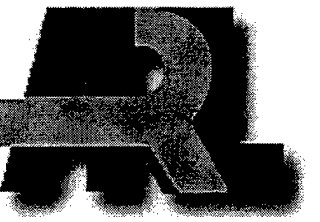
ARMY RESEARCH LABORATORY



The Properties of Dendritie Polymers II: Generation Dependence of the Physical Properties of Poly(amidoamine) Dendrimers

Srinivas Uppuluri
Petar R. Dvornic
Nora C. Beck Tan
Gary Hagnauer

ARL-TR-1774 JANUARY 1999

19990202 066

DTIC QUALITY INSPECTED 4

AUTHENTICATED U.S. GOVERNMENT INFORMATION GPO

Approved for public release; distribution is unlimited.

Starburst® is a registered trademark of Dendritech, Inc.

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

Citation of manufacturer's or trade names does not constitute an official endorsement or approval of the use thereof.

Destroy this report when it is no longer needed. Do not return it to the originator.

Army Research Laboratory
Aberdeen Proving Ground, MD 2 10055066

ARL-TR- 1774 January 1999

The Properties of Dendritic Polymers II: Generation Dependence of the Physical Properties of Poly(amidoamine) Dendrimers

Srinivas Uppuluri
Petar R. Dvornic
Michigan Molecular Institute

Nora C. Beck Tan
Gary Hagnauer
Weapons & Materials Research Directorate, ARL

Approved for public release; distribution is unlimited.

Abstract

Dendritic polymers, or dendrimers, represent a new class of macromolecules characterized by an ultra-branched molecular architecture generated by a novel synthetic route developed in the mid-1980s. As the synthetic science of these molecules matures, the search for applications of them is becoming increasingly active. However, a lack of physical property data has made the identification of suitable application and technology areas that are ripe for exploitation of dendrimers difficult. The purpose of this series of reports is to compile, in the most concise form possible, some fundamental physical property information about dendrimers. The focus is on the behavior of poly(amidoamine) or PAMAM dendrimers, which were developed in the United States and are produced domestically by Dendritech, Inc., of Midland, Michigan. In this report, the second in our series, the effect of molecular size or "generation" of the dendritic polymers on their physical properties is highlighted. The first report, ARL-TR-1606 was published in May 1998 and was focused on the general physical behavior of a mid-sized (Generation 5) PAMAM dendrimer. The third report, slated for completion in early 1999, will focus on "end group" chemistry dependence of PAMAM dendrimers.

TABLEOFCONTENTS

INTENTIONALLY LEFT BLANK

LIST OF FIGURES

INTENTIONALLY LEFT BLANK

LIST OF TABLES

INTENTIONALLY LEFT BLANK

THE PROPERTIES OF DENDRITIC POLYMERS II: GENERATION DEPENDENCE OF THE PHYSICAL PROPERTIES OF POLY(AMIDOAMINE) DENDRIMERS .

1. INTRODUCTION

Beginning in 1996, the U.S. Army Research Laboratory partnered with the Michigan Molecular Institute in a new venture aimed at scientifically exploring dendritic polymers. Dendritic polymers, or "dendrimers," are an emerging technology in polymer science growing from a breakthrough in chemistry that allowed for the synthesis of polymers having an ultra-branched macromolecular architecture. This novel architecture lends unusual properties to dendritic polymers, such as low viscosity and high reactivity, and makes them attractive candidates for use in a variety of technologies. Specific application areas in which dendrimers have been identified as having potential for exploitation include coatings, fiber-matrix coupling agents, adhesives, compatibilizers for polymer blends, toughening agents for brittle polymers, sensors, environmental remediation, catalysis, molecular organic devices, fire suppression agents, antibacterial delivery agents, and medical diagnostic tools.

Although the synthesis of dendritic polymers is taking place throughout the world at universities and other research institutions, the commercialization of this technology is in its infancy. As a result, dendritic polymers are available only in research quantities and from only three commercial sources world wide, one of which is domestic. Because of the limited availability of these materials, very little is known about their general physical properties. As a first step toward the successful integration of dendritic polymers into useful materials systems, we endeavored to compile some fundamental physical property information about these materials and the unique behavior that they display as a result of their unusual molecular structure.

In this report, the second in our series, we focus on the size or "generation" dependence of the physical properties of dendrimers having a poly(amidoamine) chemistry. These materials were developed in the United States and are currently produced domestically by Dendritech, Inc., of Midland, Michigan, under the trade name "Starburst®". A general introduction to the synthesis of poly(amidoamine) dendrimers and the associated nomenclature has been included, followed by a compilation of the properties related to their synthesis (purity, chemical structure, molecular weight), and finally, some physical properties of the materials in solution and bulk forms. The information contained herein has been compiled in a format that stresses brevity, and the document is intended for use primarily as a guide to general properties. References have been included when available. A previous report in this series focused on a thorough investigation of the properties of

a mid-sized, Generation 5 poly(amidoamine) dendrimer. A third study, scheduled for release in mid- 1999, will highlight the dependence of dendrimer properties on "end group" chemistry.

2. SYNTHESIS, NOMINAL PROPERTIES, AND NOMENCLATURE

2.1. Synthetic Procedures

The preparation of poly(amidoamine) (PAMAM) dendrimers involves typical divergent synthesis via a two-step growth sequence that consists of the Michael addition reaction of amino groups to the double bond of methyl acrylate (MA) followed by amidation of the resulting carbomethoxy, $COCH_3$, intermediate with ethylenediamine (EDA) [1]. When EDA is used as the initiator core reagent, the synthesis may be represented as shown in Figure 1.

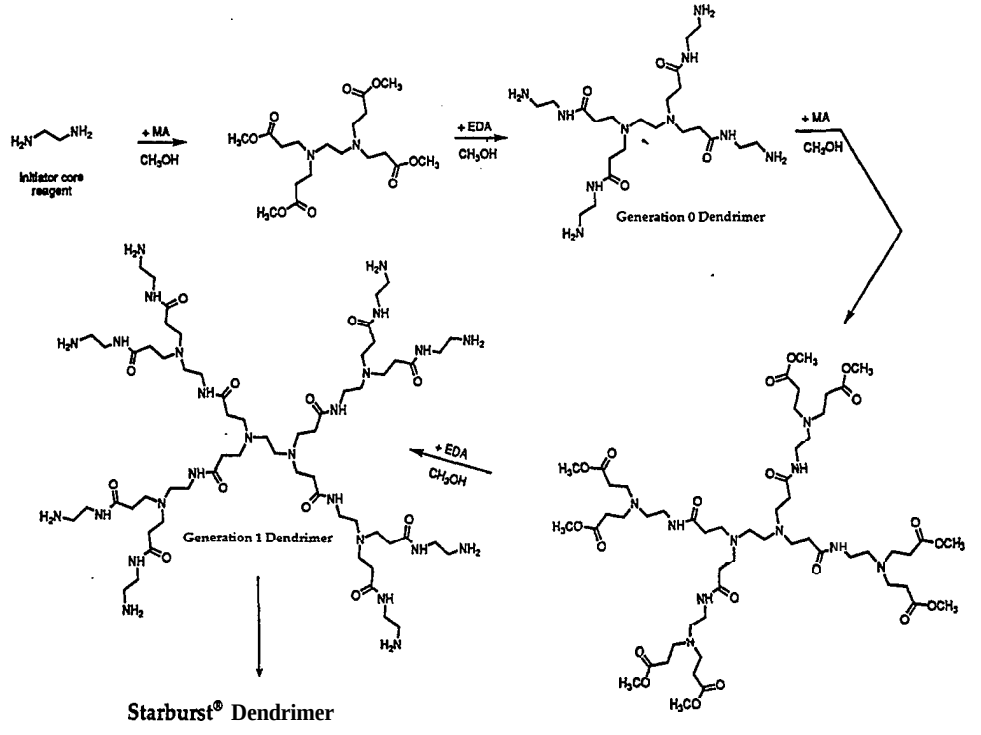


Figure 1. Synthesis of PAMAM Dendrimers.

In the first step, EDA is allowed to react under an inert nitrogen atmosphere with a 20-mole percent excess of MA at 25° C for about 48 hours. The resulting tetra ester is referred to as generation -0.5 PAMAM. The next step involves reacting this tetra ester with excess EDA to produce generation 0 PAMAM tetramine. This amidation reaction is also performed under inert nitrogen in methanol and requires about 48 hours at 0" C for completion.

The preparation of tetramine completes the first full reaction sequence employed in the divergent synthesis of PAMAM dendrimers, producing a "generation 0" dendrimer. Further reiteration of this reaction sequence results in the formation of a series of higher generation species. Half and full reaction sequences produce half and full generation intermediates (i.e., ester- and amine-terminated PAMAMs, respectively). The yields are essentially quantitative through generation 10.

2.2 Nominal Pronerties

Selected idealized molecular characteristics of generations 0 through 10, EDA core PAMAM dendrimers are listed in Table 1 and are illustrated in Figure 2. The nominal number of end groups per molecule (NEG) and molecular weights per generation (G) were calculated using the following Equations (1 and 2), respectively.

$$N_{EG} = N_c N_b^G \tag{1}$$

$$M = M_c + N_c\left[M_{RU}\left(\frac{N_b^G - 1}{N_b - 1}\right) + M_E\left(\frac{N_b^G}{N_b - 1}\right)\right] \tag{2}$$

In these equations, M is PAMAM molecular weight at generation G, M_c is molecular weight of the core (i.e., 280 for EDA-derivative core), M_{RU} is the molecular weight of the PAMAM repeat unit which is equal to 169, and M_E is molecular weight of the end groups, which is equal to 59 for full generation species.

Table 1. Molecular Characteristics of Amine-terminated EDA Core PAMAM Dendrimers

GENERATION	MOLECULAR FORMULA[a]	NUMBER OF END GROUPS	NOMINAL MOLECULAR WEIGHT[b]
0	$C_{22}H_{48}N_{10}O_4$	4	517
1	$C_{62}H_{128}N_{26}O_{12}$	8	1,430
2	$C_{142}H_{288}N_{58}O_{28}$	16	3,256
3	$C_{302}H_{608}N_{122}O_{60}$	32	6,909
4	$C_{622}H_{1248}N_{250}O_{124}$	64	14,215
5	$C_{1262}H_{2528}N_{506}O_{252}$	128	28,826
6	$C_{2542}H_{5088}N_{1018}O_{508}$	256	58,048
7	$C_{5102}H_{10208}N_{2042}O_{1020}$	512	116,493
8	$C_{10222}H_{20448}N_{4090}O_{2044}$	1024	233,383
9	$C_{20462}H_{40928}N_{8186}O_{4092}$	2048	467,162
10	$C_{40942}H_{81888}N_{16378}O_{8188}$	4096	934,720

[a]Assuming ideal structure.

[b]In order to account for the isotope effect, molecular weights were calculated using atomic weights with two decimal points.

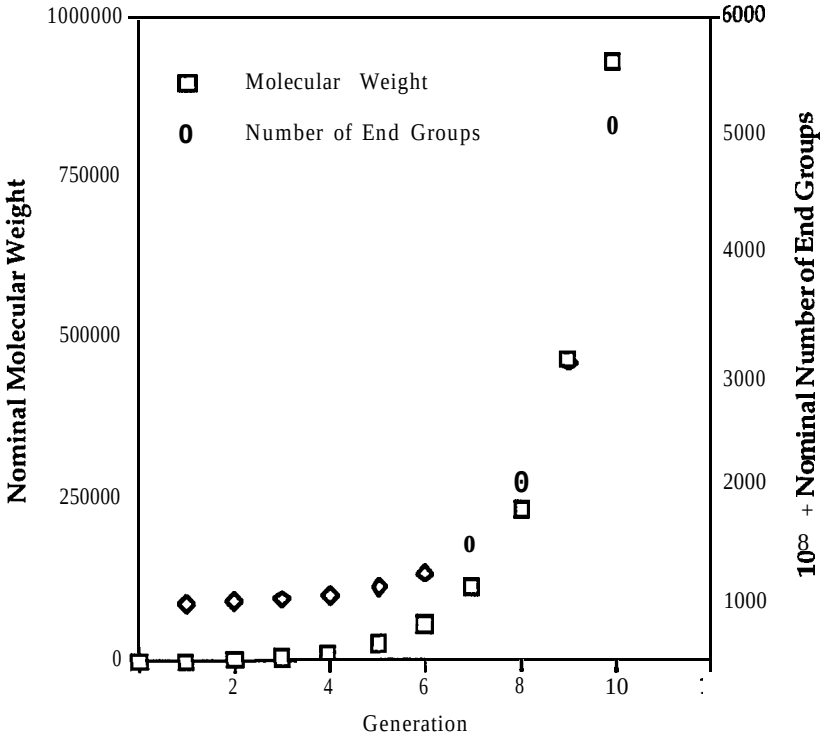


Figure 2. Dependence of Nominal Molecular Weight and Number of End Groups on Generation.

2.3 Nomenclature

A generalized structural formula of Starburst® PAMAM dendrimers may be represented as shown in Figure 3 **[1]**:

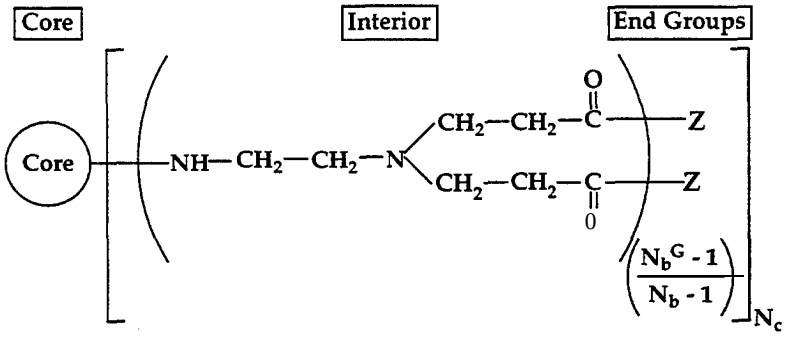


Figure 3. Structural Representation of the PAMAM Dendrimer.

In this structure, if the core is an EDA derivative -$[CH_2N[CH_2CH_2CO]_2]_2$, its functionality, N_c, is 4, the functionality of the branch junctures, N_b, is 2, and G is the number of generations surrounding the core and containing the repeating units $[NHCH_2CH_2N[CH_2CH_2CO]_2]$. Z represents terminal groups, which for PAMAM dendrimers is either -OCH_3 or -$NHCH_2CH_2NH_2$.

3. MOLECULAR PROPERTIES

3.1 Purity [2]

Purity is routinely determined by reverse phase, ion pair high performance liquid chromatography (HPLC), on a Beckman system consisting of a 126 Pump and a 168 Detector and operating with the Nouveau System Gold software. It is defined as the percent area of the main peak in the chromatogram, which corresponds to the amount of pure "monodendrimer" in the sample. Typical data for generations 0 through 6 are shown in Table 2 and Figure 4.

Table 2. Typical PAMAM Purity as Determined by HPLC

GENERATION	WEIGHT PERCENT OF MONODENDRIMER IN THE MAIN FRACTION
1	76
2	91
3	91
4	87
5	91
6	92

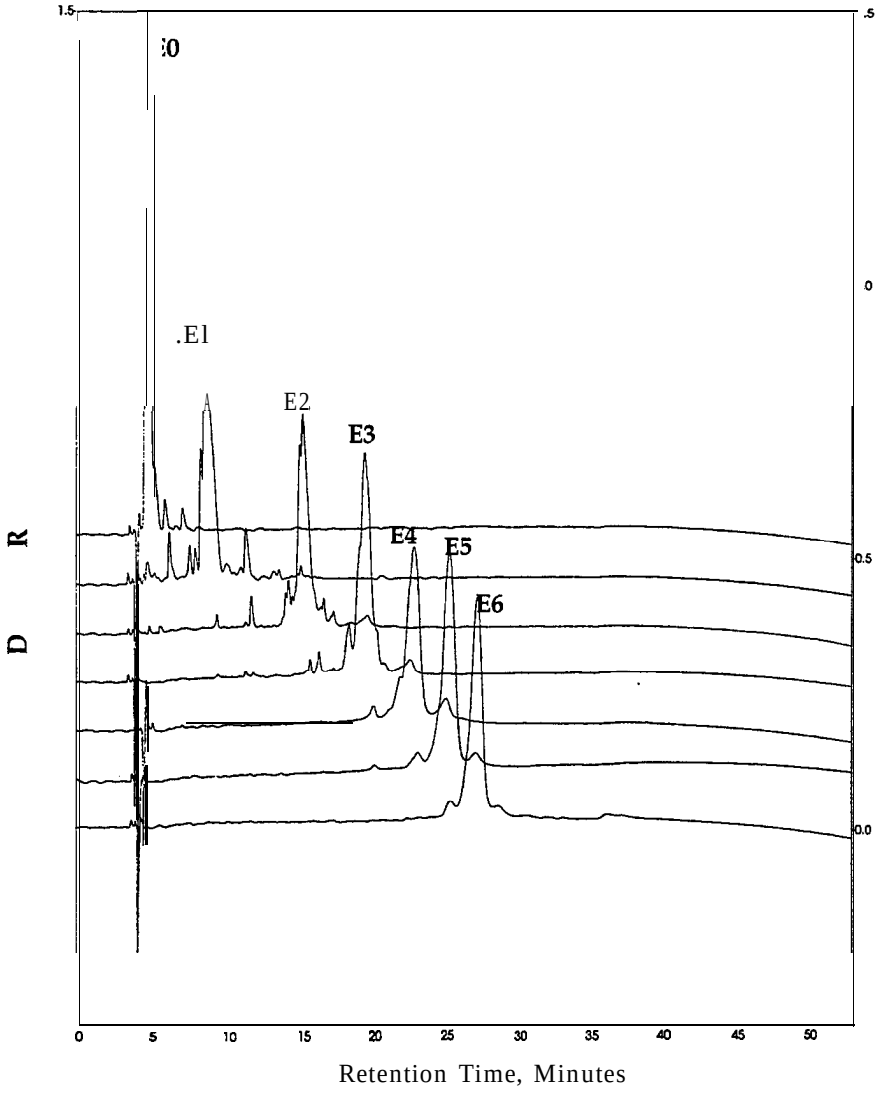


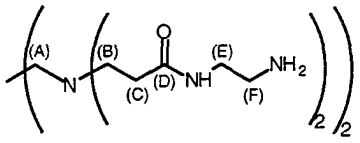
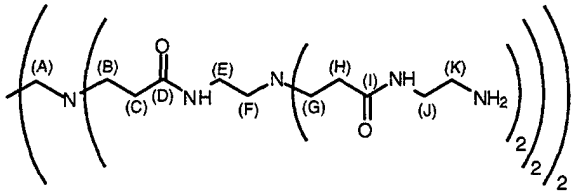
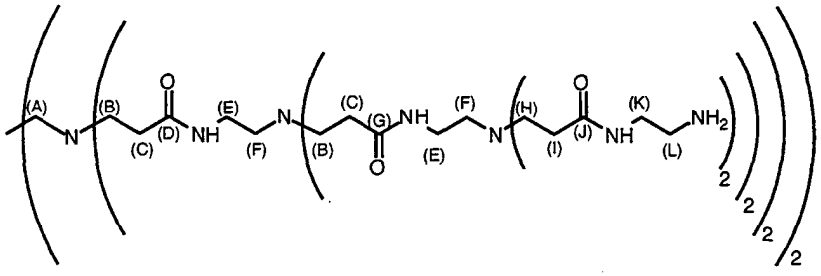
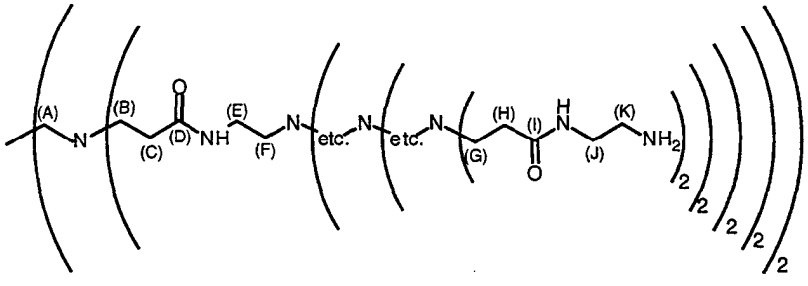
Figure 4. HPLC of PAMAM Dendrimers of Various Generations in Aaueous Solution.

3.2. Compositional Identification

3.2.1 *^{13}C Nuclear Magnetic Resonance (NMR)* [3]

NMR spectra were obtained in D_2O using 1,4 p-dioxane as the reference on a Varian 300-MHz superconducting magnet at 30" C. Characteristic peaks shift with increasing generation numbers until generation 3, after which, no further changes can be observed. Peak assignments for generations 0 through 3 and a representative spectrum for higher generations are given in Table 3 and Figure 5, respectively. It can be seen from the data that peak shifts between generations are small.

Table 3. Peak Assignments for ^{13}C NMR Spectra of PAMAM Dendrimers

Generation	Structure	^{13}C NMR Assignment	(δ, ppm)
0		(A) (B) (C) (D) (E) (F)	49.88 49.03 32.54 174.83 41.58 39.87
1		(A) (B) (C) (D) (E) (F) (G) (H) (I) (J) (K)	50.04 49.17 32.84 174.51 38.84 51.32 49.17 32.89 174.98 41.81 39.89
2		(A) (B) (C) (D) (E) (F) (G) (H) (I) (J) (K) (L)	50.11 49.23 32.81 174.25 38.88 51.40 174.38 49.23 32.94 174.78 41.78 39.99
3		(A) (B) (C) (D) (E) (F) (G) (H) (I) (J) (K)	49.84 48.93 32.54 174.13 174.22 174.31 38.59 51.11 48.93 32.88 174.72 41.54 39.68

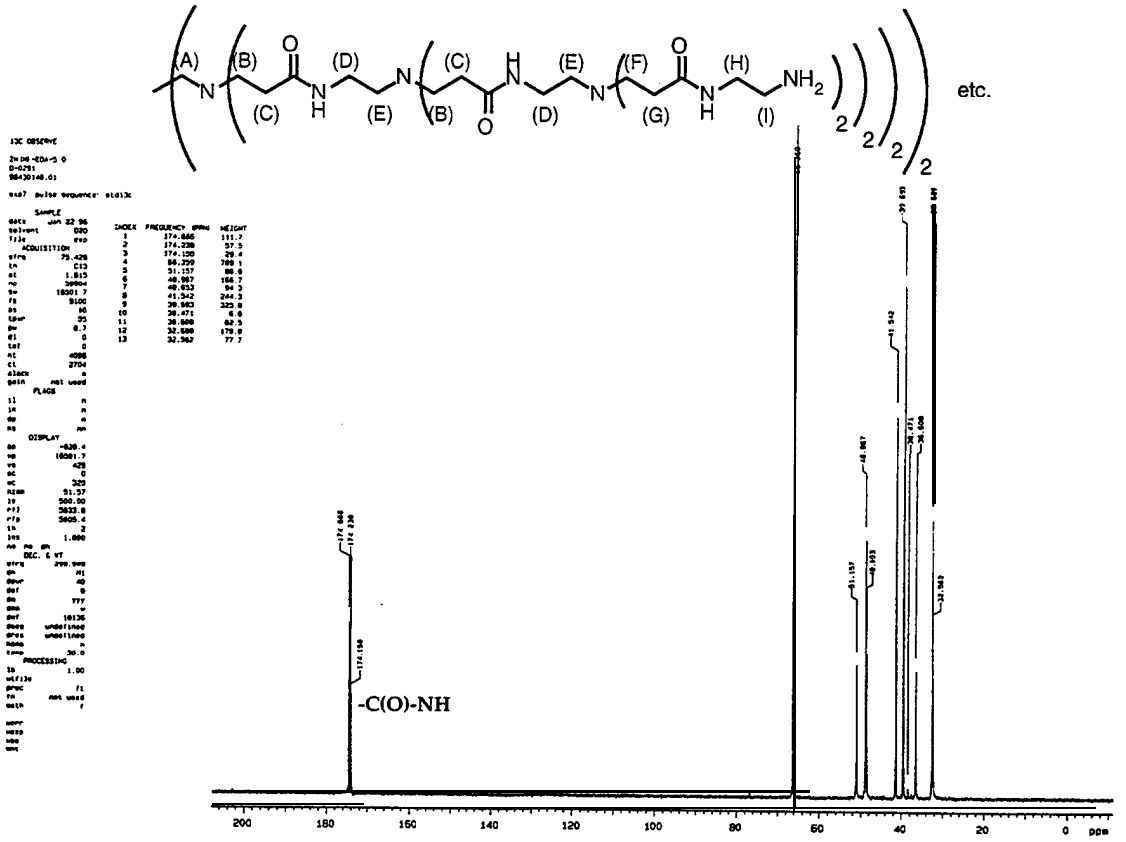


Figure 5a. Full Scale ^{13}C NMR Spectrum of a PAMAM Dendrimer of Generation 4 or Higher.

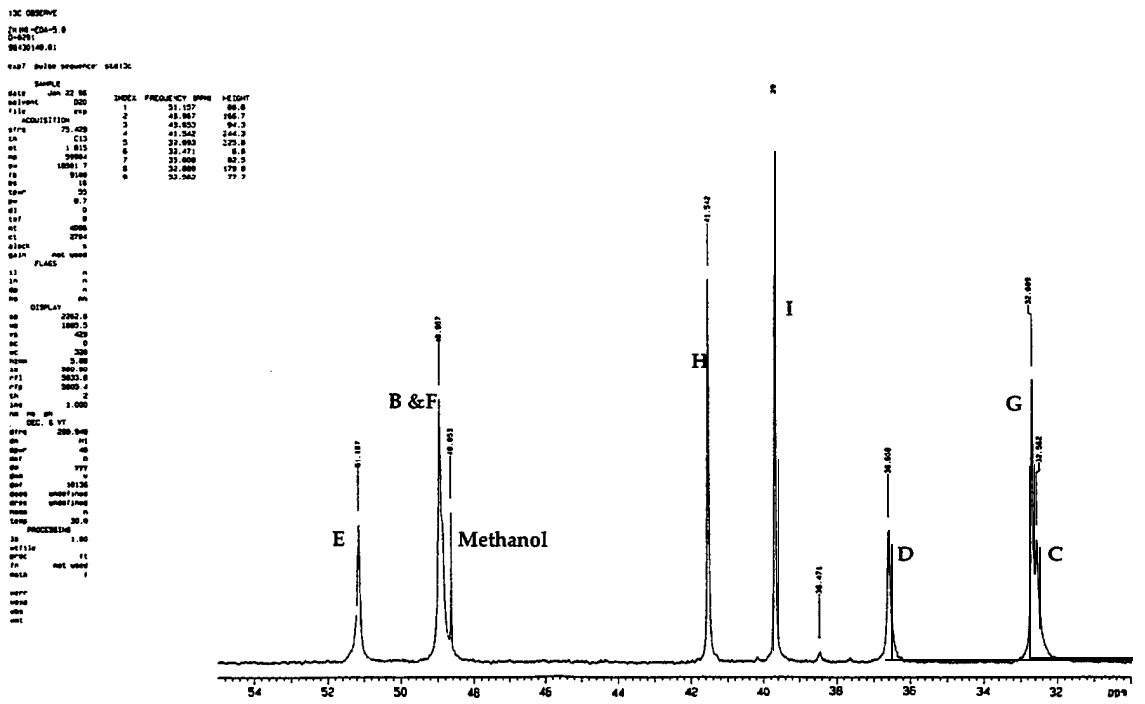


Figure 5b. The 25- to 50-parts-per-million (ppm) Region of the ^{13}C NMR Spectrum of Figure 5a.

3.2.2 Fourier Transform Infrared Spectroscopy (FTIR) **[4]**

Spectra were obtained from dry thin films cast on potassium bromide pellets using a Nicolet 20DXB FTIR spectrometer. All PAMAM generations show practically identical spectra. A typical example is illustrated in Table 4 and Figure 6.

Table 4. Peak Assignments for FTIR Spectra of PAMAM Dendrimers

FREQUENCY	MOIETY
3,250, 3,050 cm^{-1}	-NH-
2,750, 1,450 cm^{-1}	$-CH_2-$
1,650, 1,550 cm^{-1}	-HN-CO-

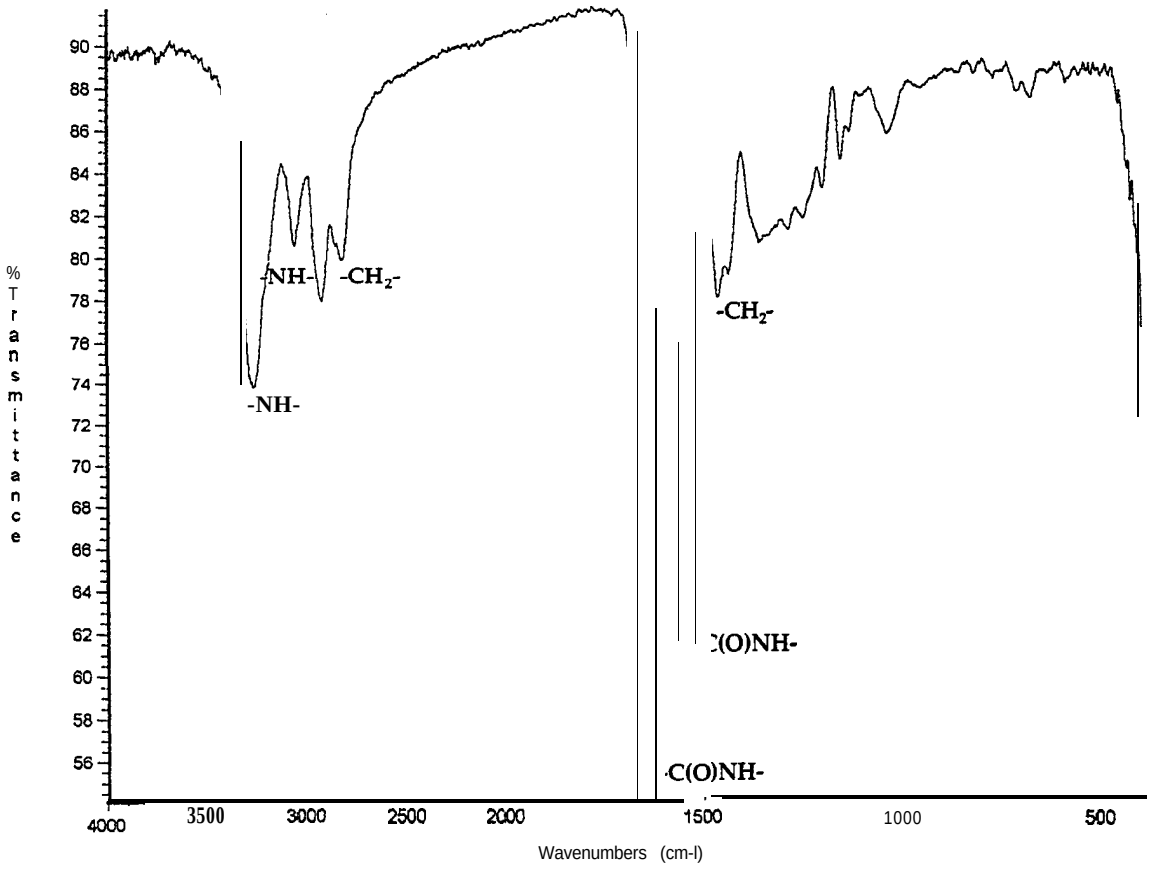


Figure 6. Typical FTIR Spectrum of a PAMAM Dendrimer.

3.3 Molecular Weight and Polydisnersitv

Molecular weights were determined by size exclusion chromatography (SEC) [5] and by mass spectrometry (MS). Mass spectrometry included electrospray ionization (ESI) [6] for lower generations (i.e., until generation 3) and matrix-assisted laser desorption time-of-flight mass spectrometry (MALDI-TOF) [6] for higher generation dendrimers. SEC was conducted using a Waters Model 4 10 differential refractometer during acidic conditions (acetic acid buffer, pH = 2.4) at 30" C. The molecular weight data are interpreted, based on ultra-high purity dendrimer standards, while the polydispersity data are given relative to linear poly(ethylene glycol) (PEG) standards. ESI-MS was performed on a Finnigan MAT TSQ 700 mass spectrometer, while MALDI-TOF was performed on a Vision 2000 Finnigan instrument with samples prepared on dihydroxy benzoic acid matrix. Representative results are shown in Tables 5 and 6 and Figures 7 through 9.

Table 5. Molecular Weights and Polydispersities From the Chromatograms of Figure 7

GENERATION	NOMINAL MW[a]	SEC (M_{peak})	SEC (M_w)	SEC (M_n)	PDI[b]
0	517	539	529	493	1.1
1	1,430	1,336	1,360	1,215	1.1
2	3,256	2,988	3,204		1.2
3	6,909	7,158	7,395	2,692 5,195	1.4
4	14,215	15,900	19,064	12,376	1.5
5	28,826	30,740	35,200	25,607	1.4
6	58,048	58,704	66,940	48,244	1.4
7	116,493	112,530	133,759	90,767	1.5
8	233,383	215,625	269.3 16	159.379	1.7
9.	467.162	421.959	5341370	264.393	2.0
10	934,720	1,037,217	1,350,203	496,615	2.8

[a]MW = molecular weights from Table 1.
[b]PDI = polydispersity index = M_w/M_n

Table 6. Molecular Weights and Polydispersities From ESI and MALDI-TOF MS

GENERATION	NOMINAL MW	MS (M_{peak})	MS (M_w)	MS (M_n)	PDI
0	517	517			
1	1,430	1,430			
2	3,256	3,256			
3	6,909	6,910			
4	14,215	13,379	13,060	12,853	1.02
5	28,826	28.292	29,391	28,722	1.02
6	58,048	54,124	54,523	53,726	1.01

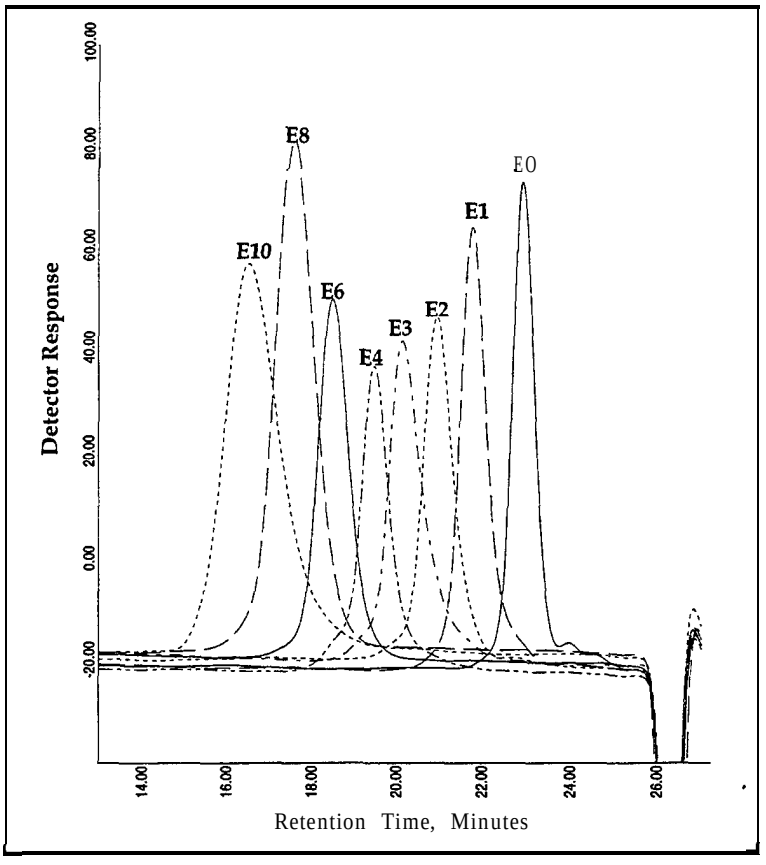


Figure 7. SEC of PAMAMs of Generations 0 Through 10 in Buffered Aqueous Solution.

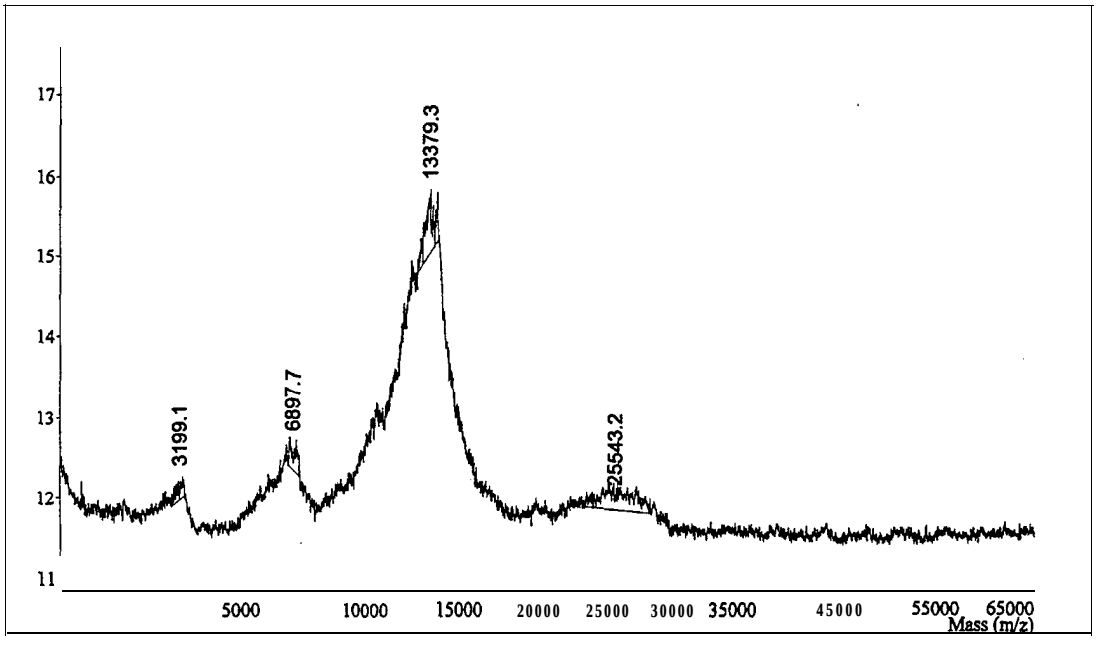


Figure 8. MALDI-TOF Spectrum of Generation 4, EDA Core, PAMAM Dendrimer.

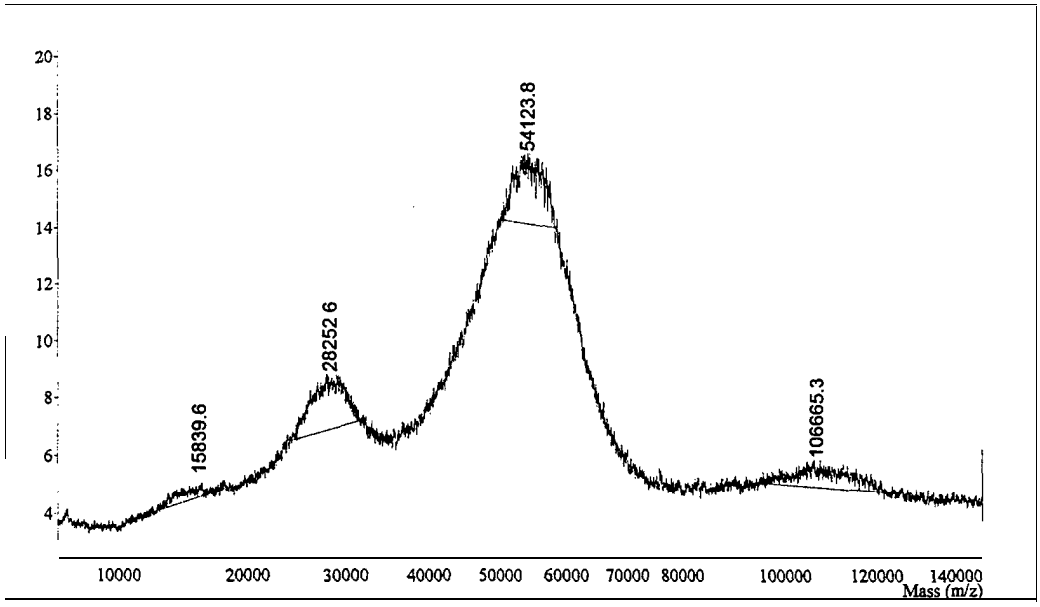


Figure 9. MALDI-TOF Spectrum of Generation 6, EDA Core, PAMAM Dendrimer.

3.4. Molecular Size and Shape

Molecular sizes and shapes of PAMAM dendrimers have been probed using a variety of techniques including SEC **[7]**, dilute solution viscometry (DSV) **[8]**, small angle neutron scattering (SANS) **[9]**, and molecular modeling based on Molecular Dynamics Polygraph software (ratio of moduli of inertia, I_Z/I_X) **[10]** and Monte Carlo on diamond lattice calculations (asphericity parameter) **[11]** . The results are summarized in Table 7 and Figure 10.

Table 7. Molecular Sizes and Shapes of PAMAM Dendrimers of Various Generations[a]

GENERATION	R_h, SEC (Å)[b]	R_h, DSV (Å)[b]	R_g, SANS (Å)[b]	I_Z/I_X	ASPHERICITY
0	7			4.5	
1	11	10		4.1	0.46
2	14	14		2.8	0.39
3	18	18	12	1.6	0.31
4	22	23	16	1.3	0.24
5	27	30	23	1.3	0.21
6	38	37	27	1.3	0.15
7	40		31		
8	48		40		
9	57		49		
10	67		57		

[a]Note: For an ideal sphere, $I_Z/I_X = 1.0$ and asphericity = 0.0

[b]R_h is the hydrodynamic radius of an equivalent sphere, while R_g is the radius of gyration. For an ideal sphere, $R_g = (3\,1/2/5)\,R_h$.

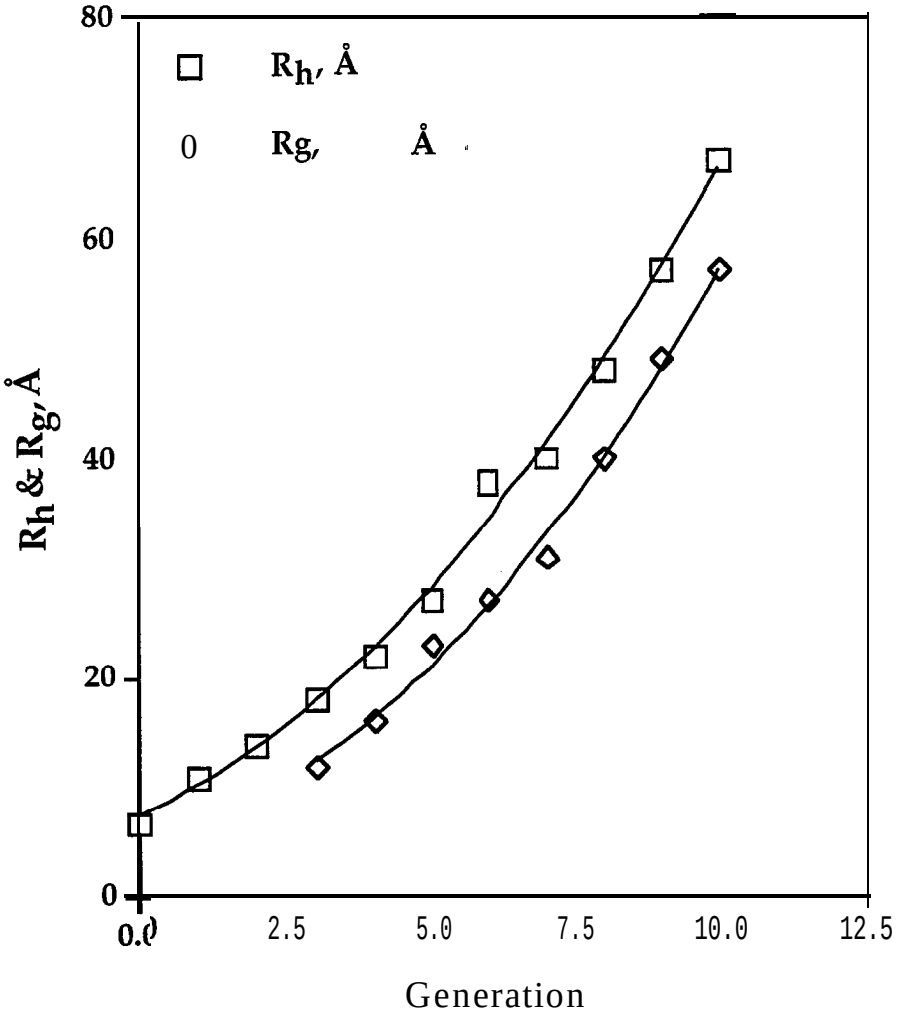


Figure 10. Hydrodynamic Radius as Determined From SEC and the Radius of Gyration Determined From SANS as a Function of Generation.

4. SOLUTION PROPERTIES

4.1 Solubilities [12]

Solubilities of various generations of PAMAM dendrimers were determined according to the standardized American Society for Testing Materials (ASTM) D 3 132-84 procedure. In all cases, concentrations were approximately 1 weight percent (wt %), and tumbling was performed for 24 hours. Solubilities were judged visually. In Table 8, solvents are arranged from top to bottom in increasing order of solubility parameter, the value of which is given for each solvent in the parentheses. Even though studies have not been conducted according to the ASTM procedure, dendrimers of all generations are known to be soluble in water.

Table 8. Solubilities of PAMAM Dendrimers of Various Generations (En=Generation n) in Common Solvents

Solvent	E0		E1		E2		E3		E4		E5		E6		E10	
	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Pentane (7.00)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Methyl cylcohexane (7.80)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Cyclohexane (8.19)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Toluene (8.90)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Tetrahydrofuran (9.10)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Chloroform (9.16)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Pyridine (10.62)	I	I	I	I	I	I	I	I	I	I	B	B	I	I	G	G
2-Pentanol (10.77)	I	S	S	S	S	S	S	S	S	S	B	S	S	S	I	S
Dimethylacetamide (10.80)	S	S	S	S	S	S	S	S	S	S	B	S	S	S	I	I
Butanol (11.40)	S	S	S	S	S	S	S	S	S	S	S	S	S	S	I	S
Acetonitrile (11.90)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
Dimethylformamide (12.10)	S	S	S	S	S	S	S	S	S	S	B	S	B	S	I	I
Ethyl alcohol (12.80)	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
Dimethyl sulfoxide (13 .00)	B	S	B	S	B	S	B	S	B	S	B	S	B	S	B	S
Ethylene glycol (17.10)	B	S	B	S	B	S	B	S	B	S	S	S	B	S	B	S

1 - Solubility 15 minutes after addition of solvent
2 - Solubility after 24 hours of tumbling
B - Borderline G - Gel-like I - Insoluble S – Soluble

4.2 Viscosity

4.2.1 *Intrinsic Viscosity* [7]

Reduced viscosities of dendrimer solutions were measured using an Ubbelohde semi-micro dilution viscometer within a concentration range from 1 to 0.1 g/dL. Intrinsic viscosities were determined by extrapolation to zero concentration. The results are listed in Table 9. The solvent was 5 wt % sodium chloride (NaCl) in water and the temperature was 20" C ±0.01°. The maximum error in these measurements did not exceed 10% of the value of $[\eta]$.

Table 9. Intrinsic Viscosities of PAMAM Dendrimers of Various Generations in 5 wt % NaCl Solution in Water

Generation	Intrinsic Viscosity (dL/g)
1	0.041
2	0.048
3	0.052
4	0.054
5	0.059
6	0.055

4.2.2 Zero-Shear Viscosity [7, 13, 14]

Zero-shear viscosities of dendrimer solutions in EDA were measured using a controlled stress low inertia (CSL) 100 Carri-Med stress-controlled cone-and-plate rheometer. The cone angle was 2° and the radius was 4 cm. All measurements were performed in a nitrogen atmosphere, and a trap was used to minimize evaporation of the solvent. The results for 40 wt % dendrimer solutions are shown in Table 10 and Figures 11 through 13.

Table 10. Zero-shear Viscosities of 40 wt % EDA Solutions of PAMAM Dendrimers of Various Generations

GENERATION	TEMPERATURE, °C	VISCOSITY, POISE
0	15	0.18
0	25	0.13
0	40	0.09
1	15	0.51
1	25	0.36
1	40	0.25
2	15	0.95
2	25	0.70
2	40	0.56
3	15	1.46
3	25	0.97
3	40	0.69
4	15	2.68
4	25	1.79
4	40	1.17
5	15	4.23
5	25	2.87
6	15	5.95
6	25	3.90
6	40	2.82

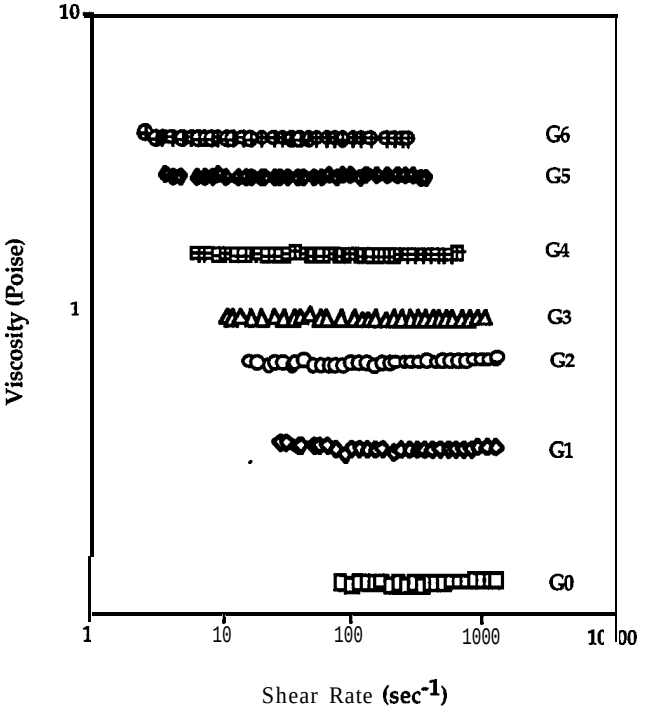


Figure 11. Viscosities of Generations 0 Through 6. PAMAM Dendrimers in EDA Solvent at 25° C and 40 wt % Solution Concentration [14].

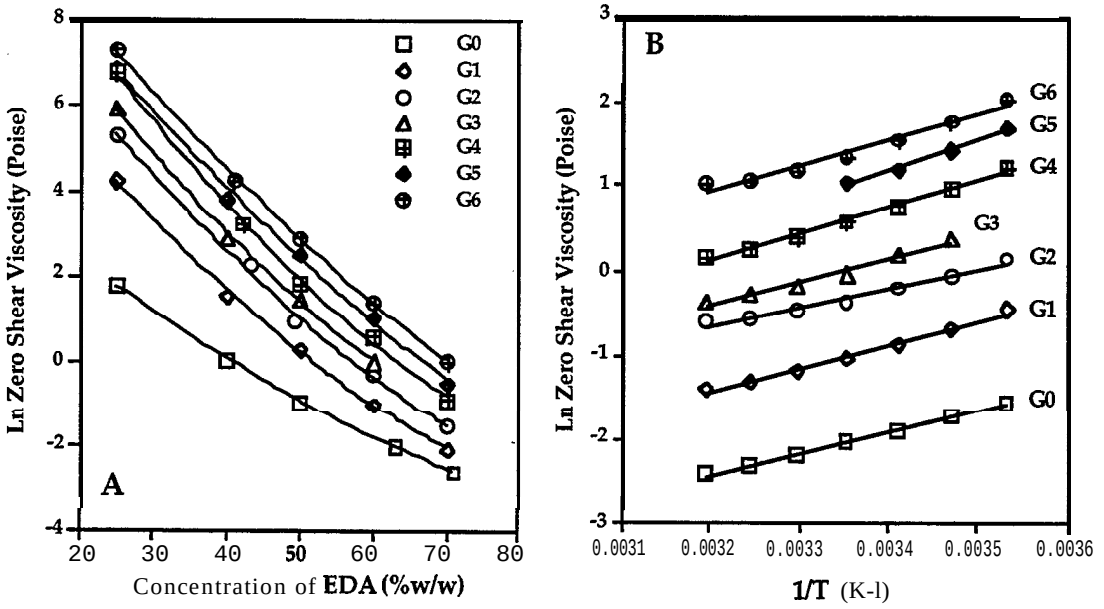


Figure 12. Zero-shear Viscosities of Generations 0 Through 6. PAMAM Dendrimers in EDA Solvent at (a) 25° C and (b) 40 wt % Solution Concentration [14].

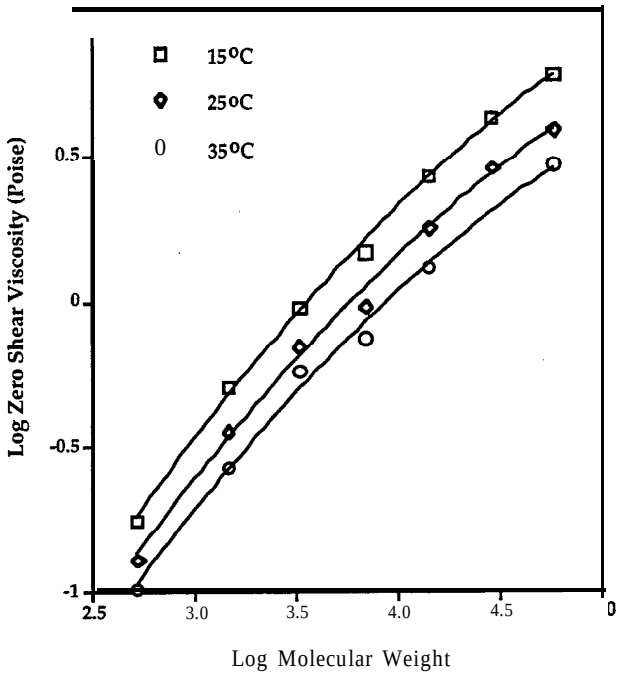


Figure 13. Dependence of Zero-Shear Viscosities on Molecular Weight of Generations 0 Through 6, PAMAM Dendrimers in EDA Solvent at 15", 25" and 35° C [14].

5. BULK PROPERTIES

5.1 Densities [7, 15]

Densities of dry neat EDA core, PAMAM dendrimers were measured pycnometrically in a hydrophobic non-solvent phenetole. A water bath was used for temperature equilibration, and densities were determined from the weights of dendrimers and volumes of the non-solvent and pycnometer at specified temperatures. Temperature measurements were accurate within ±0.1° C. The results are given in Table 11 and are illustrated in Figure 14.

Table 11. Bulk Densities of Generations 0 Through 5 PAMAM Dendrimers

Temp, °C	Density (g/cm^3)					
	Generation					
	0	1	2	3	4	5
10	1.187f0.001	1.204f0.001	1.216±0.001	1.228±0.007	1.238±0.005	1.230f0.010
20	1.178±0.003	1.196±0.001	1.214±0.002	1.219±0.007	1.224f0.002	1.220±0.010
30	1.160f0.002	1.176±0.002	1.195±0.008	1.190±0.006	1.195±0.002	1.203±0.004
40	1.152f0.002	1.169±0.005	1.188f0.001	1.187±0.008	1.188±0.001	1.195f0.009

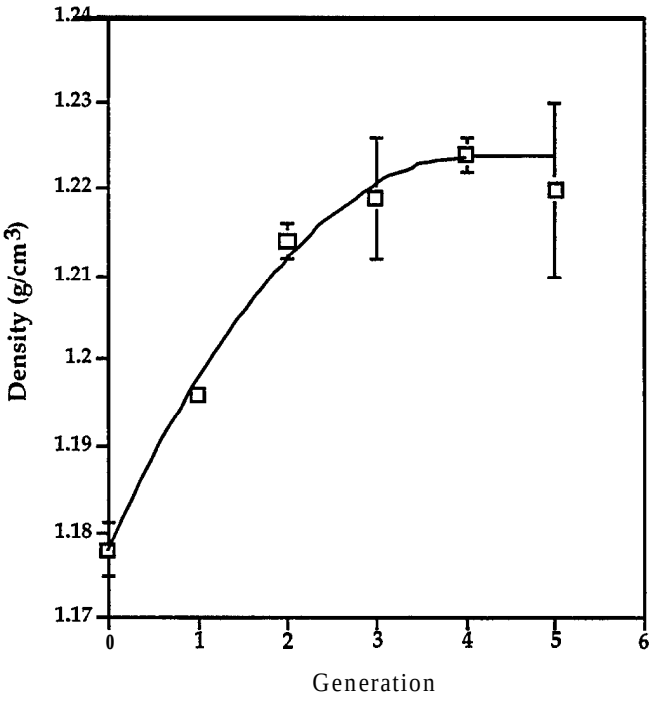


Figure 14. Densities of PAMAM Dendrimers as a Function of Generation at 20° C.

5.2 Glass Transition Temperatures [7]

Glass transition temperatures were determined using a DuPont Instruments 9 10 differential scanning calorimeter (DSC) at a heating rate of 20" C/min. Results are listed in Table 12 and are illustrated in Figure 15.

Table 12. Glass Temperatures of PAMAM Dendrimers of Various Generations

GENERATION	ONSET OF GLASS TEMPERATURE (°C)	GLASS TEMPERATURE (°C)
0	-15	-11
1	-10	-3
2	-8	0
3	6	11
4	6	14
5	6	14
6	9	16
10	18	24

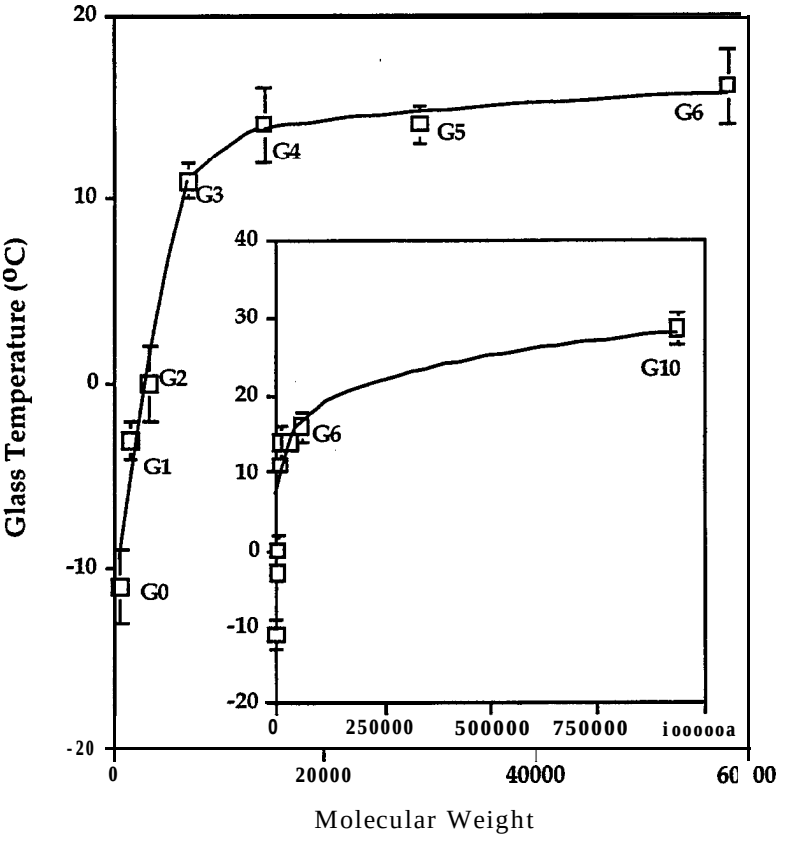


Figure 15. Glass Temnerature of PAMAM Dendrimers as a Function of Generation.

5.3 Thermal Stability [7]

Thermal stability and degradation behavior were evaluated using a DuPont Instruments thermogravimetric analyzer Model 95 1 between generations 3 and 7. Typically, about 10 mg of the sample was loaded onto a platinum pan, and a temperature sweep was performed in both nitrogen and air, between room temperature and 1000" C at a heating rate of 20° C/min. All generations studied showed similar degradation behavior. Dry dendrimers may be effectively used without considerable degradation (< 5%) at temperatures as great as 140° C for 16 hours. The presence of residual solvent may adversely affect thermal stability. Results are given in Table 13 and are illustrated in Figure 16.

Table 13. Thermal Gravimetric Analysis (TGA) of PAMAM Dendrimers

ATMOSPHERE	DEGRADATION	VALUES
Nitrogen	Onset	215° C
	5% weight loss	240° C
	50% weight loss	320° C
	End	465° C
	Maximum loss	96 wt %
	Temperature for maximum rate of degradation	320° C
	Maximum rate of degradation	0.97 wt %/°C
	Weight loss at maximum rate of degradation	32 wt %
Air	Onset	215° C
	5% weight loss	250° C
	50% weight loss	325° C
	End	685° C
	Maximum loss	~100 wt %
	Temperature for maximum rate of degradation	320° C
	Maximum rate of degradation	0.97 wt %/°C
	Weight loss at maximum rate of degradation	32 wt %

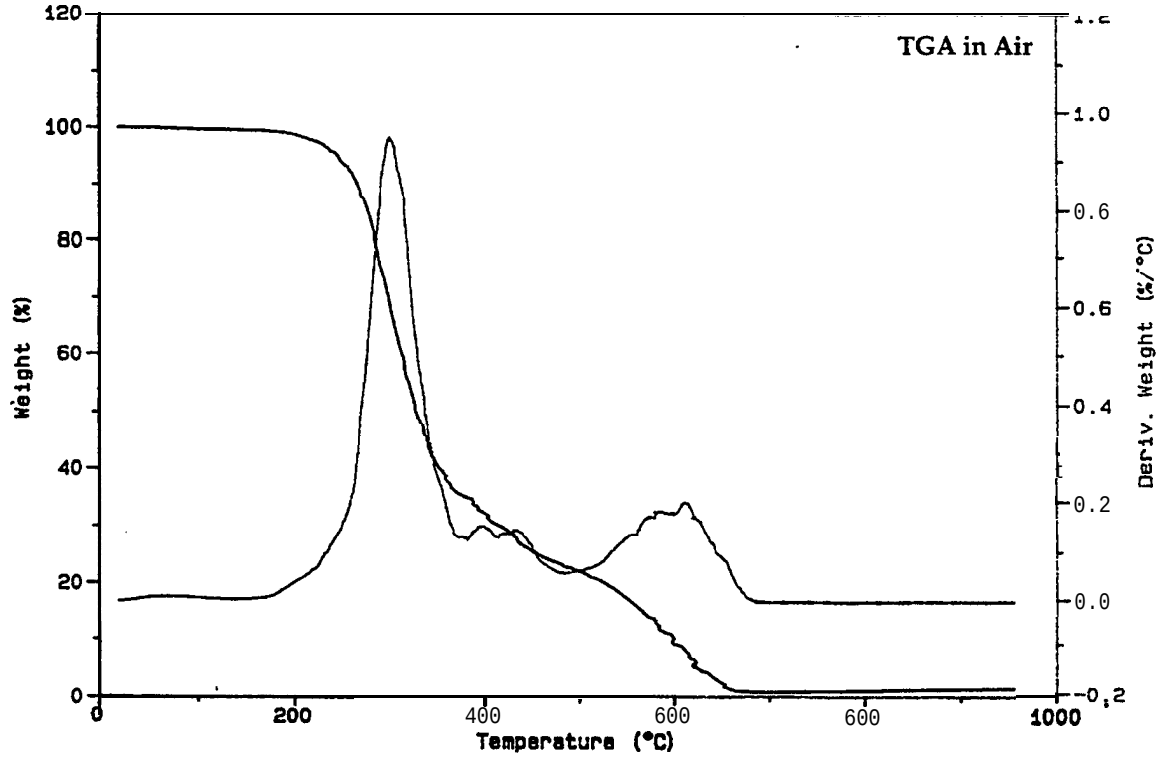


Figure 16a. TGA Thermograms of PAMAM Dendrimers of Various Generations (weight loss as a function of temperature in air).

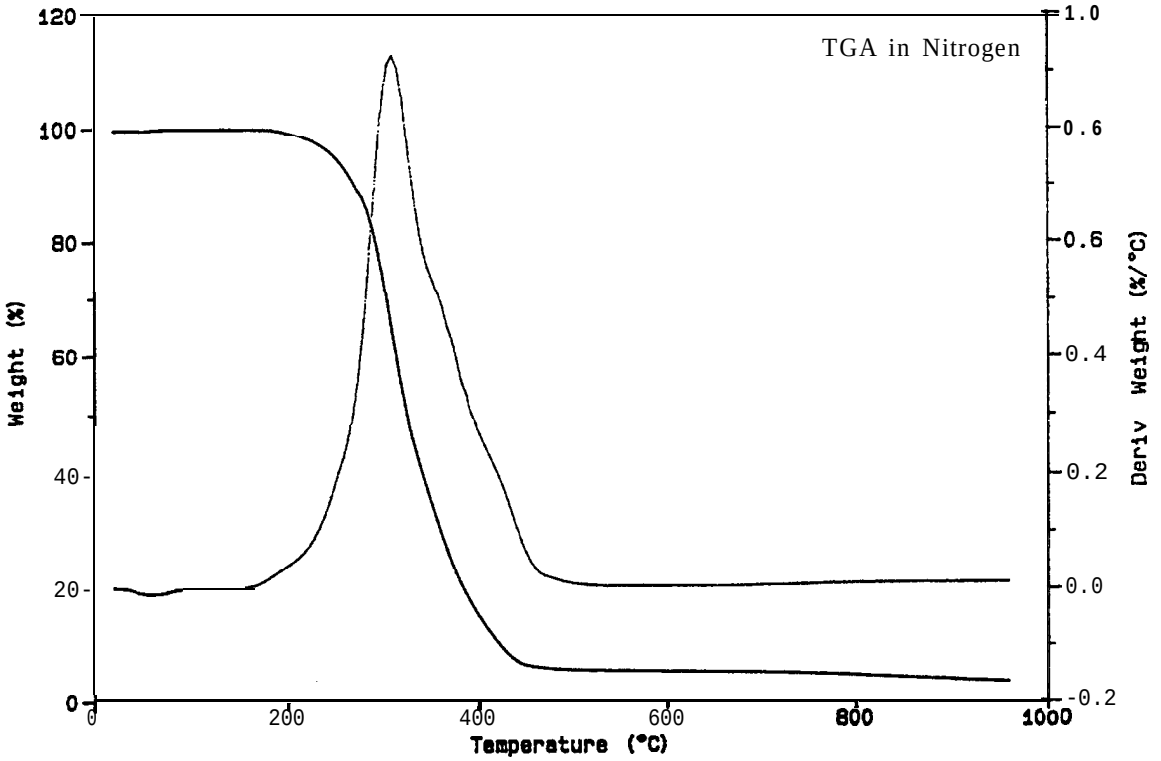


Figure 16b. TGA Thermograms of PAMAM Dendrimers of Various Generations (weight loss as a function of temperature in nitrogen).

5.4 Viscosities [7]

Viscosities of dry neat EDA core, PAMAM dendrimer samples were measured using a CSL^2 500 Carri-Med stress-controlled cone-and-plate rheometer. The cone was varied, depending on generation. For generations 0 through 4, a cone with a 4-cm radius and 2" angle was used, whereas for higher generations, a 2-cm/1° cone was employed. All measurements were performed in a nitrogen atmosphere. Results are given in Table 14 and are illustrated in Figure 17.

Table 14. Viscosities of PAMAM Dendrimers, Generations 0 Through 7, at Various Temperatures

TEMPERATURE, °C	VISCOSITY (POISE)							
	GENERATION							
	0	1	2	3	4	5	6	7
40	567	20,333	349.532					
50	178	4,563	54,304					
60	66	1,317	12,214		194,393			
70	26	452	3,468	12,581	44,110	195,000	355,593	598,340
75	18	285	2,038	6,912	22,875	98,000	197,638	366,670
80	13	181	1,212	3,964	12,663	52,000	114,651	240,970
85	9	118	752	2,382	7,434	30,000	68,175	190,600
90	7	80	483	1,475	4,450	18,000	43,406	145,390
95	5	54	320	943	2,778	11,000	27,675	84,794

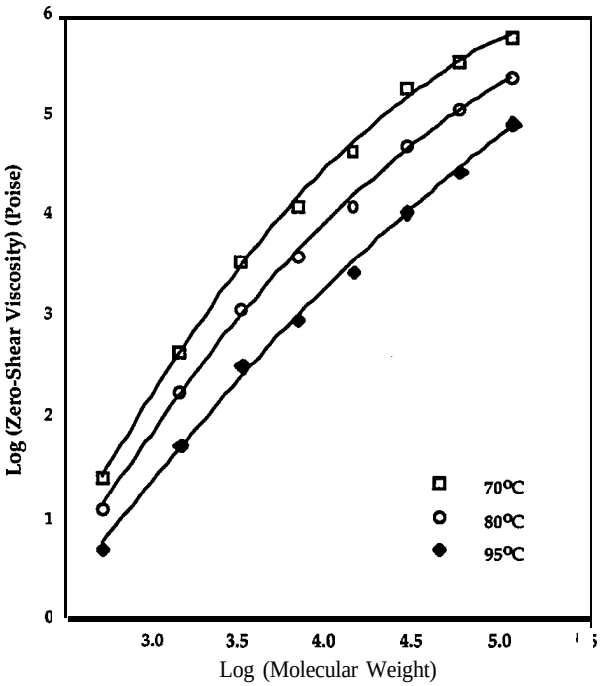


Figure 17. Viscosity as a Function of Molecular Weight of Generation 0 Through 7 PAMAM Dendrimers Between 70° and 95" C.

6. SUMMARY

The properties of poly(amidoamine) or PAMAM dendrimers have been compiled. Their dependence on molecular size or "generation" has been highlighted. The dendritic molecules have molecular weights and surface functionality that increase exponentially with generation. This relationship is a consequence of their highly branched architecture and is one of the most intriguing and potentially useful characteristics of the molecules.

Our characterization efforts have revealed that Starburst® PAMAM dendrimer products above generation 1 have reasonably high purity (~90%). The actual molecular weights of the PAMAM dendrimers are also in good agreement with nominal molecular weights predicted, assuming perfection in the synthetic sequence. However, there is some disparity in the molecular weights and polydispersities determined by different methods (i.e., SEC, MALDI, ESI). This discrepancy is a consequence of the difficulty associated with characterizing these molecules, which are compact compared to conventional materials and have high surface reactivity which is known to interfere with the accuracy of conventional chromatographic characterization methods.

The size of PAMAM dendrimers was found to increase nearly linearly with generation, corresponding to a logarithmic dependence of molecular size on molecular weight. This is a unique feature of dendritic polymers. In comparison, the linear analog of the molecule would display an $n=0.5$ power law dependence of size on molecular weight, having considerably larger size than the dendritic architecture at a given molecular weight.

We have verified that the properties of the polymers that are typically controlled by their chemistry, such as FTIR and NMR absorptions, solubility, and degradation temperatures, are essentially generation independent for the PAMAM dendrimers. Physical properties such as molecular size, glass transition temperature, density and intrinsic viscosity all show generation dependence of a similar nature. These properties show strong dependence on generation at lower molecular weights, until about generation 4, and then become relatively insensitive to generation in the higher molecular weight regime.

INTENTIONALLY LEFT BLANK

7. REFERENCES

1. Dvomic, P.R., and D.A. Tomalia. "Dendritic Polymers, Divergent Synthesis: Starburst Poly(amidoamine) Dendrimers." In J.C. Salamone, ed., The Polymeric Materials Encyclonedia: Synthesis, Properties and Applications. CRC Press, Boca Raton, FL, 1996.

2. Wetmore, A.M., and R. Spindler, unpublished data, 1998.

3. (a) Klimash, J.W. Unpublished results, 1996; (b) Dvomic, P.R., and D.A.Tomalia. "Starburst® Dendrimers: Technical Review," Dendritech Inc., Midland, MI, 1995.

4. Uppuluri, S., P.L. Parham, and J.W. Klimash. Unpublished results, 1997.

5. Mulford, L.C., S.A. Chapman, and R. Spindler, unpublished results, 1998.

6. Hedstrand, D., unpublished results, 1997.

7. Yin, R., unpublished results, 1995.

8. Uppuluri, S. Doctoral Dissertation, "Structure-Property Relationships of Polyamidoamine Dendrimers: Evaluation of the Skeletal Macromolecular Isomerism Principle." Michigan Technological University, 1997.

9. (a) Prosa, T.J., B.J. Bauer, E.J. Amis, D.A. Tomalia, and R. Scherrenberg. Journal of Polymer Science, Part B: Polymer Physics, **35,** 2913, 1997;
(b) Bauer, B.J., A. Topp, T.J. Prosa, E.J. Amis, R. Yin, D. Qin, and D.A. Tomalia. "SANS and SAXS Investigation of the Internal Structure of Dendritic Molecules," Polymer Material Science and Engineering, 77, 87, 1997.

10. Tomalia, D.A., A.M. Naylor, and W.A. Goddard III. "Starburst Dendrimers: Molecular-Level Control of Size, Shape, Surface Chemistry, Topology, and Flexibility from Atoms to Macroscopic Matter," Angewandte Chemie International Edition in English, **29(2),** 138, 1990.

11. Mattice, W. "Masses, Sizes, and Shapes of Macromolecules from Multifunctional Monomers. " Chapter 1 in G.R. Newkome, C.N. Moorefield, and F. Vogtle, eds., Dendritic Molecules, VCH Publishers, Inc., Weinheim, New York, 1996.

12. Uppuluri, S., unpublished results, 1998.

13. Dvomic, P.R., S. Uppuluri, and D.A. Tomalia. "Rheological Properties of Starburst® Polyamidoamine Dendrimers in Concentrated Ethylenediamine Solutions," Polymer Material Science and Engineering, **73,** 131, 1995.

14. Uppuluri, S., Keinath, S., Tomalia, D.A., Dvomic, P.R. "Rheology of Dendrimers: I. Newtonian Flow Behavior of Medium and Highly Concentrated Solutions of Polyamidoamine (PAMAM) Dendrimers in Ethylenediamine (EDA) Solvent," Macromolecules, **31,** 4498, 1998.

15. Uppuluri, S., D.A. Tomalia, and P.R. Dvomic. "A "Dense-Shell" Model for Intramolecular Morphology of Polyamidoamine Dendrimers Based on Experimental Rheological Data," Polymer Material Science and Ennineering, 77, 116, 1997.

NO. OF COPIES	ORGANIZATION
2	ADMINISTRATOR DEFENSE TECHNICAL INFO CENTER ATTN DTIC OCP 8725 JOHN J KINGMAN RD STE 0944 FT BELVOIR VA 22060-62 18
1	DIRECTOR US ARMY RESEARCH LABORATORY ATTN AMSRL CS AL TA REC MGMT 2800 POWDER MILL RD ADELPHI MD 20783-I 197
1	DIRECTOR US ARMY RESEARCH LABORATORY ATTN AMSRL CI LL TECH LIB 2800 POWDER MILL RD ADELPHI MD 207830-l 197
1	DIRECTOR US ARMY RESEARCH LABORATORY ATTN AMSRL CS AL TP TECH PUB BR 2800 POWDER MILL RD ADELPHI MD 20783-l 197
1	DIRECTOR US ARMY RESEARCH LABORATORY ATTN AMSRL D DR R WHALIN 2800 POWDER MILL RD ADELPHI MD 20783-l 197
1	DIRECTOR US ARMY RESEARCH LABORATORY ATTN AMSRL DD J J ROCCHIO 2800 POWDER MILL RD ADELPHI MD 20783-l 197
20	DR SRINIVAS UPPULURI MICHIGAN MOLECULAR INSTITUTE 1910 WEST ST ANDREWS RD MIDLAND MI 48640-2696 DR GUISEPPE PALMESE CENTER FOR COMP MATERIALS UNIVERSITY OF DELAWARE NEWARK DE 19716
1	MR ZHISHENG CHEN DEPT OF CHEMICAL ENGINEERING UNIVERISTY OF DELAWARE NEWARK DE 19716-3110

NO. OF COPIES	ORGANIZATION
1	DR BARRY BAUER BLDG 224/ POLYMER BLENDS GROUP NATL INST OF STANDARDS & TECH GAITHERSBURG MD 20899
1	MR KEN LAVERDURE DEPT OF POLYMER SCIENCE UNIVERSITY OF MASSACHUSETTS AMHERST MA 01003
1	DR ANDRE M STRIEGEL USDA/ARS/NCAUR 1815 N UNIVERSITY ST PEORIA IL 61604
1	DR GARY WASHINGTON DEPT OF CHEMISTRY US MILITARY ACADEMY WEST POINT NY 10996
1	DR JOHN WALKER US ARMY NATICK RD & E CENTER BIOTECHNOLOGY/MATERIALS DIV SCIENCE & TECH DIRECTORATE KANSAS ST NATICK MA 0 1760-5020
1	PROF JIMMY MAYS DEPT OF CHEMISTRY CHEMISTRY BLDG RM 201 UNIV OF ALABAMA AT BIRMINGHAM BIRMINGHAM AL 35294
1	DR BOUALEM HAMMOUDA REACTOR DIVISION NATL INST OF STANDARDS & TECH GAITHERSBURG MD 20899
1	DR WILLIAM BELL TDA RESEARCH INC 12345 WEST 52ND AVENUE WHEAT RIDGE CO 80033
1	DR DOUGLAS KISEROW US ARMY RESEARCH OFFICE DIV OF CHEM & BIOLOGICAL SCIENCES 4300 S MIAMI BLVD PO BOX 12211 RSCH TRIANGLE PARK NC 27709-22 11

NO. OF COPIES ORGANIZATION

1 DR HEIDI SCHREUDER GIBSON
US ARMY SOLDIER SYSTEMS CMD
ATTN NRDEC (SSCNC YM)
KANSAS ST
NATICK MA 01760-5020

1 DR PAUL PAINTER
POLYMER SCIENCE & ENGINEERING
320 STEIDLE BUILDING
PENN STATE UNIVERSITY
UNIVERSITY PARK PA 16802-5007

1 DR ANTHONY MCHUGH
DEPT OF CHEMICAL ENGINEERING
UNIVERSITY OF ILLINOIS
600 S MATTHEWS ST
URBANA IL 61801

1 DR JEARLDINE NORTHRUP
ENERGY AND UTILITY SYSTEMS
US ARMY CORPS OF ENGINEERS
CONST ENG RSCH LABORATORIES
PO BOX 9005
CHAMPAIGN IL 61826-9005

1 DR W M CHEW
US ARMY AVIATION & MISSILE CMD
MISSILE RD&E CENTER
REDSTONE ARSENAL AL 35898-5249

1 DR ALBERT MCMANUS
US ARMY INST OF SURGICAL RSCH
3400 RAWLEY CHAMBERS ROAD
FT SAM HOUSTON TX 78234-6315

1 DR MORTON M DENN
DEPT OF CHEMICAL ENGINEERING
UNIVERSITY OF CALIFORNIA
BERKELEY CA 94720

1 DR ERIC AMIS
POLYMERS DIVSION BLDG 224
NIST
GAITHERSBURG MD 20899

1 DR ROBERT BRIBER
DEPT OF MATERIALS & NUCLEAR ENGINEERING
UNIVERSITY OF MARYLAND
COLLEGE PARK MD 20742

NO. OF COPIES ORGANIZATION

1 DR CHRIS TOPRAKCIOGLU
DEPARTMENT OF PHYSICS
UNIVERSITY OF PATRAS
PATRAS 26500
GREECE

ABERDEEN PROVING GROUND

2 DIRECTOR
US ARMY RESEARCH LABORATORY
ATTN AMSRL CI LP (TECH LIB)
BLDG 305 APG AA

1 US ARMY ERDEC
ATTN SCBRD RTL DRRUI YIN
5232 FLEMING ROAD BLDG E3 150
APG MD 21010

23 US ARMY RESEARCH LABORATORY
ATTN AMSRL WM MA
NORA BECK TAN (20 CYS)
GARY HAGNAUER
STEVEN MCKNIGHT
DANIEL DESCHEPPER
BLDG 4600
APG MD 21005-5069

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington. VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	January 1999	Final

4. TITLE AND SUBTITLE

The Properties of Dendritic Polymers II: Generation Dependence of the Physical Properties of Poly(amidoamine) Dendrimers

5. FUNDING NUMBERS

PR: 611102.H42

6. AUTHOR(S)

Uppuluri, S.; Dvornic, P.R. (both of Michigan Molecular Institute); Beck Tan, N.C.; Hagnauer, G. (both of ARL)

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

U.S. Army Research Laboratory
Weapons & Materials Research Directorate
Aberdeen Proving Ground, MD 2 10 1 O-5066

8. PERFORMING ORGANIZATION REPORT NUMBER

3. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Research Laboratory
Weapons & Materials Research Directorate
Aberdeen Proving Ground, MD 21010-5066

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

ARL-TR-1774

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution is unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum* 200 words)

Dendritic polymers, or dendrimers, represent a new class of macromolecules characterized by an ultra-branched molecular architecture generated by *a* novel synthetic route developed in the mid-1980s. As the synthetic science of these molecules matures, the search for applications of them is becoming increasingly active. However, a lack of physical property data has made the identification of suitable application and technology areas that are ripe for exploitation of dendrimers difficult. The purpose of this series of reports is to compile, in the most concise form possible, some fundamental physical property information about dendrimers. The focus is on the behavior of poly(amidoamine) or PAMAM dendrimers, which were developed in the United States and are produced domestically by Dendritech, Inc., of Midland, Michigan. In this report, the second in our series, the effect of molecular size or "generation" of the dendritic polymers on their physical properties is highlighted. The first report, ARL-TR-1606 was published in May 1998 and was focused on the general physical behavior of a mid-sized (Generation 5) PAMAM dendrimer. The third report, slated for completion in early 1999, will focus on "end group" chemistry dependence of PAMAM dendrimers.

14. SUBJECT TERMS

dendrimers
dendritic polymers
generations

15. NUMBER OF PAGES

40

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	