Acrylamide-Based Amphiphilic Block Copolymers via Nitroxide-Mediated Radical Polymerization

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ABSTRACT: Nitroxide-mediated polymerization is shown to produce well-defined poly(*N*,*N*-dimethylacrylamide) samples. In the presence of SG1, a *β*-phosphonylated nitroxide, the free radical polymerization of *N*,*N*-dimethylacrylamide indeed exhibits a "living"/controlled character, provided the nitroxide is used in excess and its concentration finely tuned as compared to that the free radical initiator (AIBN). Poly(*N*,*N*-dimethylacrylamide-*b*-butyl acrylate) diblocks copolymers were subsequently derived by sequential polymerization of the two corresponding monomers.

Introduction

Nitroxide-mediated radical polymerization (NMP),[1] atom transfer radical polymerization (ATRP),[2,3] and reversible addition−fragmentation chain transfer (RAFT)[4] are three methodologies that exhibit the essential features of "living"/ controlled systems under conditions of regular free radical reactions. Compared to ionic "living" systems, these methodologies are easier to carry out and therefore offer an opportunity to revitalize the field of macromolecular engineering. Well-defined complex architectures including block copolymers, stars, dendrimer-like polymers, etc., have lately been obtained rather easily by either technique previously mentioned.[5] The versatility and robustness of these methodologies were further strengthened after it was demonstrated that they can well serve to control the polymerization of a number of functional monomers.[6]

The radical nature of these methodologies and the tolerance of radicals toward polar functions are indeed additional advantages over ionic systems, which generally require the protection of these groups or very drastic conditions. However, there are few exceptions where the functional monomer can poison the system responsible for the control of the radical polymerization. For instance, acrylic acid cannot be polymerized by ATRP under controlled conditions because of its presumable reaction with Cu^{II} species, the activation/deactivation process being thereby disrupted.[6] *N*,*N*′-Dimethylacrylamide (DMAA) is another monomer whose controlled polymerization via ATRP was quite challenging. Catalytic systems based on CuBr and 2,2′-bipyridine, PMETA, or even Me_4Cyclam as ligands failed to bring about a controlled polymerization of the latter monomer.[7] However, diblock copolymers containing a α,*ω*-PDMAA block could be derived using a well-defined *ω*-bromopoly(butyl (meth)acrylate) as macroinitiator.[7] Recently, Matyjaszewski and co-workers showed that DMAA can be polymerized under controlled conditions, provided Me_6TREN is used as ligand in conjunction with CuCl and appropriate chlorinated initiators.[6] Sawamoto and co-workers[8] also reported controlled polymerization of DMAA in toluene in the presence of their catalytic system based on $RuCl_2(PPh_3)_3$/$Al(Oi\text{-}Pr)_3$ and an alkyl halide-type initiator, although resulting polydispersities were higher than 1.6.

The RAFT process does not involve such limitations with monomers containing polar functions. Rizzardo and co-workers showed that PDMAA-*b*-PS diblock copolymers could be obtained with a narrow polydispersity by chain extension, using *ω*−thiocarbonylthio-PS as initiator and AIBN as radical source.[9] The McCormick team also contributed to this field with their report on the controlled polymerization of sulfonate- and butanoate-containing acrylamido monomers in the presence of dithiobenzoate and a radical source.[10] The same authors recently reported the synthesis of narrowly distributed samples of PDMAA by RAFT polymerization, but they could not precisely control their molar mass.[11,12]

Nitroxide-mediated polymerization is another main methodology of control of radical polymerization which employs this family of stable scavenging radicals to reversible trap growing radicals and thereby suppresses irreversible termination. Li and Brittain[13] and also other contributors attempted to polymerize DMAA in the presence of TEMPO but could not control the growth of PDMAA chains with such nitroxide, obtaining samples with rather large polydispersities (1.55−2). Using 2,2,5-trimethyl-4-phenyl-3-azahexane 3-nitroxide, Hawker and co-workers demonstrated the ability of the latter α-hydrogen-bearing stable radical to bring about the controlled polymerization of DMAA at 120 °C.[14] *N*-*tert*-Butyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl)-*N*-oxyl (DEPN), now available under the trademark of SG1, is another highly valued α-hydrogen-bearing nitroxide that gives rise to alkoxyamines functioning below 100 °C.[15]

In this paper we report on the ability of SG1 to control the free radical polymerization of DMAA through the classical mechanism of capture and release of growing transient radicals. The experimental conditions that allow for a precise control over the molar mass and polydispersity of the samples formed were in particular investigated. In our continuing efforts to expand the

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applicability of SG1-mediated polymerization, we also wished to derive poly(*N*,*N*′-dimethylacrylamide-*b*-*n*-butyl acrylate) (PDMAA-*b*-PBuA) amphiphilic block copolymers from the PDMAA−SG1 precursor.

Experimental Section

Materials. *N*-Butyl acrylate (BuA) from Aldrich and *N*,*N*-dimethylacrylamide (DMAA, Aldrich) were purified by distillation over CaH_2 prior to their use. *N*-*tert*-Butyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1, 84−90%) was provided by TotalFinaElf and used as received. 2,2′-Azobis(isobutyronitrile) (AIBN, Merck) was recrystallized from methanol. All reagents were stored at 3 °C under nitrogen after purification. All the solvents were of analytical grade and used without further purification. Water was purified using a Millipore Milli-Q system.

A Schlenk flask was charged with AIBN (0.0523 g), SG1 (0.25 g), and DMAA (8.06 g). The reaction mixture was thoroughly deoxygenated by three freeze−pump−thaw−N_2 cycles. The Schlenk flask was placed into a preheated oil bath and stirred at 120 °C. The polymerization was discontinued and stopped after 60% monomer consumption (7 h). After quenching in liquid N_2 dichloromethane was added, and the polymer was precipitated in cyclohexane (1×) or *n*-pentane (2×) (overall yield: 70−80%). The colorless polymer powder was dried under vacuum without heating.

SG1-terminated poly(*N*,*N*-dimethylacrylamide) (PDMAA−SG1) (0.504 g), excess SG1 (0.0056 g), and *n*-butyl acrylate (64.63 mL) were charged in a Schlenk flask. Then the system was deoxygenated by three freeze−pump−thaw−N_2 cycles, placed into a preheated oil bath, and heated at 110 °C for the required duration (∼20 h). The reaction mixture was then quenched in liquid N_2. Tetrahydrofuran was added prior to precipitation ($MeOH/H_2O$; 0 °C). Precipitations of copolymers of lower molecular masses were centrifuged (10 min, 10 000 rpm) before filtering. The copolymer was recovered as a colorless film after drying under vacuum at room temperature.

Aliquots for kinetic studies were removed by a syringe under a N_2 stream. Subsequently, the reaction mixture was deoxygenated by another three heat and thaw cycles. Excess monomer was removed by evaporation at room temperature, and conversion was determined gravimetrically.

Characterization. Molar mass and molar mass distribution of PDMAA samples were determined by size exclusion chromatography (SEC). The latter was calibrated using PDMAA samples whose molar masses were determined by ^{13}C NMR. A linear variation of M_n as a function of elution times was obtained for the calibration curves. The SEC measurements were performed at room temperature with dimethylformamide (DMF) as eluent using an equipment consisting of a Tosohaas guard, three Tosohaas TSK-Gel HR columns, a Jasco PU-1580 pump, and a Jasco RI-1530 differential refractometer.

^1H NMR spectra were recorded using a Bruker AC 250 MHz spectrometer using $CDCl_3$ as solvent. A Bruker ARX/300 (300 MHz) spectrometer was used for ^{13}C NMR spectroscopy.

Results and Discussion

Poly(*N*,*N*-dimethylacrylamide) has found wide use in the pharmaceutical/personal care industries, owing to its remarkable properties such as water solubility and biocompatibility. As our main aim is the preparation of PDMAA-based amphiphilic block copolymers for subsequent studies of their structure−property relationships in bulk, it was essential to first synthesize PDMAA in a controlled fashion, i.e., with predetermined molar mass and molar mass distribution.

The polymerization was triggered upon heating DMAA at 120 °C in the presence of AIBN and SG1 used as bicomponent initiating/controlling system. With a [AIBN]/[SG1] ratio of 2 (stoichiometric amount) the polymerization went out of control, adopting a somewhat explosive regime. The following sequence of events might have occurred that can explain the loss of control of the polymerization and its lack of reproducibility. As initiation by the radicals released by the decomposition of AIBN is almost instantaneous at 120 °C ($t_{1/2}$ = 44 s at 123 °C), the concentration of propagating radicals can reach quite high values within a very short period of time. For monomers with large propagating rate constant, k_p, such as DMAA,[16] it is essential that the growing radicals could be efficiently scavenged by the nitroxide present in the medium or self-terminate to counterbalance their fast propagation. Otherwise, monomer conversion is bound to increase sharply and reach completeness in a few minutes. As such a scenario is also accompanied by a rapid increase of temperature due to the exothermicity of polymerization, the latter may well get out of control and lead to an explosion. This is exactly what was observed in our case where a conversion as high as 90% was reached within a few minutes.

As previously experimented by several authors,[17,18] including us,[15] and also theorized by Fukuda[19] and lately by Fischer,[20] the only strategy to prevent such a catastrophic evolution is to add an excess of scavenging nitroxides before triggering polymerization. The excess of nitroxide that is necessary to control polymerization can be calculated beforehand, using the theoretical work recently published by Fischer and co-workers.[20] They demonstrated that the following well-known relation established by Georges[21] and used by others[18]

$$\ln([M]_0/[M]) = k_p[P^\bullet]t = k_pK([P{-}X]_0/[X^\bullet]_0)t \quad (1)$$

holds only if $[X^\bullet]/[P{-}X]$ is larger than $(3 \ln 10\ Kk_t/([P{-}X]_0k_p))^{1/2}$ for a period of time (t) comprised between t_1 and t_2, where t_1 ($t_1 = 1/k_c[X^\bullet]_0$) is in the millisecond region and t_2 ($t_2 = [X^\bullet]_0^3/3K^2[P{-}X]_0^2k_t$) corresponds to 90% monomer conversion. In this relation, k_p represents the rate constant of propagation, k_t the rate constant of self-termination, K the equilibrium constant between active and dormant chains

$$P{-}X \underset{k_c}{\overset{k_d}{\rightleftharpoons}} P^\bullet + X^\bullet; \quad K = k_d/k_c$$

and $[M]_0$ the initial monomer concentration.

Under these conditions only would [PDMAA$^\bullet$] experience a stationary state and $\ln\{[M]_0/[M]\}$ increase linearly with time (Figure 1). As no reliable and trustable values of k_p and k_t are available for DMAA in the literature, we did not try to determine K nor did we manage to calculate the excess of nitroxide $[SG1]_{exc} = [SG1]_0 - 2f_a[AIBN]_0$ (with $f_a < 1$) precisely required for eq 1 to hold. In addition, the focus of the current work was placed on the preparation of well-defined block copolymers rather than kinetics. These are the reasons that led us to use the rate and equilibrium constant values reported for the *n*-butyl acrylate/SG1 system for the calculation of the approximate excess of nitroxide required in the present case. Considering the chemical structure of both DMAA and BuA and the fact that the polymerization of the latter monomer also runs out of control in absence of initial SG1 excess, one can hypothesize without major risk that they should behave similarly. Applying eq 1 with the rate and equilibrium

Table 1. Polymerization of *N,N′*-Dimethylacrylamide Initiated by AIBN in the Presence of SG1

[AIBN] (10^{-2} mol L^{-1})	[SG1] (10^{-1} mol L^{-1})	time (h)	conv[b] (%)	$\bar{M}_{n,th}$ (g mol^{-1})	$\bar{M}_{n,exp}$[a] (g mol^{-1})	PDI (SEC)
9.1	2.2	11	70	3200	3400	1.13
5.7	1.38	10	70	4500	4400	1.12
5.8	1.35	10	60	5000	5200	1.07
5.6	1.34	10	60	5000	6300	1.14
5.5	13.1	10	60	5300	6300	1.10
3.7	0.86	7	40	7900	6400	1.08
1.1	0.82	8	50	27100	19000	1.07
1.3	0.26	16.5	90	22000	37400	1.16

[a] Determination by SEC calibrated with $\bar{M}_n$ values obtained from NMR characterization. [b] Evaluation by gravimetric measurements.

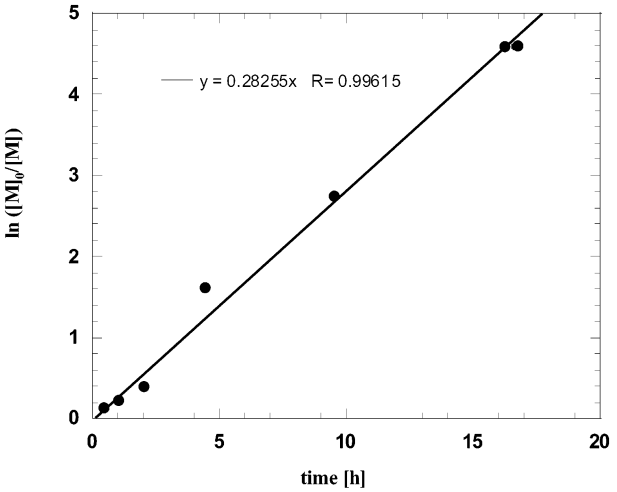

Figure 1. Evolution of $\ln\{[M]_0/[M]\}$ vs time for the polymerization of DMAA carried out at 120 °C in the presence of SG1.

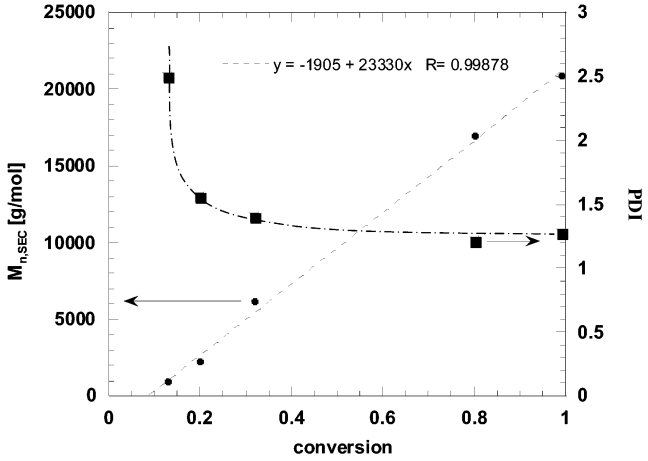

Figure 2. Evolution of $\bar{M}_n$ vs conversion and PDI vs conversion for the polymerization of DMAA at 120 °C and in the presence of SG1.

constants reported for the *n*-butyl acrylate/SG1 system[15,22] affords

$$[SG1] > (3 \ln 10\, K k_t/([P{-}SG1]_0 k_p))^{1/2}$$

with $K_{BuA/SG1,120°C} = 1.2 \times 10^{-10}$, $k_{p,BuA,120°C} = 9 \times 10^4$ L mol^{-1} s^{-1}, and $k_{t,BuA} = 2 \times 10^8$ L mol^{-1} s^{-1}.

According to this calculation, the initial concentration in SG1 should be at least 3.0−3.5 mol % larger than $[AIBN]_0$ −assumed to be equal to 0.5[P−SG1]−for propagation to occur under "living"/controlled conditions at 120 °C. For example, for a concentration of dormant species (PDMAA−SG1) equal to 1.14×10^{-1} mol L^{-1} ($[AIBN]_0 = 5.7 \times 10^{-2}$ mol L^{-1}), more than 4×10^{-3} mol L^{-1} excess of SG1 would be necessary to maintain [PDMAA•] constant and to control polymerization. In general, we added a larger excess of nitroxide than these calculated values (see Table 1, line 2).

In the presence of such an excess of nitroxide which is certainly not an optimized one, the polymerization of DMAA proceeded smoothly and exhibited a "living"/controlled character: indeed, the two criteria of livingness, which are a linear increase of $\ln\{[M]_0/[M]\}$ with time and a linear variation of $\bar{M}_n$ with conversion, are satisfied (Figures 1 and 2). The $\bar{M}_n$ of low molar mass samples were determined using ^{13}C NMR, the values obtained serving to calibrate the SEC columns. Both expected and experimental molar masses were found to agree in a range extending from a few thousand to more than 3×10^4 g mol^{-1}; the polydispersity index of the samples prepared under these conditions never exceeded 1.2 (Figure 3, Table 1).

Next to these syntheses poly(*n*-BuA) blocks were grown from these poly(DMAA-SG1) macroinitiators. To avoid the presence of dead chains in a detectable amount, the samples of PDMAA that subsequently served as macroinitiator were all isolated after discontinuing polymerization at moderate conversion (≈60%). Whatever their size and the size of the PBuA block targeted, an excess of SG1 (≈1%) was introduced in the reaction medium along with *n*-BuA. The PBuA blocks could be grown upon heating both monomer and macroinitiator to 110 °C. The diblock copolymer samples obtained were purified by precipitation and characterized by ^1H NMR. Knowing the molar mass of the PDMAA block, it was easy to deduce that of the second block from the ratio of the signal at 3.8−4.2 ppm due to $-OCH_2$ protons of *n*-BuA units to that attributable to

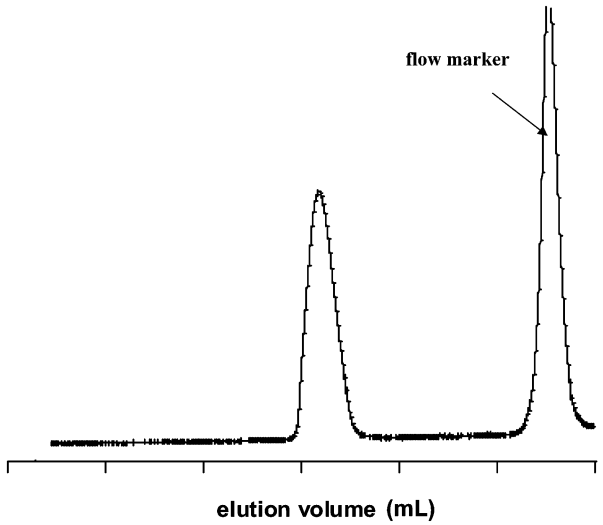

Figure 3. SEC trace of a PDMMA sample of 6400 g mol^{-1} and a PDI of 1.08.

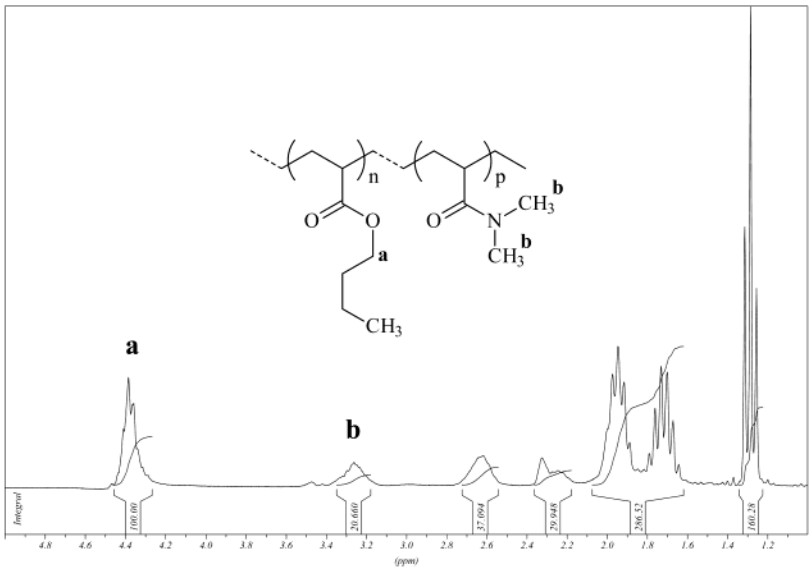

Figure 4. ^{1}H NMR spectrum of a PDMAA-*b*-PBuA copolymer.

Table 2. Polymerization of *n*-Butyl Acrylate at 110 °C from PDMAA−SG1 Macroinitiator

PDMAA precursor		PBuA blocks		PDMAA-*b*-PBuA	
PDMAA−SG1 $\bar{M}_n$ (g mol^{-1})	[PDMAA−SG1]$_0$ (mol L^{-1}) × 10^{-3}	conv[a] (%)	$\bar{M}_{n,NMR}$ (g mol^{-1})	$\bar{M}_{n,SEC}$ (g mol^{-1})	PDI (SEC)
6400	4.1	20	12 900	25 100	1.17
6400	4.1	79	50 500	76 400	1.10
6400	4.1	89	57 500	88 000	1.22
5200	5.4	20	31 400	58 800	1.12
5200	5.4	24	38 200	73 000	1.13
5200	5.4	33	51 800	103 200	1.08
5200	5.4	37	57 600	103 700	1.10
4500	2.4	21	64 500	60 500	1.20
3500	1.1	18	77 500	80 500	1.19
6000	4.1	56	58 500	90 000	1.34
10500	1.1	30	130 000	161 500	1.40

[a] Evaluation by gravimetric measurements.

the six dimethylamino protons of DMAA at 2.7−3 ppm (Figure 4). The molar mass obtained for the PBuA blocks through this calculation were all found in excellent agreement with the targeted values, attesting to the controlled growth of the second PBuA blocks (Table 2). PBuA blocks of rather large size could be grown under these conditions: the SEC characterization of these diblock copolymer samples all revealed symmetrical traces and narrow molar mass distribution (Figure 5, Table 2). No shoulder in the lower molar mass region indicating the presence of residual PDMAA could be detected, nor in the higher molar mass side that would have revealed the presence of recombined chains. Both the ln([M$_0$]/[M]) vs time plot and the $\bar{M}_n$ vs conversion evolution varied perfectly linearly, confirming that the polymerization of BuA occurred under "living"/controlled conditions with PDMAA−SG1 as macroinitiator and an excess of SG1 (Figures 6 and 7).

In contrast, attempts to obtain the same PDMAA-*b*-PBuA diblocks from PBuA−SG1 macroinitiators afforded samples exhibiting a poor blocking efficiency (0.7−0.8). This demonstrates that the order of monomer addition and polymerization matters and that the blocking efficiency is subordinated to a favorable interplay between different reactions/equilibria, i.e., rate constant of cross addition, rate constant of propagation of the second monomer, and equilibrium constants between the respective dormant and active species of the two monomers.[22]

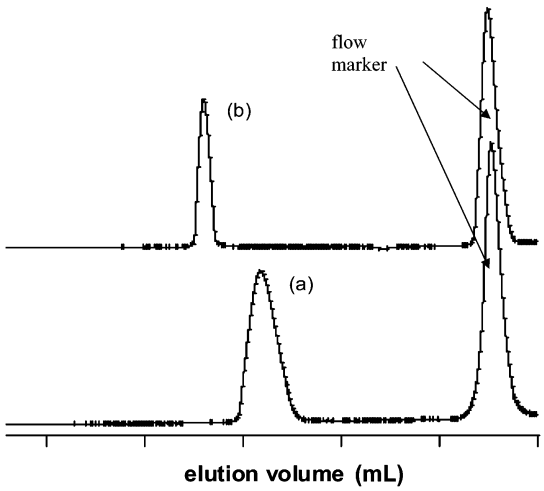

Figure 5. SEC traces of a PDMAA−SG1 macroinitiator (a) and of the resulting PDMAA-*b*-PBuA diblock copolymer (b).

Conclusion

The polymerization of *N*,*N*-dimethylacrylamide initiated by AIBN in the presence of an excess of SG1 proved to be well-controlled, affording poly(DMAA) samples whose polydispersities ranged from 1.07 to 1.20. Those PDMAA−SG1 precursors were further used to grow a second poly(BuA) block with an accurate control of both molar masses and polydispersities. No homopolymer

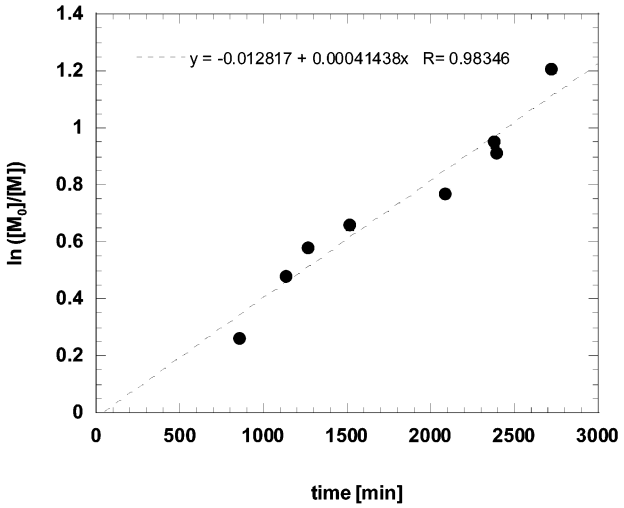

Figure 6. Evolution of $\ln\{[M]_0/[M]\}$ vs time for the polymerization of BuA initiated by a PDMMA−SG1 precursor of 6250 g mol^{-1} molar mass at 110 °C.

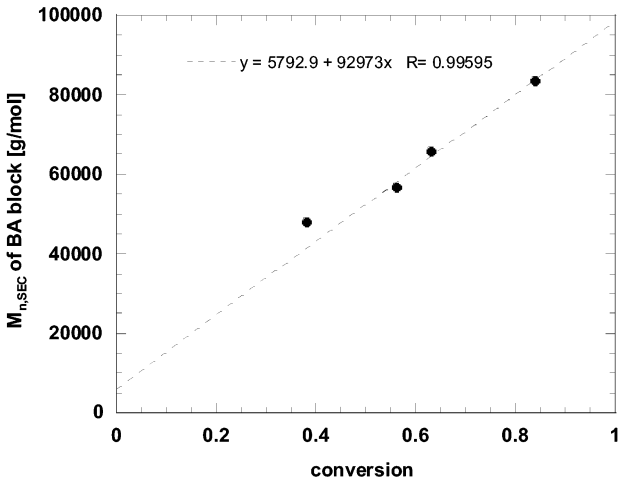

Figure 7. Dependence of $\bar{M}_n$ on conversion for the BuA block in the system of PDMAA-*b*-PBuA copolymer. $\bar{M}_n$ of PDMAA−SG1 precursor: 6250 g mol^{-1}.

contamination could be detected. Well-defined PDMAA-*b*-PbuA diblocks could be obtained in a wide range of mass and composition. Interest in such diblocks arises from the combination of the hydrophilic character of the PDMAA blocks and the low-T_g poly(BuA) blocks.

Current investigations to correlate the composition to the nanostructure of these copolymers will be presented in a forthcoming paper.

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