Synthesis and Properties of Novel Linear–Dendritic Block Copolymers. Reactivity of Dendritic Macromolecules toward Linear Polymers

Ivan Gitsov, Karen L. Wooley, Craig J. Hawker, Pavlina T. Ivanova, and Jean M. J. Fréchet*

Baker Laboratory, Department of Chemistry, Cornell University, Ithaca, New York 14853-1301

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ABSTRACT: The reactivity of benzylic dendritic polyethers toward linear polymers was investigated using coupling reactions of preformed dendritic and linear blocks in solution and in the melt. It was found that the rate constants for the Williamson reaction of poly(ethylene oxide)s (PEO) or poly(ethylene glycol)s (PEG) with dendritic bromides of various sizes increased with the length of the linear block and the generation of the dendrimer. This anomalous behavior is attributed to the increased reactivity of the PEO and PEG alcoholate anions due to the solvation of the counterion by the linear block and to the conformation changes occurring after attachment of the first dendritic block to PEG. It was shown that the functional group at the "focal point" of the dendrimer preserves its accessibility and reactivity even in highly restrictive medium and is able to participate in transesterification reactions with PEO and PEG in the melt. Thus, block copolymers that differ by a single linking bond between the linear and dendritic blocks were formed.

Introduction

Interactions of linear macromolecules with reactive groups within organized and restricted media play an important role in many processes in nature. The increasing availability of dendrimers with different chemical composition and architecture that might mimic certain features of biological substances makes the modeling of such processes possible.[1] The two basic strategies employed for the synthesis of these compounds start the construction of the dendritic macromolecules from the center[2] ("starburst", or divergent growth) or from the periphery or chain ends[3] (convergent growth). One of the characteristics of the "convergent-growth" approach is that it produces dendrimers with a single functional group at their "focal point". This group may react further, enabling the formation of higher generations, or it may be used in the preparation of other compounds with unique architectures. The key requirement for the success of this synthetic path is the preservation of the reactivity of the focal-point group, in spite of the growing steric hindrance around it. In his classical book, Flory stated that the reactivity of a functional group placed in a polymer chain should be independent of the chain length.[4] However, he also concluded that under certain conditions (e.g., large macromolecules and dilute solutions), the terminal groups might be shielded by the chain coil and thus their reactivity would be hampered.[5] This assumption fostered the theory of the "excluded kinetic volume effect" and led to numerous studies, some supporting and some denying its existence.[6-9]

In light of the above it appears likely that difficulties may be encountered both in the convergent growth of dendrimers at high generation numbers and in the reaction of dendrimers with high molecular weight reagents. Indeed, during convergent growth, the dendrimer yields tend to decrease with increasing generation.[3] However, the functional groups placed at the focal point of dendrimers still appear to retain their accessibility and reactivity even in high generations as confirmed by chemical modifications of the functional groups at the focal point.[3,10]

Surprisingly, our investigations have also shown that, in spite of the steric hindrance, unique linear–dendritic block copolymers could be easily formed in high yields even by reaction of dendritic bromides with anions of linear high polymers.[11,12] This type of reaction is quite interesting, from both theoretical and practical points of view since it can serve as a suitable model for reactions occurring in highly restricted media (excluded volume effect) while also providing access to totally novel molecular architectures that may exhibit unique properties. In this study, the quantitative evaluation of the reactivity of the functional group at the focal point is gained by tracing the influence of the size of dendrimer on its reactivity toward the linear polymers of different chain length under both mild and highly restrictive conditions (in solution and in the melt, respectively).

Experimental Section

Materials. PEGs with nominal molecular weights between 1000 and 20000 and narrow molecular weight distributions were purchased from Scientific Polymer Products, Inc. PEOs with molecular weights 4000 and 5000 were synthesized in our laboratories via living anionic polymerization of ethylene oxide initiated by (diphenylmethyl)potassium.[13] The other PEOs were purchased from Millipore Corp. (Waters Chromatography Division). The molecular weight characteristics of the polymers used are summarized in Table I. All PEGs and PEOs were dried by azeotropic distillation of benzene before use. Tetrahydrofuran (THF) (Aldrich) was dried by benzophenone–potassium under nitrogen and transferred to the reaction flask prior to use. Sodium hydride (NaH, dry, 95%), dibutyltin diacetate ($Bu_2Sn(OAc)_2$), titanium(IV) butoxide ($Ti(OBu)_4$), and cobalt(II) acetate tetrahydrate ($Co(OAc)_2 \cdot 4H_2O$—all from Aldrich—were used without further purification. The dendritic bromides of first up to fourth generation, [G-1]–Br to [G-4]–Br, were synthesized as described in ref 3a.

Methods. Size exclusion chromatography (SEC) analyses were performed on a Nicolet LC/9560 liquid chromatograph using as the mobile phase THF at 40 °C or methanol/water (1:1 v/v) at 30 °C and nominal flow rates of 1 mL/min. The separations were achieved across a bank of three 5-μm PL Gel columns with porosities 500 Å, 1000 Å, and Mixed C in THF and two Waters/Shodex Protein KW 802.5 and 804 columns for the aqueous SEC measurements. ^1H NMR spectra were recorded at room temperature on solutions in $CDCl_3$ on a Bruker WM 300 (300 MHz) spectrometer, the solvent proton signal being used as a standard.

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Table I. Molecular Weight Characteristics of PEGs and PEOs

designation	M_w[a]	M_w/M_n[a]	M_w[b]	M_w/M_n[b]
PEG1100	1060	1.01	1050	1.03
PEG2000	2064	1.05	2400	1.03
PEG5000	5000	1.05	5300	1.01
PEG11000	10900	1.19	10700	1.04
PEG20000	19700	1.34	19700	1.11
PEO1200[c]	1200		1100	1.15
PEO4000			3900	1.04
PEO5000			5200	1.03
PEO26000	26000	1.20	21400	1.01
PEO46000	46000	1.10	38300	1.01

[a] Value supplied by the vendor. [b] Value determined by aqueous SEC with PEG and PEO standards. [c] PEO1200 is poly(ethylene glycol) monolauryl ether: $C_{12}H_{25}$-$(OCH_2CH_2)_{23}$-OH commercially available from Aldrich as Brij 35.

Table II. Pseudo-First-Order Rate Constants for the Williamson Reaction of PEOs with Dendritic Bromide [G-4]-Br

PEO mol wt	k_1 (h^{-1})
1900	0.36[a]
3900	0.84 ± 0.01
5200	1.06 ± 0.02
26000	1.22 ± 0.03
46000	1.36 ± 0.02

[a] Rate constant for the reaction of PEG1900 monomethyl ether with *n*-octyl bromide.[15]

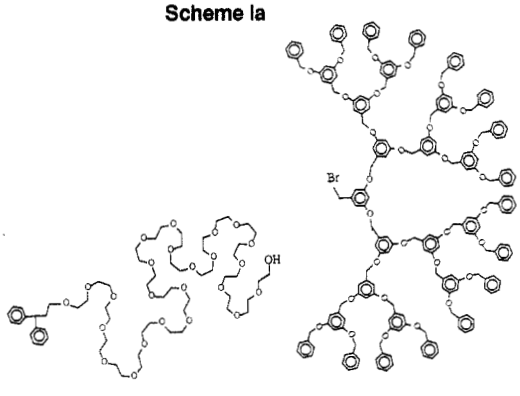
^{13}C NMR spectra were recorded on the same instrument at 75 MHz with the use of $CDCl_3$ as the solvent and the solvent carbon signal as an internal standard. Infrared spectra were recorded on a Nicolet IR/44 spectrophotometer as thin films on NaCl disks. The thermal characteristics of each sample were measured by differential scanning calorimetry using a Mettler DSC 30 low-temperature cell coupled to a TC10A TA processor. Heating rates were 10 °C/min. T_g and T_m were taken as the midpoints of the inflection tangents.

[G-3]-CO_2Me (1). A mixture of [G-2]-Br (**2**) (2.50 g, 3.09 mmol), methyl 3,5-dihydroxybenzoate (**3**) (0.25 g, 1.49 mmol), potassium carbonate (0.45 g, 3.3 mmol), and 18-crown-6 (0.08 g, 0.30 mmol) in acetone (50 mL) was stirred vigorously and heated at reflux under nitrogen for 16 h. The solvent was then removed under reduced pressure, and the residue was partitioned between dichloromethane (50 mL) and water (50 mL). The aqueous layer was extracted with dichloromethane (3 × 50 mL), and the combined organic layers were dried over $MgSO_4$ and evaporated to dryness under reduced pressure. The crude product was purified by flash chromatography, eluting with 5% hexanes/dichloromethane to give **1** as a colorless glass: yield 88%; IR 3050, 2920, 2870, 1720, 1595, 1497, 1450, 1375, 1344, 1321, 1298, 1157, 1051 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.89 (s, 3 H, CO_2CH_3), 4.97, 4.99, and 5.02 (each s, 28 H, Ar and $PhCH_2O$), 6.55–6.58 (m, 6 H, Ar*H* of monomer units), 6.67–6.69 (m, 13 H, Ar*H* of monomer units), 6.80 (t, 2 H, J = 2 Hz, Ar*H* of monomer unit), 7.2–7.5 (m, 40 H, Ph*H*); ^{13}C NMR ($CDCl_3$) δ 52.18, 69.69, 101.31, 106.10, 106.78, 108.15, 127.27, 127.68, 128.28, 131.84, 136.57, 138.72, 139.02, 159.44, 159.62, 159.88, 166.29.

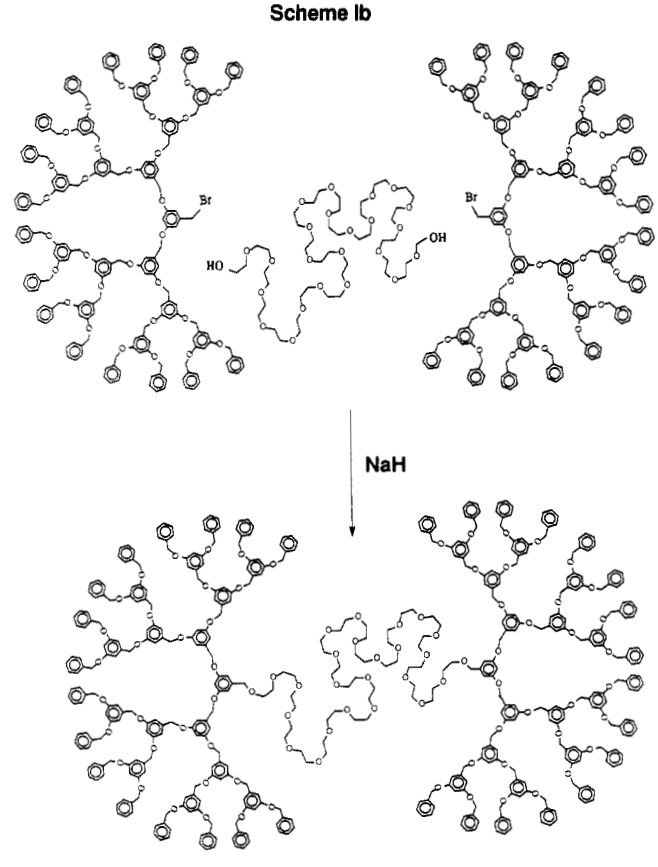
[G-4]-CO_2Me (4). A mixture of [G-3]-Br (**5**) (2.35 g, 1.42 mmol), **3** (0.114 g, 0.68 mmol), potassium carbonate (0.21 g, 1.50 mmol), and 18-crown-6 (0.04 g, 0.15 mmol) in acetone (50 mL) was stirred vigorously and heated at reflux under nitrogen for 16 h. The solvent was then removed under reduced pressure, and the residue was partitioned between dichloromethane (50 mL) and water (50 mL). The aqueous layer was extracted with dichloromethane (3 × 50 mL), and the combined organic layers were dried and evaporated to dryness under reduced pressure. The crude product was purified by flash chromatography, eluting with dichloromethane to give **4** as a colorless glass: yield 87%; IR 3050, 2920, 2870, 1720, 1597, 1497, 1453, 1375, 1345, 1321, 1298, 1159, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (s, 3 H, CO_2CH_3), 4.92-5.02 (each s, 60 H, Ar and $PhCH_2O$), 6.54–6.57 (m, 14 H, Ar*H* of monomer units), 6.66–6.68 (m, 29 H, Ar*H* of monomer units), 6.77 (t, 2 H, J = 2 Hz, Ar*H* of monomer unit), 7.26–7.42 (m, 80 H, Ph*H*); ^{13}C NMR ($CDCl_3$) δ 52.18, 69.93, 70.03, 101.44, 101.59, 106.34, 107.13, 108.44, 127.50, 127.93, 128.52, 132.02, 136.74, 138.90, 139.18, 159.64, 160.02, 160.06, 160.11, 166.33.

General Procedure for Williamson Coupling Reactions and Kinetic Measurements. The solution reactions were

Scheme Ia



Scheme Ib



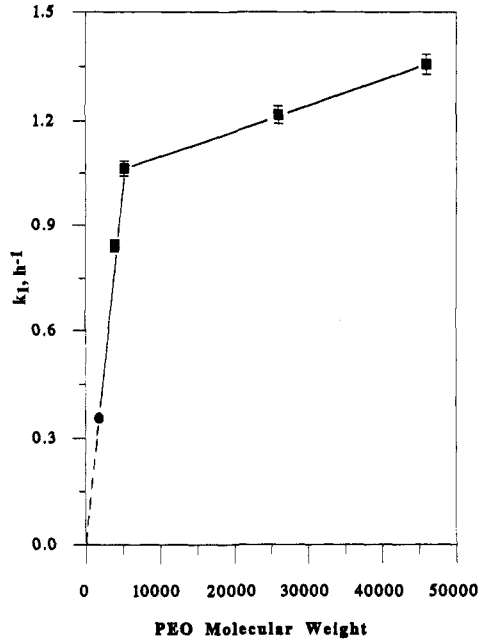


Figure 1. Dependency of the pseudo-first-order rate constant (k_1) for the Williamson reaction of PEO and [G-4]–Br on the molecular weight of the linear polyether: () this work; () *n*-octyl bromide.[15]

Table III. Dependence of the Pseudo-Second-Order Rate Constants on the Molecular Weight of PEGs in Their Williamson Reaction with Dendritic Bromide [G-4]–Br

PEG mol wt	$k_2 \times 10^3$ (M^{-1} h^{-1})
1100	1.006
5000	1.907
10700	3.091
19700	4.771

performed under dry argon following a procedure already described.[12] The kinetic measurements were carried out under similar conditions, but using a fivefold excess of the linear polyether. The consumption of the dendrimer can be monitored readily by SEC in THF of aliquots taken from the reaction mixture. The height of the dendritic bromide peak is directly proportional to its concentration in the solution. A typical experiment is described: PEG11000 (0.108 g, 1×10^{-5} mol) and dendritic bromide [G-4]–Br (0.003 g, 1×10^{-6} mol) were placed in a flask and dissolved with slight heating in 40 mL of dry THF (0.28 wt %). The solution was purged with dry argon and allowed to cool to room temperature for 10 min NaH (0.001 g, 4.2×10^{-5} mol) was added at once, and the reaction mixture was stirred vigorously. At certain intervals 0.5 mL of the solution was taken by a syringe and diluted with 0.5 mL of THF, and 0.17 mL of the resulting solution was injected in the SEC system.

The reactions in the melt are described below:

AB Block Copolymer [G-3]–$CO_2(CH_2CH_2O)_{23}C_{12}H_{25}$ (6). To a 25-mL round-bottom flask connected to a rotary vacuum pump with a liquid nitrogen trap were added 1 (0.50 g, 0.31 mmol), PEO1200 (7) (0.90 g, 0.75 mmol), and cobalt(II) acetate tetrahydrate (0.20 g, 0.80 mmol). After high vacuum (0.03 mmHg) was achieved, the flask was placed into an oil bath heated to 210 °C, and the mixture was stirred, heated, and evacuated for 16 h. The reaction mixture was then dissolved in THF and purified by precipitation into hexanes and precipitation into methanol. The mixture was then further purified by flash chromatography, eluting with 10% ether/dichloromethane and then 10% methanol/dichloromethane to give the block copolymer 6 as a glass: yield 82%; IR 3050, 2922, 2870, 1720, 1595, 1497, 1453, 1375, 1346, 1323, 1298, 1260, 1155, 1107, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, J = 3 Hz, CH_3), 1.25 (br s, 20 H, CH_2), 1.60 (t, 2 H, J = 3 Hz, CH_2), 3.49 (t, 2 H, J = 3 Hz, CH_2), 3.68 (br s, 88 H, OCH_2CH_2), 4.43 (t, 2 H, J = 3 Hz, CO_2CH_2), 4.95, 4.98, 5.03 (each s, 28 H, Ar and $PhCH_2O$), 6.55–6.58 (m, 6 H, Ar*H* of monomer units), 6.67–6.69 (m, 13 H, Ar*H* of monomer units), 6.80 (t, 2 H, J = 2 Hz, Ar*H* of monomer unit), 7.25–7.44 (m, 40 H, Ph*H*); ^{13}C NMR ($CDCl_3$) δ 13.97, 22.44, 25.81, 29.12, 29.28, 29.42, 29.45, 31.65, 64.07, 68.87, 69.74, 70.23, 71.31, 101.30, 106.12, 106.73, 108.34, 127.29, 127.72, 128.28, 131.74, 136.48, 138.60, 159.72, 159.86, 165.91.

AB Block Copolymer [G-4]–$CO_2(CH_2CH_2O)_{23}C_{12}H_{25}$ (8). To a 25-mL round-bottom flask were added 4 (0.23 g, 0.069 mmol), 7 (0.20 g, 0.17 mmol), and $Bu_2Sn(OAc)_2$ (60 μL, 0.073 g, 0.20

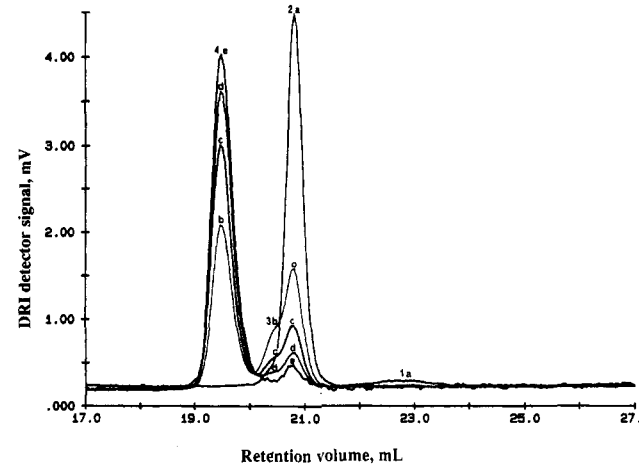


Figure 2. Time changes in the SEC traces during Williamson reaction of PEG1100 (peak 1) and [G-4]–Br (peak 2). Peak 3: reaction intermediate; peak 4: [G-4]–PEG1100–[G-4]. Time: (a) 0 min; (b) 10 min; (c) 20 min; (d) 45 min; (e) 3 h. Eluent: THF at 1 mL/min, 40 °C, 5-μm PL Gel columns 500 Å, 1000 Å, and Mixed C.

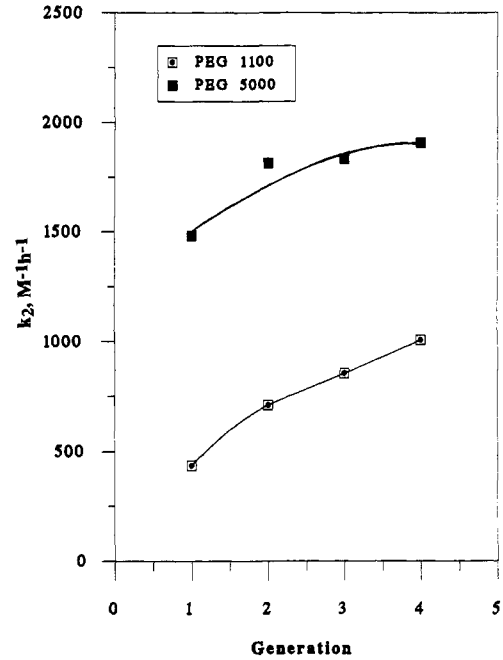
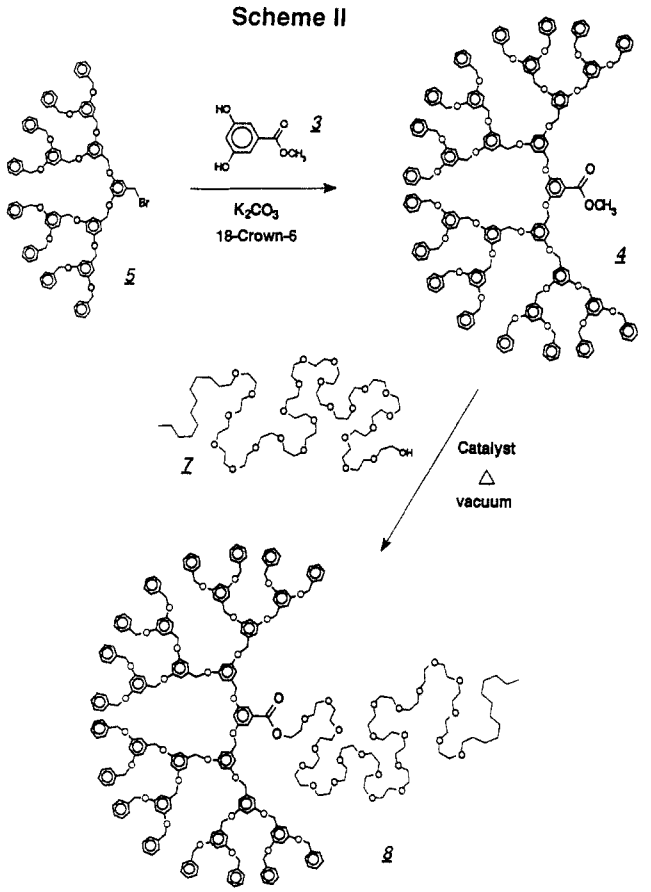


Figure 3. Dependency of the pseudo-second-order rate constants (k_2) for the Williamson reaction of PEGs and dendritic bromides on the molecular weight of the linear polyether and the generation of the dendrimer.

Table IV. Generation Dependence of the Pseudo-Second-Order Rate Constants in the Williamson Reaction of Dendritic Bromides and PEGs

PEG mol wt	generation	$k_2 \times 10^3$ (M^{-1} h^{-1})	correlation coeff
1100	1	0.435	0.983
1100	2	0.710	0.987
1100	3	0.854	0.985
1100	4	1.006	0.983
5000	1	1.483	0.906
5000	2	1.814	0.966
5000	3	1.834	0.974
5000	4	1.907	0.985

Scheme II



mmol). This reaction mixture was placed into a 160 °C oil bath and stirred under N_2. After 4 h, an additional amount of $Bu_2Sn(OAc)_2$ was added, and a vacuum was applied with a flow of N_2 to maintain the pressure at 10 mmHg. After 2 h, the reaction mixture was allowed to cool. The mixture was then dissolved in tetrahydrofuran and purified by precipitation into hexanes and precipitation into methanol. The mixture was then further purified by flash chromatography, eluting with 10% ether/dichloromethane and then 10% methanol/dichloromethane to give the block copolymer **8** as a glass: yield 68%; IR 3050, 2922, 2870, 1720, 1595, 1497, 1453, 1375, 1345, 1321, 1298, 1260, 1155, 1107, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3 H, J = 3 Hz, CH_3), 1.27 (br s, 18 H, CH_2), 1.59 (t, 2 H, J = 3 Hz, CH_2), 3.49 (t, 2 H, J = 3 Hz, CH_2CH_2O), 3.66 (br s, 90 H, OCH_2CH_2O), 4.45, (t, 2 H, J = 3 Hz, CO_2CH_2), 4.94, 4.98, 5.02 (each s, 60 H, Ar and $PhCH_2O$), 6.54–6.57 (m, 14 H, Ar*H* of monomer units), 6.66–6.68 (m, 29 H, Ar*H* of monomer units), 6.77 (t, 2 H, J = 2 Hz, Ar*H* of monomer unit), 7.25–7.48 (m, 80 H, Ph*H*); ^{13}C NMR ($CDCl_3$) δ 13.92, 22.43, 25.83, 29.09, 29.23, 29.35, 29.37, 31.65, 64.02, 68.84, 69.75, 70.28, 71.25, 101.28, 106.06, 106.17, 106.68, 108.31, 127.27, 127.71, 128.29, 131.77, 136.50, 138.60, 138.93, 159.39, 159.78, 159.85, 165.85. The AB block copolymer, [G-4]–$CO_2(CH_2CH_2)_{23}C_{12}H_{25}$ (**8**), could also be prepared in 71% yield by the cobalt acetate procedure described above.

ABA Block Copolymer [G-4]–$CO_2(CH_2CH_2O)_{46}OC$–[G-4] (9). To a 25-mL round-bottom flask were added **4** (1.00 g, 0.31 mmol), PEG2000 (0.28 g, 0.14 mmol), and cobalt(II) acetate tetrahydrate (0.075 g, 0.30 mmol). After high vacuum was achieved (0.03 mmHg), the flask was placed into an oil bath heated to 210 °C, and the mixture was stirred, heated, and evacuated for 16 h. The reaction mixture was then dissolved in THF and purified by precipitation into hexanes and precipitation into methanol. The mixture was then further purified by flash chromatography, eluting with 10% ether/dichloromethane and then 10% methanol/dichloromethane to give the triblock barbell-shaped macromolecule **9** as a glass: yield 51%; IR 3050, 2922, 2870, 1720, 1595, 1496, 1455, 1375, 1346, 1323, 1298, 1260, 1155, 1107, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.68 (br s, 176 H, OCH_2CH_2), 3.85 (br t, 4 H, J = 3 Hz, $CO_2CH_2CH_2$), 4.50 (br t, 4 H, J = 3 Hz, CO_2CH_2), 4.98, 5.01, 5.04 (each s, 120 H, Ar and $PhCH_2O$), 6.54–6.57 (m, 28 H, Ar*H* of monomer units), 6.66–6.68 (m, 58 H, Ar*H* of monomer units), 6.77 (t, 4 H, J = 2 Hz, Ar*H* of monomer unit), 7.27–7.46 (m, 160 H, Ph*H*); ^{13}C NMR ($CDCl_3$) δ 64.11, 68.94, 69.85, 70.35, 101.39, 106.18, 106.29, 106.79, 108.40, 127.36, 127.80, 128.25, 128.38, 131.87, 136.59, 138.69, 139.01, 159.49, 159.89, 159.96, 165.96.

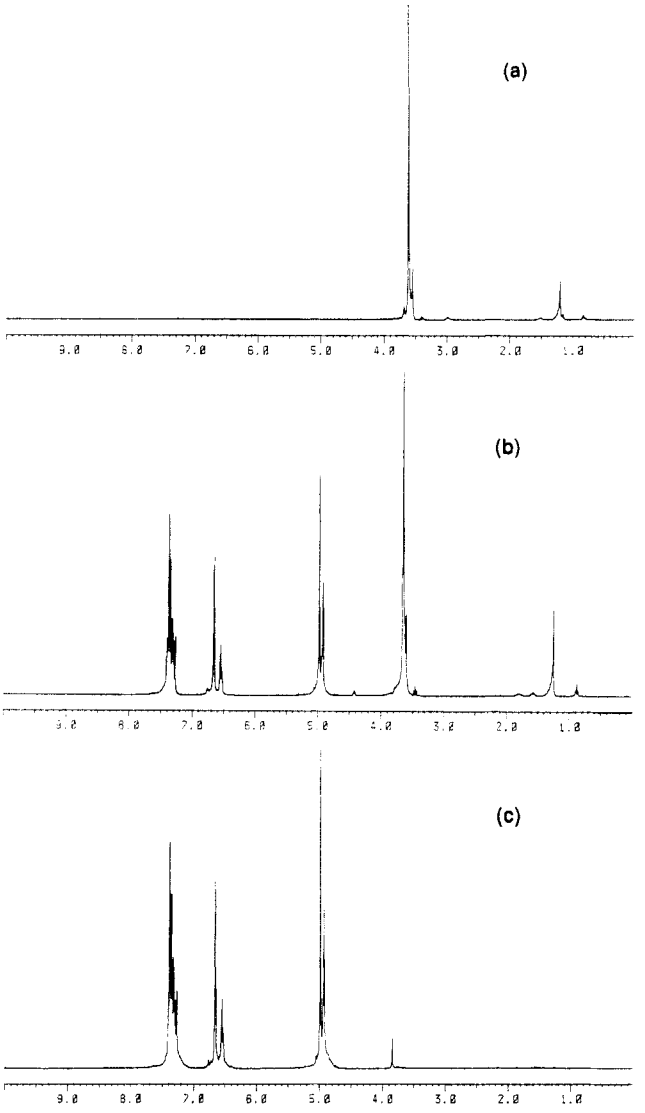


Figure 4. ^1H NMR spectra for linear PEO1200 (a), block copolymer [G-4]–CO_2–PEO1200 (b), and dendrimer [G-4]–CO_2–CH_3 (c).

Results and Discussion

1. Reactions in Solution. The reaction of PEO anion with a fourth-generation dendritic bromide ([G-4]–Br) is presented in Scheme Ia. It is believed that the reactivity of two macromolecular reagents in solution is affected by their mutual compatibility, the solvent selectivity toward each of the reacting polymers, their molecular weights, and their concentration in the reaction mixture.[14] Due to the globular nature of the dendritic macromolecule, the linear polymer may experience steric hindrance in its approach to the focal point. All of these factors contribute to the enhancement or reduction of polymer coil interpenetration. In our system, the two reacting blocks may not be compatible because of the considerable differences in their properties. For example, the dendritic block is amorphous while PEO is crystalline, and the solubility behavior of both components is markedly different. In addition, the reaction conditions[12] were chosen to meet the requirements for the "excluded volume effect": high dendrimer generation, low concentration (0.3 wt %, ca. 1 × 10^{-5} mol/L), and solvent which preferentially dissolves the dendritic reagent. Surprisingly, our investigations

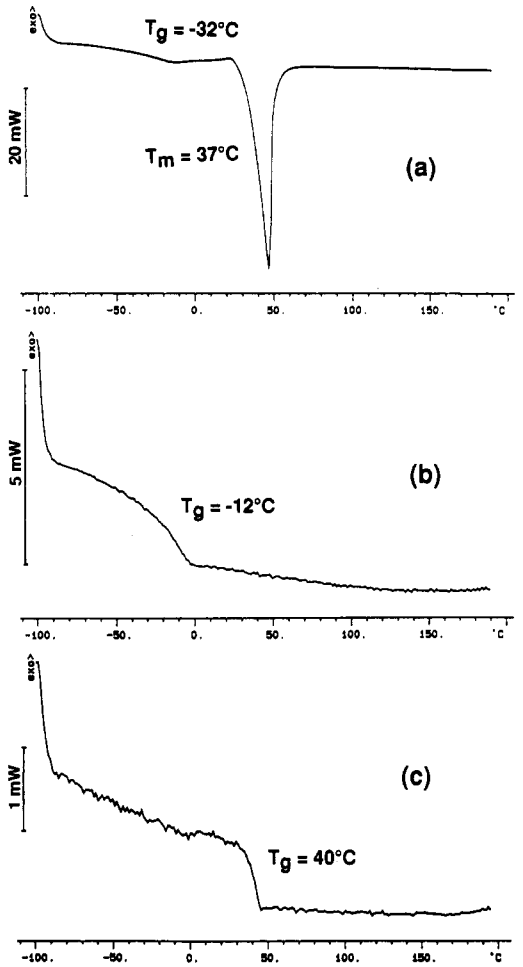


Figure 5. DSC traces for linear PEO1200 (a), block copolymer [G-4]–CO_2–PEO1200 (b), and dendrimer [G-4]–CO_2CH_3 (c).

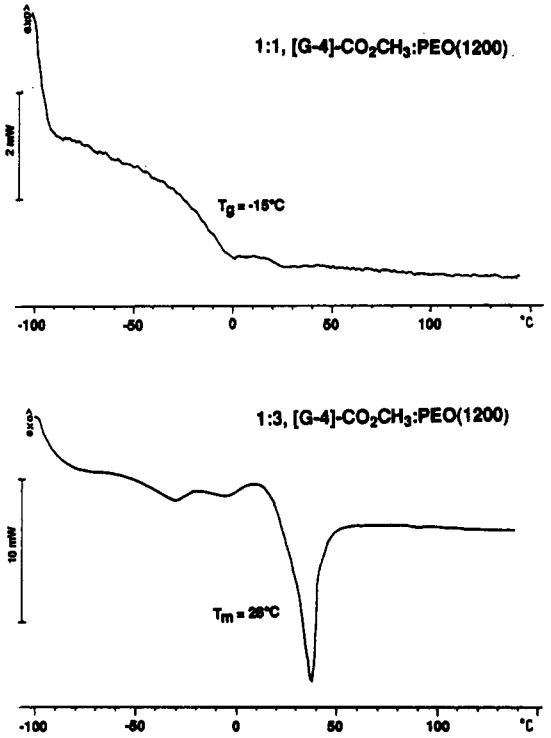


Figure 6. DSC traces for physical mixtures of [G-4]–CO_2CH_3 and linear PEO1200: (a) 1:1 molar ratio; (b) 1:3 molar ratio.

show that the reaction proceeds at a high rate and is completed within 3 h at room temperature.

Repeated experiments show that the pseudo-first-order rate constants for the reaction of PEO with [G-4]–Br increase with the molecular weight of the linear polyether (Table II). The data reported by Harris et al.,[15] although obtained for nondendritic bulky bromides, also fit the same rate law (Table II, Figure 1). This molecular weight effect might seem surprising at first in terms of the "excluded kinetic volume effect". However, it can be explained by the autosolvation of the sodium counterion by the PEO leading to the formation of a loose ion pair or even a "naked" anion with a much higher reactivity. The assumption is supported by the increase in ion-pair dissociation of sodium and potassium salts upon addition of PEO to their THF solutions reported earlier by Panayotov et al.[16] A similar molecular weight dependency of the rate of a Williamson reaction on PEO addition has been described for the system sodium phenolate/alkyl bromide in THF.[17] Regrettably, in this earlier study, determination of the direct relationship between the molecular weight of the additive and the reaction rates was impeded by the precipitation of the phenolate/PEO complex. In the present investigation the PEO anion is the only nucleophilic reagent in the system, and its reactivity may only be affected by the autosolvation if other reaction parameters are kept constant.

The influence of the chain length can also be observed in the reaction of [G-4]–Br with PEGs of different molecular weights (Scheme Ib, Table III). When the reaction is performed with a 2:1 ratio of dendrimer to PEG, a small shoulder on the dendrimer peak corresponding to monoalkylated product is observed in the SEC traces of the reaction mixture but disappears with time (Figure 2, peak 3). This absence of significant buildup of monoalkylated product may be due to increased reactivity of the monofunctionalized PEG. Similar behavior has been observed for attachment of [G-4]–Br to polyphenolic compounds.[18] However, the consumption of [G-4]–Br in the kinetic experiments fits pseudo-second-order reaction kinetics with correlation coefficients between 0.934 and 0.999. It should be mentioned that regardless of the bulkiness of both reagents the values obtained are in the range of fast organic reactions.[19]

It was reported that the rate of esterification of dendritic phenols with aromatic acid chlorides decreases only slightly from generation 1 to generation 2 with no further decrease in reaction rate to the next generation.[20] In this study the effect of the dendrimer size on the reaction rates in the Williamson reaction was measured for reagents with much higher molecular sizes—PEG1100 and PEG5000 and dendritic bromides of generations 1–4. The results are given in Table IV and Figure 3. The pseudo-second-order rate constants increase with the dendrimer size in both cases; however, the increase is more pronounced with PEG1100. A plausible explanation for this strange phenomenon may be that, after attachment of the first dendritic block, the conformation of the PEG chains is favorably altered and their solubility (and reactivity) in THF is increased.

2. Reactions in the Melt. The versatility of the convergent growth approach allows a variety of different functional groups to be placed at the focal point of dendritic macromolecules. This not only increases the range of possible copolymers that can be synthesized but it also allows a number of different chemistries to be used. For example, the hybrid polyether linear–dendritic block copolymers discussed above can be prepared using different chemistry at the point of attachment.

To be consistent with the hybrid polyethers prepared above, PEOs and PEGs were also employed as the linear component. Much literature describing the synthesis of esters[21] and polyesters[22,23] by transesterification exists. This suggests that the focal point group could be a methyl ester used in a transesterification with the poly(ethylene

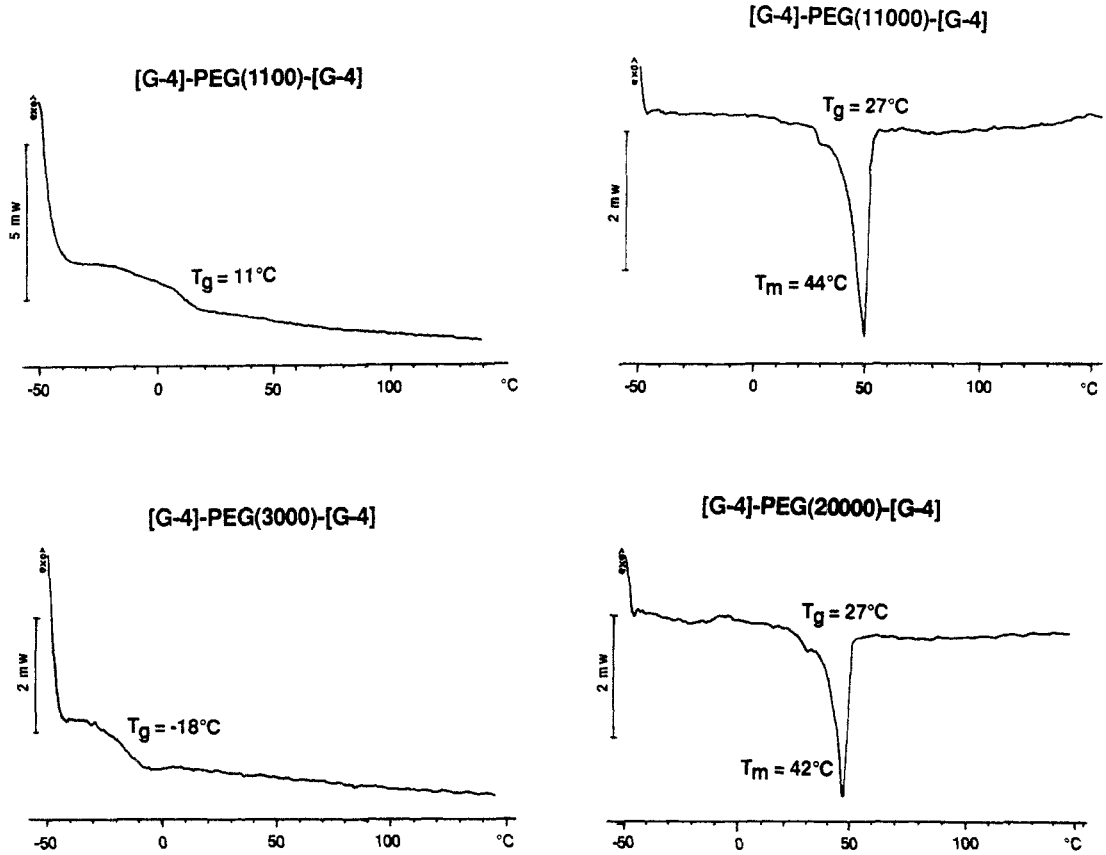


Figure 7. DSC traces for triblock copolymers with varying linear PEG chain length: (a) [G-4]–PEG1100–[G-4]; (b) [G-4]–PEG3000–[G-4]; (c) [G-4]–PEG11000–[G-4]; (d) [G-4]–PEG20000–[G-4].

glycol) to liberate methanol and afford the hybrid polymer with its two components linked through an ester bond. As shown in Scheme II, the starting dendritic unit, a fourth-generation fragment containing a methyl ester group at the focal point, **4**, was obtained in 87% yield by reaction of [G-3]–Br (**5**) with methyl 3,5-dihydroxybenzoate (**3**). Similarly, reaction of [G-2]–Br (**2**) with **3** gave the third-generation methyl ester, **1**, in 88% yield.

For the synthesis of AB hybrid linear–dendritic block copolymers by transesterification, the reaction of **1** with PEO1200 (**7**) was studied under a variety of conditions and catalysts. Initially, [G-3]–CO_2CH_3 (**1**) and **7** were heated at 150 °C under a stream of N_2 with dibutyltin diacetate ($Bu_2Sn(OAc)_2$), titanium(IV) butoxide ($Ti(OBu)_4$), or cobalt(II) acetate ($Co(OAc)_2$) as catalyst to determine the efficiency of each of the catalysts in the transesterification coupling reaction.[24,25] Aliquots were removed at time intervals during the reactions and analyzed. From this simple experimental comparison, $Bu_2Sn(OAc)_2$ was found to be significantly more effective as catalyst, with 55% block copolymer formed after 3 h (as determined by SEC) versus 44% for $Ti(OBu)_4$ and 5% for $Co(OAc)_2$.

Optimum reaction conditions for a 1:1 mixture of the two components included heating the neat mixture of dendritic methyl ester and linear poly(ethylene glycol) at 160 °C in the presence of $Bu_2Sn(OAc)_2$ under a stream of N_2 for 4 h and then under a vacuum of 10 mmHg for 2 h. Under these reaction conditions, the linear–dendritic block copolymer, [G-4]–CO_2–PEO1200 (**8**) was prepared from reaction of **4** with **7** (Scheme II) in 68% yield. Higher vacuum could not be used due to the low boiling point of $Bu_2Sn(OAc)_2$ (139 °C, 5 mmHg). Reaction of **4** with **7** using $Co(OAc)_2$ as catalyst and harsher conditions (210 °C, 0.03 mmHg, 16 h) gave similar results and a yield of 71% for **8**, while reaction of **1** with **7** and $Co(OAc)_2$ under the same conditions gave the hybrid block copolymer [G-3]–CO_2–PEO1200 (**6**) in 82% yield. Purification was by flash chromatography, eluting the unreacted dendritic starting methyl ester with 10% ether/CH_2Cl_2 followed by elution of the hybrid linear–dendritic structure with 10% methanol/CH_2Cl_2.

The preparation of the ester-linked hybrid ABA block copolymers was similarly accomplished using a telechelic linear polymer as the starting material. Therefore, reaction of **4** with PEG2000 at 210 °C under a high vacuum (0.03 mmHg) in the presence of cobalt(II) acetate afforded the ABA block copolymer **9** in 51% yield after purification by precipitation and flash chromatography. It should be emphasized that even at temperatures above 200 °C the linear block does not undergo any chain cleavage.

3. Characterization of the Hybrid Linear–Dendritic Copolymers. Characterization and control of the purity of the hybrid block copolymers formed in both the solution and the melt reactions are of particular importance and were accomplished by a variety of spectroscopic, chromatographic, and thermal techniques. For example, comparison of the ^1H and ^{13}C NMR spectra of the hybrid polymer **8** formed in the melt with the two starting materials reveals a number of differences as well as similarities (Figure 4). The resonance for the methyl ester of the dendritic starting material **4** disappears on reaction, and the spectra of the resulting product show resonances for both the linear and the dendritic units. This, coupled with the appearance of new resonances at 4.40 ppm (^1H NMR) and 64.02 ppm (^{13}C NMR) for the methylene group of PEO1200 attached to an ester oxygen, demonstrates that the linear and dendritic units are covalently bound through the ester linkage. The purity of the products formed was confirmed by SEC studies which show the signals for the hybrid products as single peaks of lower polydispersity than the starting PEO or PEG and at lower retention volumes (higher molecular weights) than either of the starting materials. Similar spectroscopic and

chromatographic behavior was observed for the ether-linked hybrid block copolymers as well.[12]

Differential scanning calorimetry (DSC) traces for the two starting blocks (4 and 7) and the hybrid structure from attachment of the two blocks through an ester linkage (8) are shown in Figure 5. PEO1200 (7) is a crystalline polymer exhibiting a glass transition temperature (T_g) at −32 °C and a melting transition at 37 °C. Dendrimer [G-4]–CO_2CH_3 (4) is an amorphous material having a glass transition at 40 °C. The hybrid structure 8 shows no melting transition and a single glass transition at −12 °C (261 K). This glass transition is 29 °C below the theoretical value of 17 °C (290 K) calculated from the Fox equation[26] for linear block copolymers. These data suggest that the two blocks can mix and plasticize each other. To study this, DSC measurements on physical mixtures of the two blocks were done. As shown in Figure 6, the thermal behavior of a mixture consisting of a 1:1 molar ratio (1:0.36 mass ratio) of the dendritic and linear blocks resembles the hybrid structure, giving a single T_g at −15 °C and no melting transition. However, when the molar ratio of the crystalline poly(ethylene glycol) was increased to 1:3 (1:1 mass ratio, dendrimer:linear), the melting transition reappeared due to the ability of the PEG to phase separate and crystallize. It is unclear what causes the other thermal transitions occurring at temperatures below the melting transition. With the observed reappearance of the melting transition in the physical mixtures, hybrid structures with varying sizes of dendritic and linear units were investigated. Figure 7 demonstrates the changes in thermal properties due to changes in the microscopic phase structure of triblock hybrid block copolymers in which the molar ratio remains 2:1, while the mass ratio varies. [G-4]–PEG1100–[G-4][12] has a dendritic to linear block mass ratio of 1:0.15 and displays a single glass transition temperature at 11 °C. When the amount of PEG is increased to 1:0.46 in [G-4]–PEG3000–[G-4],[12] a single T_g is still observed, but at a lower temperature, −18 °C, due to the increased influence of the PEG block. In agreement with the physical mixtures, when the amount of the PEG is greater than a 1:1 mass ratio, the melting transition reappears, as observed for [G-4]–PEG11000–[G-4][12] (1:1.7, dendrimer:linear) and [G-4]–PEG20000–[G-4][12] (1:2.9). The melting transition at ca. 43 °C confirms that the PEG unit is phase-separating to form crystalline domains, while it may be deduced that the glass transition at 27 °C is the result of domains of dendrimer contaminated with the attached PEG block; thus the observed T_g is lower than that of the pure dendrimer. Therefore when the dendritic block is in excess, the two blocks mix. However, when the linear PEG is in excess, phase separation occurs, the driving force being crystallization of the PEG.

Conclusion

This study demonstrates that novel linear–dendritic hybrid block copolymers can be prepared using either solution or melt reaction conditions. The rate of reaction of dendritic aromatic polyether fragments having a single bromomethyl group at the focal point with linear poly(ethylene glycol) was shown to increase with increasing molecular weight of the dendritic fragment as well as with increasing molecular weight of the linear fragment. This demonstrates that the functionality at both the focal point of the dendrimer and the chain end of the linear polymer is not only very accessible but also reactive. The results from the melt reaction of dendritic esters with poly(ethylene glycol) support this conclusion. At low molecular weights of the linear poly(ethylene glycol) a single glass transition temperature was observed for the hybrid polymers; however, at higher molecular weights phase separation occurs to give domains of crystalline poly(ethylene glycol) and domains of predominantly dendritic polyether.

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References and Notes

(1) Tomalia, D. A.; Naylor, R.; Goddard, W., III. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 138.
(2) (a) Buhleier, E.; Wehner, W.; Vogtle, F. *Synthesis* **1978**, 155. (b) Newkome, G. R.; Yao, Z.; Baker, G. R.; Gupta, V. K. *J. Org. Chem.* **1985**, *50*, 2004. (c) Tomalia, D. A.; Baker, H.; Dewald, J.; Hall, M.; Kallos, G.; Martin, S.; Roeck, J.; Ryder, J.; Smith, P. *Polym. J.* **1985**, *17*, 117.
(3) (a) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638. (b) Miller, T. M.; Neenan, T. X.; Zayas, R.; Blair, H. E. *J. Am. Chem. Soc.* **1992**, *114*, 1018.
(4) Flory, P. J. *Principles of Polymer Chemistry*; Cornell University Press: Ithaca, NY, 1953; p 75.
(5) Flory, P. J. In ref 4, p 78.
(6) Morawetz, H.; Cho, J.-R.; Gans, P. *Macromolecules* **1973**, *6*, 624.
(7) Morawetz, H.; Wang, Y. *Macromolecules* **1990**, *23*, 1753.
(8) Okamoto, A.; Shimanuki, Y.; Mita, I. *Eur. Polym. J.* **1982**, *18*, 545.
(9) Okamoto, A.; Toyoshima, K.; Mita, I. *Eur. Polym. J.* **1983**, *19*, 341.
(10) Hawker, C. J.; Fréchet, J. M. J. *Polymer* **1992**, *33*, 1507.
(11) Gitsov, I.; Wooley, K. L.; Hawker, C. J.; Fréchet, J. M. J. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1991**, *32* (3), 631.
(12) Gitsov, I.; Wooley, K. L.; Fréchet, J. M. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1200.
(13) Berlinova, I. V.; Panayotov, I. M. *Makromol. Chem.* **1989**, *190*, 1515.
(14) Gnanou, Y.; Lutz, P. *Makromol. Chem.* **1989**, *190*, 577.
(15) Harris, J. M.; Case, M. G. *J. Org. Chem.* **1983**, *48*, 5390.
(16) Panayotov, I. M.; Tsvetanov, C. B.; Berlinova, I. V.; Velitchkova, R. S. *Makromol. Chem.* **1970**, *134*, 313.
(17) Yamazaki, N.; Hirao, A.; Nakahama, S. *J. Macromol. Sci., Chem.* **1979**, *A13*, 321.
(18) Wooley, K. L.; Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1991**, *113*, 4252.
(19) Eremin, E. N. *Basics of Chemical Kinetics*, II ed.; Vysshaya Shkola: Moscow, 1976; p 540.
(20) Miller, T. M.; Kwock, E. W.; Neenan, T. X. *Macromolecules* **1992**, *25*, 3143.
(21) Bender, M. L. *Chem. Rev.* **1960**, *53*, 60.
(22) Allen, G. *Comprehensive Polymer Science*; Pergamon Press: New York, 1985; Vol. 5, pp 275–314.
(23) Bartl, H.; Falbe, J. *Methoden Der Organischen Chemie*, Band E20, Teil 2; Georg Thieme Verlag: Stuttgart, New York, 1987; pp 1405–1422.
(24) Tomita, K.; Ida, I. *Polymer* **1975**, *16*, 185.
(25) (Carborundum), Economy, J.; Nowak, B. E. French Patent 1 568 152, 1969; *Chem. Abstr.* **1970**, *72*, 13412.
(26) Fox, T. G. Bull. Am. Phys. Soc. **1956**, *1*, 123.