Development of Branching in Living Radical Copolymerization of Vinyl and Divinyl Monomers

Iveta Bannister,[†] **Norman C. Billingham,***[,†] **Steven P. Armes,***[,‡] **Steven P. Rannard,**[§] **and Paul Findlay**[§]

Department of Chemistry, University of Sussex, Falmer, Brighton, East Sussex, BN1 9QJ, UK;
Department of Chemistry, University of Sheffield, Brook Hill, Sheffield, South Yorkshire, S3 7HF, UK;
and Unilever Research Centre, Port Sunlight, Quarry Road East, Bebington, Wirral, CH63 3JW, UK

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ABSTRACT: The branching copolymerization of 2-hydroxypropyl methacrylate (HPMA) with either ethylene glycol dimethacrylate (EGDMA) or bisphenol A dimethacrylate (BPDMA) as the branching agent has been carried out using atom transfer radical polymerization (ATRP) in methanol at 20 °C. With EGDMA, soluble branched copolymers were obtained provided that less than one branching agent was incorporated per primary chain: higher levels of EGDMA led to gelation, as expected. Analysis of the changes in the molecular weight and polydispersity of the polymers shows that the formation of highly branched chains occurs only at high (>90%) conversions. Chain coupling is close to the ideal behavior predicted by the Flory−Stockmayer theory, suggesting that all double bonds are equally reactive and that there is no significant cyclization, in contrast to conventional free radical polymerization. This analysis is confirmed by comparison of the consumption of the EGDMA branching agent with predictions from both theory and simulation. With BPDMA as the branching agent, similar results are obtained although branching is slightly less efficient.

Introduction

Radical polymerization of vinyl monomers normally produces high molecular weight chains, which are very easily cross-linked since it is only necessary to introduce an average of two branch points into each chain to convert the whole reacting mass into a network.[1] Thus, free radical solution copolymerization of a vinyl monomer with even a small percentage of a divinyl monomer leads to gelation, unless the reaction is carried out at very high dilution, when microgels are formed. Gelation in the presence of a divinyl monomer typically occurs at low conversions even when only a few percent of comonomer is used because radical polymerization gives polydisperse polymers with some chains significantly longer than the average, which cross-link even more easily.

Sherrington et al.[2−6] have recently described a new "Strathclyde" route to branched vinyl polymers which involves the addition of a chain transfer agent (typically a thiol) to a conventional free radical copolymerization of a vinyl and a divinyl monomer. In the presence of the chain transfer agent, the molecular weight of the primary chains is limited, gelation can be suppressed, and soluble, branched polymers are obtained as the sole product. Although the basic concept of using a chain regulator to suppress gelation (effectively by ensuring that the primary chain length is too short to allow gelation at finite conversion) is more than 50 years old,[7] Sherrington et al. were the first to show that this approach can be used to produce soluble, branched polymers at high conversion.

To date, most of this work has focused on the polymerization of hydrophobic monomers, notably methyl methacrylate (MMA). For example, in their first report Sherrington and co-workers used a cleavable diacrylate branching agent to prepare branched PMMA, which was then degraded via ozonolysis to produce the linear primary PMMA chains.[2] In subsequent work, a comparison of conventional free radical and catalytic chain transfer polymerization was made for the copolymerization of MMA with tripropylene glycol diacrylate.[3] ^{1}H NMR spectroscopy provided detailed analysis of the soluble branched PMMA chains, allowing quantification of the terminal thiol groups, the branching agent content, and the pendent unreacted vinyl groups under favorable circumstances.[4]

The effect of varying the functionality of the branching agent has also been explored, and the influence of the degree of branching on mechanical properties such as the glass transition temperature was assessed for PMMA.[5] Finally, a comparison of copolymerizations of three divinyl monomers with MMA revealed some intriguing differences, with divinylbenzene producing more regular, less polydisperse branched polymers than either a diacrylate or a dimethacrylate branching agent.[6]

Atom transfer radical polymerization (ATRP) is a form of living radical polymerization developed independently by Sawamoto et al.[8] and Matyjaszewski et al.[9] The ATRP formulation typically comprises an alkyl halide initiator, a copper catalyst with suitable ligand(s), and a styrenic, acrylic, or methacrylic monomer. The catalyst reversibly caps the growing polymer radicals with halogen atoms, which lowers the instantaneous polymer radical concentration and significantly reduces the probability of chain termination relative to propagation. ATRP is best described as "pseudo-living" rather than truly living; nevertheless, it has been extensively used to prepare a wide range of well-defined copolymers with block, graft, and hyperbranched architectures.[10−14] One disadvantage of ATRP is that the reduced polymer radical concentration can often lead to rather low polymerization rates for nonpolar monomers such as styrene or MMA, even for bulk polymerizations at 110 °C.[10,15]

Zhu et al. studied the homopolymerization of ethylene glycol dimethacrylate (EGDMA) using ATRP in bulk monomer at 70 °C.[16] Gelation occurred at relatively low conversions (<10%), as expected for a divinyl monomer, although the reaction did

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[†] University of Sussex.
[‡] University of Sheffield.
[§] Unilever Research Centre.
* To whom correspondence should be addressed.

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not show the autoacceleration typical of normal free-radical polymerization. ESR spectroscopy showed a large increase in both radical and Cu(II) concentrations at high conversion, indicating that the polymerization changes from ATRP to a conventional free radical mechanism as the mobility of the ATRP catalyst becomes increasingly retarded in the gel.

Recently, we showed that soluble branched polymers can be prepared by the Strathclyde approach using both ATRP and group transfer polymerization (GTP).[17,18] In addition, Li and Armes[19] obtained water-soluble branched polymers by the statistical copolymerization of 2-(dimethylamino)ethyl methacrylate with EGDMA using oxyanionic initiation, and Liu et al.[20] used reversible addition fragmentation chain transfer (RAFT) polymerization to produce branched PMMA via the one-pot copolymerization of MMA and EGDMA mediated by 2-(2-cyanopropyl) dithiobenzoate.

Recently, Li and Armes[21] synthesized a series of branched 2-hydroxypropyl methacrylate (HPMA) copolymers using a dimethacrylate branching agent containing a disulfide bond. This approach allowed the branched copolymer chains to be cleaved at every branch point, which led to the production of near-monodisperse primary chains essentially indistinguishable from those produced without the dimethacrylate. This confirms that these branched copolymers comprise statistically linked low polydispersity primary chains and also indicates that branching by chain transfer to polymer is negligible during such ATRP syntheses.

Although all of these studies describe branched copolymer syntheses, they do not discuss the kinetics of polymerization or the development of branching with conversion in any detail. The statistical theory of gel formation in copolymerization of vinyl and divinyl monomers was elaborated by Flory[1,22−24] and by Stockmayer[25,26] in the 1940s, based on the assumptions that all vinyl groups are equally reactive and that no double bonds are wasted in cyclization. However, subsequent experimental studies have suggested that neither of these assumptions is truly valid in many conventional free radical polymerizations. For example, Landin and Macosko[27] showed that the copolymerization of MMA and small amounts of EGDMA leads to cyclization of about 3−4% of the pendent vinyls when the reaction is carried out in bulk monomer and that this fraction increases rapidly with dilution; others[28−30] have suggested both cyclization and reduced reactivity of the pendent vinyl groups.

Wang and Zhu[31] have recently reported a study of gelation in the ATRP of MMA and EGDMA in bulk monomer at 70 °C. Their study focuses on the relation of the gel point to conversion, and they conclude that the reaction under ATRP conditions is essentially statistical, closely following the predictions of Flory and Stockmayer. In a similar study[32] they showed that this copolymerization experiences autoacceleration at high conversions in bulk, suggesting the onset of diffusion-controlled radical deactivation. Like Li and Armes,[21] Wang and Zhu[32] also used a cleavable branching agent (in their case based on ester hydrolysis) to show that the gel fraction was made up of primary chains with the same molecular weight and polydispersity as those produced in the absence of the branching agent.

Although the studies reported to date have focused on gelation, in principle living techniques also offer a number of benefits in the synthesis of soluble branched copolymers. In the case of ATRP these include the following: (i) the ability to control the primary chain length by adjusting the monomer/initiator molar ratio without the need for a transfer agent; (ii) relatively low polydispersities, which minimizes the probability of (higher molecular weight) chains containing more than the two branching units minimally required for a highly branched polymer; (iii) the ability to polymerize functional or hydrophilic monomers directly and efficiently under mild conditions; (iv) a range of branching agents can be evaluated and compared; (v) the possibility of preparing branched block copolymers via either the macroinitiator approach or sequential monomer addition.[17]

In previous work, we have shown that the ATRP of a wide range of hydrophilic methacrylates proceeds rapidly in polar solvents such as water or lower alcohols at ambient temperature.[33−35] ATRP syntheses in water are too fast to be well-controlled,[33,36] but in methanol relatively low polydispersities and good blocking efficiencies can be achieved.[33−35,37] Moreover, it is much easier to sample ATRP syntheses without causing premature termination than is the case for anionic polymerization.

Some of the advantages of ATRP are illustrated in the present study, in which we examine the statistical copolymerization of 2-hydroxypropyl methacrylate [HPMA] with EGDMA using ATRP in methanol at room temperature. In particular, the evolution of the branching of the copolymers with conversion is investigated by periodic sampling of the reaction to gain a better understanding of the copolymerization mechanism.

Experimental Section

Materials. Unless otherwise stated, materials were purchased from Aldrich and used without further purification. HPMA (97%) was donated by Cognis Performance Chemicals (Hythe, UK), and was used as received. EGDMA was passed through a column of activated STD grade aluminum oxide to remove the polymerization inhibitor and was stored at −25 °C prior to use. The column chromatography grade silica gel 60 (0.063−0.200 mm) used for the removal of the copper ATRP catalyst from the copolymers was purchased from E. Merck (Darmstadt, Germany).

Synthesis of the 2-(*N*-Morpholino)ethyl-2-bromoisobutyrate (ME-Br) ATRP Initiator. 2-Hydroxyethylmorpholine (9.36 g, 71.4 mmol), triethylamine (16.25 g, 107.1 mmol), and toluene (300 mL) were placed in a 1 L round-bottomed flask and purged with nitrogen for 30 min. 2-Bromoisobutyryl bromide (24.62 g, 107.1 mmol) was added to the solution via a cannula, slowly with stirring. A white precipitate of triethylammonium bromide formed immediately, and the reaction mixture was stirred for a further 10 h, prior to removal of the precipitated salt by filtration. The toluene solution was washed with three 100 mL aliquots of 0.1 M Na_2CO_3 solution, followed by three 100 mL aliquots of deionized water to remove traces of unreacted 2-bromoisobutyryl bromide, and dried using $MgSO_4$. The solvent and excess triethylamine were removed by rotary evaporation to give a pale yellow liquid (yield 12.5 g, 80%). ^{1}H NMR (in $CDCl_3$): δ_H 4.3 (2H, t, CH_2-O), 3.6 (4H, t, CH_2-O), 2.7 (2H, t, CH_2-N), 2.4 (4H, t, CH_2-N), 1.8 (6H, s, CH_3-C-Br).

Kinetic Studies of the ATRP of Homopolymerization of HPMA and of Formation of Branched HPMA-based Copolymers in Methanol at 20 °C. *Linear PHPMA Homopolymer.* This synthesis was carried out according to the general protocol described by Save et al.[34] In a typical synthesis, HPMA monomer (11.67 g, 81.00 mmol) and ME-Br initiator (0.45 g, 1.62 mmol; target degree of polymerization = 50) were placed into a 100 mL round-bottomed flask equipped with a stir bar. The flask was placed in a water bath at room temperature to eliminate any polymerization exotherm. After the flask was sealed with a rubber septum, the solution was deoxygenated using a nitrogen purge for 20 min and maintained under nitrogen. HPLC grade methanol was degassed separately and subsequently added to the monomer/initiator mixture by syringe to give a 50% v/v mixture based on the HPMA monomer. The Cu(I)Cl catalyst (0.16 g, 1.62 mmol) and 2,2′-bipyridine (bpy) ligand (0.63 g, 4.05 mmol) were added to the reaction mixture under a positive nitrogen flow. Samples (∼0.8 mL) of the reaction mixture were taken at regular intervals and diluted into 1 mL of methanol, and the polymerization was stopped by exposing the reaction to the air. The mixture changed rapidly from brown to green, indicating termination of the polymerization due to the aerial oxidation of Cu(I) to Cu(II). The degree of polymerization of each copolymer was determined by ^{1}H NMR via end-group analysis using the well-resolved signals at δ 2.2 and δ 2.4 due to the initiator fragment, and molecular weights and polydispersities were obtained from SEC measurements (see below for further details). Theoretical molecular weights were calculated using the formula M_n = ([HPMA]/[ME-Br]) × conversion × molecular weight of monomer. The target degree of polymerization was adjusted to be either 30 or 50 by choosing the appropriate [HPMA]/[ME-Br] molar ratio. The [ME-Br]:[Cu(I)]:[bpy] molar ratios were 1:1:2.5 in all syntheses.

Branched PHPMA Copolymer. Branched copolymers were prepared by copolymerizing the EGDMA brancher with HPMA. In a typical experiment, HPMA (11.67 g, 81.00 mmol), EGDMA (0.32 g, 1.62 mmol), and ME-Br initiator (0.45 g, 1.62 mmol; target degree of polymerization of primary chains = 51), including units derived from the brancher, were placed into a 100 mL round-bottomed flask equipped with a stirrer bar. The flask was placed in a water bath at room temperature. After the flask was sealed with a rubber septum, the solution was deoxygenated using a nitrogen purge for 20 min and maintained under nitrogen. HPLC grade methanol was degassed separately and subsequently added to the comonomer/initiator mixture by syringe to give 50% v/v based on the HPMA monomer. The Cu(I)Cl catalyst (0.16 g, 1.62 mmol) and bpy ligand (0.63 g, 4.05 mmol) were added to the reaction mixture under a positive nitrogen flow. Samples (~0.8 mL) of the reaction mixture were taken at regular intervals, diluted into 1 mL of methanol, and exposed to air to terminate the reaction. The color of the reaction mixture changed from brown to green. The average degree of polymerization of the primary chain of each copolymer was determined by ^{1}H NMR via end-group analysis, and molecular weights and polydispersities were obtained from SEC measurements (see below for further details). Theoretical molecular weights were calculated using the formula M_n = ([HPMA + EGDMA]/[ME-Br]) × conversion × molecular weight of monomer. The target degree of polymerization of the primary chain was adjusted by varying the [HPMA + EGDMA]/ [ME-Br] molar ratio. The [ME-Br]:[Cu(I)]:[bpy] molar ratios were 1:1:2.5 in all syntheses. The potential degrees of branching were controlled by varying the [brancher]/[initiator] molar ratios. Finally, additional ATRP syntheses were carried out in which the HPMA was copolymerized with a second brancher, bisphenol A dimethacrylate (BPDMA), rather than EGDMA.

Nuclear Magnetic Resonance Spectroscopy. ^{1}H NMR spectra were recorded in CD_3OD or $CDCl_3$ using a 300 MHz Bruker Avance DPX 300 spectrometer. ^{1}H NMR was used to determine the extent of polymerization by comparing the peak integrals due to monomer vinyl signals at δ 5.6 and δ 6.2 (in CD_3OD) with those due to the methacrylate backbone at δ 0.5−1.9. In addition, the number-average degree of polymerization was estimated by comparing the appropriate methacrylate peaks with those due to the initiator at δ 2.2 and δ 2.4 (in CD_3OD). It was assumed that each chain contained one morpholine group, that the initiator efficiency was 100%, and that chain transfer was negligible. These assumptions have been confirmed in other studies[21,34] to be valid for the ATRP of methacrylic monomers such as HPMA conducted in methanol at ambient temperature.

Dual Detection Size Exclusion Chromatography (DD-SEC). Molecular weights and polydispersities of the PHPMA homopolymers and the branched PHPMA−EGDMA copolymers were measured by size exclusion chromatography (SEC) using HPLC grade THF, stabilized with 2,6-di-*tert*-butyl-4-methylphenol (BHT) as eluent, at a flow rate of 1.0 mL min^{-1}. The DD-SEC setup comprised a VE 7510 SEC solvent degasser, VE 1121 solvent pump, VE5200 autosampler, DM400 data manager (all from Viscotek), three 7.5 × 300 mm PLgel Mixed-B 10 μm columns (Polymer Laboratories), a laser light scattering mini-DAWN detector (Wyatt) operating at 690 nm, and an 1100 series refractive index (RI) detector (Agilent), operating at 30 °C and calibrated with a series of aqueous NaCl solutions at various concentrations. All analyses were in fact carried out on unpurified, unfiltered aliquots (about 0.4 mL) of the reaction mixture), diluted into 1.5 mL of THF eluent, 100 μL of which was then injected. There is an in-line filter and a precolumn; otherwise, the samples were not isolated or purified prior to NMR or SEC analysis. The molecular weight distributions were analyzed with Astra software (Wyatt) using the known refractive index increment, d*n*/d*c*, and concentration detector calibration constant. The d*n*/d*c* of a $PHPMA_{50}$ homopolymer (M_n ~ 9000 g mol^{-1}) was determined using an Optilab DSP (λ = 633 nm) interferometric refractometer (Wyatt) in off-line mode at 30 °C. A series of six copolymer solutions of differing concentrations (the highest being 1 g L^{-1}) in HPLC grade THF eluent were successively injected using a syringe pump, and the resulting signals were analyzed using the Wyatt software. The d*n*/d*c* value was calculated to be 0.0918 ± 0.0037 mL g^{-1}. The weight-average molecular weights of the branched copolymers were calculated using the d*n*/d*c* value determined for the linear homopolymer, assuming that the presence of the small amount of EGDMA had a negligible effect on d*n*/d*c*.

Analysis of Branching Agent Consumption. Consumption of the EGDMA branching agent was measured by GC analysis of the reaction mixture at various times, using an Agilent Technology 6890N GC with HP-5 column (length 30 m). The carrier gas was helium at 1 mL/min, and the column temperature was increased from a starting value of 100 °C at sample injection to a maximum of 450 °C at 10 °C/min. Identification of the peaks was confirmed by GC-MS using a Quattro Micro mass spectrometer with electron impact ionization at 70 V in positive mode and also by injecting samples of pure HPMA and EGDMA. The ratio of HPMA and EGDMA in the mixture was determined using calibration constants measured by injection of standard mixtures of known composition.

Simulation of EGDMA Consumption. To validate the developed theory, the consumption of EGDMA was simulated by a computer model. A Monte Carlo program was written in C# to run on a standard personal computer. In essence, an array of numbers is set up in which each cell initially contains either 1 (denoting a double bond from an HPMA molecule) or 2 (denoting a double bond of an EGDMA molecule with both double bonds intact). The cells are selected randomly, and the content changed as appropriate to either 0 (denoting a reacted double bond) or 3 (denoting a double bond of an EGDMA molecule with the other double bond reacted). When some desired fraction of the cells has been modified, a subprogram counts the fractions of each type of double bond remaining, and the proportion of cells retaining the value 2 (denoting unreacted EGDMA) is determined.

Gretton-Watson et al.[38,39] have recently reported a modeling study of the kinetics of branching under “Strathclyde” conditions, i.e., for conventional free radical polymerization with continuous initiation and simultaneous chain transfer and termination. Their approach involves numerical solution of the set of differential equations for the kinetics of all of the individual elementary reactions. Branching copolymerizations under living conditions are much simpler to model by Monte Carlo methods, which require no knowledge of rate constants. In principle, the approach of Gretton-Watson et al. could be used to model living reactions, whereas the nonliving case is not amenable to our Monte Carlo approach. In the present work, we are concerned solely with modeling the consumption of the branching agent; extension of our model to predict molecular weight−conversion relationships is under development and will be reported elsewhere in due course.

Results and Discussion

Background. The synthesis of branched copolymers using living polymerization is different to the use of conventional free radical chemistry as described by Sherrington et al.[2−6] Under the latter conditions, high molecular weight chains are obtained at relatively low conversions, so that highly branched copolymers can be formed even in the early stages of the polymerization. In contrast, for living (or pseudo-living) polymerizations such as ATRP all the chains are initiated at approximately the same time and grow together at similar rates to reach a mean degree of polymerization dictated solely by the monomer/initiator molar ratio. If the formulation is such that there is less than one brancher per copolymer chain based on the final degree of polymerization, and assuming that the mono- and divinyl monomers copolymerize ideally, then during the early stages of the polymerization the number of branching sites per chain is substantially less than unity. Thus, to a first approximation, the degree of branching is expected to be negligible at lower conversions. At what conversion does branching begin to become significant? The answer to this fundamental question can be obtained by periodic sampling of the copolymerizing solution, followed by SEC and NMR analyses of these aliquots. Such studies have been undertaken in the present work.

Our choice of HPMA was governed by two facts. Save et al.[34] had already shown that the ATRP of this monomer is well controlled and can give high conversions in convenient times at ambient temperature in methanol. Bories-Azeau et al.[40] showed that the hydroxyl groups in HPMA can be esterified with succinic anhydride to yield polyacids, and Graham et al.[41] showed that the polyelectrolyte effect is much reduced in branched polyacids prepared via normal free radical chemistry. Since the synthesis and characterization of polyelectrolytes prepared by ATRP is a theme of our current research, the facile polymerization of HPMA and the straightforward conversion of the polymer to a polyacid were attractive. EGDMA was chosen as the brancher as it has already been used to demonstrate the concept of branching in free radical polymerization of other systems, as mentioned above. For comparison, a second branching agent, bisphenol A dimethacrylate (BPDMA), was chosen on the basis that it should not have significantly different reactivity to that of EGDMA or HPMA but it might, on steric grounds, have a different propensity towards cyclization.

As already mentioned, ATRP typically yields polymers with predictable molecular weights and relatively narrow weight distributions (M_w/M_n about 1.1−1.3). Figure 1 shows the results of a typical kinetic analysis of ATRP homopolymerization of HPMA for a target degree of polymerization (DP) of 50. The semilogarithmic plot of monomer concentration vs time is linear, indicating its consumption by first-order kinetics and implying a constant concentration of active centers during the polymerization. SEC analyses showed symmetrical unimodal molecular weight distributions, and M_n increased linearly with conversion, indicating a negligible contribution from chain transfer or other side reactions under these conditions. The polydispersity decreased rapidly with conversion and remained constant at around 1.1 above ∼50% conversion. Similar results were obtained for a target DP of 30, although the final polydispersity of the $PHPMA_{30}$ polymer was slightly higher at 1.3.

Branching Statistics. It is reasonable to expect that the ATRP copolymerization of a divinyl and a vinyl monomer should result in branched polymers, in which primary chains of predictable molecular weight and relatively narrow molecular weight distribution are randomly linked when the pendent vinyl bonds of the brancher copolymerize and therefore yield dimers, trimers, etc., of the primary chains. However, because of the statistical nature of the process, a complex mixture of products with different molecular weights and architectures is expected (see Scheme 1).

Following Wang and Zhu,[31] with some modifications and with the confidence generated by prior studies using cleavable branching agents,[21,32] we consider the average branched product at any fractional conversion of monomer as a collection of chains identical to those produced in a linear ATRP at the same conversion, but coupled via EGDMA units in which both double bonds have been polymerized, and also containing pendent vinyl groups resulting from incorporation of only one end of the branching agent.

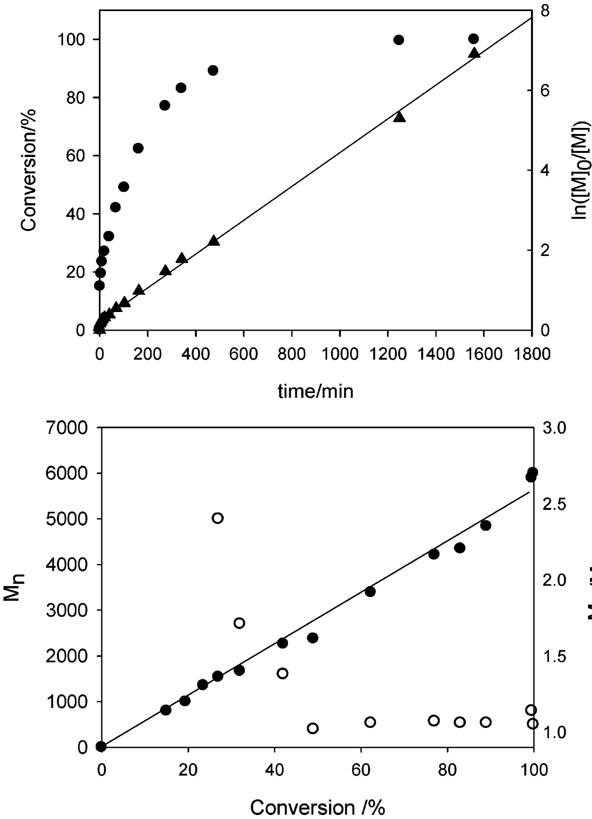

Figure 1. ATRP kinetics for the homopolymerization of HPMA in methanol at 20 °C. The [HPMA]:[Cu(I)Cl]:[bpy]:[initiator] molar ratio was 50:1:2.5:1. Upper figure shows conversion (●) and $\ln([M]_0/[M])$ (▲) vs time. Lower figure shows the evolution of M_n (●) and M_w/M_n (○) with conversion.

If $M_{n,b}$ and $M_{n,l}$ are respectively the molecular weights of the branched polymer and of the linear polymer produced at the same conversion in the absence of brancher, then the average number of primary chains per polymer molecule is simply $M_{n,b}/M_{n,l}$, and the average number of EGDMA units with both double bonds reacted which are incorporated into each copolymer chain, n_b, is given by

$$n_b = \frac{M_{n,b}}{M_{n,l}} - 1 \tag{1}$$

Following Flory,[1] the branching density, ρ, can be defined as the number fraction of repeat units which are in branch points. Since the molecular weight of HPMA is 144, if we neglect the small error introduced by the presence of (typically less than 2 mol %) of EGDMA, then the branching density is given by

$$\rho = \frac{144 n_b}{M_{n,b}} \tag{2}$$

According to the statistical theory of gelation, as developed by Flory and Stockmayer,[1] the critical condition for an infinite network to be formed by linking monodisperse chains is the point where the product of the probability that a branched unit is in a primary chain containing another branch unit (ρ) and

Scheme 1. Schematic Formation of a Branched Copolymer by ATRP: Primary PHPMA Chains with Relatively Low Polydispersity ($M_w/M_n = 1.2-1.3$) are Statistically Linked by the EGDMA Brancher Units.

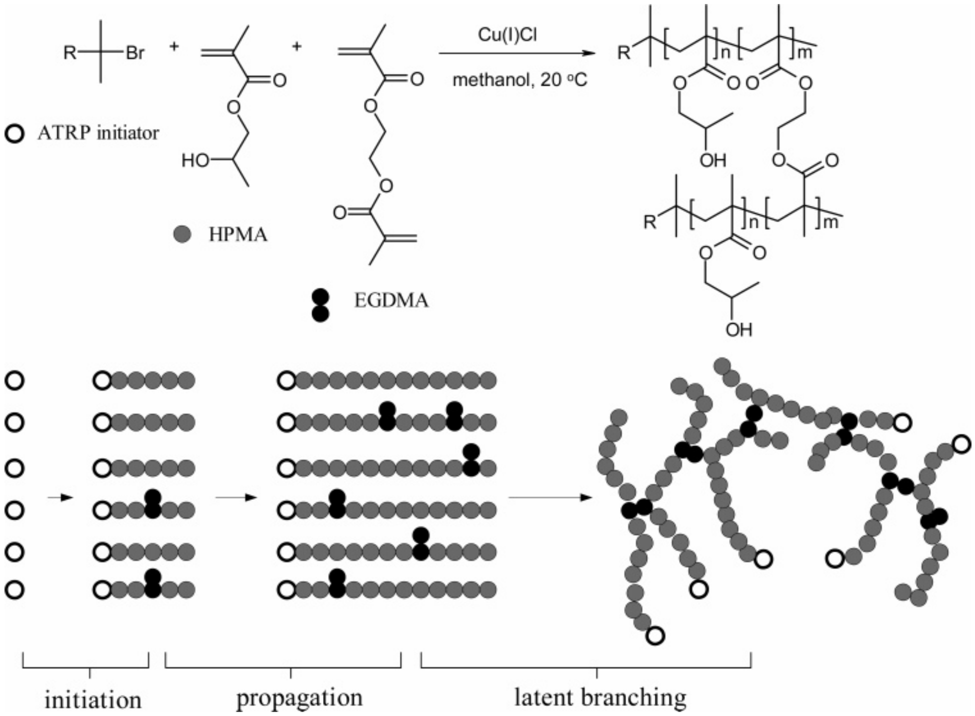

Table 1. Summary of Branched PHPMA Copolymers Prepared with Varying Concentration of Branchers[a]

		^{1}H NMR		THF GPC				
monomer	x	DP	M_n	M_w	M_w/M_n	n_b	ρ_b	$(M_n^b - M_n^1)/M_n^b$
				HPMA/initiator/brancher = 50				
linear PHPMA		51	6000	6300	1.05	0	0.000	0.00
EGDMA	0.7	53	29 000	106 000	3.6	4	0.019	0.79
EGDMA	0.8	54	66 000	190 000	2.9	10	0.022	0.91
EGDMA	0.9	51	192 000	645 000	3.4	31	0.023	0.97
EGDMA	1.0	50	243 000	365 000	1.5	40	0.023	0.98
EGDMA	1.1	gel	gel	gel	gel	gel	gel	gel
BPDMA	0.7	50	30 000	57 000	1.9	4	0.019	0.80
BPDMA	0.8	52	69 000	302 000	4.4	10	0.022	0.91
BPDMA	0.9	51	112 000	319 000	2.9	18	0.023	0.95
BPDMA	1.0	52	131 000	363 000	2.8	2.1	0.023	0.95
BPDMA	1.1	gel	gel	gel	gel	gel	gel	gel
				HPMA/initiator/brancher = 30				
linear PHPMA		34	4700	6000	1.3	0	0.000	0.00
BPDMA	0.7	33	36 000	125 000	3.5	5	0.020	0.87
BPDMA	0.8	31	82 000	235 000	2.9	13	0.022	0.94
BPDMA	0.9	gel	gel	gel	gel	gel	gel	gel

[a] n_b is the average number of brancher units per molecule = $(M_{n,b}/M_{n,l} - 1)$, ρ_b is the branching density = the fraction of brancher units per molecule = $144n_b/M_n^b$. The critical point for the formation of an infinite network is $(M_{n,b} - M_{n,l})/M_{n,b} = 1$.

the degree of polymerization, P, of the primary chain is equal to unity. For polydisperse chains, the condition is $\rho P_{w,l} = 1$, where $P_{w,l}$ is the weight-average chain length (because the longer chains in a polydisperse polymer form a network earlier). If the primary chains are homogeneous then, to a first approximation, $M_{n,l} \approx M_{w,l}$, and at the gel point we have

$$\rho P_{n,l} = \frac{\rho M_{n,l}}{144} = \frac{M_{n,b} - M_{n,l}}{M_{n,l}} = 1 \tag{3}$$

where the quantity $\rho(M_n^l/144)$ is the branching coefficient.

Branching Copolymerizations. A series of copolymerizations of HPMA with two different target degrees of polymerization of the primary chains (50 and 30) and varying contents of EGDMA or BPDMA branchers were performed. In each case the reaction was allowed to proceed to high conversion and judged to be complete (>99% conversion) when no vinyl bonds could be detected by ^{1}H NMR analysis of the reaction mixture (see Figure 2). The resulting copolymers were analyzed by SEC with dual detection and the molecular weight data are summarized in Table 1.

The polymerization of HPMA alone gives a polymer of low polydispersity ($M_w/M_n = 1.05$). When the branching agent is introduced, the polydispersity increases. Both M_n and M_w/M_n increased steadily with increasing BPDMA content, for a given primary chain length. When EGDMA was used as the branching agent, the polydispersity fell at the end of the reaction, which may reflect the formation of a small amount of very high molecular weight material (possibly microgel), which is not detected in the SEC analysis. In all cases the number of primary chains per molecule, n_b, also rose with increasing brancher content, as expected.

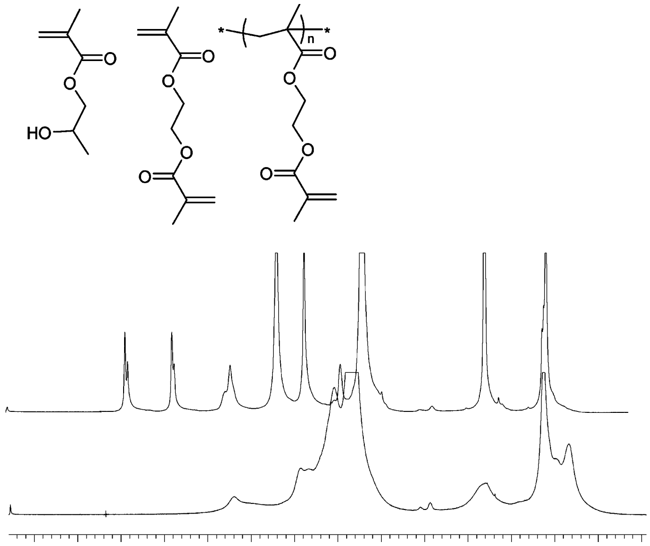

Figure 2. ^{1}H NMR spectra recorded for a PHPMA$_{50}$−EGDMA$_{0.90}$ reaction mixture at 12% conversion and also at the end of the reaction. The monomer conversion was judged to be complete when no signal due to vinyl protons was detectable. The vinyl protons due to the HPMA and EGDMA comonomers were not distinguishable.

Table 2. Molecular Weight and Branching Characteristics of Soluble PHPMA Copolymers from Various Reaction Mixtures Prior to Gelation[a]

	$M_{n,b}$	% conversion	n_b	ρ_b	$(M_{n,b} - M_{n,l})/M_{n,b}$
PHPMA$_{50}$−EGDMA$_{1.1}$	461 000	95	80	0.025	0.99
PHPMA$_{50}$−BPDMA$_{1.1}$	258 000	84	51	0.028	0.98
PHPMA$_{30}$−BPDMA$_{0.90}$	1 550 000	96	332	0.031	1.00

[a] The $M_{n,l}$ at a given conversion was calculated from the linear regression for the appropriate linear analogue.

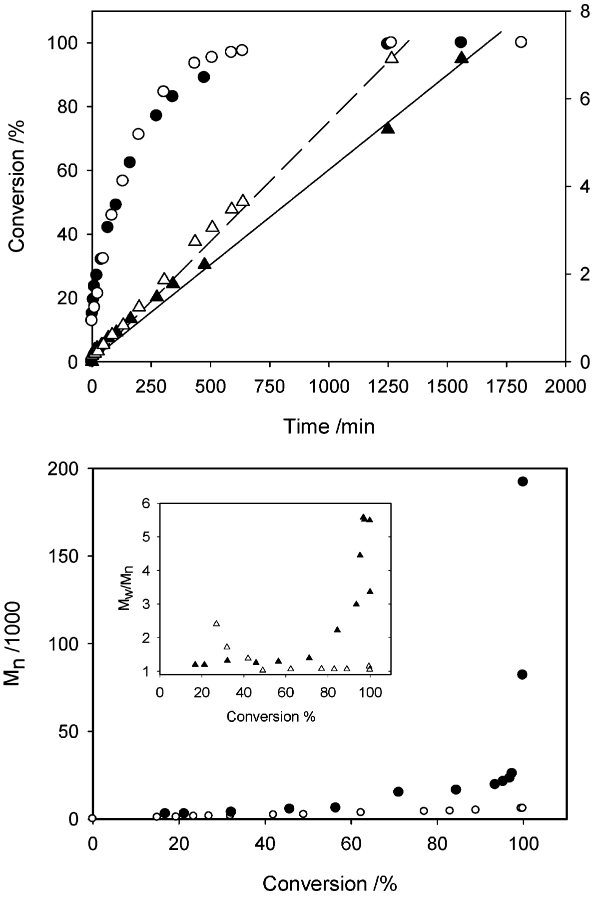

Figure 3. ATRP kinetic data obtained during the synthesis of PHPMA$_{50}$−EGDMA$_{0.90}$ branched copolymer. Upper curve shows conversion (●) and ln([M]$_0$/[M]) (▲) vs time. Lower curve shows M_n (●) and (inset) M_w/M_n (▲) vs conversion. Unfilled points are for the linear HPMA homopolymerization in the absence of any EGDMA.

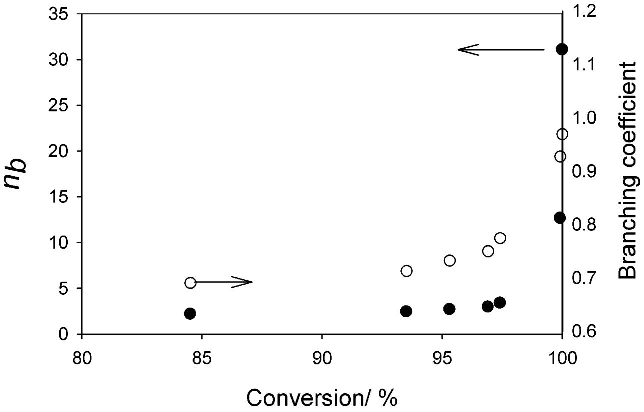

Figure 4. Change in the number of branches per molecule n_b and $\rho(M_n^l/144)$ with conversion for the ATRP of PHPMA$_{50}$−EGDMA$_{0.90}$ copolymer at high conversion. (The M_{nl} for a particular monomer conversion was interpolated from the linear regression of the polymerization kinetics obtained for PHPMA$_{50}$ homopolymer.)

For the copolymers prepared with EGDMA, the average number of primary chains per molecule at 100% conversion rises rapidly with increasing EGDMA content to reach a value of 40 for one EGDMA molecule per primary chain. The critical product $\rho P_{n,l}$, as defined by eq 3, was less than unity for the soluble polymers and 0.99 for one EGDMA per primary chain. This implies that the system is very close to gelation ($\rho P_{n,l} = 1$), as confirmed by the fact that a reaction mixture containing 1.1 mol of EGDMA per primary chain gelled before all of the monomer was consumed.

These results imply that the branching reaction in the HPMA/EGDMA system is close to ideal, since any nonreactivity or cyclization of pendent double bonds would lead to a reduction in the value of $\rho P_{n,l}$. The same calculation for the last copolymer sample extracted from reactions that gelled revealed that $\rho P_{n,l}$ is close to unity in all cases (see Table 2).

The HPMA/BPDMA mixture gels below 100% conversion at a BPDMA:HPMA ratio of 1.1:50. However, at 1.0:50 the PHPMA−BPDMA chains produced at 100% conversion are slightly less branched than those formed with the EGDMA brancher, having on average only 20 primary chains per molecule, as compared to 40 in the case of EGDMA. As shown in Table 2, soluble but highly branched copolymer ($\rho P_{n,l} = 0.98$) can be formed at 85% conversion when the BPDMA:HPMA ratio is 1.1:50. These data suggest that the BPDMA is somewhat less efficient in branching the copolymer, but there is not a dramatic deviation from ideality.

In contrast to the soluble branched copolymers with a target primary chain length of 50 HPMA units, where the use of up to 1 mol of brancher per primary chain is possible, gelation was observed for the polymers with target DP of 30 when only 0.8 mol of brancher per primary chain was used. However, the polydispersity of the primary chains (1.28) is somewhat higher at this chain length. Since longer chains gel more easily, the broader the molecular weight distribution, the fewer branching units are required to produce gelation. If M_n is replaced with M_w in the calculation, the critical branching product is 0.98 for 0.80:50 BPDMA:HPMA, again suggesting that the branching is not far from the ideal, statistical copolymerization.

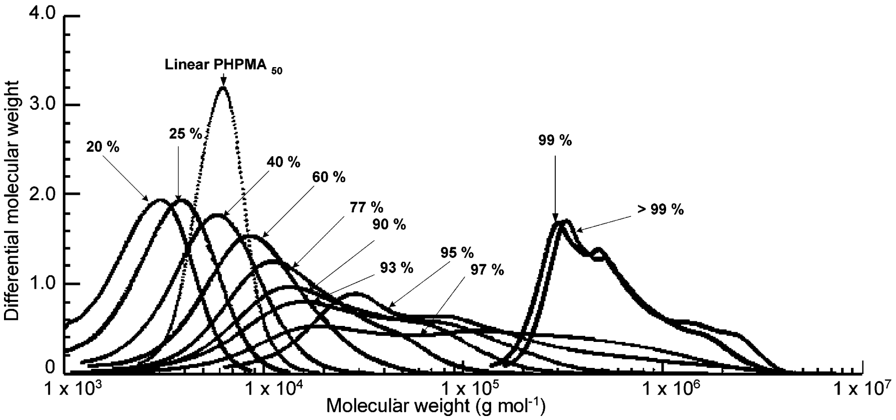

Figure 5. Evolution of the differential molecular weight distribution with conversion for a PHPMA$_{50}$−EGDMA$_{1.0}$ branched copolymer.

We carried out a more detailed analysis during the synthesis of PHPMA$_{50}$−EGDMA$_{0.9}$, taking samples at intervals throughout the reaction. Figure 3 shows the results. The conversion−time curves are quite similar for both the linear and branched reactions over a wide range of monomer conversion. The semilogarithmic plots suggest that the polymerization in the presence of brancher is actually slightly faster up to around 95% conversion. However, we observed that the last 5% of monomer consumption, which corresponds to the onset of substantial branching, requires much longer times than that needed for an equivalent linear polymerization. For example, 99% conversion is attained within 8 h at 20 °C in the absence of EGDMA brancher, whereas the same polymerization in the presence of 0.9 mol of EGDMA requires at least 48 h to reach the same conversion. This marked retardation is presumably due to the very rapid increase in the viscosity of the copolymerizing solution in the last 5% conversion. This is in contrast to the results of Wang and Zhu[31] for copolymerization of MMA and EGDMA in bulk monomer, where autoacceleration was observed at high conversions. The present results suggest that the presence of 50% solvent in our reactions is enough to maintain good control even at high conversions.

Where the branching agent is present, M_n increases more or less linearly up to about 90% conversion, closely resembling the linear regression for the PHPMA homopolymer, and only increases steeply in the last 10% conversion.

Figure 4 shows the changes in n_b and the branching coefficient with conversion for the same reaction in the high conversion range. The average number of primary chains per molecule, n_b, rises very rapidly after 95% conversion, showing that the most significant branching takes place in the last few percent of conversion after the unreacted EGDMA monomer in the reaction mixture is almost exhausted. The branching coefficient also rises rapidly in this range. Thus, the pendent vinyl bonds of the incorporated EGDMA monomer react mainly in the last stages of the reaction, when the concentration of the free monomer is very low, linking the primary chains in a statistical manner.

Further evidence that the most significant branching occurs mainly during the later stages of the reaction can be seen in Figure 5, which shows the evolution of the differential molecular weight distribution of PHPMA$_{50}$−EGDMA$_{1.0}$ with conversion. At low conversions the distribution curves are monomodal. At around 80% conversion there is clear evidence that multiples of the primary chains are formed at high conversion. Above 97% conversion, there is a very marked shift of the distribution to much higher molecular weights.

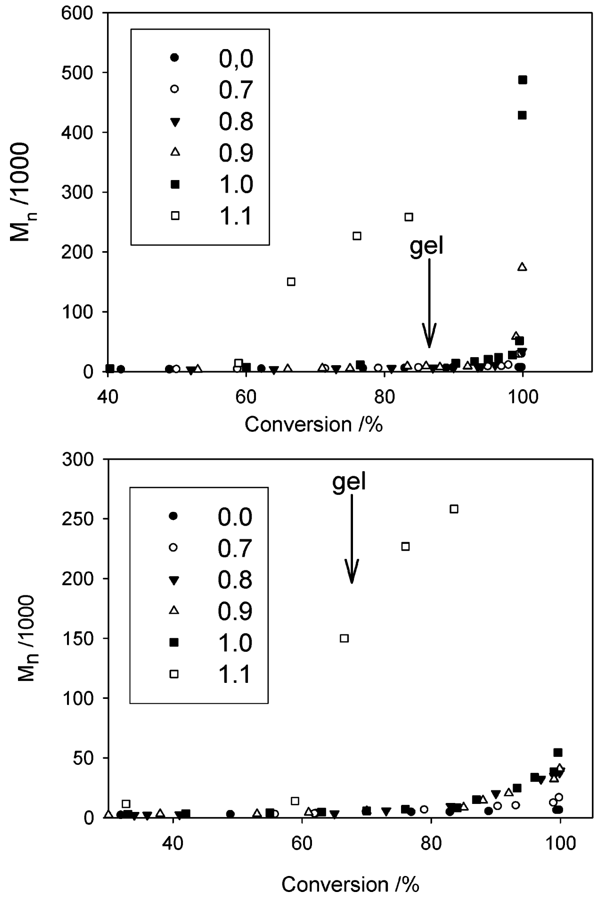

Figure 6. Variation of molecular weight with conversion for the ATRP of HPMA copolymerized with varying mole fractions of branching agent (upper figure, EGDMA, lower figure BPDMA) at a HPMA/initiator molar ratio of 50. Molar contents of branching agent per 50 HPMA units are indicated.

Figure 6 summarizes the change in M_n with conversion for the copolymerization of HPMA to a target degree of polymerization of 50 with varying proportions of both EGDMA and BPDMA branchers. The onset of significant branching occurs earlier for the copolymers with BPDMA brancher (at around 80−85% conversion) than in copolymers where EGDMA was used (at around 90−95% conversion). When 1.1 mol of BPDMA or EGDMA brancher per primary chain is used, the polymer forms an insoluble network, but unlike conventional polymerization, gelation does not occur until very high conversion.

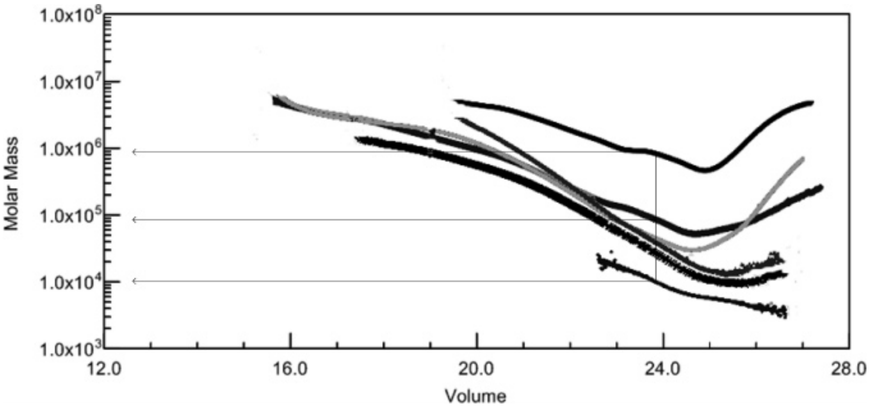

Figure 7. Relationship between molar mass and SEC exclusion volume for the PHPMA$_{50}$−EGDMA$_x$ copolymers at 100% conversion, where x varies from 0 to 1.1. These data were generated using a dual detector SEC instrument.

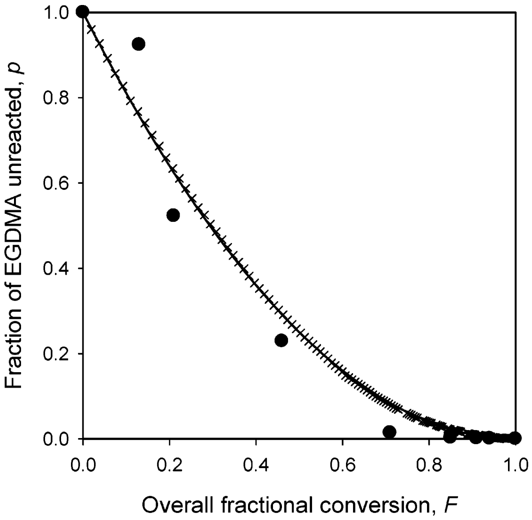

Figure 8. Fraction of unreacted EGDMA monomer, p (measured by GC analysis), as a function of overall conversion, F (measured by ^{1}H NMR), during the synthesis of PHPMA$_{50}$−EGDMA$_{0.90}$ branched copolymer. Experimental points (●) are compared with both eq 4 (solid line) and also a Monte Carlo simulation of the statistical reaction of double bonds (×).

Figure 7 shows the relationship between SEC elution volume and molecular weight derived from the dual detector SEC data obtained for the PHPMA$_{50}$−EGDMA$_x$ copolymers at >99% conversion, where x was varied from 0 to 1.1. It is clear that for a given hydrodynamic radius (or elution volume) the molecular weights of branched copolymers are up to 2 orders of magnitude higher than those of linear PHPMA because the hydrodynamic radius of a branched copolymer is smaller than a linear homopolymer of the same molecular weight. The curvature of the plots for the most highly branched copolymers confirms that they contain copolymer chains with the same molecular weight but quite different elution volumes, due to their different degrees of branching. Similar results were also obtained for the BPDMA-containing copolymers.

Consumption of Branching Agent. Although the analysis of molecular weights and distributions outlined above provides convincing evidence that the polymerization closely follows the ideal Flory−Stockmayer model, further confirmation can be obtained by comparing the predicted and actual curves for consumption of the branching agent as a function of overall conversion. To follow the incorporation of the EGDMA brancher into the primary PHPMA chains, the amount of unreacted EGDMA in the reaction solution was determined by gas chromatography. (The signals due the vinyl protons of the HPMA and EGDMA monomers are not clearly distinguishable in the ^{1}H NMR spectrum.) This analysis gave the relative concentrations of the two monomers at different stages of the reaction. The fraction of the unreacted EGDMA remaining in the reaction mixture is plotted against the overall fractional conversion in Figure 8. As expected, the plot is nonlinear: the concentration of free EGDMA falls more rapidly at the start of the reaction since reaction of only one of its double bonds is sufficient to remove the free brancher from the solution, leaving a pendent double bond.

Theory (see Appendix) shows that, for random consumption of double bonds, the fraction, p, of the EGDMA molecules which remain unreacted should vary with the overall fractional conversion of all double bonds, F, according to

$$p = (1 - F)^2 \tag{4}$$

The validity of eq 4 was tested by a Monte Carlo simulation, and both eq 4 and the simulation results are plotted in Figure 4. The excellent agreement between theory and simulation provides confirmation of the theory, and the fit of the theory to the experimental data supports the view that the double bonds react statistically, with no preference for any particular type.

Conclusions

We have monitored the ATRP copolymerization of HPMA with either EGDMA or BPDMA as branching agents at a fixed mean degree of polymerization of either 50 or 30 and a variable amount of EGDMA branching agent in order to elucidate the mechanism of branching for a living (or in this case pseudo-living) polymerization. As expected, branching is negligible during the early stages of the copolymerization, with polydispersities remaining low up to 70−80% conversion. However, substantial branching occurs in the later stages of the reaction.

Analysis of the branching statistics suggests that the network formation is almost perfectly fitted by the classic Flory−Stockmayer model for gelation in reactions of this type. This is in marked contrast to the similar reaction of MMA and EGDMA by conventional free radical chemistry, where substantial reduction of the efficiency of the branching agent due to cyclization reactions has been reported. This conclusion is confirmed for the HPMA/EGDMA system by an analysis of the consumption of the EGDMA monomer.

This study has clarified several aspects of branched living polymerizations under ATRP conditions. First, the final degree of branching is remarkably sensitive to the precise final conversion, since the molecular weight increases asymptotically in this regime. Indeed, we suggest that degrees of branching are meaningless in such systems unless the corresponding conversions are also stated. Second, as the gel point condition of one branching agent per chain is approached, the syntheses become more irreproducible, with gelation occasionally occurring when this was not predicted. Presumably this is because the degree of branching is very sensitive to relatively small differences in the formulation.

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Appendix. Derivation of Eq 4

A growing copolymer radical has the choice of three double bonds with which to react: those on HPMA molecules, those on EGDMA molecules with two unreacted double bonds, and those on EGDMA molecules with one remaining unreacted double bond, the other having already reacted.

Let (X_n,Y_n) be the numbers of unreacted and singly reacted EGDMA molecules when n of the double bonds on EGDMA molecules have already reacted. At time $t = 0$ or conversion $x = 0$ we have $X_0 = S$, $Y_0 = 0$. The distribution of unreacted and singly reacted EGDMA molecules is independent of the number of HPMA molecules which have reacted since reaction of an HPMA molecule does not change the EGDMA molecules.

(X, Y) develops as a bivariate Markov chain (X_0, Y_0), (X_1, Y_1), (X_2, Y_2), etc. If $X_n = x$, $Y_n = y$, we have that (X_{n+1}, Y_{n+1}) is either: $(x - 1, y + 1)$, with probability $2x/(2x + y)$ or $(x, y - 1)$ with probability $y/(2x + y)$. (This is because one of the remaining $(2x + y)$ double bonds is selected at random to be the next one reacted on the EGDMA molecules.)

Thus, if $(X_{n+1},Y_{n+1}) = (x',y')$, the *average* values are

$$x' = ((x - 1)(2x) + xy)/(2x + y) \quad \text{and} \quad y' = ((y + 1)(2x) + (y - 1)y)/(2x + y)$$

We can simplify and look at differences:

$$x' - x = -2x/(2x + y), \quad y' - y = (2x - y)/(2x + y)$$

Treating x and y as continuous functions, we can divide them to get the (estimated) differential equation

$$\frac{dy}{dx} = -\frac{2x - y}{2x}$$

This equation can be solved by putting $y = \upsilon x$, which leads to

$$2x\frac{d\upsilon}{dx} = -(\upsilon + 2)$$

Separating the variables and integrating, with the initial condition that $\upsilon = 0$ when $x = S$ gives

$$2x = y = 2\sqrt{Sx}$$

Assuming that double bonds are reacted sequentially over time, the rate of change of x with time, t, then becomes

$$\frac{dx}{dt} = \frac{-2x}{2\sqrt{Sx}} = -\sqrt{\frac{x}{S}}$$

This easily integrates to give $x = (2S - t)^2/(4S)$.

Using the *proportion* of unreacted EGDMA molecules, i.e., $p = x/S$, this becomes

$$p = \left(1 - \frac{t}{2S}\right)^2$$

If it is assumed that all double bonds are equally reactive, then the $2S$ double bonds in EGDMA are consumed in proportion to the overall conversion, so that we can write $t = 2FS$, where F is the fractional conversion. This ensures that the reaction stops when $F = 1$ and $S = 0$ and leads to the final relation between p and F in the attractively simple form

$$p = (1 - F)^2$$

This approach gives only *average* behavior, but the actual trajectory will be close to the average because (in the (x,y) format) if Y_n happens, by random chance, to be “too big” (or “too small”), the weights of the two possible next steps are such as to tend to return it to average.

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