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Mechanistic study of Atom Transfer Radical Polymerization in the Presence of an Inimer: Toward Highly Branched Controlled Macromolecular Architectures through One-Pot Reaction

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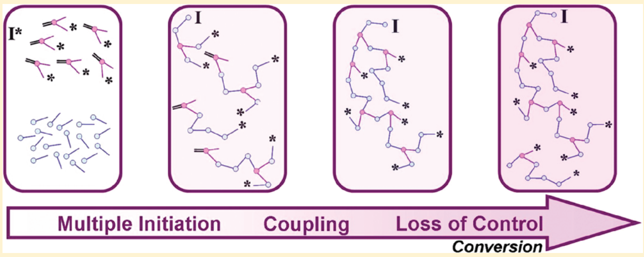
Supporting Information



ABSTRACT: Highly branched polymethacrylates have recently offered new perspectives in lithographic performance and drug delivery. The control of branching remains yet challenging and requires fundamental investigation to consider new applications. Therefore, an advanced study of the formation mechanism of branched polymers synthesized by self-condensing vinyl copolymerization (SCVCP) of a methacrylic AB* inimer, 2-(2-bromoisobutyryloxy)ethyl methacrylate (BIEM), with methyl methacrylate (MMA) via atom transfer radical polymerization (ATRP) has been performed. Evidence of branched structures was obtained with a conventional GPC apparatus equipped with a multiangle light scattering detector and detailed ^{1}H NMR analyses. A three-step reaction scheme is suggested according to the dependence of molecular weight with conversion. Controlled radical polymerization mainly occurs until moderate conversions, with the participation of inimer as chain initiator. Then the polymerization of small macromolecules, through consumption of polymerizable moiety, dramatically increases the molecular weight of polymer. Finally, a loss of control partially due to thermal decomposition of residual comonomers occurs at high conversion. This mechanistic methodology will allow, with adequate reaction process, the one-step preparation of controlled branched macromolecular architectures leading to functional materials.

1. INTRODUCTION

Dendritic and hyperbranched structures are of particular interest in polymer science.[1−11] This is mainly due to their promising use in various industrial applications thanks to inherent specific characteristics compared to linear counterparts.[12−14] For example, their unusual globular and highly branched structure increases their compactness while providing a high density of functional sites on their periphery. They are consequently widely used as viscosity modifiers,[15] catalyst supports[16,17] and drug carriers.[18−23] However the control of the architecture remains challenging. Several polymerization techniques, such as step-growth polymerization and ring-opening polymerization, can lead to various branched structures.[11,24−26] Free radical copolymerization of a monofunctional monomer and a multifunctional comonomer, also called a cross-linking agent, has also been performed[27] but showed limitations in the synthesis of well-defined branched structures despite the use of chain transfer agents.[28] In order to control the architecture while simplifying synthesis, Fréchet and co-workers have developed a one-pot synthesis, self-condensing vinyl polymerization (SCVP),[29] that has been statistically described in terms of molecular weight distribution and branching degree.[30,31] SCVP has been adapted to various polymerization techniques such as living ionic,[32,33] group transfer,[34] and controlled/"living" free-radical processes.[35−39] Regarding the atom transfer radical polymerization (ATRP), a specific monomer named inimer (AB*) is employed. This monomer can undergo a polymerization with its vinyl function (A) and/or can initiate a new branch from its halogen site (B*). ATRP offers a good control over polymer architecture and is versatile enough to control the chain length between two branching points simply by adjusting the monomer to inimer concentration ratio.[40−42]

This convenient polymerization technique has already been performed by our team for the synthesis of polymers dedicated to lithographic applications.[43] To consider new perspectives in this field, it is now essential to precisely understand the formation of the branching architecture. Therefore, a fundamental study has been performed on a model chemical system. In this work, we report on our investigations on the formation mechanism of highly branched polymers (HB) via atom transfer radical polymerization. Multidetection GPC coupled with ^{1}H NMR analyses allow us to suggest a general scheme for the formation of highly

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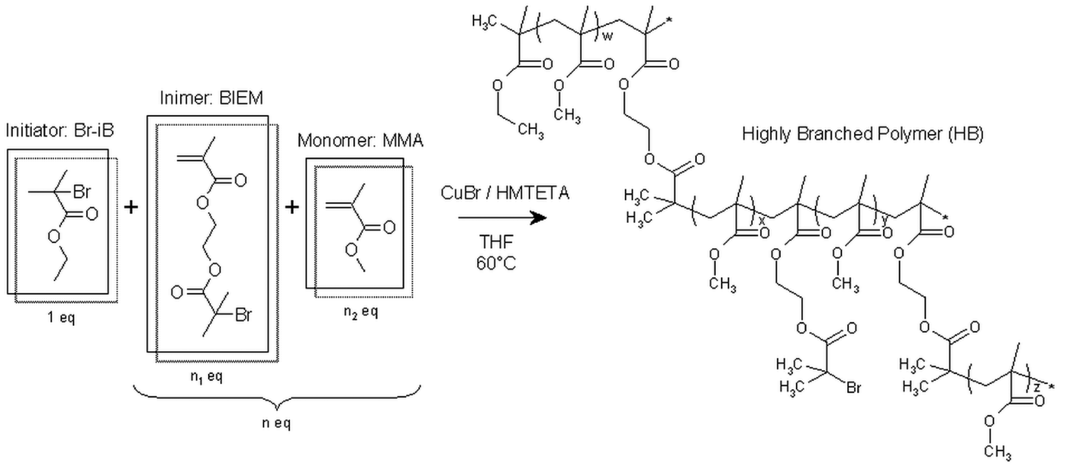
Scheme 1. Synthetic Route to Highly Branched Polymethacrylate by SCVCP of BIEM and MMA



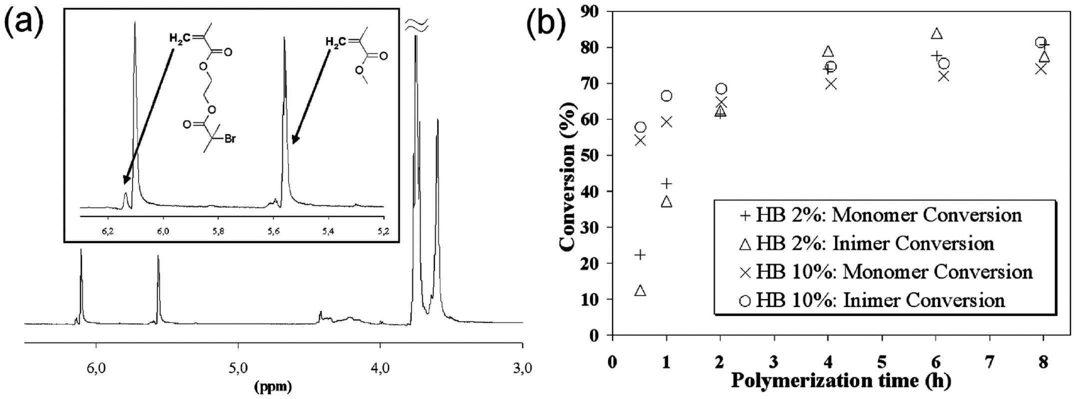


Figure 1. (a) ^{1}H NMR spectrum ($CDCl_3$) of a typical reaction mixture containing 90−10% MMA-BIEM after 6 h of polymerization. (b) Monomer and inimer conversions (in %) with polymerization time (in h) for SCVCP of BIEM and MMA (feeding ratios are MMA/BIEM/Br-iB/CuBr = 294/6/1/1.8 and 270/30/1/5) at 60 °C, in 50 wt % THF. HB X% means highly branched polymer containing X% inimer.

branched polymethacrylates by SCVCP via ATRP and to describe the evolution of this polymerization method from low to high conversions. The fine-tuning of this versatile polymerization process could allow further improvements in the control of the macromolecular branched architectures.

2. RESULTS

2.1. Synthesis of Branched Polymethacrylates through One-Pot ATRP. Controlled radical polymerization of linear polymers via ATRP involves the use of an initiator that determines the number-average degree of polymerization ($\overline{DP_n}$) of the polymer at full conversion[44] ($\overline{DP_n}$ = [monomer]/[initiator]). As can be seen in Scheme 1, a common ATRP-initiator, 2-ethyl bromoisobutyrate (Br-iB), was used for the synthesis of branched polymers, in order to obtain a reference regarding molecular weight that could be compared to the linear counterpart. For theoretical calculations, we have considered that all chains have been initiated by Br-iB. One Br-iB equivalent is thus added to the n equivalents mixture of comonomers. The initial comonomer mixture (for one equivalent of initiator Br-iB) contains n_1 equivalents of inimer 2-(2-bromoisobutyryloxy)ethyl methacrylate (BIEM) and n_2 equivalents of methyl methacrylate (MMA). The chemical composition of the synthesized polymethacrylates is defined by the percentage of each of the two comonomers, and particularly by the inimer (BIEM) content in the polymer, defined to the following: Inimer(BIEM)% = $(n_1/n) \times 100 = (n_1/(n_1 + n_2) \times 100)$. In this case, BIEM is considered as a monomer that reacts with its methacrylate double bond (A) and whose addition increases the length of the vinyl chain.

2.2. Investigation on the Reactivity of Both Comonomers. After the optimization of the catalyst content[38,41,45] (for more details see section C in the Supporting Information), a kinetic study was conducted, at two different inimer contents (2% and 10% inimer) to compare the mechanism for comonomers incorporation in the polymer chain. Conversions of MMA and BIEM could be separately determined by ^{1}H NMR, as shown in Figure 1a (see also section B in the Supporting Information for precise ^{1}H NMR chemical shifts and NMR calculations). BIEM and MMA seem to be incorporated into the polymer chains at similar rates (see Table 1 and Figure 1b). Hence, the comonomer composition in the polymer at intermediate conversions is in fair agreement with the composition in the feed. This observation is further supported by the estimation of the reactivity ratios ($r_1 = k_{11}/k_{12}$ and $r_2 = k_{22}/k_{21}$) of comonomers MMA (1) and BIEM (2).

Table 1. Conversions and C═C Content in the Polymer by ^{1}H NMR for Branched Polymers[a]

reaction conditions		comonomers conversions[c] (%)			C═C % in the polymer	
inimer content (mol %)[b]	polymerization time (h)	MMA	BIEM	inimer % that initiates a branch[c]	theoretical[d]	experimental[c]
2	0,5	22	12	61		
2	1	42	37	87	reference	1.10
2	2	61	62	82	0.75	0.76
2	4	74	79	85	0.62	0.26
2	6	78	84	73	0.59	0.22
2	8	81	78	87	0.57	0.30
10	0,5	54	58	48		
10	1	59	66	50	reference	1.57
10	2	65	68	51	1.45	1.65
10	4	70	75	49	1.34	0.94
10	6	72	75	49	1.30	0.65
10	8	74	81	43	1.26	1.11

[a] Copolymerization of BIEM and MMA (feeding ratios are MMA/BIEM/Br-iB = 294/6/1 and 270/30/1) at 60 °C with optimized CuBr/HMTETA quantity in 50 wt % THF. [b] BIEM feeding ratio in the comonomer feed. [c] Determined by ^{1}H NMR. [d] Calculated using C═C % in the polymer after 1 h of reaction time as reference and considering a controlled radical process until the end of the reaction (linear increase of molecular weight with conversion and no further chain initiation).

Table 2. Molecular Weights, Polydispersity Indexes, and $R_M = \overline{M}_{w\text{-RI}}/\overline{M}_{w,GPC\text{-}MALS}$ Values for Linear and Branched Polymers[a]

BIEM[b] %	$M_{w,GPC\text{-}RI}$[c]	$M_{w,GPC\text{-}MALS}$[d]	M_w/M_n[c]	R_M
0	17 100	16 400	1.20	1.04
2	14 300	15 800	1.75	0.91
10	13 900	17 900	1.63	0.78
20	12 200	17 200	2.11	0.71

[a] (Co)polymerization of BIEM and MMA at 60 °C in 50 wt % THF, polymers with targeted similar molecular weight. [b] Determined by the comonomers feeding ratios. [c] With refractive index detector. [d] With multi-angle light scattering detector.

Using the Fineman−Ross (F-R) linearization method,[46,47] the reactivity ratios r_1 and r_2 were found to be equal to 0.99 and 1.56, respectively (see section D in the Supporting Information for more details). Given that both values are close to 1, we can consider that MMA and BIEM are incorporated into polymer chains with proportions similar to the comonomer feeding ratio. This observation also suggests that the polymerization continues to occur through the A* site (corresponding to the methacryloyl radical or halide) after inimer incorporation, which is necessary to obtain branching points in the architecture.

2.3. Branching Characterization by GPC Multidetection.

The incorporation of inimer was also characterized through its branching ability as the inimer can initiate polymerization with its bromoester (B*) group and generate branching points in the structure. Linear and branched polymers were then characterized by conventional GPC-RI, using PMMA standards for calibration, and GPC-MALS as mass-sensitive detector, to confirm the branching architecture of the polymers. The apparent average molecular weight determined by GPC-RI ($\overline{M}_{w-RI}$) is based on the hydrodynamic volume of the chains; while the absolute molecular weight of the polymer is determined with the online MALS detector ($\overline{M}_{w-MALS}$). Considering that branched structures are more compact than linear polymers for a given molecular weight the ratio between $\overline{M}_{w-RI}$ and $\overline{M}_{w-MALS}$ gives qualitative information about the degree of branching of the polymers. As can be seen in Table 2, the ratio $R_M = \overline{M}_{w\text{-RI}}/\overline{M}_{w\text{-MALS}}$ significantly varies as polymer architecture moves from linear (R_M = 1.04, theoretically 1.00) to highly branched architectures (R_M = 0.71). This parameter thus indicates a trend of branching density of the synthesized polymers.

2.4. Quantitative Measurements of Topological Structure.

The topological structure of branched polymers has been precisely investigated through detailed ^{1}H NMR analyses, demonstrating the presence of branching points in the polymer. A branching point is created when an inimer unit is incorporated in the polymer chain and when both reactive sites (A* and B*) of the inimer continue to add new comonomer units. We have previously shown that reactivity of both comonomers is quite similar; we can thus consider that a branched structure is formed if B* is capable of initiating a new branch when the inimer is incorporated in the polymer chain. As can be seen in Figure 2 (especially Figure 2, panels b and c), two peaks distinctly characterize branch initiation.

Copolymers obtained by SCVCP of MMA and BIEM show peaks at 2.6−2.9 ppm attributed to methylene protons geminal to a bromine atom. The peak comes from the creation of a new active site under the form A* or M* (corresponding to the methacryloyl radical/halide from the AB inimer or from the M monomer respectively) and above all to a new branching point in the structure. Obviously this new peak is not observed in the linear analogue (Figure 2a). The normalized integral ratio of peaks at 2.6−2.9 ppm and peaks at 4.0−4.5 ppm, which correspond to ethylene protons in ethylene glycol spacer, is independent of molecular weights.[30] This ratio characterizes end groups and, in the same way, the incorporated inimer that really initiates a new branch. As can be shown in Table 1, for polymer containing 2% inimer, about 80% of the incorporated inimer initiate a new branch whereas only 50% of the incorporated inimer create branching points in the case of polymer containing 10% inimer (for more details, see also section B in the Supporting Information). This difference can be partially explained by steric hindrance and the difficulty associated with bringing reactive

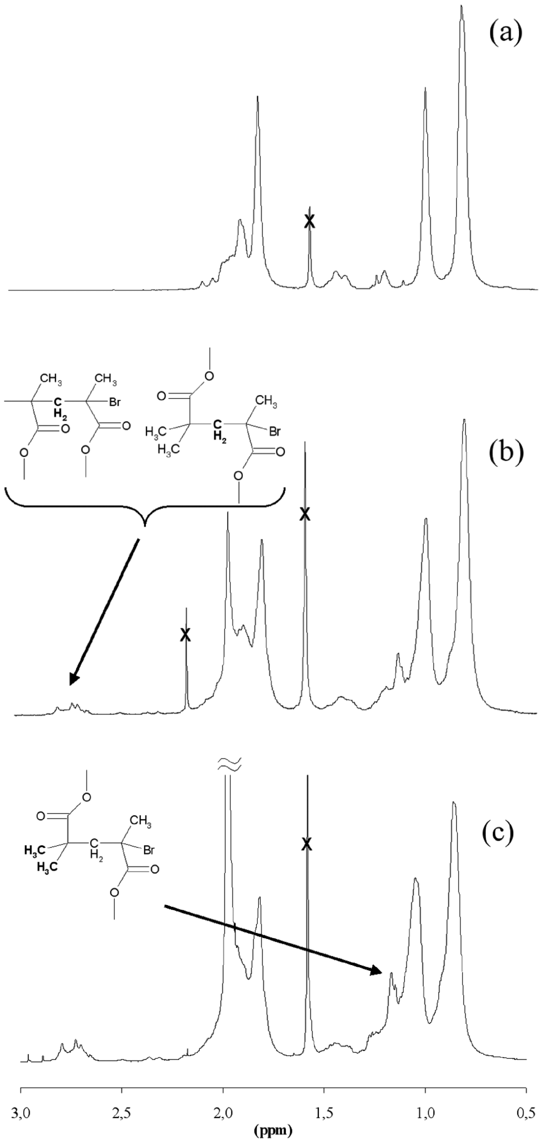


Figure 2. ^{1}H NMR spectra ($CDCl_3$) of a typical polymethacrylate containing (a) 100% MMA, (b) 90−10%: MMA-BIEM, and (c) 80−20%: MMA-BIEM.

species to all the bromine sites at high inimer content, when the structure is more compact.

Furthermore, the broad peaks at 0.7−1.5 ppm are attributed to the methyl group in the backbone. When inimer content increases, peaks at 1.1−1.2 ppm are convoluted with the methyl group peaks (see Figure 2c). The peaks at 1.1−1.2 ppm can be attributed to the six methyl protons previously adjacent to a bromine atom of free inimer (at 1.93 ppm) and then included in the backbone near the branching point. Unfortunately no quantitative result concerning the peaks at 1.1−1.2 ppm can be obtained because of the overlap of methyl groups in the backbone. This further supports the formation of a branched architecture. The advanced characterization by ^{1}H NMR consequently confirms the results suggested by the comparison of GPC results (GPC-RI vs GPC-MALS). The branched architecture of poly(MMA-co-BIEM) has been observed and partially quantified by the calculation of the incorporated inimer rate, whose bromine atom initiates polymerization by adding new comonomer units.

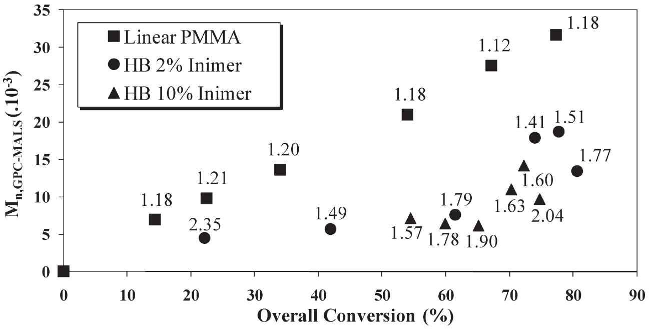


Figure 3. Evolution of the controlled/"living" character of the reaction according to molecular weight $\overline{M}_{\rm n}$ (from GPC-MALS analysis) as a function of overall conversion (in %). The polymerization consists in ATRP of MMA (linear PMMA) and SCVCP via ATRP of MMA and BIEM (feeding ratios are MMA/BIEM/Br-iB/CuBr = 294/6/1/1.8 and 270/30/1/5) at 60 °C, in 50 wt % THF. The PDI obtained from GPC-RI analysis is shown for each sample.

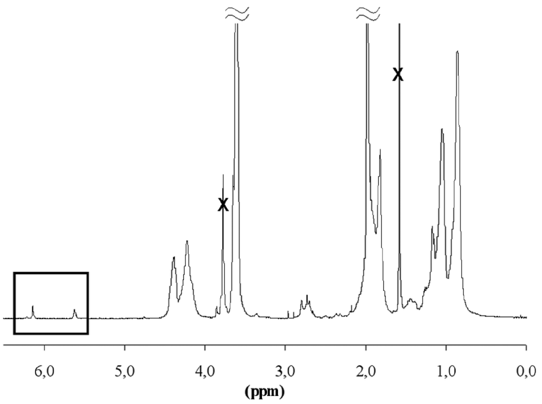


Figure 4. ^{1}H NMR spectra ($CDCl_3$) of a typical polymethacrylate containing 90−10%: MMA-BIEM.

2.5. Kinetics Investigations Correlated with Chain Ends Determination. To investigate the formation of the branched architecture, a kinetic study has been performed for several inimer feeding ratios. As shown in Figure 3, the evolution of absolute number-average molecular weight $\overline{M}_{\rm n-MALS}$, determined using $\overline{M}_{\rm w-MALS}$ and PDI results from GPC measurements ($\overline{M}_{\rm n-MALS} = \overline{M}_{\rm w-MALS}/{\rm PDI}$), was plotted as a function of overall comonomer conversion, determined by ^{1}H NMR. The PDIs of the samples were given for each sample. The study, carried out for linear poly(methyl methacrylate), validates the conclusion that molecular weights ($\overline{M}_{\rm n-MALS}$) increases linearly with conversion and that PDIs of the obtained samples are low.

The linear increase of molecular weight with conversion is not observed for branched polymers. To more precisely investigate the polymer samples, ^{1}H NMR analyses were performed on the purified polymer samples (recovered by precipitation of the polymerization reaction media). As can be seen in Figure 4, protons from the CH_2 group at 6.14 or 5.59 ppm from the double bond of the inimer were still present in polymer chains and were sufficiently well-defined compared to the baseline noise. This allowed for approximate integrals to be calculated. By comparing the integral of these peaks and the normalized integral of peaks at 4.0−4.5 ppm, corresponding to methylene glycol linkage of all incorporated BIEM, it is possible to calculate the proportion of

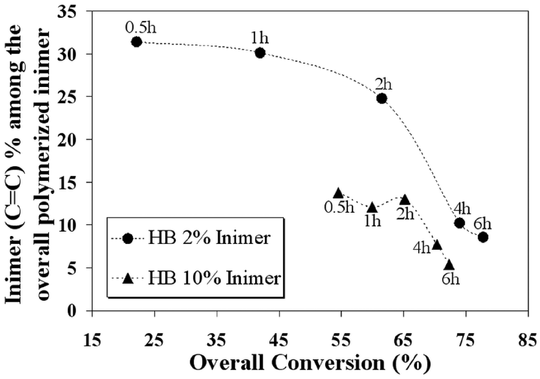


Figure 5. Inimer % (determined by ^{1}H NMR) among the overall polymerized inimer that initiates a polymer chain as a function of overall conversion. The polymerization consists in SCVCP of typical polymethacrylates containing 98−2% and 90−10%: MMA-BIEM. The polymerization time is mentioned on the curves.

inimer that plays the role of chain initiator among all of the incorporated comonomers. According to numerical values in Table 1, after 1 h of polymerization, 1.10% or 1.57% of the incorporated comonomers are inimers under the form of chain initiators (with a double bond), for copolymers containing 2% or 10% inimer respectively. As shown in Figure 5, the presence of inimer as the chain initiator corresponds to above 30% or 10% (depending on the inimer content) of the overall polymerized inimer (for more details, see also section B in the Supporting Information).

In addition, it is possible to evaluate the percentage of inimer as chain initiator (C=C) in the polymer as a function of conversion by taking samples after one hour of polymerization as references for calculation. In these calculations, we consider that all polymer chains have been initiated during this first hour and that polymer chains have grown simultaneously, which are reasonable assumptions for controlled/”living” polymerization. Theoretical percentages of inimer as chain initiator (C=C) in polymer were evaluated (see Table 1 and section B in the Supporting Information for more details) for each sample. As described below, these kinetics results correlated with advanced ^{1}H NMR analyses of purified polymer samples, allowing us to suggest a mechanism for the formation of highly branched architectures.

3. DISCUSSION

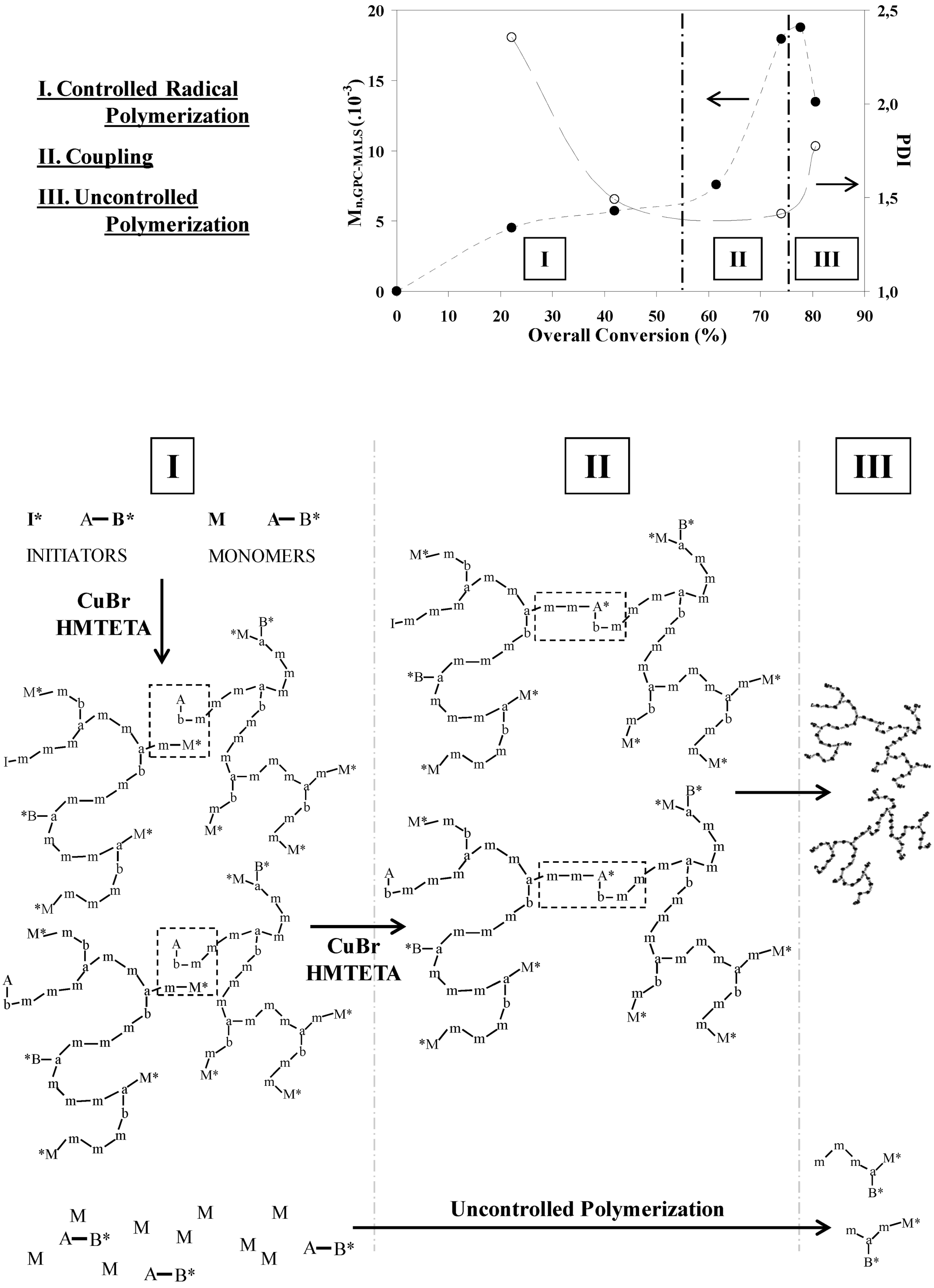
Copolymerization of MMA and BIEM does not exhibit a linear evolution of molecular weight with conversion from the beginning to the end of the reaction (see Figure 3). Three domains can be distinguished on the collected experimental results. The first domain (I) corresponds to conversions from 0 to 55%. The second domain (II) occurs between conversions from 55% to 75%, and the third domain (III) is attributed to higher conversions (>75%). In the following, a possible polymerization mechanism for the formation of the branched architecture is suggested. This study aims at highlighting the predominant phenomenon at the origin of chain growth for each domain.

Domain I has been mainly attributed to a controlled radical polymerization process because of a linear evolution of the molecular weight with conversion (Figure 3). This can also be correlated to a decrease of polydispersity from more than 2.4 to 1.8. However, the number-average molecular weight corresponding to an extrapolated curve is three times lower than the theoretical molecular weight, which is calculated taking into account the assumption that all of the polymer chains were initiated by a Br-iB initiator. This apparent low molecular weight has been attributed to a participation of the inimer to chain initiation step. As well as Br-iB initiator, BIEM also has the ability to initiate polymer chain from its bromine atom (B*). When inimer initiates a polymer chain, a carbon−carbon double bond is located at the end of the macromolecule, as shown via ^{1}H NMR analyses of purified polymer samples. This has been confirmed by the synthesis of a branched polymer (containing 10% BIEM) carried out without the Br-iB initiator. Kinetics results were similar for samples with or without the presence of this initiator (for more details see section E in the Supporting Information).

The predominant behavior in the second domain of Figure 3, proceeding from 55 to 75% conversion, can be attributed to a convergence phenomenon. This means that low molecular weight chains, created by controlled radical polymerization during the first step, couple. As can be seen in Figure 3, the average molecular weight approximately doubles while polydispersity decreases. This two-by-two macromolecular coupling is confirmed by ^{1}H NMR analyses, summarized in Table 1. A great difference between theoretical and experimental percentages of inimer as chain initiator (C=C) in polymer can be observed at approximately 70% conversion. Experimental values are about 2 times lower than the theoretical ones. This difference can be explained by a disappearance of double bonds caused by the inimer playing the role of initiator in the polymer chain. This tendency can also be observed in Figure 5, where the quantity of inimer as initiator (C=C) among the overall polymerized inimer dramatically decreases after 2 h of polymerization. The double bond of a first macromolecule reacts with an active species (*) of a second macromolecule; as a result molecular weight sharply increases. This coupling can also occur at lower conversion but the effect on the polymer properties, especially on its molecular weight, is more significant in the second domain. If convergence occurred until the end of the reaction, PDI would continue to decrease with conversion and all polymer chains would have the same final $\overline{DP_n}$ with one initiator molecule (of 2-ethyl bromoisobutyrate) at the end of each chain.

Nevertheless, coupling generates large compact structures and limits further polymerization because of diffusion limitations. A phase separation appears in the Schlenk at high conversion (in the third domain of Figure 3): one very colored phase being rich in catalyst, even turning dark green and another phase being less colored. GPC analyses, made selectively on the less colored phase, showed similar molecular weight to the one obtained on the entire sample. This result suggests that similar macromolecules are present in both phases and that the concentration of cupper does not influence largely the polymerization process at high conversion. Furthermore, the dark color of the catalyst probably reveals a loss of catalyst efficiency. These observations let us think that controlled/“living” ATRP is no more the predominant phenomenon responsible for chain growth at high conversion. Even though coupling step could still occur at high conversion, gelation should be maintained at a reasonable rate due to the presence of Br-iB initiator that induces the presence of a minimum number of polymer chains. In addition, even if some

Scheme 2. Proposition of Reaction Scheme for the Formation of Highly Branched Polymethacrylates by SCVCP via ATRP



gelation may occur, it is probably not the main phenomenon as, despite the filtration of the sample before GPC analysis, very high molecular weights would also be present on the chromatogram if coupling of high molecular weights occurred, which is not the case. Finally, we suggest that uncontrolled polymerization is most likely conducted at high conversion (>75%) (for more details see section F in the Supporting Information). Methacrylates are indeed capable of pure thermal initiation[48] and this phenomenon could become more visible than previously during the polymerization if controlled/"living" or coupling phenomena are largely unfavored. After six hours of polymerization, molecular weight decreases and polydispersity increases. These characteristics could actually arise from an increase of the number of chains and from their probable short length, due to low concentration of residual comonomers.

Scheme 2 summarizes the suggested three-step polymerization mechanism for the formation of highly branched polymethacrylates. In this scheme, the curved lines represent polymer chains. B* and M* are active units, whereas a, b, and m are incorporated ones. A corresponds to a methacryloyl group of BIEM and M stands for MMA unit. Polymerization can be mainly seen as a controlled radical polymerization predominantly initiated by a part of inimer until moderate conversion. Then convergence of low molecular weight macromolecules significantly increases the molecular weight and finally a loss of control, supported by uncontrolled polymerization of residual comonomers, may occur.

4. CONCLUSIONS

In this work, we have suggested a precise mechanism of SCVCP via ATRP, using a fine analytical methodology, for the one-pot synthesis of branched polymer architectures. Even though the polydispersity was quite low, the dependence of the molecular weight with conversion was not linear during the entire reaction, contrary to what is expected for classical controlled/"living" radical polymerization process. We investigated the polymerization process (from low to high conversions) on a model chemical system (MMA and BIEM), which enabled the suggestion of a three-step mechanism, based upon the predominant mechanism at the origin of chain growth. First, controlled radical polymerization mainly occurred with the participation of inimer mainly as a chain initiator. Then, incorporation of these formed macro-monomers through copolymerization led to a sudden increase of average molecular weight. Finally, neither ATRP nor coupling phenomena mainly occurred but uncontrolled polymerization thermally initiated by residual comonomers contributes to molecular weight evolution at high conversion. Thus, the present work using model monomers with simple chemical structures, allows us to better understand the synthesis of highly branched architecture. This mechanistic study of the SCVCP via ATRP will help to further develop controlled highly branched polymer architectures by influencing the polymerization process using various configurations of chemical reactor systems. It is expected that a continuous-flow microprocess (instead of a batch reactor) might provide significant benefits[49,50] to the discussed polymerization reaction as it has been demonstrated for the synthesis of homo-[51] and copolymers[52,53] through nitroxide-mediated polymerization (NMP). Therefore, through a convenient polymerization technique and an adapted reaction process, other comonomers could be considered for the material design based on highly branched polymers depending on the targeted applications. For instance, drug delivery systems offering versatile functionalization and/or branching density might be synthesized thanks to the control of macromolecular architecture resulting from the present and future works.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. A. Experimental section; B. summary of ^{1}H NMR main chemical shifts and NMR calculations; C. optimization of the catalyst amount for ATRP; D. Fineman−Ross linearization method for the determination of reactivity ratios r_1 and r_2; E. comparison of the polymerization kinetics with and without 2-ethyl bromoisobutyrate initiator, for the synthesis of branched polymers; F. uncontrolled polymerization occurring at high conversion (domain III). This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) Tomalia, D. A. *Polym. J.* **1985**, *12*, 117–132.
(2) Tomalia, D. A.; Fréchet, J. M. J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2719–2728.
(3) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665–1688.
(4) Caminade, A.-M.; Majoral, J.-P. *Acc. Chem. Res.* **2004**, *37*, 341–348.
(5) Hawker, C.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638–7647.
(6) Grayson, S. M.; Fréchet, J. M. J. *Chem. Rev.* **2001**, *101*, 3819–3867.
(7) Helms, B.; Meijer, E. W. *Science* **2006**, *313*, 929–930.
(8) Matthews, O. A.; Shipway, A. N.; Stoddart, J. F. *Prog. Polym. Sci.* **1998**, *23*, 1–56.
(9) Gao, C.; Yan, D. *Prog. Polym. Sci.* **2004**, *29*, 183–275.
(10) Kim, Y. H. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 1685–1698.
(11) Fréchet, J. M. J. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3713–3725.
(12) Tomalia, D. A.; Naylor, A. M.; Goddard, W. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 138–175.
(13) Tande, B. M.; Wagner, N. J.; Mackay, M. E.; Hawker, C. J.; Jeong, M. *Macromolecules* **2001**, *34*, 8580–8585.
(14) De Brabander-van Den Berg, E. M. M.; Meijer, E. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1308–1311.
(15) Sendijarevic, I.; McHugh, A. J. *Macromolecules* **2000**, *33*, 590–596.
(16) Crooks, R. M.; Zhao, M.; Sun, L.; Chechik, V.; Yeung, L. K. *Acc. Chem. Res.* **2001**, *34*, 181–190.
(17) Astruc, D.; Chardac, F. *Chem. Rev.* **2001**, *101*, 2991–3023.
(18) Stiriba, S. E.; Frey, H.; Haag, R. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 1329–1334.
(19) Boas, U.; Heegaard, P. M. H. *Chem. Soc. Rev.* **2004**, *33*, 43–63.
(20) Lee, C. C.; MacKay, J. A.; Fréchet, J. M. J.; Szoka, F. C. *Nat. Biotechnol.* **2005**, *23*, 1517–1526.
(21) Patri, A. K.; Majoros, I. J.; Baker, J. R. *Curr. Opin. Chem. Biol.* **2002**, *6*, 466–471.

(22) Liu, M.; Fréchet, J. M. J. *Pharm. Sci. Technol. Today* **1999**, *2*, 393–401.

(23) Nanjwade, B. K.; Bechra, H. M.; Derkar, G. K.; Manvi, F. V.; Nanjwade, V. K. *Eur. J. Pharm. Sci.* **2009**, *38*, 185–196.

(24) Jikei, M.; Kakimoto, M. A. *Prog. Polym. Sci.* **2001**, *26*, 1233–1285.

(25) Haag, R.; Sunder, A.; Stumbé, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 2954–2955.

(26) Stumbé, J. F.; Bruchmann, B. *Macromol. Rapid Commun.* **2004**, *25*, 921–924.

(27) Poly, J.; James Wilson, D.; Destarac, M.; Taton, D. *Macromol. Rapid Commun.* **2008**, *29*, 1965–1972.

(28) O'Brien, N.; McKee, A.; Sherrington, D. C.; Slark, A. T.; Titterton, A. *Polymer* **2000**, *41*, 6027–6031.

(29) Fréchet, J. M. J.; Henmi, M.; Gitsov, I.; Aoshima, S.; Leduc, M. R.; Grubbs, R. B. *Science* **1995**, *269*, 1080–1083.

(30) Müller, A. H. E.; Yan, D.; Wulkow, M. *Macromolecules* **1997**, *30*, 7015–7023.

(31) Yan, D.; Müller, A. H. E.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 7024–7033.

(32) Paulo, C.; Puskas, J. E. *Macromolecules* **2001**, *34*, 734–739.

(33) Baskaran, D. *Macromol. Chem. Phys.* **2001**, *202*, 1569–1575.

(34) Simon, P. F. W.; Radke, W.; Müller, A. H. E. *Macromol. Rapid Commun.* **1997**, *18*, 865–873.

(35) Hawker, C. J.; Fréchet, J. M. J.; Grubbs, R. B.; Dao, J. *J. Am. Chem. Soc.* **1995**, *117*, 10763–10764.

(36) Gaynor, S. G.; Edelman, S.; Matyjaszewski, K. *Macromolecules* **1996**, *29*, 1079–1081.

(37) Matyjaszewski, K.; Gaynor, S. G.; Kulfan, A.; Podwika, M. *Macromolecules* **1997**, *30*, 5192–5194.

(38) Wang, Z.; He, J.; Tao, Y.; Yang, L.; Jiang, H.; Yang, Y. *Macromolecules* **2003**, *36*, 7446–7452.

(39) Weimer, M. W.; Fréchet, J. M. J.; Gitsov, I. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 955–970.

(40) Matyjaszewski, K.; Gaynor, S. G. *Macromolecules* **1997**, *30*, 7042–7049.

(41) Mori, H.; Seng, D. C.; Lechner, H.; Zhang, M.; Müller, A. H. E. *Macromolecules* **2002**, *35*, 9270–9281.

(42) Mori, H.; Walther, A.; André, X.; Lanzendörfer, M. G.; Müller, A. H. E. *Macromolecules* **2004**, *37*, 2054–2066.

(43) Chochos, C. L.; Ismailova, E.; Brochon, C.; Leclerc, N.; Tiron, R.; Sourd, C.; Bandelier, P.; Foucher, J.; Ridaoui, H.; Dirani, A.; Soppera, O.; Perret, D.; Brault, C.; Serra, C. A.; Hadziioannou, G. *Adv. Mater.* **2008**, *21*, 1121–1125.

(44) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921–2990.

(45) Matyjaszewski, K.; Pyun, J.; Gaynor, S. G. *Macromol. Rapid Commun.* **1998**, *19*, 665–670.

(46) Roos, S. G.; Müller, A. H. E.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 8331–8335.

(47) Fineman, M.; Ross, S. D. *J. Polym. Sci.* **1950**, *5*, 259–262.

(48) Nising, P.; Meyer, T.; Carloff, R.; Wicker, M. *Macromol. Mater. Eng.* **2005**, *290*, 311–318.

(49) Hessel, V.; Serra, C.; Löwe, H.; Hadziioannou, G. *Chem. Ing. Tech..* **2005**, *77*, 1693–1714.

(50) Bally, F.; Serra, C. A.; Hessel, V.; Hadziioannou, G. *Macromolecular React. Eng.* **2010**, *4*, 543–561.

(51) Rosenfeld, C.; Serra, C.; Brochon, C.; Hadziioannou, G. *Chem. Eng. Sci.* **2007**, *62*, 5245–5250.

(52) Rosenfeld, C.; Serra, C.; Brochon, C.; Hessel, V.; Hadziioannou, G. *Chem. Eng. J.* **2007**, *135* (SUPPL. 1), S242–S246.

(53) Rosenfeld, C.; Serra, C.; Brochon, C.; Hadziioannou, G. *Lab . Chip* **2008**, *8*, 1682–1687.