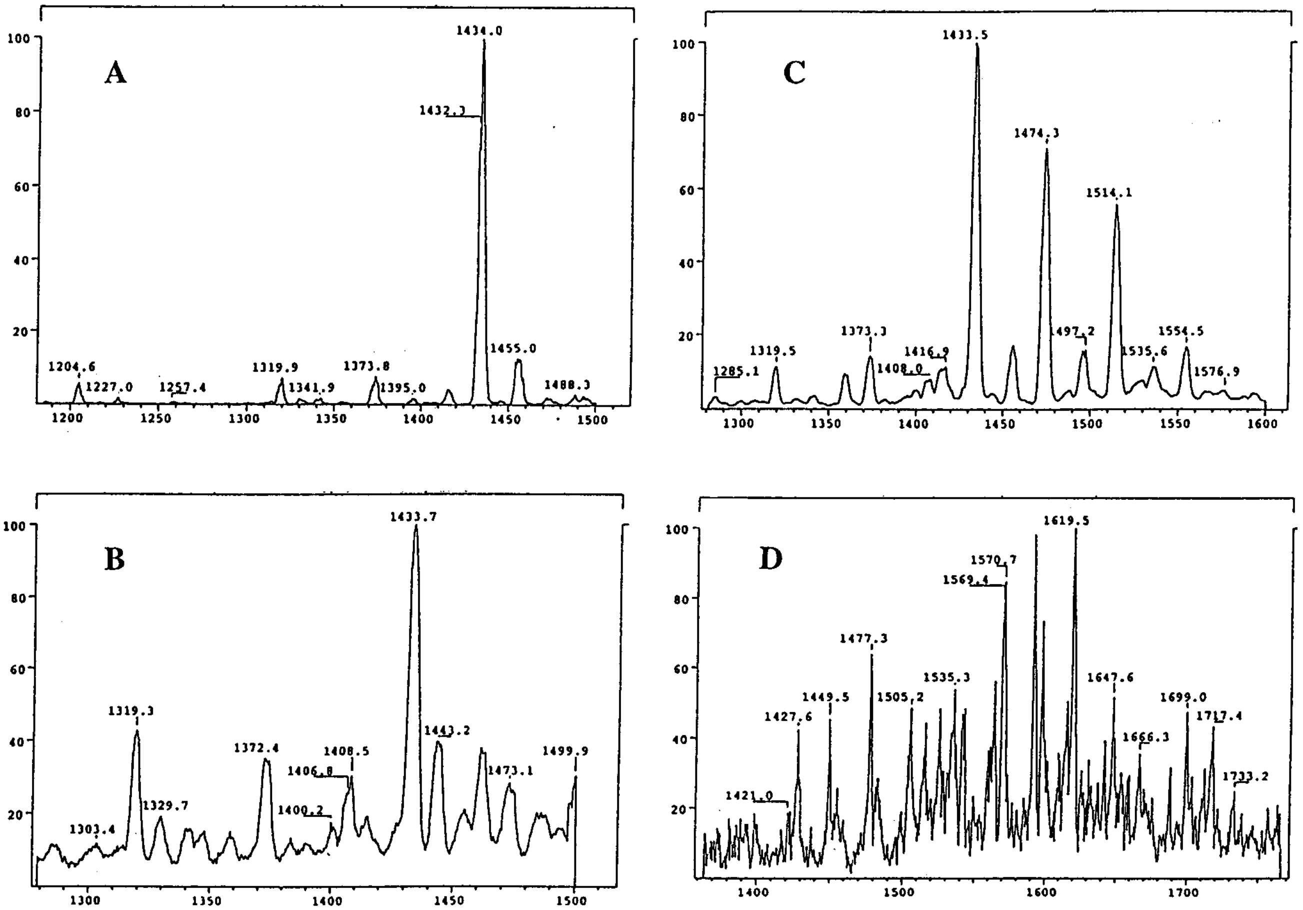


Figure 7. Electrospray–ionization mass spectra of generation 1 PAMAM before (A) and after 24 h exposure to the following solvents at 80 °C: NMP (B), DMSO (C), and DMF (D).

this purpose, the procedure consisted either of following the decrease of intensity of signals from $-NH-C\boldsymbol{H}_2-Si(CH_3)_3$ or $-NH-CH_2-Si(C\boldsymbol{H}_3)_3$ groups (at 2.22 and 0.12 ppm, respectively) with reaction time or monitoring the increase in intensity of signals from fully substituted amino groups $-N[C\boldsymbol{H}_2-Si(CH_3)_3]_2$ and/or $-N[CH_2-Si(C\boldsymbol{H}_3)_3]_2$ at 2.05 and 0.07 ppm, respectively (see Figure 8). As shown in Figure 9, in ^{13}C NMR, partially substituted secondary amino groups were represented by signals H_1, I_1, J_1, and K_1, of which the former three shifted with the progress of reaction from 175.7 to 175, 39.7 to 40.0, and 53.6 to 54, respectively, while K_1 remained stationary at 38 ppm. In the same spectra, fully substituted tertiary amines were represented by signals H_2, I_2, J_2, and K_2 at 174.4–174.2, 38.2, 61.3, and 51.4 ppm, respectively, so that monitoring of the reactions could be performed by following either the disappearance of the secondary amino group signals or the appearance and increase in intensity of those from the tertiary ones.

In ^{29}Si NMR, relevant signals for the monitoring purposes included decreasing $-NH-CH_2-\boldsymbol{Si}(CH_3)_3$ singlet (which shifted with the progress of the reaction from 0.5 to 0.25 ppm) and increasing $-N[CH_2-\boldsymbol{Si}(CH_3)_3]_2$ singlet, which shifted from −1 to −1.3 ppm, as shown in Figure 10.

In all PAMAMOS preparations, product workup procedures involved reaction mixture filtration and dialysis in $MeOH/H_2O$. If acid acceptor was not used in the synthesis, filtration was always preceded by neutralization with Na_2CO_3.

Regardless of the method of synthesis, mass spectra of higher generation PAMAMOS dendrimers (i.e., those obtained from generations 3 and 4 PAMAMs) were difficult to interpret, but conclusive proofs of structures were obtained from their lower generation derivatives. To illustrate this, Figure 11 shows ESI-MS of PAMAMOS dendrimer **14** prepared by chloroalkylation of generation 1 PAMAM (the ideal structure of which is expected to have 16 reactive NH groups) with chloromethyltrimethylsilane (**16**). The ^{13}C NMR spectrum of this product indicated 93% NH substitution, hence an average number of 14.9 trimethylsilyl (TMS) groups per molecule and 2710 average molecular weight. In excellent agreement with this, ESI-MS data of Figure 11 show predominantly 15-arm substituted molecules (i.e., $m/z = 2721$ corresponding to the molecular weight of the expected structure + 1H), but also a substantial amount of completely siliconized structure (i.e., molecules in which all 16 NH groups of the original PAMAM reagent were converted into $-CH_2-Si(CH_3)_3$ units), as identified by the signal at $m/z = 2807$ (i.e., the expected molecular weight + 1H). The third most prominent signal in this spectrum (at $m/z = 2648$) is most likely due to a 14-arm substituted homologue (in accordance with ^{13}C NMR results), although the reason for its deviation from expected position at $m/z = 2634$ is not clear from these data alone.

GPC analysis of PAMAMOS dendrimers was performed at 80 °C, relative to PAMAM dendrimer standards using PLgel columns and NMP containing 0.1%

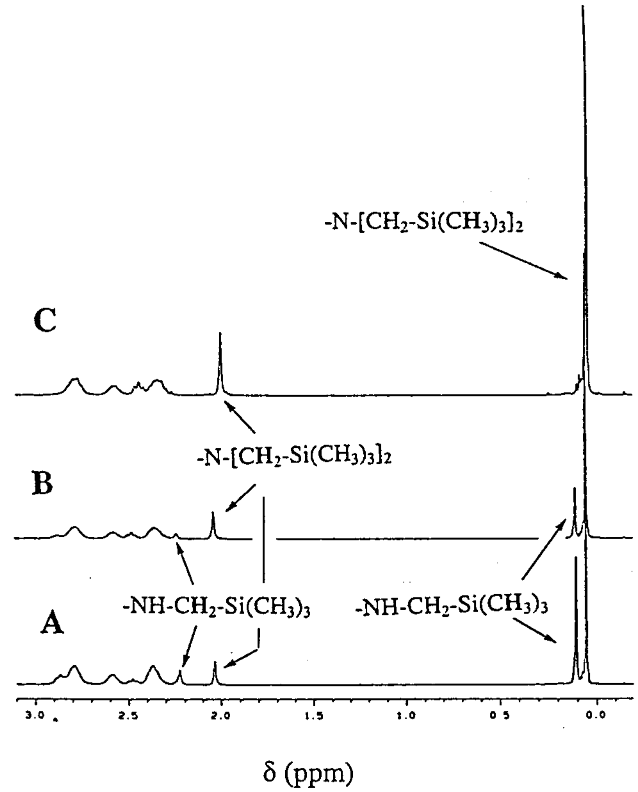


Figure 8. Monitoring of the synthesis of PAMAMOS dendrimer **14** by haloalkylation of generation 3 PAMAM dendrimer (**6**) with chloromethyltrimethylsilane (**16**) in NMP at 80 °C by ^{1}H NMR. CD_3OD was used as NMR solvent and traces shown correspond to 68% (A), 82% (B), and 100% (C) conversion of NH groups.

(w/v) LiBr. All examined dendrimers were readily soluble in this solvent system with no indication of undesired interaction(s) with the columns. It should be particularly noted that in this approach both PAMAMOS samples and PAMAM standards had identical molecular architecture. To illustrate the results obtained, Figure 12 shows typical chromatograms of PAMAMOS dendrimers **14** prepared from generations 4 and 1 PAMAMs and chloromethyltrimethylsilane (**16**) in comparison to those of generations 0−5 PAMAM standards (shown in the inset). It can be seen that not only did all of these dendrimers show similarly shaped signals attributable to narrow molecular size distributions but also the order of their retention times followed the order of expected molecular sizes. Thus, PAMAMOS dendrimer **14** obtained from generation 1 PAMAM (B of Figure 12) showed a peak at 1006 s (comparable with 1028 and 998 s for generations 1 and 2 PAMAMs, respectively), while the peak for its homologue prepared from generation 4 PAMAM (A of Figure 12) appeared at 941 s (comparable with 954 and 938 s for generations 4 and 5 PAMAMs, respectively).

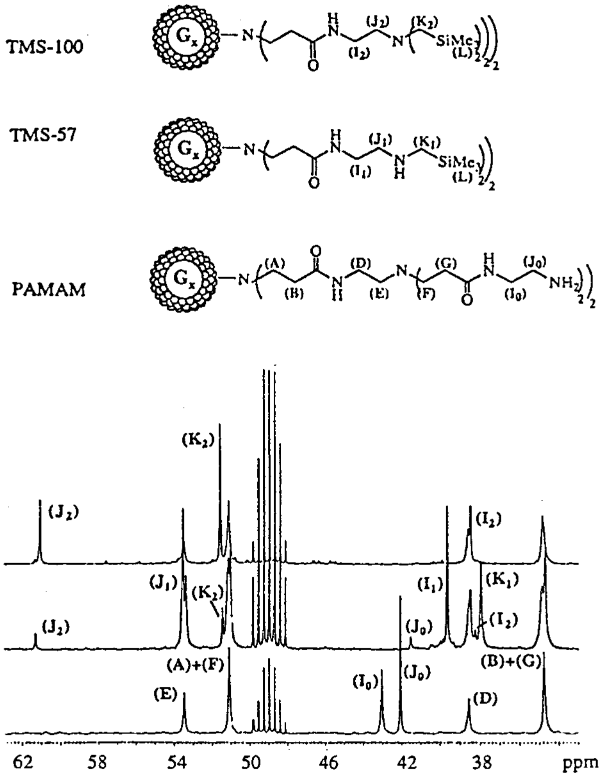


Figure 9. Monitoring of the synthesis of PAMAMOS dendrimer **14** by haloalkylation of generation 3 PAMAM dendrimer (**6**) with chloromethyltrimethylsilane (**16**) in NMP at 80 °C by ^{13}C NMR. CD_3OD was used as NMR solvent and traces shown from the bottom to the top correspond to 0% (i.e., unmodified PAMAM), 57%, and 100% TMS substitution, respectively. Note: disappearance of signals I_0 and J_0 characteristic for unmodified PAMAM; appearance and subsequent disappearance of signals K_1, J_1 and I_1 characteristic for secondary silylated amines; and appearance of signals K_2, J_2, and I_2 characteristic for silylated tertiary amines with the progress of reaction occurrence.

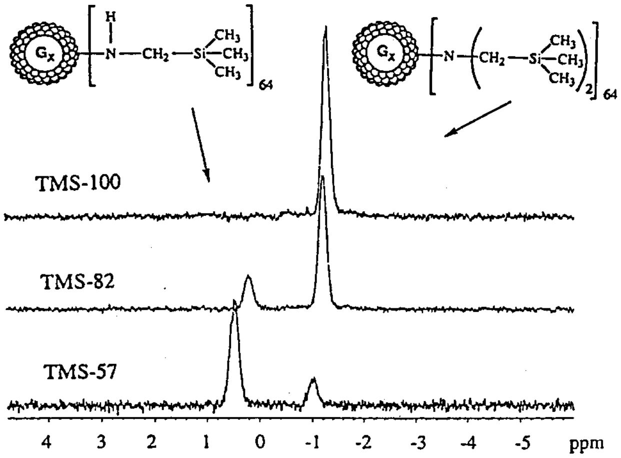


Figure 10. Monitoring of the synthesis of PAMAMOS dendrimer **14** by haloalkylation of generation 3 PAMAM dendrimer (**6**) with chloromethyltrimethylsilane (**16**) in NMP at 80 °C by ^{29}Si NMR. CD_3OD was used as NMR solvent, and traces shown correspond to the indicated degrees of TMS substitution in percent.

Physical Properties of PAMAMOS Dendrimers. Inherent to the concept of compositionally copolymeric dendrimers is the expectation that their properties will reflect not only their unique architecture but also combined specific features of the participating components. Accordingly, PAMAMOS dendrimers exhibit typical dendrimer-like properties such as highly regular structure (see Figure 11), relatively narrow molecular weight distribution(s) (see Figure 12), and lack of crystalline order (hence no melting transition), but also unique composition related solubility, specific glass temperatures, and thermal/thermooxidative degradation behavior.

Solubility. Solubility of PAMAMOS dendrimers was examined in different solvents, and some of the results obtained are illustrated in Table 2 for derivatives of trimethylsilyl (TMS)-terminated PAMAMOS **14** pre-

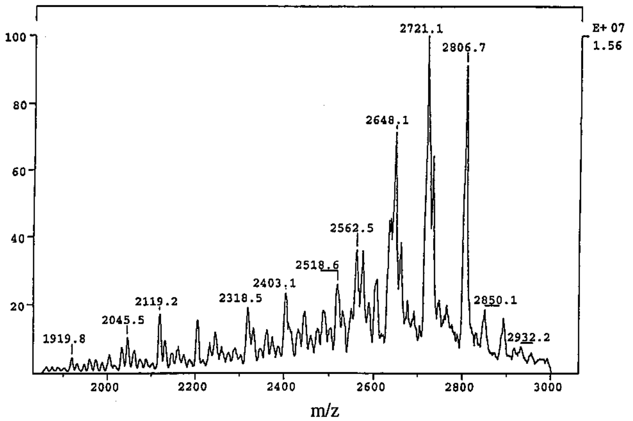


Figure 11. Electrospray–ionization mass spectrum of PAMAMOS dendrimer **14** obtained by haloalkylation of generation 1 PAMAM dendrimer (**6**) with chloromethyltrimethylsilane (**16**). ^{13}C NMR of this product indicated 93% NH substitution.

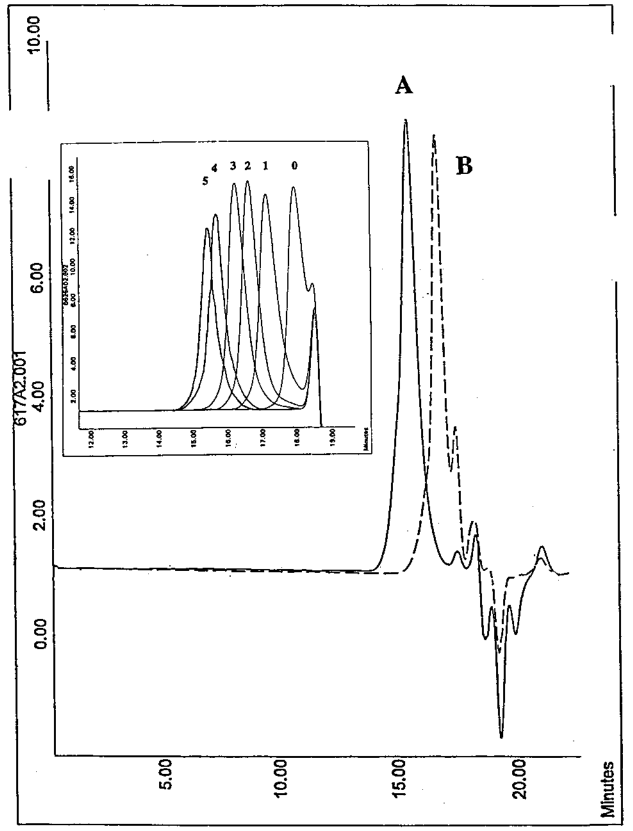


Figure 12. GPC traces of PAMAMOS dendrimers **14** from generation 4 (A) and generation 1 (B) PAMAMs and of the corresponding PAMAM standards (inset) in NMP/0.1% (w/v) LiBr at 80 °C.

pared from generation 4 PAMAM precursor.

It changed continuously with the nature of the dendrimer end groups (i.e., with the degree of NH conversion into $-CH_2-Si(CH_3)_3$, TMS, units), resulting in complete turnaround from hydrophilic, unsubstituted PAMAMs (which are generally highly soluble in water and methanol but insoluble in hydrocarbons), to hydrophobic, 100% TMS-substituted PAMAMOS **14** (which was insoluble in water but quite soluble in toluene). The partially modified intermediate obtained at about 50% conversion (i.e., at the stage at which end groups were predominantly secondary amino units, $-N(H)-CH_2-Si(CH_3)_3$) acquired solubility in polar organic solvents (such as chloroform and tetrahydrofuran) in which unmodified PAMAM precursors are insoluble, while the derivative obtained at about 68% conversion of NH groups (i.e., at the stage at which more than two-thirds of end groups were TMS units) lost solubility in water, which is so characteristic for unmodified PAMAMs. Most strikingly, however, intermediates as well as the completely silylated PAMAMOS dendrimers retained solubility in methanol, which was also characteristic for the starting PAMAM precursors. This was unexpected because methanol is a well-known nonsolvent for high molecular weight methylsiloxane polymers of traditional macromolecular architectures and was anticipated to interact in a similar manner with TMS end groups of PAMAMOS dendrimers as well. Clearly, the unique architecture and geometry of dendrimer molecules must cause the difference, which, as revealed by a computer modeling study (see Figure 13), results from the fact that even in completely silylated PAMAMOS **14**, the "coverage" of the PAMAM interior with $-CH_2-Si(CH_3)_3$ end groups is insufficient to block interactions of that interior with the surrounding environment. In fact, it appears from similar modeling considerations that at least three layers of OS branch cells are needed to cover the PAMAM interior to an extent where PAMAMOS insolubility in methanol may be expected.

Glass Temperatures. Glass temperatures of selected PAMAMOS dendrimers and their corresponding PAMAM precursors are listed in Table 3. Because of pronounced tendency of PAMAMs to absorb moisture, all samples were thoroughly dried under reduced pressure and transferred into the DSC pans in a dry nitrogen atmosphere.

Several interesting observations can be made from these data. First, both [3,1] and [4,1] PAMAMOS dendrimers (i.e., those from generations 3 and 4 PAMAMs, respectively, having a single layer of OS branch cells surrounding the PAMAM interiors) had only slightly higher T_g's than the corresponding unmodified PAMAMs. For example, while for PAMAMOS [3,1] this difference was practically negligible (i.e., only about 1–2 °C depending on the end groups; compare TMS- and DMVS-terminated PAMAMOS [3,1] with generation 4 PAMAM), for the [4,1] derivative with TMS end groups it amounted to 8 °C with respect to T_g of the corresponding generation 5 PAMAM. From these data, it seems that T_g's of these dendrimers were more influenced by the composition of their interiors than by the nature of their end groups.[11] Second, T_g's of PAMAMOS dendrimers ceased to change after about 50% of original PAMAM NH end groups converted into the OS units (compare generation 4 PAMAM and PAMAMOS [4,1] TMS at 57 and 100% conversion, respectively). This is also consistent with the observation that in PAMAMOS [*x*,1] series the end groups have only a limited effect on this dendrimer property. Third, similar to what is often found for linear silicon-containing polymers,[12] replacement of one methyl group in TMS end units by a rodlike vinyl group resulted in a slight but clear decrease in T_g, as seen for PAMAMOS [3,1] TMS and PAMAMOS [3,1] DMVS, respectively. However, the most significant effect on PAMAMOS dendrimer T_g was the introduction of the second layer of OS branch cells in the [3,2] derivatives. For example, T_g decreased by as much as 63 °C (i.e., from about 16 °C to about − 47 °C) from PAMAMOS [3,1] TMS to PAMAMOS [3,2] TMSOS. This behavior is not only consistent with the well-known flexibility of the siloxane building blocks, but it also

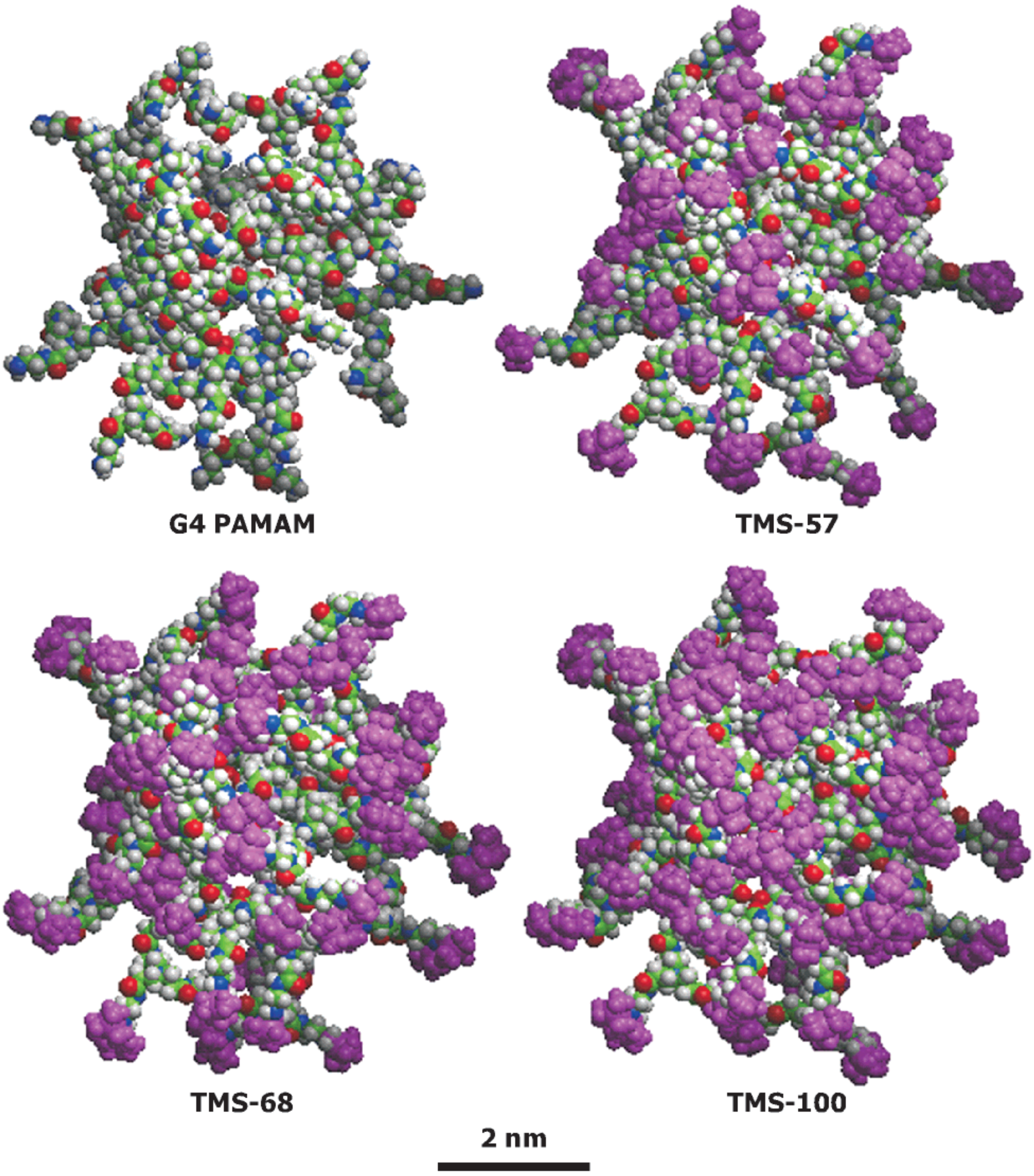


Figure 13. Energy-minimized molecular models of generation 4 PAMAM (top left) and the corresponding PAMAMOS dendrimers **14** with 57, 68, and 100% of TMS end groups, respectively. Whole TMS groups are painted magenta.

clearly demonstrates the importance of the copolymer concept in tailor-making dendrimer properties for desired applications.

Thermal and Thermooxidative Stability. In contrast to solubility and glass temperature behavior, thermal and thermooxidative stability of PAMAMOS dendrimers was not significantly different from that of their PAMAM precursors. For example, when examined by dynamic thermal gravimetric analysis (DTGA) in air (see Figure 14), PAMAMOS [3,1] TMS showed a degradation pattern very similar to those of its generation 3 and 4 PAMAM precursors. All showed a two-step weight loss process in which the first step started at about 190−200 °C, went through a rate maximum at about 280 °C, and ended at about 350 °C with the total weight loss of about 65 wt %, while the second step started at about 350−370 °C, went through a rate maximum between about 550−600 °C, and ended at about 650 °C. However, at the end of their degradation PAMAMs were completely annihilated, whereas both PAMAMOS dendrimers lost in the second step only about 20−25 wt %, leaving a thermally stable residue of about 5−10 wt % of the original sample weight. The residue was pure white silica, but its relative amount was lower than expected from the silicon content of the original sample, indicating that a significant quantity of organosilicon volatiles were formed during this degradation.

Table 3. Glass Temperatures of Selected PAMAMOS Dendrimers[a]

dendrimer[b]	% modification[c]	T_g (°C)[d]
PAMAM, G = 3 (**6**)		11
PAMAM, G = 4 (**6**)		14
PAMAM, G = 5 (**6**)		14
PAMAMOS [3,1] TMS (**14**)	91	16
PAMAMOS [3,1] DMVS (**15**)	100	15
PAMAMOS [4,1] TMS (**14**)	57	21.5
PAMAMOS [4,1] TMS (**14**)	100	22
PAMAMOS [3,2] TMSOS (**3**)	63	−47

[a] By DSC at a heating rate of 10 °C/min. [b] *G* values in PAMAM notation refer to the respective dendrimer generation. Pairs of numbers enclosed in squared brackets in PAMAMOS notation refer to the generation of PAMAM precursor (first number of each pair) and to the number of OS layers surrounding this PAMAM interior. For example, [3,2] denotes a PAMAMOS dendrimer in which 2 layers of OS branch cells surround interior that corresponds to a generation 3 PAMAM dendrimer. Suffixes in PAMAMOS notation refer to the nature of the silicon-containing end groups, as follows: TMS = trimethylsilyl; DMVS = dimethylvinylsilyl; TMSOS = trimethylsiloxysilyl. Bold numerals in parentheses refer to the numeration system used in Schemes 1 and 3. [c] % conversion of PAMAM =NH groups into the corresponding OS branch cells, as determined by NMR. [d] T_g values were determined by DSC, at half-distance between the first deflection from the baseline and its subsequent reestablishment.

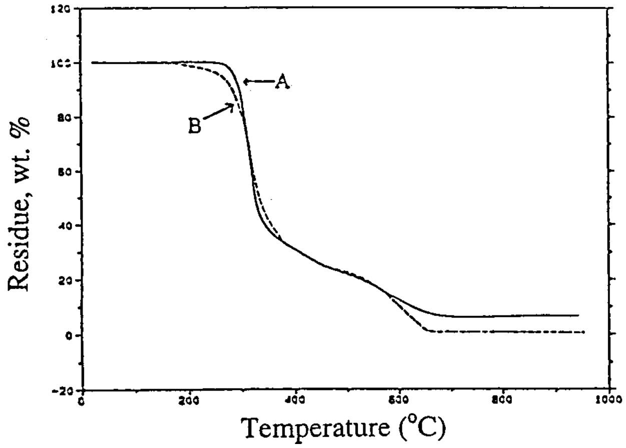


Figure 14. Dynamic thermal gravimetric analysis (DTGA) in air of PAMAMOS [3,1] TMS dendrimer **14** (A) and generation 4 PAMAM dendrimer (B). Both traces were obtained at the same heating rate of 20 °C/min.

In nitrogen, PAMAMOS dendrimers degraded in a single weight-loss step. As with unmodified PAMAMs,[13] they also showed the onset of weight loss at about 150 °C, reached maximum rate of the process at about 300 °C, and ended in complete annihilation at about 500 °C. Clearly, the degradation of these copolymeric dendrimers originated from the same weak link(s) as the degradation of their PAMAM precursors, which have been determined to decompose above about 140 °C most probably by a series of retro-Michael reactions.[14] Thus, it follows from these data that while dendrimer solubility and glass temperature behavior seem to be the properties that are influenced by both their molecular architecture and chemical composition, their thermal and thermooxidative stability are mostly determined by the “weakest” compositional link(s) present in the latter.

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