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Synthesis of dendritic macromolecules hybrid dendritic-linear block copolymers

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**Synthesis of Dendritic Macromolecules
and
Hybrid Dendritic-Linear Block Copolymers**

**A Thesis
presented to
The Faculty of the Department of Chemistry
San Jose State University**

**In Partial Fulfillment
of the Requirements for the Degree
Master of Science**

**By
Archana Desai
December, 1997**

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Abstract

Part I. A series of polyether monodendrons based on 3,5-dihydroxybenzyl alcohol as the monomer unit were synthesized using a convergent growth strategy. The synthesis involved the condensation of two equivalents of a benzylic bromide with the two phenolic groups of the monomer, 3,5-dihydroxybenzyl alcohol, under phase transfer conditions. A benzylic alcohol functionality was then converted into corresponding bromide and these procedures repeated until a fifth generation dendritic wedge was obtained. The bromomethyl group at the focal point was then converted into the desired amino functionalized dendritic fragment.

Part II. Unlike anionic procedures which are incompatible with a large number of functional groups, nitroxide mediated 'living' free radical procedures have the potential to be tolerant to a wide variety of functional groups. This new polymerization technique may therefore offer an unparalleled opportunity in the synthesis of reactive linear polymers with controlled molecular weight and low polydispersity. Using this new technique, the one-step synthesis of active ester substituted linear polymers was examined.

Part III. The reactive linear polymers with active ester functional groups were next coupled with the monoamino substituted dendrons to give high molecular weight hybrid dendritic linear block copolymers. These materials were fully characterized, and the relationship between dendrimer size and percent incorporation was determined.

*This work is dedicated to my son
Preet Desai*

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PART I : SYNTHESIS OF DENDRONS

1. INTRODUCTION

The ultimate goal of this project was to develop a highly efficient and versatile synthetic route to hybrid dendritic linear block copolymers in which numerous dendritic fragments are attached to a linear polymer backbone. As the name implies, dendritic macromolecules are highly branched, three dimensional structures that resemble the growth pattern of trees. Initially dendritic macromolecules were prepared by a divergent growth approach in which the synthesis begins at a polyfunctional core and proceeds radially outward with an ever increasing number of chain ends. Subsequently, Hawker and Frechet¹ at Cornell University developed a new approach to dendrimer synthesis known as the convergent approach. In the convergent mode of dendrimer construction of polymeric arms (dendrons or dendritic fragments) are synthesized from the "outside-in" and are characterized by a single reactive functional group at the center or focal point of the macromolecule.¹ The first phase of this research project involves the development of a synthetic strategy for the preparation of polyether dendritic fragments containing a single amine group at the focal point group via the convergent growth approach.

2. BACKGROUND

One of the reasons for studying highly branched macromolecules, such as dendrimers, is because they will have fundamentally different, and potentially new properties when compared to traditional linear polymers. These highly branched, three dimensional macromolecules are divided into two main classes, dendritic and hyperbranched macromolecules, which differ in their structure and mode of synthesis.² Dendritic macromolecules have a regular or perfectly branched architecture with at least one branch point per monomer unit, whereas hyperbranched macromolecules have randomly branched structure and contain significant amounts of linear segments.² Dendrimers differ from linear polymers in terms of the three different architectural components; they contain (a) an interior core, (b) interior layers (generations), and (c) exterior functional groups.^{3,4}

2.1 Dendrimer Synthesis

Tomalia⁵ and Newkome⁶ independently reported in 1985 the first syntheses of true dendrimers or starburst macromolecules. Both groups used a two step, divergent growth approach in which growth is started at a central polyfunctional core and proceeds radially outward with an increasing number of chain ends. Tomalia's two step synthetic strategy for the synthesis of polyamidoamine (PAMAM) is shown in Scheme I.^{5a,b} Step A, involves the Michael reaction of ammonia with methyl acrylate to form a triester, followed by the reaction of a large excess of ethylenediamine with the triester (step B) to give the first generation dendrimer which has six primary amino groups compared to three for the starting ammonia core. Repetition of this two step sequence produces higher and higher generations. Although the divergent growth approach has proved extremely successful for the preparation of dendritic macromolecules, it does suffer from a number of drawbacks. Firstly, any incomplete reaction would lead to imperfections in

Scheme 1. Synthetic scheme of polyamidoamine (PAMAM) dendrimers

the next sequence and the probability of failure in any sequence increases as the molecular weight increases. Secondly, as extremely large amounts of reagents are required to force the reaction to completion and to avoid any side reactions, purification becomes very difficult in the later stages of the growth.

To overcome this problem, Hawker and Frechet⁷ developed a convergent growth strategy for the synthesis of dendrimers and employed this novel technique to prepare dendritic polyether wedges up to sixth generation, [G-6]-Br. A general structural notation to represent various generation dendritic molecules is [G-x]-f where [G-x] refers generation number ($x = 0, 1, 2, 3, \dots$) and f refers to functionality attached at the focal point. In the "convergent" mode strategy, branched polymeric arms (dendron or dendritic fragments) are synthesized from the "outside-in". This convergent growth approach is actually opposite of the divergent growth approach and permits dendrimers with fewer defects to be synthesized because separation and purification is simpler. It also permits the synthesis of a variety of block copolymers due to the presence of the single unique functionality at the focal point of the dendron.

2.2 Properties and Characterization

Traditional linear polymers are characterized by a random coil structure with only two chain ends. The contribution from these chain ends are therefore negligible at high molecular weights and the physical properties are dominated by chain entanglements and the presence or absence of functionalities attached to the polymer backbone.⁸ Unlike linear polymers, a fundamental feature of dendrimers and hyperbranched molecules is the presence of a large number of chain ends which would be expected to play a major role in determining the physical properties of dendrimers. For example, due to their highly branched structure, crystallization is not likely to occur and chain entanglement is not likely to be a dominant process.⁹

A simple analogy for the comparison of linear polymers and dendrimers is that the linear polymers resemble "cooked spaghetti" while dendrimers resemble "green peas."¹⁰ In the bulk state linear polymers are heavily entangled in contrast to dendrimers which due to their globular structure would be expected to have little or no entanglements.¹⁰ Therefore, dendrimers are expected to have unusual physical and chemical properties. For example, the viscosity of classical linear polymers such as poly(styrene), increases sharply with molecular weight according to the Mark-Houwink-Sakurada equation:

$$[\eta] = k M^a$$

in which $[\eta]$ is the intrinsic viscosity of the polymer, M is its molecular weight, and k and a are constants specific to each solvent-polymer combination at a given temperature.^{10,11} Dendrimers, however, do not obey this relationship once a threshold molecular weight is reached (Figure 1).¹² In this case, the intrinsic viscosity for poly(benzyl ether) dendrimers has been shown to pass through a maximum and then actually decrease as the molecular weight increases.¹³ This discrepancy can be better understood if it is realized that like spheres, the volume (V) of a dendrimer increases cubically ($V = 4/3\pi r^3$) with increasing generation number (G) while the mass of the dendrimers doubles at each of the successive generations and increases exponentially [$MW \sim 2^{(G-1)}$]. This relationship is unique for the dendrimers and illustrates why these are a novel, new class of polymeric materials and have attracted considerable interest.

The beauty of the dendrimers is that their size and architecture can be specifically controlled in their syntheses. As dendritic polymers have numerous chain-ends which can be functionalized easily, numerous structural domains with different properties can be synthesized. Researchers in the field are developing a variety of uses for dendritic

Figure 1. Log intrinsic viscosity as a function of log molecular weight for dendrimers, linear and hyperbranched polymers.

macromolecules. These include nanoscale catalysts and reaction vessels, micelle mimics, imaging studies, chemical sensors, high performance polymers, adhesives and coatings, etc. and a number of other applications such as agents for delivering drugs or genes into cells have been proposed.¹⁴

Before continuing it is necessary to summarize a number of important procedures and concepts in polymer science that are used throughout this thesis.

2.3 Molecular Weights and Averages

Once a polymer has been synthesized, it is essential to determine its molecular weight. This calculation can be done either by absolute or relative methods (secondary methods). An absolute method gives direct values of the M_w and M_n (see below for definitions), whereas a secondary method would give only a relative measure of the polymer's molecular weight. Absolute methods are well established both theoretically and experimentally but are generally expensive, and also time-consuming. Therefore, molecular weight determinations are predominantly performed by much faster and simpler secondary methods, usually solution viscosity or gel permeation chromatography (GPC) which typically involves calibration against known standards. A summary of important methods for determining molecular weights of polymers and the results obtained from them are shown in Table I.¹⁵

Table I. Summary of molecular weight methods and results¹⁵

	Absolute	Relative	M_n	M_w	Other
GPC		x	x	x	mol. wt. distribution
Light-scattering	x			x	R_g^2 (a), A_2 (b)
Osmometry	x		x		A_2
Intrinsic Viscosity		x			M_v (c)

(a) R_g - Radius of gyration, (b) A_2 Second virial coefficient, (c) M_v Viscosity average molecular weight

In our case, the method chosen to determine relative molecular weight was GPC. It operates on the principle that polymer molecules separate according to their size, i.e. hydrodynamic volume.¹⁶ The separation is based on the fact that polymer molecules of varying molecular weight or degree of polymerization have different hydrodynamic volumes in their dissolved state.

The GPC procedure involves injecting a dilute solution of a polymer into a continuous flow of solvent passing through a series of columns containing microporous gel particles. The size of these gel particles is in the range 5 - 10 μm in order to give efficient packing with pore sizes from 0.5 to 10^5 nm, which correspond to the effective size range of polymer molecules.¹⁷ In the separation process, small molecules permeate through a greater number of pores than the larger molecules and therefore have a greater mean path and have longer elution times. Thus, time or elution volume is inversely proportional to molecular weight. The molecular weight of a polymer is usually given in terms of either a number-average molecular weight, M_n , or weight-average molecular weight, M_w , which are explained below.

The **degree of polymerization (DP)** of a polymer chain is defined as the average number of repeat units (mers) per chain. For example, $M = \text{DP}(w_x)$ where, M is the molecular weight of the polymer, DP is the degree of polymerization, and w_x is the molecular weight of the repeat unit.

The **number-average molecular weight, M_n** , is defined as the total weight of all molecules in a polymer sample divided by the total number of moles present and it is biased towards low molecular weight fractions (eq 1)

$$M_n = W/N = \sum n_x M_x / \sum n_x = n_1 M_1 / \sum n_x + n_2 M_2 / \sum n_x + \dots = \sum (n_x/N) M_x$$

(eq 1)

where W = total sample weight = $\sum w_x = \sum n_x M_x$

n_x = number of moles of x-mer

M_x = molecular weight of x-mer

(n_x/N) = mole fraction of x-mer

The **weight-average molecular weight, M_w** , is defined as the summation of the weight fractions of all molecules times their molecular weights and it is biased towards high molecular weight fractions (eq 2)

$$M_w = \sum w_x M_x / \sum w_x = w_1 M_1 / \sum w_x + w_2 M_2 / \sum w_x + \dots = \sum (w_x/W) M_x \quad (\text{eq 2})$$

where w_x = weight of x-mer in sample = $n_x M_x$

(w_x/W) = weight fraction of x-mer in sample

For any polydisperse system M_n is always smaller than M_w , since the smaller individuals in polydisperse mixtures make a larger contribution on counting the molecules. The ratio of M_w / M_n is used to determine the polydispersity (PD) in a polymer sample and gives the statistical variation in molecular weight for a given sample. Unlike natural polymers, such as proteins, which are monodisperse, man-made polymers are inherently polydisperse (i.e. they contain a range of molecular weights) due to limitations of current synthetic methods. In fact, dendrimers are the only example of synthetic polymers which can be considered as monodisperse. Polymers prepared by anionic polymerizations have narrow molecular weight distribution, with polydispersity indices less than 1.05 while those prepared by traditional free radical polymerizations have polydispersities in the range of 1.5 - 3.0. Typical molecular weight distributions obtained by the more commonly employed polymerization methods are shown in Table II.¹⁵

Table II. Typical molecular weight distribution¹⁵

Method	Polydispersity	Stereospecificity
Natural Proteins	1.0	Perfect
Anionic polymerization	1.02-1.05	None
Chain polymerization	1.5-3.0	None
Step Polymerization	2.0-4.0	None
Ziegler-Natta	2.0-40	High
Cationic	Broad	None

2.4 Glass transition temperature

The practical utility of polymers and their different properties depend heavily on their glass transition temperatures, T_g . For example, polystyrene, with a T_g of 100°C , is a hard glassy material at room temperature whereas ethylene propylene copolymer with a T_g of -60°C is used as a rubber at room temperature. The T_g of a polymer depends on the chain geometry, chain flexibility and the type of the molecular aggregates formed. In an effort to manipulate the physical properties of polymeric materials (e.g. T_g) many researchers have examined random copolymers. The net effect of the interaction between two different monomeric components of a copolymer on the T_g value is as though the copolymer is a mixture of two homopolymers. The T_g value of random copolymers, therefore, depends on the T_g value of the individual homopolymers and on the ratio of the two monomer components.¹⁷

The glass transition temperature of a random copolymer can be predicted by using the well known Fox equation:

$$1/T_{g(AB)} = W_A/T_{g(A)} + W_B/T_{g(B)}$$

where $T_g(A)$, $T_g(B)$ and $T_g(AB)$ are the glass transition temperatures of two homopolymers A and B and the copolymer AB respectively and W_A and W_B are the weight fractions of the respective monomer components in the copolymer. From this equation, it can be seen that the glass transition temperature of a copolymer will be in-between those of the respective homopolymers.

The most popular technique for determination of T_g is differential scanning calorimetry (DSC), shown schematically in Figure 2.¹⁸ A typical plot obtained from such a measurement made is shown in Figure 3.¹⁸ In DSC, small samples of polymer (10-15 mg) and an inert reference substance (one that undergoes no transitions in the temperature range of interest) are mounted in a block containing heaters for each and thermocouples to monitor heat flow. In DSC, both sample (S) and reference (R) are maintained at the same temperature by controlling electrically the rate at which heat is transferred to them. The amount of heat that has to be supplied to S and R to achieve this equivalence in temperature is constantly measured over the temperature range employed. This recorded heat flow gives a measure of the amount of energy absorbed or evolved in a particular transition and hence gives calorimetric measurements directly. The thermodynamic property being monitored is the enthalpy. At T_g , the heat capacity of the sample suddenly increases, requiring more power (relative to reference) to maintain the same temperature .

Figure 2. Schematic representation of DSC

Figure 3. Schematic DSC record

3. RESULTS AND DISCUSSION

The synthetic scheme leading to the first generation bromide [G-1]-Br was achieved in three steps as shown in Scheme II. The first step involved the reaction of methyl 3,5-dihydroxybenzoate (1), with benzyl bromide (2), under phase transfer conditions to give the ester 3 in 88% yield. This phase transfer catalyzed alkylation (PTC, as explained below) was carried out using a mixture of potassium carbonate, and 18-crown-6 ether. Reduction of the ester 3, with LiAlH_4 gave the first generation benzylic alcohol [G-1]-OH (4) in 89 % yield and subsequent bromination of 4 with $\text{CBr}_4/\text{PPh}_3$ gave the corresponding bromide [G-1]-Br (5) in 89% yield.

Having obtained the first generation bromide, the convergent growth approach was employed next to give larger dendritic fragments (Scheme III). The second generation synthesis involved a similar two step procedure. An initial Williamson reaction of [G-1]-Br (5) with the monomer unit 3,5-dihydroxybenzyl alcohol (6) under PTC gave the second generation alcohol [G-2]-OH (7) in 88% yield after recrystallization. In this reaction, alkylation of the monomer unit 6 occurs only at the phenolic hydroxy groups, leaving the hydroxymethyl group at the focal point intact. C-alkylation of phenols¹⁹ is a well known side reaction, however no detectable amounts of C-alkylation was observed by ^1H NMR. The second step involved activation of the hydroxymethyl group by conversion to a bromide with $\text{CBr}_4/\text{PPh}_3$ to give [G-2]-Br (8) in 91% yield. Repetition of these alkylation and bromination procedures gave higher dendritic fragments up to a fifth generation. Before coupling of the bromide with the monomer unit, the excess of $\text{CBr}_4/\text{PPh}_3$, as well as the reaction byproducts, were removed by flash chromatography and then by precipitation in ether. High yields, greater than 85%, were obtained for all the steps, except in the fifth generations, where lower yields were obtained, presumably due to increasing steric congestion around the focal

point group. Materials up to the second generation were crystalline, whereas all materials from the third generation onwards were glassy solids and were purified by standard flash chromatography.

The alkylation reactions shown in Scheme II and Scheme III used phase transfer catalysis (PTC) which can be explained as follows. A catalyst which allows PTC process involves immiscible reactants which react by bringing one of the reactants into the other phase. In solid-liquid phase transfer catalysis, an organic compound and the catalyst, for example crown ether (18-C-6), are dissolved in an organic solvent. The cation of the insoluble inorganic salt is complexed by the 18-C-6. The anion of the salt is unchanged but follows the complex cation into solution in the organic phase where it may react with the organic substrate. Crown ethers are effective as PTC catalysts due to their ability to form complexes with a wide variety of cationic substrates such as alkali and alkaline earth metals cations and ammonium ions.^{20a-c} Thus, this cation-complexation leads to the solvent separated ion pairs or free ion pairs. As a result, the anion generated in PTC is more nucleophilic than those solubilized in aqueous media.

In contrast to all other synthetic polymers for which a distribution in molecular weights is obtained (which in turn complicates characterization), the elucidation of dendrimer structures is greatly facilitated by their high level of symmetry and the fact that they are nearly monodisperse. GPC is very useful in characterizing these dendrons, the molecular weight of which approximately doubles at each generation, so any incomplete generation growth can be easily detected. GPC traces of these materials showed narrow peaks with polydispersity (PD) about 1.02, which is consistent with their monodisperse nature. The glass transition temperatures (T_g) for all dendrons were determined by DSC and found to be around 40°C.

Infrared spectroscopy offers very little information in characterization of

Scheme II. Synthetic scheme for the preparation of [G-1]-Br

Scheme III. Synthetic scheme for the preparation of poly (aryl alkyl ether) dendrimers by convergent growth approach

Scheme III. Synthetic scheme for the preparation of poly (aryl alkyl ether) dendrimers
by convergent growth approach (continued)

dendritic wedges because the spectra become overcrowded with the dominant functional groups and the contributions from the unique focal point groups are rapidly lost. In a similar way, elemental analysis⁷ is not a reliable technique to determine changes in the structure. For example, [G-3]-OH requires C = 79.12%, H = 5.82% while [G-5]-Br requires C 78.46% and H = 5.66%.

¹H NMR spectroscopy was an important tool for confirming the structures of the various dendritic fragments. For example, the ¹H NMR spectrum of [G-3]-Br (shown in Figure 4) contains three types of resonances. The resonances for the exterior phenyl groups occur at 7.25 - 7.45 ppm, interior aromatic protons of the building blocks appears between 6.5 to 6.7 ppm, while the unique resonance for the single bromomethyl group at the focal point appears at 4.30 ppm. The chain end benzylic methylene protons give pseudosinglet at 5.00 ppm whereas the interior benzylic methylene protons give rise to pseudosinglet at 4.95 ppm. On reaction with the monomer unit, the focal point group is converted to a hydroxymethyl group which gives a new resonance at 4.60 ppm. Therefore any impurity from unreacted starting material can be easily detected. Thin layer chromatography (TLC) was also found to be extremely useful in monitoring these reactions. The structures and purities of the dendritic fragments were also confirmed by ¹³C NMR.

The synthetic routes leading to the formation of amino terminated polyether dendrons are shown in Scheme IV and Scheme V respectively. The conversion of [G-3]-Br to [G-3]-N₃ involved the nucleophilic displacement of bromide ion by azide ion and its subsequent reduction with LiAlH₄ to give [G-3]-NH₂. The products were easily purified by flash chromatography due to the large R_f difference between the starting bromide, the intermediate azide, and the resulting amine. The second, fourth and fifth generation bromides were similarly converted to corresponding azides and amines, and TLC was found to be extremely useful to check the reaction progress. Starting from

[G-3]-Br, [G-3]-N₃ was obtained in 85% yield and its subsequent reduction with LiAlH₄ gave [G-3]-NH₂ in 84% yield after purification by flash chromatography.

As discussed above, the purities and structures of the functionalized dendrimers could be determined by ¹H NMR. In this case, as the functionality at the focal point group changes from bromide to azide, the chemical shift of the focal point methylene protons moves upfield. The case of [G-3]-Br and [G-3]-N₃ (4.3 ppm to 4.2 ppm) respectively is illustrated in Figure 4 and Figure 5. Similar changes in chemical shift were observed for the methylene protons at focal point group for all other generations. ¹³C NMR spectra of [G-4]-OH and [G-4]-Br as shown in Figure 6 and Figure 7 show a similar change in chemical shift for the methylene carbons at the focal point group. The chemical shift of methylene carbons changes from 65.0 ppm to 33.5 ppm for [G-4]-OH and [G-4]-Br respectively.

The introduction of the azide group could also be observed by IR spectroscopy. Figure 8 and Figure 9 show the infrared spectra of [G-3]-N₃ and [G-4]-N₃ respectively. Both dendritic fragments, show a strong N=N=N asymmetric stretching absorption,²¹ at 2130 cm⁻¹. On reduction of the azido group to amino group subtle changes in the ¹H NMR and infrared spectra were observed. Figure 10 and Figure 11 show the ¹H NMR spectra of [G-3]-NH₂ and [G-4]-NH₂ respectively. The unique resonance for the focal point aminomethyl group is now found to be at 3.76 ppm compared to 4.17 ppm for the corresponding azido derivatives. The infrared spectra show the total absence of the azide stretch at 2130 cm⁻¹.

In conclusion, a variety of chemical modifications can be performed on the focal point group, as can be seen by the synthesis of various dendrons with hydroxymethyl functionality to aminomethyl functionality. The purities and structures of the resulting dendrimers were fully confirmed by a variety of spectroscopic techniques.

Figure 4. ^1H NMR spectrum of third generation bromide [G-3]-Br

Figure 5. ^1H NMR spectrum of third generation azide [G-3]-N₃

Scheme IV. Synthetic scheme for the preparation of [G-3]-NH₂

Scheme V. Synthetic scheme for the preparation of [G-4]-NH₂

Figure 6. ^{13}C NMR spectrum of fourth generation alcohol [G-4]-OH

Figure 7. ^{13}C NMR spectrum of fourth generation bromide [G-4]-Br

Figure 8. IR spectrum of third generation azide [G-3]-N₃

Figure 9. IR spectrum of fourth generation azide [G-4]-N₃

Figure 10. ^1H NMR spectrum of third generation amine [G-3]- NH_2

Figure 11. ^1H NMR spectrum of fourth generation amine [G-4]- NH_2

4. CONCLUSION

The synthesis of dendritic macromolecules via a convergent growth approach has a number of advantages. This approach is characterized by the continuous presence of a single functional group at the focal point of the growing dendrimer which requires only a single activation reaction and usually only two coupling reactions for generation growth. The chances of defects occurring during the generation growth are therefore decreased, as these would be easily detected and separated. Monodisperse dendritic macromolecule can be obtained via this approach. We have developed a synthetic route for the preparation of monoamino functionalized dendritic polyether macromolecules based on 3,5-dihydroxy benzyl alcohol. All dendrimers were fully characterized.

5. EXPERIMENTAL

Infrared spectra were recorded on a Perkin Elmer Spectrophotometer as thin films on NaCl. ^1H NMR spectra were recorded in CDCl_3 solution on a Bruker AM 250 (250 MHz) spectrometer, with TMS proton signal as an internal standard. ^{13}C NMR spectra were recorded at 62.5 MHz on a Bruker AM 250 spectrometer in CDCl_3 solution with the solvent carbon signal serving as internal standard. Analytical TLC was performed on commercial Merck plates coated with silica gel GF₂₅₄ (0.25mm thick). Silica gel for flash chromatography was Merck Kieselgel 60 (230-400 mesh). Size exclusion chromatography was carried out on a Waters Chromatograph connected to a Waters 410 differential refractometer. Four 5 μm Waters columns (300 x 7.7 mm) connected in series in order of increasing pore size (100A, 1000A, 10⁵A and 10⁶A) were used with THF as solvent. Glass transition temperatures (T_g) were recorded on a Perkin-Elmer DSC 7 system.

General Procedure for the Synthesis of Dendritic Benzyl alcohols

A mixture of dendritic benzyl bromide (2.00 equiv), 3,5-dihydroxybenzyl alcohol (1.00 equiv), dried potassium carbonate (2.1-2.2 equiv), and 18-crown-6 (0.2 equiv) in dry acetone (10.0 equiv) was heated at reflux and stirred vigorously under nitrogen for 48 h. The reaction mixture was cooled and evaporated to dryness under reduced pressure. The product was partitioned between CH_2Cl_2 and water and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic extracts were then dried with MgSO_4 , filtered and evaporated to dryness. Individual purification procedures are described below.

General Procedure for the Synthesis of Dendritic Benzyl Bromides

To a mixture of the appropriate dendritic benzyl alcohol (1.00 equiv) and carbon tetrabromide (1.25 equiv) in dry THF (the minimum required to ensure dissolution) was

added triphenylphosphine (1.25 equiv). The reaction mixture was stirred under nitrogen for 20 min. For fourth and fifth generations, larger excesses of CBr_4 and PPh_3 were required to force the reaction to completion; these were added in 1.25 equiv increments at 10 min intervals until TLC showed no starting material. The reaction mixture was then poured into water and extracted three times with CH_2Cl_2 . The combined extracts were dried and evaporated to dryness. The crude product was then purified by methods described below.

Methyl 3,5-dihydroxybenzoate (1)

3,5-dihydroxy benzoic acid (50.0 g, 325 mmol) was dissolved in methanol (300 mL), and concentrated sulfuric acid (5 mL) was added to it. The mixture was heated at reflux overnight and excess methanol was removed by evaporation. The product was partitioned between water and diethyl ether. The combined organic layers were dried (MgSO_4) then evaporated to dryness. The crude product was purified by recrystallization from the mixture of methanol and water to give **1** as a white solid. Yield 44.0 g (80%): ^1H NMR (CDCl_3) δ 3.85 (s, 3H, OCH_3), 6.43 (t, 1H, $J = 3\text{Hz}$, ArH), 6.90 (d, 2H, $J = 3\text{Hz}$, ArH).

Methyl 3,5-dibenzyloxy-benzoate (3)

A mixture of methyl 3,5-dihydroxybenzoate (**1**) (46.40 g, 276.0 mmol), benzyl bromide (**2**) (99.30 g, 580.0 mmol), potassium carbonate (50.00 g, 362.0 mmol) and 18-crown-6 (1.00 g, 3.79 mmol) dissolved in acetone (500 mL) was refluxed with vigorous stirring under nitrogen for 24 h. The reaction mixture was cooled, filtered and evaporated to dryness and partitioned between ether (3 x 70 mL) and water (150 mL). The aqueous layer was extracted with ether (50 mL) and combined with ether extract, dried (MgSO_4) and evaporated to dryness. The product ester **3** was obtained as a white solid product after recrystallization from methanol. Yield 85.00 g (88%); ^1H NMR (CDCl_3) δ 3.88 (s,

3H, OCH_3), 5.06 (s, 4H, $PhCH_2O$), 6.80 (t, 1H, $J = 3\text{ Hz}$, ArH), 7.23-7.44 (m, 12H, $12ArH$); ^{13}C NMR (CDCl_3) δ 54.45, 70.15, 102.12, 107.89, 127.65, 128.16, 128.49, 136.98, 140.05, 160.25, 168.90.

3,5-dibenzyloxy-benzyl alcohol, [G-1]-OH (4)

Methyl 3,5-dibenzyloxy-benzoate (3) (80.0 g, 230 mmol) was dissolved in dry THF (300 mL) and added dropwise to a mixture of LiAlH_4 (17.5 g, 461 mmol) in dry THF (250 mL). The solution was heated to reflux overnight and then 1N NaOH (30 mL) was added dropwise and stirred for 30 min, cooled, filtered and the filtrate was evaporated to dryness. The product 4 was purified by recrystallization from methanol/water. Yield 65.0 g (89%): mp 85-86 °C; IR (film) 1600, 1430, 1365, 1160, 1070 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.58 (d, 2H, CH_2OH), 5.02 (s, 4H, $PhCH_2O$), 6.58 (t, 1H, $J = 3\text{ Hz}$, ArH), 6.64 (d, 2H, $J = 3\text{ Hz}$, ArH), 7.24-7.45 (m, 10H, ArH); OH resonance not observed; ^{13}C NMR (CDCl_3) δ 64.63, 70.14, 101.89, 107.14, 127.53, 128.07, 128.55, 136.56, 139.54, 160.08.

3,5-dibenzyloxy-benzyl bromide [G-1]-Br (5)

To a solution of [G-1]-OH, (4) (60.00 g, 187.5 mmol) and carbon tetrabromide (68.48 g, 206.2 mmol) in dry THF (300 mL) was added triphenylphosphine (54.03 g, 206.2 mmol) under nitrogen. The reaction mixture was stirred for 10 min and the completion of the reaction was monitored by TLC. The reaction mixture was evaporated to dryness, partitioned between CH_2Cl_2 and water, and the aqueous layer extracted with CH_2Cl_2 (3x200 mL). The combined CH_2Cl_2 extracts were dried with MgSO_4 and evaporated to dryness. The product 5 was purified by recrystallization from 3:1 hexane/toluene. Yield 64.0 g, (90%): mp 92-93 °C; IR (film) 1600, 1595, 1435, 1370, 1160, 1075 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.40 (s, 2H, $CH_2\text{Br}$), 5.02 (s, 4H, $PhCH_2O$), 6.56 (t, 1H,

$J = 3\text{ Hz}$, ArH), 6.64 (d, 2H, $J = 3\text{ Hz}$, ArH), 7.24 -7.44 (m, 10H, ArH); ^{13}C NMR (CDCl_3) δ 32.85, 70.08, 101.77, 107.08, 127.56, 128.12, 128.62, 136.77, 139.82, 160.11.

[G-2]-OH (7)

A mixture of [G-1]-Br (5) (50.0 g, 130 mmol), 3,5-dihydroxybenzyl alcohol (6) (9.12 g, 65.2 mmol), potassium carbonate (18.0 g, 130 mmol) and 18-crown-6 (100 mg) dissolved in acetone (500 mL) was refluxed with vigorous stirring under nitrogen for 24 h. The reaction mixture was cooled, filtered, evaporated to dryness and partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2 (3 x 150 mL) and the combined organic extracts were dried (MgSO_4) and evaporated to dryness. The crude [G-2]-OH (7) was purified by recrystallization from 3:1 toluene/hexane and obtained as a white crystalline solid product. Yield 43.0 g (88%); mp 110 °C; IR (film) 1600, 1430, 1365, 1160, 1070 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.62 (d, 2H, $J = 6\text{ Hz}$, CH_2OH), 4.97 (s, 4H, $Ar\text{CH}_2\text{O}$), 5.02 (s, 8H, $Ph\text{CH}_2\text{O}$), 6.49 (t, 1H, $J = 2\text{ Hz}$, ArH), 6.55 (d, 2H, $J = 2\text{ Hz}$, ArH), 6.59 (d, 2H, $J = 2\text{ Hz}$, ArH), 6.64 (d, 4H, $J = 2\text{ Hz}$, ArH), 7.23-7.37 (m, 20H, ArH); OH resonance not observed; ^{13}C NMR (CDCl_3) δ 65.29 (CH_2OH), 69.93, 70.10 (CH_2O), 101.32, 101.54, 105.74, 106.33 (ArC), 127.54, 127.99, 128.57 ($Ph\text{CH}$), 136.75, 137.26, 143.40, 160.05, 160.15 (Ar and PhC).

[G-2]-Br (8)

To a solution of [G-2]-OH (7) (42.00 g, 56.40 mmol) and carbon tetrabromide (26.50 g, 80.00 mmol) in dry THF (150 mL) was added triphenylphosphine (20.96 g, 80.00 mmol) under nitrogen. The reaction mixture was stirred for 10 min and the completion of the reaction was monitored by TLC. The reaction mixture was evaporated to dryness, partitioned between CH_2Cl_2 and water, and the aqueous layer extracted with CH_2Cl_2 (3x100 mL). The combined CH_2Cl_2 extracts were dried (MgSO_4) and evaporated to dryness. The product was then recrystallized from 3:1 toluene/hexane to

give **8** as a white solid. Yield 41.0 g (91%); mp 129-130°C; IR (film) 1600, 1595, 1435, 1370, 1160, 1075 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.41 (s, 2H, CH_2OH), 4.97 (s, 4H, ArCH_2O), 5.04 (s, 8H, PhCH_2O), 6.53 (t, 1H, $J = 2$ Hz, ArH), 6.59 (d, 2H, $J = 2$ Hz, ArH), 6.63 (d, 6H, ArH), 7.30-7.44 (m, 20H, PhH); ^{13}C NMR (CDCl_3) δ 33.57 (CH_2Br), 69.98, 70.08 (CH_2O), 101.60, 102.16, 106.35, 108.16 (ArC), 127.53, 127.99, 128.56 (PhCH), 136.71, 139.00, 139.73, 159.92, 160.14, (Ar and PhC).

[G-3]-OH (**9**)

A mixture of [G-2]-Br (**8**) (24.64 g, 30.53 mmol), 3,5-dihydroxybenzyl alcohol (**6**) (2.08 g, 14.89 mmol), potassium carbonate (6.00 g) and 18-crown-6 (150.00 mg) dissolved in acetone (200 mL) was refluxed with vigorous stirring under nitrogen for 24 h. The reaction mixture was cooled, filtered and evaporated to dryness and partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2 (3x150 mL) and combined with CH_2Cl_2 extract, dried (MgSO_4) and evaporated to dryness. The completion of the reaction was monitored by TLC. The crude [G-3]-OH (**9**) was purified by flash chromatography, eluting with CH_2Cl_2 , and gradually increasing to 2.5% ether in CH_2Cl_2 , and finally 5% ether in CH_2Cl_2 to give the product **9** as a colorless glass. Yield 21.0 g (88%); IR (film) 1595, 1470, 1370, 1165, 1070 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.57 (d, 2H, $J = 6$ Hz, CH_2OH), 4.94 (s, 12 H, ArCH_2O), 5.0 (s, 16H, PhCH_2O), 6.52 (m, 7 H, ArH), 6.63 (m, 14H, ArH), 7.24-7.41 (m, 40H, PhH); OH resonance not observed; ^{13}C NMR (CDCl_3) δ 65.09 (CH_2OH), 69.83, 69.88, 70.01 (CH_2O), 101.15, 101.52, 105.64, 106.31 (ArC), 127.50, 127.93, 128.51 (PhCH), 136.68, 139.17, 139.26, 143.50, 159.97, 160.07 (Ar and PhC).

[G-3]-Br (**10**)

To a solution of [G-3]-OH (**9**) (23.00 g, 14.45 mmol) and carbon tetrabromide (9.59 g, 28.90 mmol) in dry THF (150 mL) was added triphenylphosphine (7.57 g, 28.90

mmol) under nitrogen. The reaction mixture was stirred for 10-15 min and the completion of the reaction was monitored by TLC. The reaction mixture was rotovapped to dryness, partitioned between CH_2Cl_2 and water, and the aqueous layer extracted with CH_2Cl_2 (3x100). The combined CH_2Cl_2 extracts were dried with MgSO_4 and evaporated to dryness. The crude product was purified by flash chromatography, eluting with 1:1 petroleum ether/ CH_2Cl_2 , 1:3 petroleum ether/ CH_2Cl_2 to 1:5 petroleum ether/ CH_2Cl_2 . The product was then precipitated into ether (800 mL) from CH_2Cl_2 (100 mL) to give **10** as a colorless glassy product. Yield 22.0 g (91%); IR (film) 1600, 1460, 1370, 1170, 1065cm^{-1} ; ^1H NMR (CDCl_3) δ 4.36 (s, 2H, CH_2Br), 4.93 (s, 12 H, ArCH_2O), 5.0 (s, 16H, PhCH_2O), 6.53 (m, 7H, ArH), 6.63 (m, 14H, ArH), 7.27-7.41 (m, 40H, PhH); ^{13}C NMR (CDCl_3) δ 33.547(CH_2Br), 69.96, 69.99, 70.07 (CH_2O), 101.56, 101.62, 102.15, 106.34, 106.41, 108.19 (ArC), 127.53, 127.97, 128.55 (Ph CH), 136.73, 139.01, 139.16, 139.77, 159.93, 160.03, 160.13 (Ar and PhC).

[G-4]-OH (**11**)

A mixture of [G-3]-Br (**10**) (23.9 g, 14.5 mmol), 3,5-dihydroxybenzyl alcohol (**6**) (0.99 g, 7.07 mmol), potassium carbonate (5.00 g) and 18-crown-6 (200 mg) dissolved in acetone (300 mL) was refluxed with vigorous stirring under nitrogen for 24 h. The reaction mixture was cooled, filtered and evaporated to dryness and partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2 (3x150 mL) and combined with CH_2Cl_2 extract, dried (MgSO_4) and evaporated to dryness. The completion of the reaction was monitored by TLC. The crude [G-4]-OH **11** was purified by flash chromatography, eluting with CH_2Cl_2 , and gradually increasing to 2.00%, 4.00%, and 6.25% ether in CH_2Cl_2 to give the product **11** as a colorless glass. Yield 20.4 g (88%); IR (film) 1596, 1470, 1360, 1156, 1050 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.54 (d, 2H, $J = 6\text{ Hz}$, CH_2OH), 4.93 (s, 28 H, ArCH_2O), 5.0 (s, 32 H, PhCH_2O), 6.53-6.57 and

6.63 -6.67 (m, 45H, *ArH*), 7.29-7.42 (m, 80H, *PhH*); OH resonance not observed; ^{13}C NMR (CDCl_3) δ 64.99 (CH_2OH), 69.85, 69.95 (CH_2O), 101.09, 101.51, 105.66, 106.30 (*ArC*), 127.46, 127.88, 128.47 (*PhCH*), 136.69, 139.17, 139.14, 139.18, 139.31, 143.51, 159.92, 159.96, 160.05 (*Ar* and *PhC*).

[G-4]-Br (12)

To a solution of [G-4]-OH (11) (19.9 g, 6.06 mmol) and carbon tetrabromide (4.02 g, 12.1 mmol) in dry THF (150 mL) was added triphenylphosphine (3.17 g, 12.1 mmol) under nitrogen. The reaction mixture was stirred for 10-15 min and the completion of the reaction was monitored by TLC. The reaction mixture was rotovapped to dryness, partitioned between CH_2Cl_2 and water, and the aqueous layer extracted with CH_2Cl_2 (3x100). The combined CH_2Cl_2 extracts were dried with MgSO_4 and evaporated to dryness. The crude product was purified by flash chromatography, eluting with 1:1 petroleum ether/ CH_2Cl_2 , 1:3 petroleum ether/ CH_2Cl_2 , 1:5 petroleum ether/ CH_2Cl_2 to CH_2Cl_2 . The product was then precipitated into ether (800 mL) from CH_2Cl_2 (100 mL) to give 12 as a colorless glassy product. Yield 20.3 g (88%); IR (film) 1597, 1470, 1376, 1210, 1160, 1050 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.36 (s, 2H, CH_2Br), 4.77 (s, 28 H, ArCH_2O), 4.96 (s, 32 H, PhCH_2O), 6.53-6.57 and 6.63 -6.67 (m, 45 H, *ArH*), 7.29-7.43 (m, 80H, *PhH*); ^{13}C NMR (CDCl_3) δ 33.54 (CH_2Br), 69.90, 69.99 (CH_2O), 101.55, 102.09, 106.33, 108.22 (*ArC*), 127.48, 127.91, 128.50 (*Ph CH*), 136.72, 139.06, 139.17, 139.71, 159.67, 159.99, 160.09 (*Ar* and *PhC*).

[G-3]-N₃ (15)

A mixture of [G-3]-Br (10) (10.0 g, 6.04 mmol) and NaN_3 (1.17 g, 18.1 mmol) in DMSO was heated to 55°C under argon, with stirring for 24 h. The reaction mixture was cooled and added to water (250 mL) and extracted with dichloromethane (4x50 mL). The combined organic layers were dried (MgSO_4), evaporated to dryness to give 15 as a

glassy solid. Yield 8.30 g (85%); IR (film) 2130, 1600, 1460, 1370, 1170, 1065 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.17 (s, 2H, CH_2N_3), 4.74 (s, 12 H, ArCH_2O), 5.0 (s, 16H, PhCH_2O), 6.52 (m, 7H, ArH), 6.62 (d, 14H, ArH), 7.23-7.40 (m, 40H, PhH).

[G-3]- NH_2 (16)

[G-3]- N_3 (15) (25.5 g, 15.8 mmol) was dissolved in dried THF (200 mL) and LiAlH_4 (4.00 g, 105 mmol) was added slowly at room temperature with constant stirring under argon. The reaction mixture was then refluxed under argon for four h. The progress of reaction was checked by TLC. To the reaction mixture, water (15 mL) was added slowly to decompose LiAlH_4 . The solution was filtered, the solid residue was washed with THF (3 x 50 mL) and combined with previous filtrate, evaporated to dryness. The solid residue was partitioned with CH_2Cl_2 and water, organic layers were dried (MgSO_4), and purified by flash chromatography eluting with CH_2Cl_2 , 5% methanol in CH_2Cl_2 with increasing solvent polarity up to 10% methanol in CH_2Cl_2 . Yield 21.00 g (84%); IR (film) 1600, 1490, 1367, 1150, 1051, 830 cm^{-1} ; ^1H NMR (CDCl_3) δ 3.76 (s, 2H, CH_2NH_2), 4.95 (s, 12 H, ArCH_2O), 5.00 (s, 16H, PhCH_2O), 6.55 (m, 7H, ArH), 6.66 (m, 14H, ArH), 7.23-7.37 (m, 40H, PhH); ^{13}C (CDCl_3) δ 33.82 (CH_2NH_2), 69.96, 69.85, 70.25 (CH_2O), 102.33, 108.33 (ArC), 127.72, 127.92, 128.40 (PhCH), 136.81, 139.96, 160.21 (Ar and PhC).

[G-4]- N_3 (17)

A mixture of [G-4]-Br (12) (23.9 g, 7.13 mmol) and NaN_3 (4.17 g, 64.21 mmol) in DMSO (100 mL) was heated to 55°C under argon, with stirring for 24 h. The reaction mixture was cooled and added to water (500 mL) and extracted with dichloromethane (4x50 mL). The combined organic layers were dried (MgSO_4), evaporated to dryness to give 17 as a glassy solid. Yield 21.8 g (92%); IR (film) 2120, 1600, 1460, 1370, 1170,

1065 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.17 (s, 2H, CH_2N_3), 4.95 (s, 28 H, ArCH_2O), 5.01 (s, 32 H, PhCH_2O), 6.50-6.63 (m, 45H, ArH), 7.21-7.37 (m, 80H, PhH).

[G-4]- NH_2 (18)

[G-4]- N_3 (17) (21.9 g, 6.60 mmol) was dissolved in dried THF (150 mL) and LiAlH_4 (1.51 g, 39.63 mmol) was added slowly at room temperature with constant stirring under argon. Next, the reaction mixture was refluxed under argon for four h. The progress of reaction was checked by TLC. To the reaction mixture, water (15 mL) was added slowly to decompose LiAlH_4 . The solution was filtered, the solid residue was washed with THF (3 x 50 mL) and combined with previous filtrate, evaporated to dryness. The solid residue was partitioned with CH_2Cl_2 and water, organic layers were dried (MgSO_4), and purified by flash chromatography eluting with CH_2Cl_2 and increasing solvent polarity up to 10% methanol in CH_2Cl_2 . Yield 17.5 g (81%); IR (film) 1606, 1496, 1367, 1150, 1051, 834 cm^{-1} ; ^1H NMR (CDCl_3) δ 3.71 (s, 2H, CH_2NH_2), 4.97 (s, 28 H, ArCH_2O), 5.01 (s, 32 H, PhCH_2O), 6.50-6.63 (m, 45 H, ArH), 7.29-7.43 (m, 80H, PhH); ^{13}C (CDCl_3) δ 33.65 (CH_2NH_2), 70.01, 70.07 (CH_2O), 101.60, 106.39 (ArC), 127.56, 127.99, 128.57 (Ph CH), 136.78, 139.22, 160.06, 160.15 (Ar and PhC).

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PART II : SYNTHESIS OF REACTIVE LINEAR POLYMERS

1. INTRODUCTION

A primary objective of this thesis was to prepare well defined reactive linear polymers with low polydispersities, and accurate control over molecular weight and chain ends. Previously these goals were only achieved by synthetically more demanding techniques such as anionic or cationic polymerizations which are incompatible with wide a range of functional groups¹. Previous attempts using free radical polymerizations were unsuccessful and produced polydisperse materials.² Recently, a number of groups^{3,4} have shown that bulk free radical polymerization of vinyl monomers, using (2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) based initiating systems, results in a living polymerization with accurate control of chain ends and molecular weight. Subsequently, living free radical procedures have been shown to be effective in synthesizing well defined graft and block copolymers with narrow polydispersities.^{3,4} To study the compatibility of reactive functional groups with typical living free radical polymerization conditions, the polymerization of two active ester containing monomer units were examined in detail. High molecular weight hybrid dendritic linear block copolymers were then prepared by coupling of these novel reactive linear polymers with the monofunctional reactive dendritic fragments described in Part I of this thesis.

2. BACKGROUND

2.1 Living polymerization

The first living polymerization was reported by Szwarc in the mid 1950s. It involved anionic polymerization of styrene and 1,3-butadiene.^{5a,b} In these living polymerizations, propagating centers do not undergo either termination or transfer reactions and a linear relationship for M_n versus conversion is obtained.^{6,7} These procedures provide a way to produce macromolecules with narrow PD and defined ends groups. Living polymerization provides a unique opportunity for the preparation of block copolymers by the sequential addition of two or more different monomers.

It has been more difficult to achieve living cationic polymerization. Both transfer and termination reactions are facile reactions in cationic systems. The major problem has been the difficulty of finding suitable reaction conditions which stabilize the reactive carbocations sufficiently to prevent transfer and termination reactions, but that still allows the propagation to occur. As both the transfer and termination reactions cannot be fully avoided, these polymerizations are quasi-living cationic and not true living cationic polymerizations.

2.2 Nitroxide-Mediated Living Free Radical Polymerizations

As described above, accurate control of polymer structure may be achieved by anionic,⁸ cationic,⁹ or ring opening polymerization techniques.¹⁰ Due to the reactivity of the propagating chain ends, these procedures have rigorous synthetic requirements and are incompatible with a wide variety of functional groups. Conversely, free radical polymerizations have less rigorous synthetic requirements but are relatively uncontrolled, typically producing polymers with polydispersities greater than 2.0. They are also

complicated by inefficient initiation, lack of molecular weight control as well as lack of control of chain ends. For example, Moad¹¹ has shown that for the benzoyl peroxide initiated polymerization of styrene, the initiation step involves the formation of at least six active species and in the final macromolecule the number of benzoyl chain ends per macromolecule varied from 1.4 to 2.3.

To overcome the above deficiencies, Hawker and coworkers¹² have developed a novel living free radical procedure utilizing TEMPO based initiators. It should be noted that while this process may not strictly obey the definition of living polymerization, it does satisfy many of the requirements, and are hence "living" or "pseudoliving" in nature. Using this technique well defined polymers with controlled molecular weights, chain ends and low polydispersities can be prepared.^{12,13}

The crucial feature of nitroxide mediated free radical polymerization is that the carbon-oxygen bond of the inactive alkoxyamine **1a**, on homolytic cleavage forms a stable nitroxide radical **1b** and the polymeric radical **1c** as shown in the Scheme I.^{13,14} This nitroxide radical does not initiate any extra chain but it does react with carbon centered free radicals. The polymeric radical **1c** can then undergo chain extension with monomer to form another polymeric radical **1d** with an increase in degree of polymerization. Recombination of **1d** with **1b** gives an inactive alkoxyamine equivalent in reactivity to **1a**, and this cycle can then be repeated.

Hawker et al.¹² synthesized a variety of TEMPO based derivatives to examine the effect of structural variation on the efficiency of these compounds as unimolecular initiators in nitroxide mediated living free radical polymerizations. For example, the effect of the α -methyl group was examined by comparison of the α -methyl benzyl initiator **4b** with the benzyl initiator **4a**.

Scheme I. Homolysis, monomer insertion and reversible combination cycle of unimolecular initiator

Pst = Polystyrene

Figure 1 shows the evolution of molecular weight with percentage conversion for the polymerization of styrene at 120 °C, in the presence of the α -methyl benzyl initiator **4b**, and the benzyl initiator **4a**. Figure 2 shows the variation of polydispersity as a function of conversion for **4b** and **4a** for the same system. As shown in the Figure 1, molecular weight evolves in a linear fashion with increasing conversion for the α -methyl benzyl initiator **4b**. This is characteristic of living polymerizations, whereas for the benzyl initiator **4a**, the molecular weight increases rapidly at low conversion and thereafter remains the same, which is a characteristic of traditional free radical polymerizations. As shown in Figure 2, the polydispersity of the polymer obtained from the benzyl initiator **4a** increases initially, reaching a value of 2.2-2.3 at higher conversion whereas the polydispersity of the polymer obtained from the α -methyl benzyl initiator **4b** decreases as the conversion increases, and reaches a constant value of 1.1-1.2 after 30% conversion. These results indicate that the stability of initiating radical affects the overall polymerization and the α -methyl group is necessary for the benzylic derivatives to act as unimolecular initiators in nitroxide mediated free radical initiator.

Figure 1. Evolution of molecular weight M_n , with percentage conversion for the polymerization of styrene using unimolecular initiators 4b ($\square$) and 4a (Δ)

Figure 2. Polydispersity of macromolecules as a function of conversion for the polymerization of styrene using unimolecular initiators 4b ($\square$) and 4a (Δ)

3. RESULTS AND DISCUSSION

The synthesis of unimolecular initiators (**4**) was carried out using Priddy and Howell's¹⁵ synthetic strategy, as shown in Scheme II. *tert*-Butyl peroxide (**2**) was added to ethylbenzene (**1**) in the presence of TEMPO (**3**) and the reaction mixture was heated at reflux under argon for sixteen h. The product was purified by flash chromatography giving **4** in 42% yield. In this reaction, the *tert*-butoxy radical abstracts a hydrogen atom from the ethyl benzene to generate the benzylic radical, which is then trapped by TEMPO to give **4**.

This living polymerization technique can be applied to reactive monomers like esters, acid chloride, amines, etc. For example, Hawker and coworkers¹⁶ carried out polymerization of 9:1 mixture of styrene and *p*-vinylbenzyl amine at 125°C in the presence of nitroxide initiator **4** to obtain linear polymers as shown in the Scheme III.

The second part of the project involved the preparation of the linear copolymers with the O-succinimide as the reactive group. The preparation of active ester monomer **12**, using 4-vinylbenzoic acid (**10**) and N-hydroxysuccinimide (NHS) (**11**) is illustrated in Scheme IV, and the similar preparation of active ester monomer **14** using acryloyl chloride (**13**) and N-hydroxysuccinimide (**11**) is illustrated in Scheme V. Active esters, **12** and **14** both were obtained in 80% yield.

In this reaction dicyclohexylcarbodi-imide (DCC) is used as a coupling agent and N,N-dimethylamino pyridine (DMAP) functions as a catalyst.¹⁷ DMAP increases the electrophilicity of carbonyl carbon and facilitates the displacement of carbodimide reagent as N,N-dicyclohexyl urea¹⁸.

Scheme II. Synthetic scheme of unimolecular initiator 4

Scheme III. Synthetic scheme of amino functionalized reactive linear polymers 7 and 9

Scheme IV. Synthetic scheme of N-oxy succinimide 4-vinylbenzoate 12

Scheme V. Synthetic scheme of N-oxy succinimide acrylate 14

To investigate the compatibility of "living" free radical polymerization with reactive functional groups the copolymerization of a 9:1 mixture of styrene (**6**), and the active ester (N-oxysuccinimide 4-vinylbenzoate) (**12**), at 125 °C in the presence of unimolecular initiator **4b** was examined. Significantly, this gave active ester functionalized reactive linear copolymers **15a,b,c,d,e** with no hydrolysis or loss of functional groups as shown in Scheme VI. The polymerization setup that was developed proved to be simple; the reaction mixture was placed in a round bottom flask with a nitrogen bubbler attached, and heated to 125 °C. In contrast, living anionic procedures require specialized glassware coupled with vacuum line techniques. The synthetic schemes leading to the formation of various linear copolymers is shown in Schemes VI, VII, VIII and IX. The molecular weights and polydispersities of the crude reactive linear polymers were improved by precipitation. The molar ratio of repeat units (styrene/active ester) and molecular weights/polydispersities for the purified reactive linear copolymers are listed in Table I. In all cases, purified yields were between 75% and 85%.

The theoretical molecular weights calculated for the linear polymers were in close agreement with the experimentally determined GPC molecular weights obtained using narrow polystyrene standards. For example, in the case of **15d**, the theoretical M_n 100,000, compares favorably with the GPC molecular weight of 93,000. This result, coupled with a polydispersity of 1.28 clearly demonstrates that reactive functional groups are compatible with living free radical polymerization and well defined polymers can be obtained.

Scheme VI. Synthetic scheme of reactive linear polymers 15 a-e

Scheme VII. Synthetic scheme of reactive linear polymer 16

Scheme VIII. Synthetic scheme of reactive linear polymer 17

Scheme IX. Synthetic scheme of reactive linear polymer 18

Table I. GPC molecular weights and polydispersities for reactive linear polymers

Compound No. ^a	Molar ratio STY/AE ^b	GPC data ^c M_n	GPCdata ^c Polydispersit y
15a	9:1	22,000	1.25
15b	9:1	30,000	1.15
15c	9:1	49,000	1.16
15d	9:1	100,000	1.28
15e	9:1	120,000	1.25
16	8:2	41,000	1.24
17	7:3	80,000	1.25
18	6:4	43,000	1.25

a) Reactive linear polymer numbers b) Molar ratio of styrene : active ester in the linear polymer c) GPC data are reported in polystyrene equivalents for reactive linear polymers

^1H NMR spectra of the active ester monomer (N-oxysuccinimide 4-vinyl benzoate) (**12**) and of the active ester functionalized reactive linear copolymer **15d** are shown in Figure 3 and Figure 4 respectively. Comparison of the two ^1H NMR spectra shows that active ester groups are incorporated in the polymer, since both **12** and **15d** contain the characteristic resonances for the active ester group at 2.9 ppm. The ^1H NMR spectrum of polymer **15d** also shows the absence of vinyl group resonances and shows the characteristic resonances for polystyrene at 1.00-2.20 ppm. The ratio of incorporation was calculated by comparison of the integration values for aromatic protons at 6.5-7.2 ppm with that of only active ester resonance at 2.9 ppm. For example, the percentage of active ester calculated from the ^1H NMR of the linear polymer **15d** was found to be 10.6% which is in good agreement with the feed stock ratio of 10%.

The infrared spectrum of reactive linear copolymer **17** also showed the presence of activated ester groups as shown in Figure 5. The strong bands at 1781 cm^{-1} and 1812 cm^{-1} are characteristic of the carbonyl stretch of the succinimide carbonyls and the strong bands at 1760 cm^{-1} are due to carbonyl stretch of the ester group which is shifted to higher frequency than the normal carbonyl stretch of the ester due to the electron withdrawing succinimide group.¹⁹ Also, bands at 1605 and 1491 cm^{-1} are due to aromatic ring stretch absorptions. A strong out of plane C-H bending vibrations at 844 cm^{-1} indicates the presence of *p*-disubstituted ring whereas two bands at 700 and 750 cm^{-1} indicates the monosubstituted ring of the styrene units. These features are fully consistent with the expected structure and clearly demonstrate the validity of this novel approach to the synthesis of reactive linear polymers.

Figure 3. ^1H NMR spectra of N-oxy succinimide 4-vinylbenzoate 12

Figure 4. ^1H NMR spectra of linear copolymer 15

Figure 5. Infrared spectra of linear polymers 17

Figure 6. Infrared spectra of linear polymers 18

Also, comparison of the infrared spectra of the benzoate linear polymers **17** (Figure 5) with the acrylate linear polymer **18** (Figure 6), shows that the C=O stretch of the ester in **18** is shifted unexpectedly to lower frequency band (1737 cm^{-1}) when compared to the linear polymer **17** (1781 cm^{-1}). Actually, unlike **17** the carbonyl group of ester in **18** is not in the conjugation with aromatic ring so the C=O stretch of the ester in **18** is expected at higher frequency but unexpectedly this was not observed. The glass transition temperatures for all the copolymers prepared in this study were between 95 and 100°C .

In summary, the new technique of living free radical polymerization is an extremely reliable method for the synthesis of reactive linear polymers with a high degree of control both in terms of molecular weight as well as polydispersity (Table I). Complete structural identification was obtained by a variety of spectroscopic techniques which clearly demonstrates the stability of reactive groups, such as activated esters, under typical nitroxide mediated conditions.

4. CONCLUSION

Living free radical polymerization technique is an efficient procedure for synthesizing reactive linear polymers. Compared to living cationic or anionic techniques, which demand pure reagents and solvents to exclude oxygen and water and, this is a better technique, and is compatible with a variety of functional groups. In a single step, using a simple experimental setup, a reactive linear polymer with low polydispersity can be easily prepared. The main advantage is that we can accurately control the molecular weight of the polymer by controlling the molar ratio of monomer to the initiator.

5. EXPERIMENTAL

1-Phenyl-1-(2', 2', 6', 6'-tetramethyl-1'-piperidinyloxy)ethane (4b)

To ethylbenzene (100 mL) was added di-tert-butyl peroxide (5.00 g, 33.0 mmol) followed by TEMPO (10.5 g, 66.0 mmol). The reaction mixture was heated at reflux under argon for 16 h and evaporated to dryness. The crude product was purified by flash chromatography eluting with hexane and slowly increasing to 1:1 hexane/dichloromethane. The TEMPO derivative **4b**, was obtained as a crystalline white solid which could be recrystallized from cold ethanol. Yield 7.2 g (42%); mp 46-47 °C; IR (neat) 2950, 1490, 1390, 1375, 1040 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.64, 1.05, 1.16, 1.36 (each br s, 12H), 1.23-1.58 (m, 6H), 1.44 (d, $J = 7$ Hz, 3H), 4.76 (q, $J = 7$ Hz, 1H), 7.25-7.35 (m, 5H).

N-oxysuccinimide 4-vinylbenzoate (12)

To a solution of carboxylic acid **10** (5.00 g, 33.7 mmol) in dry tetrahydrofuran was added N-hydroxysuccinimide (**11**) (4.27 g, 37.1 mmol), dicyclohexylcarbodiimide (7.66 g, 37.1 mmol) and 4-dimethylaminopyridine (412 mg, 3.38 mmol). The solution was stirred at room temperature under argon for 3 h. The urea which was formed was separated by gravity filtration and the filtrate evaporated to dryness. The crude product was purified by flash chromatography, eluting with 1:1 petroleum ether/ CH_2Cl_2 , CH_2Cl_2 , and finally 5-10% ether in CH_2Cl_2 . The pure yield after flash chromatography was 6.50 g (80%). ^1H NMR (CDCl_3) δ 2.9 (s, 4H), 5.42 (dd, H_a , $J_{\text{cis}} = 10$ Hz, $J_{\text{gem}} = 1$ Hz), 5.89 (dd, H_b , $J_{\text{trans}} = 18$ Hz, $J_{\text{gem}} = 1$ Hz), 6.61 (dd, H_c , $J_{\text{trans}} = 18$ Hz, $J_{\text{cis}} = 10$ Hz), 7.8 (d, 2H, $J = 7$ Hz), 8.04 (d, 2H, $J = 7$ Hz); IR (film) 1770, 1744, 1605, 995, 839 cm^{-1} .

N-oxy succinimide acrylate (14)

To a solution of acryloyl chloride (**13**) (5.00 g, 55.2 mmol) in dry tetrahydrofuran was added N-hydroxysuccinimide (**11**) (6.98 g, 60.7 mmol), and 4-dimethylaminopyridine (674 mg, 5.52 mmol). The solution was stirred at room temperature under argon for 3 h. The crude product was purified by flash chromatography, eluting with 1:1 petroleum ether/CH₂Cl₂, CH₂Cl₂, and finally 5-10% ether in CH₂Cl₂. The pure yield after flash chromatography was 7.50 g (80%); ¹H NMR (CDCl₃) δ 2.84 (s, 4H), 6.16 (dd, H_a, J_{cis} = 11 Hz, J_{gem} = 1 Hz), 6.30 (dd, H_b, J_{trans} = 17 Hz, J_{gem} = 1 Hz), 6.64 (dd, H_c, J_{trans} = 17 Hz, J_{cis} = 11 Hz); IR (film) 1772, 1738, 1630, 995, 900 cm⁻¹.

General procedures for copolymerization

Polymerization of 12 and 6 to 15d (9:1 Copolymer of 12 with styrene 6)

A mixture of the initiator **4b** (28.0 mg, 0.106 mmol) and active ester (**12**) (2.45 g, 10 mmol) were dissolved in styrene (**6**) (10.0 g, 96 mmol) and the reaction mixture heated at 125°C for 74 h. The viscous reaction mixture was cooled to room temperature, dissolved in dichloromethane (30 mL) and precipitated in methanol (800 mL) to give the reactive linear random copolymer **15d** as a white solid. The low molecular weight impurities were removed by the dropwise addition of isopropyl alcohol (170 mL) to **15d** dissolved in acetone (500 mL). Yield 9.90 g (79%); M_n = 100K, PD = 1.20; ¹H NMR (CDCl₃) δ 1.2-2.1 (m, 30H), 2.9 (s, 4H), 6.4-7.2 (m, 49H).

Polymerization of 12 and 6 to 16 (8:2 Copolymer of 12 with styrene 6)

A mixture of the initiator **4b** (50 mg, 0.19 mmol), active ester **12** (2.45 g, 10 mmol) were dissolved in styrene **6** (5.00 g, 48 mmol) and the reaction mixture heated at 125 °C for 6 h. The viscous reaction mixture was cooled to room temperature, dissolved in dichloromethane (30 mL) and precipitated in methanol (800 mL) to give the reactive

linear random copolymer **16** as a white solid. Fractional precipitation of the product **16** was done by dissolving it in acetone followed by the dropwise addition of isopropyl alcohol. Yield 6.00 g (76%); $M_n = 41K$, PD = 1.20; 1H NMR ($CDCl_3$) δ 1.2-2.1 (m, 30H), 2.9 (s, 4H), 6.4-7.2 (m, 48H).

Polymerization of 12 and 6 to 17 (7:3 Copolymer of 12 with styrene 6)

A mixture of the initiator **4b** (47 mg, 0.181 mmol), active ester **12** (10.0 g, 40.8 mmol) were dissolved in styrene **6** (10.4 g, 95.2 mmol) and the reaction mixture heated at 125°C for 6 h. The viscous reaction mixture was cooled to room temperature, dissolved in dichloromethane (30 mL) and precipitated in methanol (800 mL) to give reactive linear random copolymer **17** as a white solid. Fractional precipitation of the product **17** was done by dissolving in acetone followed by the dropwise addition of isopropyl alcohol. Yield 17.0 g (81%); $M_n = 80,000$, PD = 1.25; 1H NMR ($CDCl_3$) δ 1.2-2.1 (m, 30H), 2.9 (s, 4H), 6.4-7.2 (m, 47H).

Polymerization of 14 and 6 to 18 (6:4 Copolymer of 14 with styrene 6)

A mixture of the initiator **4b** (65 mg, 0.247 mmol), active ester **14** (12.5 g, 74 mmol) were dissolved in styrene **6** (11.9 g, 111 mmol) and the reaction mixture heated at 125°C for 6 h. The viscous reaction mixture was cooled to room temperature, dissolved in dichloromethane (30 mL) and precipitated in methanol (800 mL) to give reactive linear random copolymer **18** as a white solid. Fractional precipitation of the product **18** was done by dissolving in acetone followed by the dropwise addition of isopropyl alcohol to it. Yield 21.0 g (83%); $M_n = 43K$, PD = 1.25; 1H NMR ($CDCl_3$) δ 1.2-2.1 (m, 30H), 2.9 (s, 4H), 6.4-7.2 (m, 30H).

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PART III : SYNTHESIS OF HYBRID-DENDRITIC LINEAR BLOCK COPOLYMERS

1. INTRODUCTION

High molecular weight hybrid dendritic linear block copolymers were prepared by the coupling of the reactive linear polymers with monofunctional reactive dendrimers. These dendritic fragments (dendrons) were prepared as described in Part I using the convergent growth approach and the reactive linear polymers were prepared by a novel method as described in Part II.

To gain insight into the steric environment of the linear backbone, as well as the dendritic fragment, a detailed examination of the effect of dendrimer size and level of functionalization on the extent of dendrimer incorporation was undertaken. These hybrid products were fully characterized by various spectroscopic and chromatographic techniques.

2. BACKGROUND

A large number of different approaches to the preparation of hybrid dendritic-linear copolymers have been reported in the literature.¹ For example, Hawker et al² carried out the reaction of the fourth generation alcohol, [G-4]-OH, with p-chloromethyl styrene to form a dendritic macromonomer with a single styrene unit at the focal point. Polymerization with styrene unit using traditional free radical techniques produced a hybrid block copolymer in which globular dendritic blocks were grafted on a polystyrene backbone. However, the products obtained were polydisperse and the incorporation of the dendrimer was relatively low. In another example, Frechet used the dendritic fragment, [G-4]-OH, as a macroinitiator for the anionic ring opening polymerization of caprolactone to form hybrid linear-globular AB block copolymers.³ Again, the weight percentage of dendrimer incorporated was very low.

Recently, Karakaya and coworkers⁴ carried out the dendrimerization of hydroxyethyl-substituted poly(para-phenylene). They synthesized the first and second generation Frechet-Hawker type dendrons (dendritic fragments) with isocyanate functional group at the focal point and coupled these with hydroxyethyl-substituted poly(para-phenylene) in refluxing toluene. The purification of the product was done by standard precipitation techniques with substantial loss of polymer. While the incorporation was relatively high in this case, the product obtained was extremely ill-defined and had large polydispersity (5-10).

A large number of researchers in the field have prepared various block copolymers with unusual properties. For example, Gitsov and coworkers,^{5,6,7} prepared AB diblock, and ABA triblock structures having dendritic block, [G-4]-Br, as A block and linear polyethylene glycol as a B block. Both types of hybrid materials are amphiphilic and possess surfactant like properties.

Initially, we examined the synthesis of hybrid dendritic linear macromolecules via Hawker et al's macromonomer synthetic strategy,² using living free radical procedures. However while the samples were well defined with controlled molecular weights and low polydispersities, the incorporation of dendrimer was low due to the bulk polymerization conditions. To overcome these difficulties an efficient synthetic strategy for the preparation of low polydispersity hybrid copolymers with high incorporation of the dendritic portion was examined.

Therefore a novel approach⁸ was developed in which active ester functionalized linear copolymers were coupled with amino functionalized second, third, fourth and fifth generation dendrons in refluxing chloroform to produce the desired hybrid macromolecules.

In both approaches, living free radical procedure were employed to control the growth of the linear backbone. In the first case, copolymerization of a dendritic acrylate with styrene formed the hybrid structure, and in the second case, linear copolymers with active ester functionality were first prepared and then coupled with dendritic fragments to give well defined hybrid dendritic structures. The advantage of the latter method is that a predetermined number of active ester groups can be attached to the linear backbone and thereby accurately control the molecular weight of the hybrid, while also obtaining high loading levels.

3. RESULTS AND DISCUSSION

3.1 Dendritic macromonomer approach

One of the important goals of polymer chemistry is to synthesize polymers with controlled architecture. This goal can be done by formation of graft and star polymers and subsequent polymerization of macromonomers. Recently, Frechet and Hawker developed a new approach to hybrid dendritic linear copolymers in which dendritic macromonomers are prepared via a convergent growth approach in which a polymerizable group is attached at the focal point of dendron.² Subsequent copolymerization of this macromonomer with styrene gives the desired dendritic macromolecules. This approach is unique as this type of chemistry is not available to dendritic macromolecules produced by divergent synthetic methods.

In the convergent growth approach, there is a single functional group at the focal point of the dendron. This presents a unique point for modification and subsequent reaction. Therefore, a dendritic macromonomer, [G-3]acrylate (**3**) was formed, as shown in Scheme I, by attaching a polymerizable group at the focal point of dendron [G-3]-OH. The synthesis of this macromonomer was carried out by using [G-3]-OH (**1**) and acryloyl chloride (**2**). The reaction involves the nucleophilic displacement of chloride ion by dendritic alcoholate (alkoxide generated from [G-3]-OH). ¹H NMR, ¹³C NMR and IR were important tools to investigate the incorporation of acrylate unit at the focal point group. On comparison of the ¹H NMR spectra of [G-3]-OH (**1**) and [G-3]-acrylate (**3**), the latter shows a new vinyl resonance in the range 5.78-6.18 ppm. Also the resonance for the hydroxymethyl group has disappeared and is replaced by a small peak at 5.09 ppm for the focal point CH₂ group of [G-3]-acrylate.

The GPC analysis of macromonomer showed a single narrow peak while examination of the ¹³C NMR spectrum showed a resonance at 70.1 ppm for the

Scheme I Synthesis of [G-3]-acrylate

Scheme II Copolymerization of [G-3]-acrylate 3 with styrene 4

methylene carbon attached to the acrylate group as well as resonances for the vinyl group.

The synthetic scheme leading to the formation of the hybrid **6** via living polymerization of the dendritic acrylate **3** with styrene (**4**) is shown in Scheme II. The polymerization was carried out using a simple setup. The required quantities of the initiator, macromonomer (**3**), and styrene (**4**) were placed in a round bottom flask with a nitrogen bubbler attached and heated at 125 °C. The composition of the copolymer was determined by ^1H NMR. Integration of the resonances for the ArCH_2O group at 5.0 ppm of the dendrimer and comparison with the aromatic and aliphatic resonances of the polystyrene backbone gave the relative styrene to dendrimer composition. From the ^1H NMR the percentage of [G-3]-acrylate was found to be 10.1% (weight %) which is in good agreement with the feed ratio of 10% (weight %). Also, the GPC of **6** did not show any indication of the starting material. However all the attempts failed to increase the weight percentage of dendrimer in the hybrid structure above 40%. Only low molecular weight, low conversion materials were obtained.

3.2 Coupling strategy for hybrid dendritic linear block copolymers

The preparation of hybrid macromolecules with linear and dendritic blocks was then examined using a coupling strategy. In this approach, the hybrid macromolecules were produced using simple amide bond formation chemistry. This coupling chemistry was chosen due to the high yields, mild reaction conditions, and short reaction time associated with it. Having prepared both the sets of reactive polymers, (amino functionalized dendritic wedges and linear polymers as described in Parts I and II), the synthesis of hybrid dendritic block copolymers was achieved as shown in Scheme III and Scheme IV.

For example, a mixture of the linear polymers **7a** was refluxed with 1.5 equivalents of [G-3]- NH_2 in chloroform for 24 hours, which gave hybrid polymer **15a** in

Scheme III Synthetic scheme of hybrid polymers 9a-13a

7a, b, c, d, e

9a, 10a, 11a, 12a, 13a

Scheme IV Synthetic scheme of hybrid polymers 9b-13b

7a, b, c, d, e

9b, 10b, 11b, 12b, 13b

equivalents of [G-3]-NH₂ in chloroform for 24 hours, which gave hybrid polymer 15a in 70% yield. The fractional precipitation of hybrid product 15a was performed by first dissolving it in dichloromethane/acetone solution followed by the dropwise addition of isopropyl alcohol, a solvent in which 15a is very insoluble. This procedure removed the excess of dendrimer from the hybrid product and improved the purity of the product. Using the same approach, various hybrid materials were prepared using second, third, fourth and fifth generation dendritic amines as shown in Table I.

Based on these results, the combination of dendrimer chemistry with living free radical procedures is an extremely reliable technique for the preparation of large macromolecules. A high degree of control, in terms of molecular weights and polydispersity, can be achieved. Molecular weights/polydispersities for the purified hybrid products and the corresponding amino dendrons are listed in Table I. In all the cases, purified yields were between 60-80%.

The structure of these unique hybrid macromolecules was confirmed by a variety of spectroscopic techniques. For example, ¹H NMR of hybrid 9a as shown in Figure 1c, shows characteristic resonances for both the dendritic portions derived from [G-3]-NH₂ as well as the linear backbone. The resonance at 5.0 ppm is due to the dendritic fragment and the resonance at 1.0-2.2 ppm is due to the linear polystyrene backbone. Since the hybrid macromolecules have unique resonances for both the dendritic appendages and the linear backbone, the weight ratio and molar ratio of the linear and dendrimer portions can be accurately determined. Complementary information was obtained from the ¹³C NMR spectrum. GPC was found to be extremely useful in determining the purity of the hybrid macromolecules as well as to follow the course of reaction since there is a dramatic weight difference between the starting materials and the hybrid product (Figure 2).

Table I. SEC molecular weights, polydispersities, weight percentages, and glass transition temperatures

for the hybrid polymers

No. ^a	GPC-data ^b	No. ^c	GPC-data ^d	M theor. ^e	Wt% dendrimer ^f	Tg ^g
	Mn PD		Mn PD			
9a	22,000 1.25	[G-3]	36,000 1.13	52,000	59	69
9b	22,000 1.25	[G-4]	40,000 1.12	82,000	75	62
10a	30,000 1.15	[G-3]	51,000 1.11	70,000	62	72
10b	30,000 1.15	[G-4]	60,000 1.10	110,000	76	63
11a	49,000 1.16	[G-3]	71,000 1.14	86,000	48	74
11b	49,000 1.16	[G-4]	83,000 1.13	159,000	71	59
12a	100,000 1.28	[G-3]	160,000 1.20	323,000	63	69
12b	100,000 1.28	[G-4]	196,000 1.20	357,000	77	61
13a	120,000 1.34	[G-3]	212,000 1.21	282,000	63	68
13b	120,000 1.34	[G-4]	258,000 1.20	454,000	78	59

Table I

No. ^a	GPC-data ^b Mn PD	No. ^c	GPC-data ^d Mn PD	M theor. ^e	Wt% dendrimer ^f	Tg ^g
14a	41,000 1.24	[G-3]	74,000 1.16	134,000	78	61
14b	41,000 1.24	[G-4]	83,000 1.17	161,000	81	57
15a	80,000 1.25	[G-2]	145,000 1.40	184,000	67	70
15b	80,000 1.25	[G-3]	180,000 1.32	324,000	81	56
15c	80,000 1.25	[G-4]	215,000 1.30	604,000	93	56
15d	80,000 1.25	[G-5]	240,000 1.46	1163,000	91	56
16a	43,000 1.25	[G-2]	90,000 1.37	126,000	78	57
16b	43,000 1.25	[G-3]	135,000 1.40	238,000	88	51
16c	43,000 1.25	[G-4]	154,000 1.50	462,000	87	56

a) Hybrid polymer numbers b) GPC data are reported in polystyrene equivalents for reactive linear polymers c) Generation numbers of amino dendrons d) GPC data are reported in polystyrene equivalents for hybrid dendritic linear copolymers e) Theoretical molecular weight calculated from the composition of dendrimer and styrene determined by ¹H NMR. f) Weight % of dendrimer determined from ¹H NMR g) Glass transition temperature, Tg (°C)

Figure 1. ^1H NMR spectra of a) [G-3]- NH_2 b) Reactive linear polymer 7a
c) Hybrid polymer 9a

Figure 2. Size exclusion chromatograph of a) Dendrimer, b) Reactive linear polymer, c) Hybrid polymer

Examination of Table I shows that polystyrene equivalent molecular weight increases from 120K for linear polymer **7e** (prepared in Part II) to 250K for the hybrid **13b**, while the polydispersity remains the same. There is a dramatic difference between polystyrene equivalent molecular weight of 250K and the actual molecular weight of 450K. This dramatic weight difference suggests substantial increase in the three dimensional character of the hybrid polymer when compared to linear analogs. However, the difference can be rationalized when it is taken into account that the hybrid **13b** contains 78% dendrimer by weight.

The glass transition temperatures were determined as the inflexion points on the second heating. For the different generation dendritic fragments the glass transition temperatures were found to be around 40°C and were independent of the molecular weight (Table I). Similarly the glass transition temperatures for all the linear polymers were found to be 100°C. Therefore, using the standard Fox equation and the weight fraction of dendrimer and linear polymer as determined from ¹H NMR, theoretical glass transition temperatures for the hybrid dendritic linear macromolecules were determined. These glass transition temperatures were found to be in close agreement with the experimentally determined values. For example, the calculated value for the T_g of hybrid **9a** as determined by the Fox equation is 63°C compares favorably with the experimental value of 69°C as shown in Figure 3.

The ¹H NMR spectra of the hybrid block copolymers (Table I) based on starting linear polymer:dendron ratio of 9:1, do not show the resonance for the active ester group at 2.9 ppm. This indicates that at this functionalization ratio, complete substitution of active ester group with reactive dendrimers occurs. It was found that increasing the molecular weight of the linear backbone while maintaining the same dendrimer size, as can be seen in case of **13a**, **14a**, and **15b**, did not result in any decrease in the level of

Figure 3. DSC heating curves, a) Dendrimer b) Reactive linear polymer c) Hybrid polymer

incorporation.

However, in each case a dramatic weight difference was observed when the actual molecular weight, calculated from the compositions obtained by ^1H NMR spectroscopy, was compared with the one obtained from GPC. Increasing the ratio of functionalization from 9:1 to 8:2 was also found to result in complete dendrimer incorporation. As the intent was to get information about the extent of dendrimer incorporation on the linear backbone, the various amino terminated dendrons were attached to the same linear backbone. As can be seen in the case of **16 a, b, and c**, hybrids with the acrylate linear copolymers, the molar ratio of styrene to dendritic acrylate fragment was 6:4.

In the case of **16 a, b, and c**, a lower percentage of dendrimer incorporation on the linear backbone was observed, i.e. hybrid formation involved the displacements of fewer active ester groups. Therefore, a lower weight percentage of dendrimer incorporation was observed. Interestingly, ^1H NMR did not show the presence of unreacted active ester. This observation can be rationalized if we assume that unsubstituted active ester groups present in the vicinity of the amide NH may have been replaced in an intramolecular cyclization reaction forming a stable six membered ring. The molar ratio of styrene to dendritic acrylate fragment in **16a, b, and c**, was 6:4. Thus, there is steric crowding of the dendritic units around the linear polystyrene backbone, therefore only a fraction of the active esters may be available for substitution. The rest of the active esters must have been replaced via intramolecular cyclization. This cyclic imide formation is also confirmed by observing the infrared spectrum⁹ of **16c** (Figure 4), which clearly indicates the presence of a cyclic imide band at 1667 cm^{-1} .

A 7:3 ratio of functionalization resulted in no decrease in dendrimer incorporation for the dendrimer size of up to fourth generation, but a slight decrease in dendrimer incorporation was observed for the fifth generation dendron. This decrease may be

attributed to the large size of the fifth generation dendron (steric effect). A 6:4 ratio of functionalization (in the case of acrylates), resulted in a decrease in dendrimer incorporation which was again presumably due to the formation of stable six membered rings by intramolecular reactions.

Infrared spectra of the hybrids (excluding **16a**, **b**, and **c**) consistently showed amide I and amide II bands⁹ for secondary amides. For example, the infrared spectrum of hybrid polymer **15a** showed amide I and amide II bands at 1655cm^{-1} and 1528 cm^{-1} respectively as shown in the Figure 5. Bands at 1156cm^{-1} and 1049 cm^{-1} can be attributed to asymmetric and symmetric C-O-C stretching vibrations (from the dendritic fragment). Also, bands at 1596 and 1494 cm^{-1} are due to aromatic ring stretch absorptions. Strong out-of-plane C-H bending vibrations at 829 cm^{-1} indicate the presence of *p*-disubstituted rings whereas two bands at 697 and 741 cm^{-1} shows presence of monosubstituted rings. In summary, the presence of secondary amide groups, aryl alkyl ether groups, mono and disubstituted phenyl groups are apparent.

Figure 4. Infrared spectrum of hybrid 16c

Figure 5. Infrared spectrum of hybrid 15a

4. CONCLUSION

We have demonstrated that living free radical polymerization is an efficient procedure for synthesizing reactive linear polymers, and also the hybrid dendritic linear block copolymers derived from them. Analysis of hybrid product further indicates that dendritic wedges can be efficiently incorporated into the linear backbone. The hybrid dendritic linear block copolymers with very high molecular weights can be prepared in a small number of steps with controlled molecular weight. It is easy to fully characterize these materials by various spectroscopic and chromatographic techniques.

5. EXPERIMENTAL

Preparation of [G-3]-acrylate (3) (dendritic macromonomer)

To a solution of [G-3]-OH (1) (8.00 g, 5.03 mmol) and acryloyl chloride (2) (1.37 g; 15.1 mmol) in dry THF (100 mL) under argon was added dropwise a solution of DMAP (306.5 mg, 2.51 mmol) and pyridine (596 mg, 7.55 mmol) in dry THF (20 mL). The solution was stirred at room temperature under argon for 4 h. The progress of the reaction was checked by TLC. The reaction mixture was evaporated to dryness. The product was partitioned between dichloromethane and water and the aqueous layer extracted with CH_2Cl_2 (3x). The combined organic layers were dried and evaporated to dryness under reduced pressure. The product was purified by flash chromatography. The yield after flash chromatography was 6.8 g (82%); ^1H NMR (CDCl_3) δ 4.93 (s, 14H), 5.0 (s, 16H), 5.77 (dd, H_a , $J_{\text{cis}} = 8$ Hz, $J_{\text{gem}} = 1$ Hz), 5.82 (dd, H_b , $J_{\text{trans}} = 18$ Hz, $J_{\text{gem}} = 1$ Hz), 6.17 (dd, H_c , $J_{\text{trans}} = 18$ Hz, $J_{\text{cis}} = 8$ Hz), 6.53-6.54 (m, 21H), 7.24-7.39 (m, 40H); IR (film) 3060, 2950, 1718, 1600, 1460, 1245, 1165, 1030, 995, 700 cm^{-1} .

Polymerization of dendritic macromonomer (3) with styrene (4)

The copolymerization was carried out as described below for a 1:10 mixture (by weight) of [G-3]-acrylate 3 with styrene 4.

To the third generation macromonomer 3 (500 mg, 0.304 mmol) was added styrene (4) (5.00 g, 48.1 mmol), initiator 5 (63 mg, 0.242 mmol, 0.5 mol%) and the solution heated at 130 $^\circ\text{C}$ under argon for 48 h. The reaction mixture was then precipitated into methanol. Yield 4.4 g (80%); ^1H NMR (CDCl_3) δ 1.25-2.1 (br, backbone CH_2 and CH , 477H), 4.93 (s, $\text{Ar-CH}_2\text{O}$, 14H), 5.0 (s, 16 H, PhCH_2O), 6.3-7.2 (br m, ArH , 851H); IR (film) 3030, 2950, 1730, 1600, 1460, 1165, 1030, 700 cm^{-1} .

General Procedure for hybrid dendritic linear block copolymers

A mixture of active ester **7a** (1.0 g, 0.85 mmol, 1.00 equiv), [G-3]-NH₂, (1.62 g, 1.02 mmol, 1.2 equiv), and chloroform (30 mL) was refluxed under argon for 24 h. The reaction mixture was evaporated to dryness. The molecular weight and polydispersity of the crude polymers were improved by employing fractional precipitation techniques. The products were dissolved in CH₂Cl₂/acetone. Then isopropyl alcohol was added dropwise. This procedure removed the lower molecular weight dendrimer. The hybrid **9a** was obtained as a white powder. Yield 1.58 g (70%); ¹H NMR (CDCl₃) δ 1.2-2.1 (m, 30H), 4.9 (s, 4H), 6.5-7.2 (m, 110H).

Using the same procedure all the hybrid compounds described in the Table I were prepared.

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