Molecular Weight and Functional End Group Control by RAFT Polymerization of a Bisubstituted Acrylamide Derivative

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Received September 5, 2002; Revised Manuscript Received November 17, 2002

ABSTRACT: Controlled radical polymerization of the bisubstituted acrylamide derivative *N*-acryloylmorpholine (NAM) has the potential to yield telechelic polymers, one end of which can subsequently be grafted to latex particles. Once grafted, the other chain end of the polymer can be used as an immobilization site for species with applications in molecular biology and biomedicine. The controlled polymerization of NAM using reversible addition−fragmentation chain transfer (RAFT) is performed using two new chain transfer agents S=C(Z)−SR bearing the same functional propanoic acid group (R) and two different Z groups, benzyl (CTA 1) and phenyl (CTA 2). RAFT polymerization of NAM mediated by CTA 1 is very fast (>80% conversion in less than half an hour at 65 °C). The linear evolution of $\bar{M}_n$ and the low polydispersity indices ($\bar{M}_w/\bar{M}_n$ < 1.2) are in accord with the expected characteristics of a living polymerization. CTA 2 leads to broader $\bar{M}_w/\bar{M}_n$'s (<1.4). The resulting CTA-capped polymers were further used to yield an amphiphilic polyNAM-*block*-polystyrene. These α,ω-functionalized polyNAM chains were characterized by ^{1}H NMR and MALDI-ToF mass spectrometry.

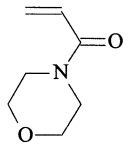
Introduction

N-Acryloylmorpholine (NAM) is a bisubstituted acrylamide derivative (Scheme 1) whose corresponding polymer can be used in molecular biology and biomedicine.[1,2] The polymer has a number of useful properties,[3−6] including solubility in water and other polar and low-polarity solvents. *N*-Acryloylmorpholine has been used for many years in biological applications[1,2,7−11] and in photocurable products such as inks.[12] Previous work by some of the present authors studied the conventional free-radical homopolymerization[13] of NAM and its copolymerization with an activated-ester monomer.[14]

The present paper shows that controlled radical polymerization can be used for this process, thereby opening up a range of potential biomedical applications for the resulting polymers. For example, one could synthesize α,ω-functionalized polymer chains, one end of which can subsequently react with appropriate functional groups introduced at the surface of the latex.[15] The other chain end could be used for the immobilization of single-stranded DNA fragment probes. The other chain end could also be functionalized by a sugar, which would lead to polymers with application in carbohydrate−protein recognition.[16−18]

Controlled radical polymerization using reversible addition−fragmentation chain transfer (RAFT)[19−21] is applicable to a wide range of monomers and can be performed in a wide variety of solvents under a broad range of conditions. In this process, a dithioester chain transfer agent (CTA), S=C(Z)−SR, reacts with either the primary radical derived from an initiator or a propagating polymer chain (P•), forming a new CTA and

Scheme 1



eliminating R•, which is able to reinitiate the polymerization. The polymerization is controlled by the transfer of the CTAs between dormant and active chains. Molecular weight control can be adjusted by the relative amount of reagents involved in the polymerization; the end-functionality of the resulting chains is controlled by the nature of the substituents Z and R on the CTA. Earlier work on RAFT-mediated polymerization of NAM has been performed using four different CTAs: *tert*-butyldithiobenzoate, carboxymethyldithiobenzoate, (1-(4-methylcyclohexan-2-onyl)-1-methyl)ethyldithiobenzoate, and 1,3-bis(2-(thiobenzoylthio)prop-2-yl)benzene; in each case, except for carboxymethyldithiobenzoate, this showed that the RAFT technique can produce well-controlled NAM polymer chains.[22] However, the R groups introduced at the chain ends were not always functional.

The reactive function introduced on the CTA must be compatible with the RAFT dithioester function. The present paper uses a carboxylic acid group as the reactive function on the CTA; it fulfills the compatibility requirement and can easily be activated into a highly reactive ester.[23] Hitherto, only a few CTAs bearing a carboxylic acid group as a R group have been used in RAFT polymerizations,[24−27] and in all cases the R leaving group was a primary radical which is not very favorable for an efficient fragmentation.

In the present paper, we investigate the syntheses of two new CTAs (Scheme 2) bearing the same functional R group, namely a propanoic acid group, which gives rise to secondary reinitiating radicals. We introduce two

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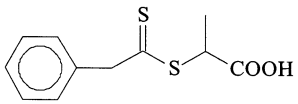
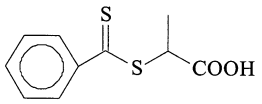
10.1021/ma025646l CCC: $25.00
Published on Web 01/08/2003

Scheme 2



CTA 1



CTA 2

different Z groups, a phenyl and a benzyl group, since previous studies[28] have reported a dependence of retardation on the nature of the Z group. Their use in the RAFT polymerization of NAM is then evaluated by performing kinetic measurements and following the evolutions of molecular weight distribution and polydispersities as a function of conversion. The living character of the process is further investigated by polymerizing styrene in the presence of polyNAM used as "macroCTA", which should lead to the formation of polyNAM-*block*-polystyrene. Polymers in all cases are analyzed by ^{1}H NMR and MALDI-ToF mass spectrometry.

Experimental Section

N-Acryloylmorpholine (NAM, 99% from Polysciences, Inc.) and styrene (99% from Aldrich) were purified by distillation under reduced pressure. Azobis(isobutyronitrile) (AIBN, 98% from Merck) as initiator was purified by recrystallization in ethanol. Dioxane (99.8% from Aldrich) was distilled over $LiAlH_4$ under reduced pressure. Tetrahydrofuran (99.8% from Lab-Scan) was distilled over sodium metal under nitrogen. Bromobenzene (95%, Ajax Chemicals) was distilled over calcium hydride. Carbon disulfide (Merck, 99.5%) was distilled over calcium hydride under nitrogen. Benzylmagnesium bromide (1 M in ether from Aldrich) was used as obtained. 2-Bromopropanoic acid (Merck, 98%) was distilled under reduced pressure before use.

The syntheses of both CTA 1 and CTA 2 were performed using methods analogous to those described by Rizzardo et al.[29,30]

Synthesis of 2-[[2-Phenyl-1-thioxoethyl]thio]propanoic Acid (CTA 1). Carbon disulfide (4 mL, 66 mmol) and dry tetrahydrofuran (40 mL) were cooled in an ice bath under nitrogen. 1 M Benzylmagnesium bromide in ether (40 mL, 40 mmol) was added slowly with stirring. After 30 min, 2-bromopropanoic acid (3.6 mL, 6.18 g, 40 mmol) was added slowly. After 48 h, the mixture was poured into ethyl acetate (200 mL) and washed with water (3 × 100 mL) and saturated sodium chloride (100 mL). The organic extract was dried with magnesium sulfate and then evaporated under reduced pressure to dryness. The excess bromopropanoic acid was removed by kugerol distillation at 120 °C and 0.5 Torr. The residue was then dissolved in ether (200 mL) and extracted with a 50:50 mixture of saturated sodium hydrogencarbonate/water (4 × 50 mL). The combined aqueous extracts were washed with ether (100 mL) and acidified carefully to pH < 1 with 2 M hydrochloric acid. The solution was extracted with ethyl acetate (2 × 100 mL), and the combined organic extracts were washed with water (2 × 50 mL), saturated sodium chloride (50 mL), and then dried with magnesium sulfate. Evaporation of the solvent gave the title compound (3.73 g, 39%) as a red liquid which slowly solidified on standing (mp 36 °C). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.54, d, J 7.40 Hz, 3H, CH_3; 4.28, s, 2H, CH_2; 4.59, q, J 7.40 Hz, 1H, CH; 7.22−7.34, m, 5H, Ar−H; 10.8−11.0, br s, 1H, COOH. ^{13}C NMR ($CDCl_3$, 50 MHz): δ 16.05, 47.65, 57.31, 127.35, 128.56, 129.05, 136.28, 177.16, 232.66. ν_{max}: 3384−2411, 1708, 1289, 1211, 1132, 1074, 986, 855, 698 cm^{-1}.

Synthesis of 2-[[2-Phenyl-1-thioxo]thio]propanoic Acid (CTA 2). Bromobenzene (2.68 mL, 4 g, 25 mmol) in dry tetrahydrofuran (10 mL) was added dropwise to magnesium turnings (607 mg, 25 mmol) in tetrahydrofuran (20 mL) with stirring under nitrogen. After the magnesium had finished reacting the solution was cooled to 0 °C and carbon disulfide (2.2 mL, 2.855 g, 37.5 mmol) was added. After 1 h, 2-bromopropanoic acid (2.249 mL, 3.824 g, 25 mmol) was added and the mixture left for 48 h. The mixture was then acidified with 2 M hydrochloric acid (40 mL) and extracted with ethyl acetate (2 × 100 mL). The combined organic extracts were dried with magnesium sulfate and evaporated to dryness. The excess bromopropanoic acid was removed by kugerol distillation at 120 °C and 0.5 Torr. Purification by silica chromatography gave two fractions, the first eluting with 15% ethyl acetate/light petroleum and the second eluting with 60% ethyl acetate/light petroleum gave the desired compound (1.57 g, 30%) as red crystals (mp 55 °C). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.72, d, J 7.39 Hz, 3H, CH_3; 4.90, q, J 7.41 Hz, 1H, CH; 7.39, t, J 7.73 Hz, 2H, Ar−H3′; 7.52, q, J 7.14 Hz, 1H, Ar−H4′; 8.00, d, J 7.25 Hz, 2H, Ar−H2′; 10.2−10.4, br s, 1H, COOH. ^{13}C NMR (50 MHz): δ 16.30, 48.14, 126.94, 128.39, 132.78, 144.06, 177.13, 225.40. ν_{max}: 3270−2463, 1698, 1284, 1211, 1038, 876, 755, 677 cm^{-1}.

The excess 2-bromopropanoic acid could not be removed from the resulting CTAs by chromatographic methods and thus was removed by distillation under reduced pressure. Recrystallizing the CTAs so obtained did not result in the complete removal of impurities. However, ^{1}H and ^{13}C NMR characterizations showed the purity of both CTAs to be higher than 97%.

Polymerization Procedure and Kinetics. Polymerizations were performed in a round-bottom flask capped with a septum. The reaction vessel was loaded with dioxane, monomer (∼2 M), trioxane (molar ratio NAM/trioxane = 6:1), CTA, and AIBN in a 10:1 CTA:AIBN molar ratio. As described by d'Agosto et al.,[13] trioxane was used as an internal reference for the determination of the conversion using NMR, by comparison with the vinyl protons of NAM, since trioxane gives a clean peak at 5.1 ppm. For accuracy, the area of this peak should be about the same as that of a NAM vinylic proton. As there are six protons in trioxane, the molar ratio of NAM/trioxane was chosen as 6:1. The mixture was purged with nitrogen for 15 min at 20 °C. The temperature was then raised to 65 or 85 °C using a thermostated oil bath. Polymerizations were carried out under a nitrogen atmosphere. The experimental conditions used in the different experiments are listed in Table 1.

Samples were withdrawn from the polymerization mixture at different reaction times and introduced into vials containing hydroquinone (inhibitor), placed in ice to stop polymerization, then stored at −20 °C. Monomer consumption was followed by ^{1}H NMR analysis of each sample. ^{1}H NMR analysis was performed without evaporation of the polymerization solvent by mixing 0.2 mL of each sample with $CDCl_3$ (1:3 v/v).

Monomer conversion was determined by comparison of the vinyl protons of NAM with the protons of trioxane as reference (Figure 1).

Polymer Characterization. Molecular weights and molecular weight distribution were determined by size-exclusion chromatography with THF as eluent (flow rate = 1 mL/min) at 25 °C using three Styragel columns (HR2, HR3, and HR4 with pore sizes 10^2, 10^3, and 10^4 Å, respectively) and a refractometric detector (Shimadzu RID 10A), using polystyrene standards for calibration. The theoretical number-average molecular weight was obtained using

$$\bar{M}_n(\text{theor}) = M_{CTA} + \frac{[NAM]}{[CTA]} M_{NAM} x_{NAM} \qquad (1)$$

where M_{CTA} and M_{NAM} are the molecular weights of RAFT agent and NAM and x_{NAM} is the fraction conversion. The

Table 1. Experimental Conditions

run	CTA	[CTA]/mM	[monomer]/M	[styrene]/M	dioxane/mL	temperature/°C
A	CTA 1	10.7	2		5	65
B	CTA 2	11.4	2		5	85
C	CTA 1	5.3	2		7.5	65
D	"macroCTA 1"[a]	7.8	1.25		2.5	65
E	CTA 1	14.7		2.7	5	85
F	"macroCTA 1"[a]	6.6		2	2.5	85

[a] Obtained by RAFT CTA1 mediated polymerization of NAM, theoretical $\bar{M}_n = 2.17 \times 10^4$, $\bar{M}_w/\bar{M}_n = 1.2$, [CTA]/[AIBN] = 10.

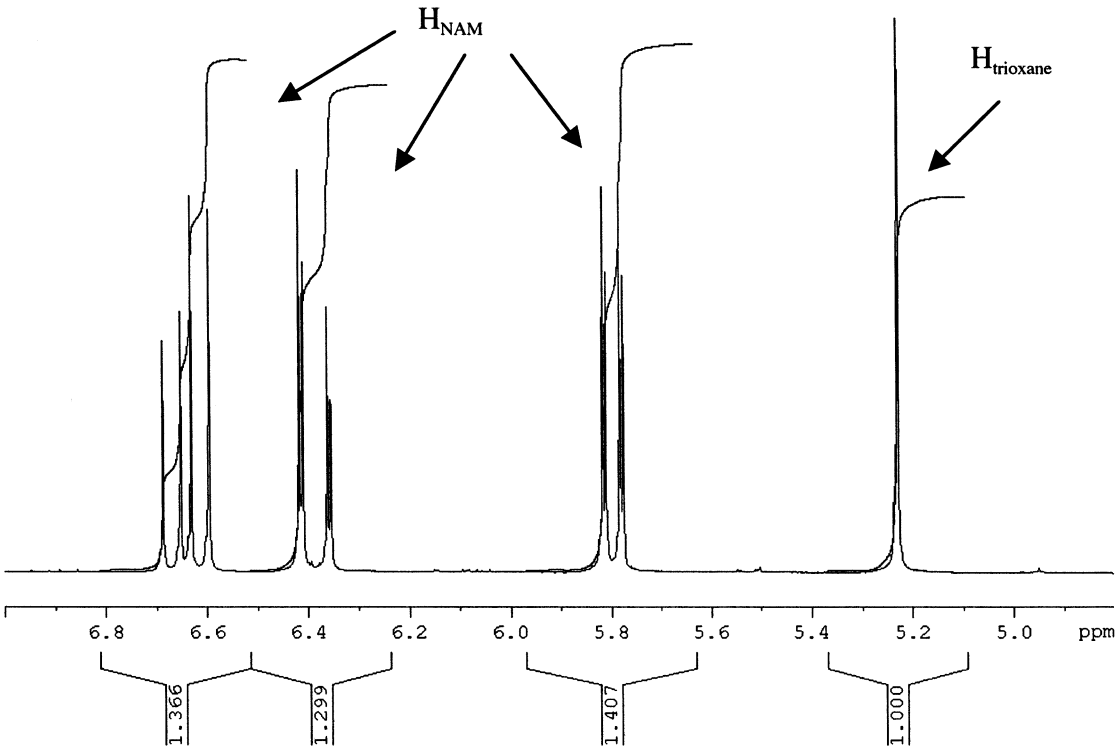


Figure 1. ^{1}H NMR spectrum of the reaction mixture during polymerization A (300 MHz, $CDCl_3$).

contribution of the molecular weight of the chains initiated by AIBN was neglected because of the high CTA:AIBN ratio used here.

For analyses by ^{1}H NMR spectrometry (Bruker Avance 300, 300 MHz, $CDCl_3$ or DMSO as deuterated solvents), polymers were precipitated out with diethyl ether, recovered by filtration, washed several times with the same solvent, and finally dried under vacuum until constant weight was attained.

MALDI-ToF mass spectrometry of the polymers was performed with sodium α-cyano-4-hydroxycinnamate as matrix. The ratio of polymer to matrix was 1:100. Spectra were recorded with a Micromass TOFSPEC E spectrometer, equipped with a 337 nm N_2 laser and 20 kV acceleration voltage, in reflectron mode.

Results and Discussion

Preliminary Comparison of CTA 1 and CTA 2. NAM was first polymerized in dioxane using CTA 1 (10.7 mM) and AIBN as initiator. The temperature was 65 °C, and a NAM:CTA 1 ratio was chosen such that $\bar{M}_n$(theor) after complete conversion should be 2.65×10^4 (entry A, Table 1). Samples were withdrawn from the polymerization mixture at different times. Each sample was analyzed by ^{1}H NMR to determine conversion. The time dependence of conversion is given in Figure 2 (for later reference, this also shows data for 5.3 mM CTA); note that the data in Figure 2 at low conversions (≤5%) are subject to the highest uncertainty, inherent in the measurement technique. The polymerization of NAM under these conditions is

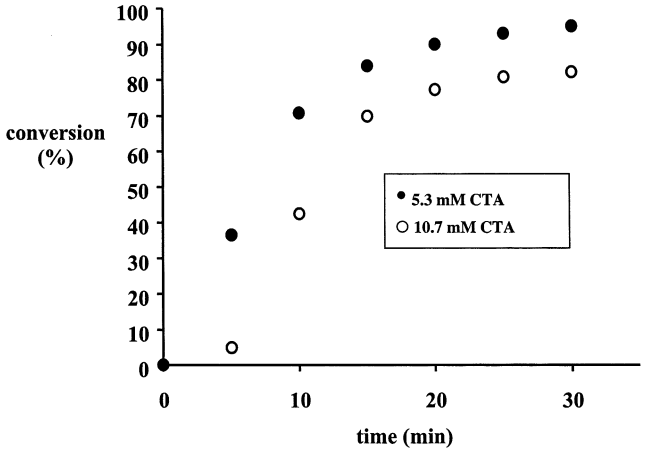


Figure 2. Conversion as a function of time for polymerization of NAM with CTA 1 (65 °C) for runs A (10.7 mM RAFT) and C (5.3 mM RAFT); see Table 1.

rapid: ~80% conversion is reached within half an hour. The conversion dependences of $\bar{M}_n$ values (which are relative to polystyrene standards and hence "apparent" $\bar{M}_n$) and of polydispersity (obtained by DRI−SEC analysis of the untreated samples) are given in Figure 3. Within experimental uncertainty, the apparent $\bar{M}_n$ values are linear with conversion, consistent with polymerization proceeding in a controlled fashion. Now, the apparent $\bar{M}_n$ values are not in agreement with those

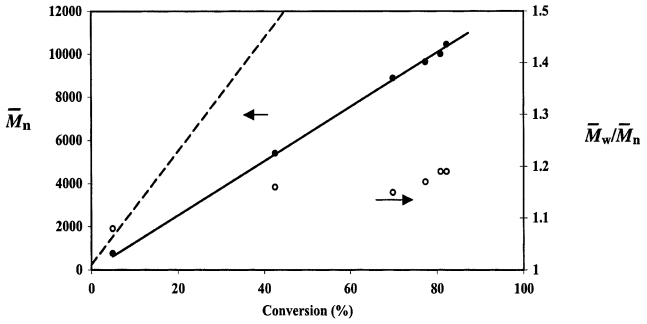


Figure 3. Points: experimental $\bar{M}_n$ and polydispersity as functions of conversion for polymerization of NAM with CTA 1 at 65 °C (run A, Table 1). Broken line: $\bar{M}_n$(theor); full line, best fit to experimental $\bar{M}_n$. Molecular weights are relative to styrene standards.

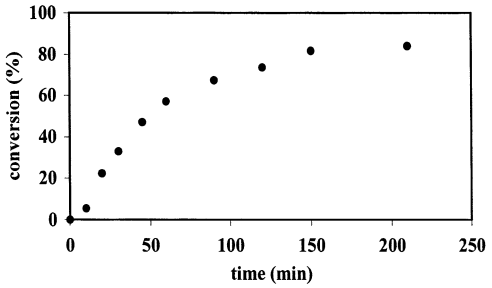


Figure 4. Conversion as a function of time for polymerization of NAM with 10.2 mM CTA 2 (85 °C) for run B (Table 1).

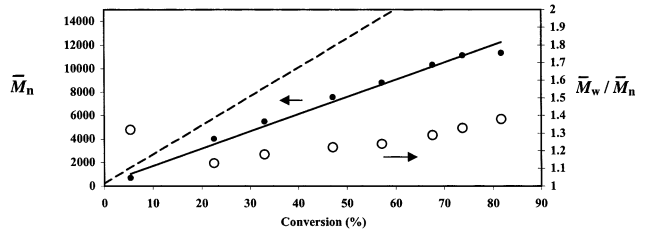


Figure 5. Points: experimental $\bar{M}_n$ and polydispersity as functions of conversion for polymerization of NAM with 11.4 mM CTA 2 at 85 °C. Broken line: $\bar{M}_n$(theor); full line, best fit to experimental $\bar{M}_n$. Molecular weights are relative to styrene standards.

expected from eq 1; this may be an artifact arising from the use of polystyrene standards to obtain these apparent $\bar{M}_n$ values. The polydispersity, which never exceeds 1.2, may increase slightly with conversion. However, this is not a firm conclusion, because $\bar{M}_n$ is rather sensitive to baseline subtractions, etc.; a number of workers[19,26,31] have previously reported an increasing $\bar{M}_w/\bar{M}_n$ for several monomers such as *N*-isopropylacrylamide and other acrylamide-based monomers.

NAM was polymerized in the presence of CTA 2 under the same conditions as for CTA 1, such that $\bar{M}_n$(theor) after complete conversion should be 2.49×10^4 (entry B, Table 1). Polymerization with CTA 2 was much slower than with CTA 1: at 65 °C, only a few percent conversion was reached after 5 h. At 85 °C, 80% conversion was obtained after just over 2 h, as shown in Figure 4; $\bar{M}_n$ and polydispersities are shown in Figure 5. The observed difference between the behaviors of CTA 1 and CTA 2 could be related to the nature of their Z group, benzyl and phenyl respectively, as suggested by Barner-Kowollik et al.,[28] who reported a significant decrease in "macroCTA" radical lifetimes in the RAFT polymerization of styrene when going from cumyl

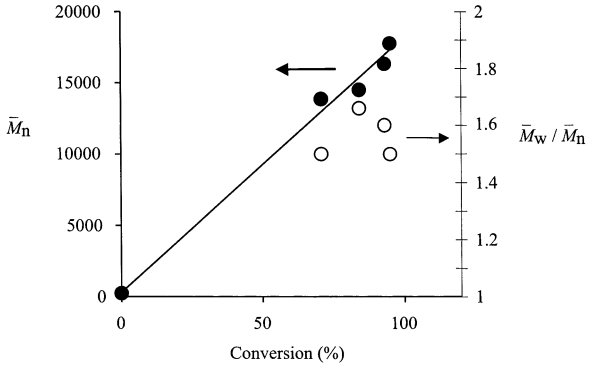


Figure 6. Points: experimental $\bar{M}_n$ and polydispersity as functions of conversion for polymerization of NAM with CTA 1 at 65 °C (run C, Table 1). Full line, best fit to experimental $\bar{M}_n$. Molecular weights are relative to styrene standards.

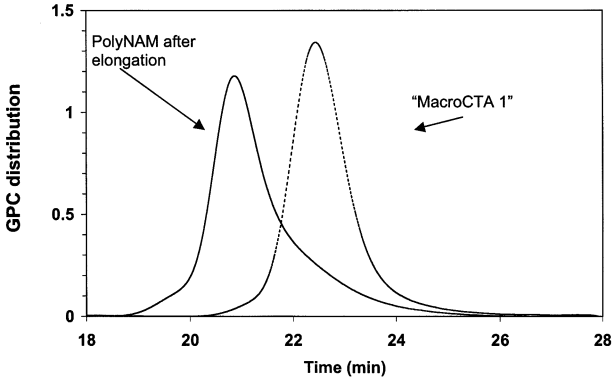


Figure 7. SEC chromatograms (GPC distributions as a function of elution time) for a starting CTA-capped polyNAM ("macroCTA 1") and for the species resulting after second-stage polymerization of this with NAM.

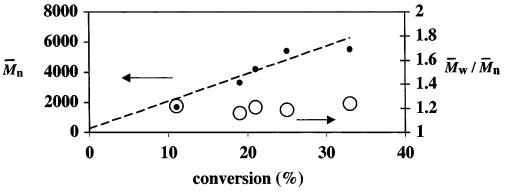


Figure 8. Points: experimental $\bar{M}_n$ and polydispersity as functions of conversion for polymerization of NAM with CTA 1 at 85 °C (run E, Table 1). Broken line: $\bar{M}_n$(theor).

dithiobenzoate (Z = phenyl, R = cumyl) to cumyl phenyldithioacetate (Z = benzyl, R = cumyl). Fukuda and co-workers[32] have suggested that retardation, in the case of a styrene/dithiobenzoate system, could be additionally explained by the formation of stars arising from reversible or irreversible termination reactions of the intermediate radicals. Although molecular weight control in the present CTA 2 system seems adequate, as suggested by the almost linear increase of $\bar{M}_n$ with conversion, polydispersities ($M_w/M_n \leq 1.4$) are higher than those observed with CTA 1. Again, $\bar{M}_n$ values calculated on the basis of a polystyrene calibration are not in agreement with the theoretical values.

It is interesting to compare the experimental M_n values from SEC measurements obtained for CTA 1 and CTA 2. These should be the same for a given conversion regardless of the calibration; however, those for CTA 2 are consistently ~20% higher than for CTA 1. This result may arise from different amounts and types of impurities in the CTAs (see above remarks) or from the degradation of CTA 2 at the reaction temperature (85

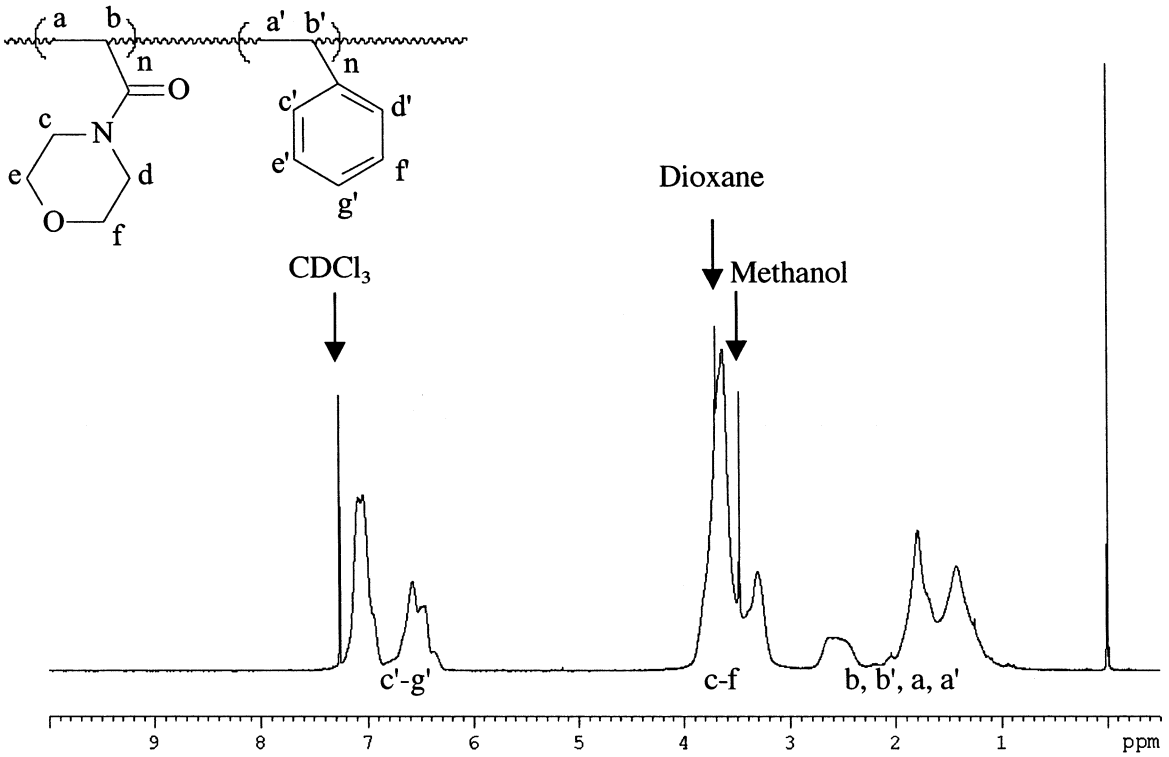


Figure 9. ^{1}H NMR analysis of the block polymer from run F, recovered after precipitating twice from methanol (300 MHz, $CDCl_3$).

Table 2. Solubilities of Polymers in Different Solvents

	methanol	ether	water
"macroCTA 1" (polyNAM capped with CTA 1)	soluble	insoluble	soluble
polyNAM-*block*-polystyrene capped with CTA 1	insoluble	swollen	insoluble
polystyrene	insoluble	insoluble	insoluble

°C for several hours instead of 65 °C for less than an hour for CTA 1). The amount of actual CTA 2 available for polymerization would then be overestimated, and consequently $\bar{M}_n$(theor) will be higher (eq 1). The high $\bar{M}_w/\bar{M}_n$ values can be explained in the same way.

Detailed Study of CTA 1. As the RAFT polymerization with CTA 1 exhibited several advantages over that with CTA 2 (lower polydispersity, higher polymerization rate), this system was investigated further. With lower [CTA] (run C, Table 1; Figure 2), the rate is faster and closer to that of the corresponding system in the absence of CTA.[13] In a pure RAFT process, the polymerization rate should be independent of the CTA concentration, but retardation may occur and originate from different factors such as a too low fragmentation rate or a too slow reinitiation.[33] Polydispersities are much larger with lower [CTA] (Figure 6). No meaningful comparison can be made between the observed and theoretical $\bar{M}_n$ because of the lack of absolute molecular weights. (Because of possible mass bias in ablation, MALDI-ToF cannot be used reliably to find $\bar{M}_n$ in these systems with relatively high molecular weights and moderate polydispersity.)

PolyNAM Used as a "MacroCTA". An important criterion of true living character is the successful extension of chains or the synthesis of a block copolymer using preformed polymer chains as a "macroCTA"; linear increase of the molecular weight should ensue. To investigate this point, we first performed the polymerization of NAM mediated by a polyNAM "macroCTA" (run D, Table 1), referred to as "macroCTA 1" ($\bar{M}_n = 2.17 \times 10^4$; $\bar{M}_w/\bar{M}_n = 1.2$), obtained by RAFT polymerization of NAM mediated by CTA 1. This homopolymer second growth was undertaken because its molecular weight analysis avoids difficulties that can arise in the determination of the molecular weight distribution of a block copolymer, discussed later. The polymerization was performed at 65 °C, and the ratio NAM/"macroCTA 1" was such as the expected chain extension should approximately double the original $\bar{M}_n$ (i.e., $\bar{M}_n$(theo, extension) $= 2.27 \times 10^4$). After 3 h, the conversion was 89%. The polymer was recovered by precipitation in diethyl ether. Comparison of SEC chromatograms of the starting polyNAM and the second-growth polymer shows that the extension was successful (Figure 7). However, a small amount of residual low molecular weight dead chains remains in the final product. Also, a small shoulder appears at high molecular weight, probably corresponding to bimolecular termination by combination.

Growing a Block Copolymer. As mentioned in the Introduction, as a part of a program to synthesize latex particles with "hair" (i.e., grafted layer) of controlled chain length and functionality, obtaining block copolymers of NAM and styrene is of importance, e.g., when considering their use as surfactants in emulsion polymerization. On the basis of the previous result, the synthesis of a block copolymer was investigated by polymerizing styrene in the presence of the same "macroCTA 1". One requirement for forming a narrow polydispersity AB block copolymer is that the first-formed polymeric CTA should have a high transfer

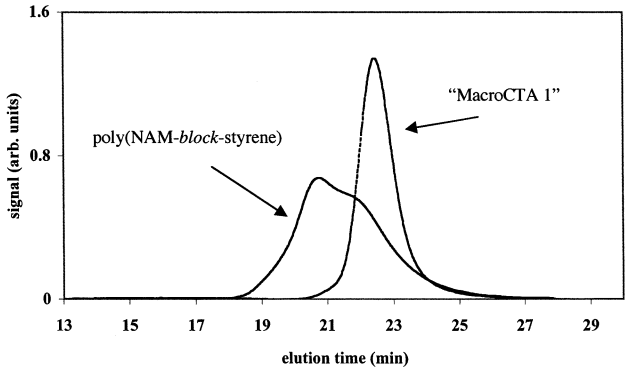


Figure 10. SEC chromatograms of the parent "macroCTA 1" and of the block copolymer obtained after polymerization with styrene (run F, Table 1).

constant in the subsequent polymerization step to give the B block. This requires that the leaving-group ability of propagating radical A is comparable to or greater than that of the propagating radical of B. We could have chosen to form the polystyrene block first; however, with a view to introducing our R group at the end of the hydrophilic part, we decided to start with a polyNAM "macroCTA 1".

Prior to the synthesis of this block copolymer, the polymerization of styrene mediated by CTA 1 was investigated (run E, Table 1). As is expected that styrene would be slower to polymerize than NAM (styrene having a low propagation rate coefficient[34]), a temperature of 85 °C was chosen to avoid long polymerization times (noting however that the half-life of AIBN is ∼15 min at this temperature). After polymerization for 10 h, 35% conversion was obtained, and conversion leveled off at this value. Experimental $\bar{M}_n$ values agreed very well with the theoretical ones and polydispersities were low (Figure 8), consistent with controlled polymerization. The fast polymerization rate observed for CTA 1 mediated polymerization of NAM is consistent with supposing a higher apparent propagation rate coefficient of acrylamide derivatives (e.g., the propagation rate coefficient for *N*-isopropylacrylamide in water at 65 °C is[35] $\sim 8 \times 10^4$ M^{-1} s^{-1}) combined with a lower termination rate coefficient for NAM arising from steric hindrance provided by the bulky morpholine group.[13]

The polymerization of styrene using "macroCTA 1" to form polyNAM-*block*-polystyrene was then undertaken (run F, Table 1), with the ratio styrene/"macroCTA 1" chosen so that $\bar{M}_n$(theor) of the polystyrene block was 3.1×10^4 after 100% conversion. Conversion leveled off at 40% after 10 h.

Solubilities in various solvents of this supposedly block copolymer and of the parent "macroCTA 1" are given in Table 2. The final polymer was recovered by precipitation in methanol. Whereas "macroCTA 1" is precipitated out in diethyl ether, the supposedly block copolymer was only swollen by the same solvent. On the other hand, it precipitated out in methanol wherein "macroCTA 1" is soluble. These solubility results are consistent with the formation of a block copolymer.

Figure 9 shows the ^{1}H NMR spectrum of the supposedly block copolymer, purified by two successive precipitations in methanol. One sees the presence of peaks corresponding to polystyrene and polyNAM. Integration under the appropriate peaks (in which the contributions of residual solvents, dioxane at 3.7 ppm and methanol at 3.4 ppm, and of $CDCl_3$, are neglected) gives a composition of 44% styrene and 56% NAM. This is in agreement with the theoretical composition, 47% styrene and 53% NAM, calculated at the conversion where polymerization was stopped. Taking into account these compositions and the molecular weight of "macroCTA

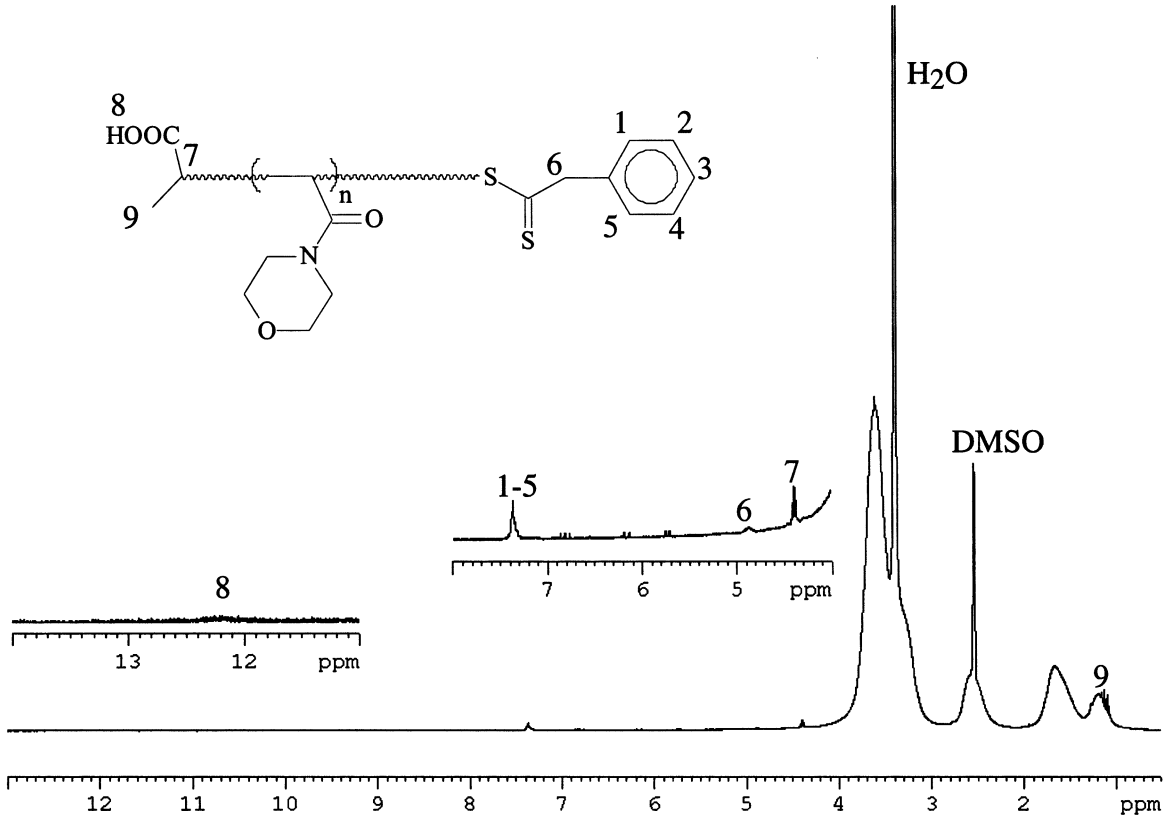


Figure 11. ^{1}H NMR spectrum (256 scans) of polyNAM synthesized in the presence of CTA 1 (300 MHz, DMSO).

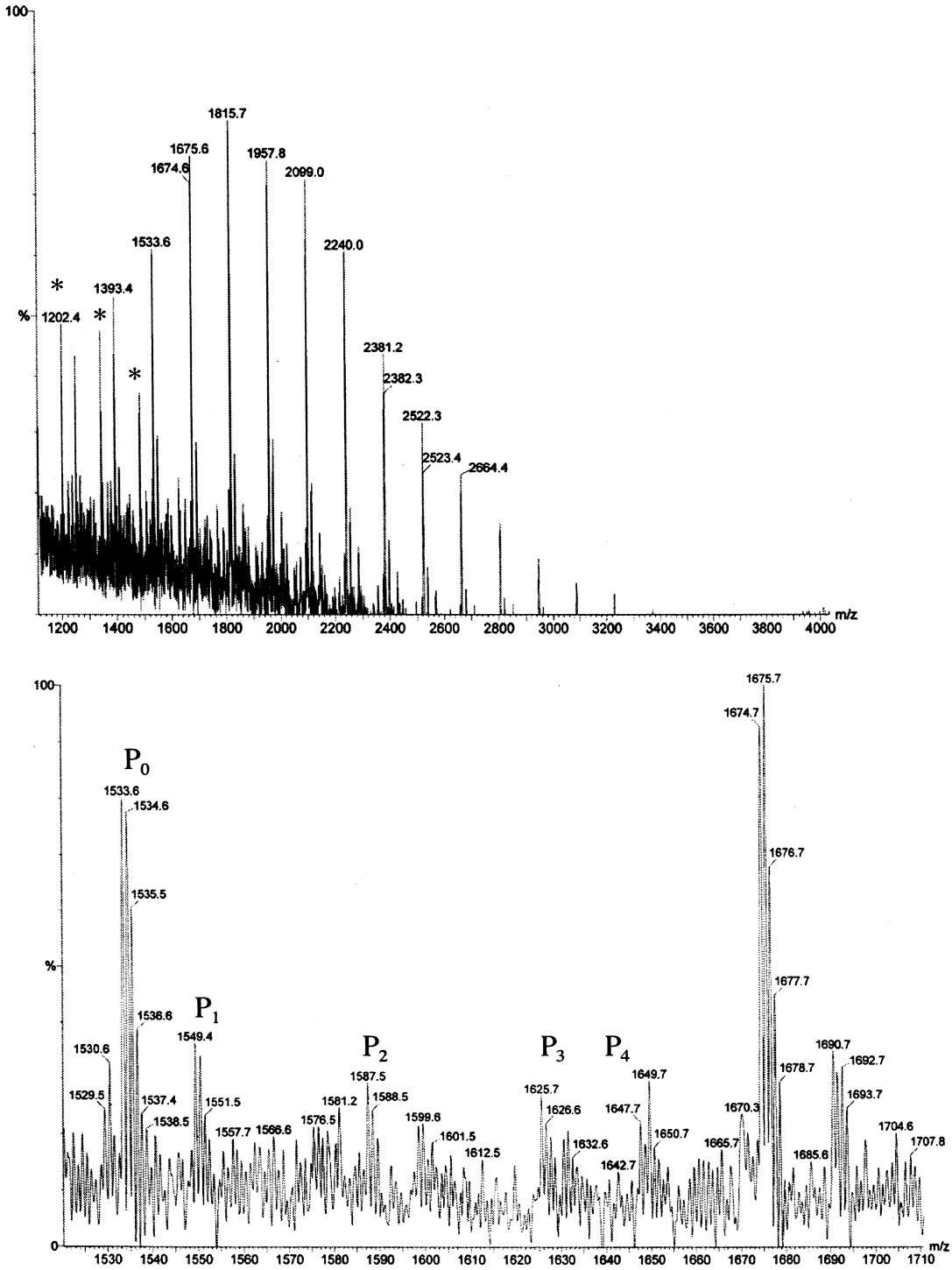


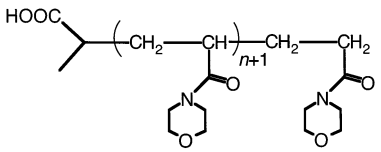
Figure 12. MALDI-ToF mass spectrum (reflectron mode) of polyNAM over the range 1200−4000 Da and enlargement of the region from 1500 to 1710 Da. Matrix: α-cyano-4-hydroxycinnamate; cationization agent: Na^+.

1", a $\bar{M}_n$(exp) of 1.25×10^4 for the polystyrene block was obtained (M_n(theor) at this conversion being calculated to be 1.24×10^4). SEC analysis of the starting "macroCTA 1" and the block copolymer given in Figure 10 shows a shift of the distribution toward higher molecular weights. However, termination reactions seem to occur more readily, as evidenced by the shape of the chromatogram and the larger polydispersity (1.60). More detailed information as to the microstructure of the formed polymer (e.g., the presence of any residual polyNAM homopolymer) would require more sophisticated techniques such as two-dimensional polymer chromatography.[36]

Characterization of the Polymer Chain-End Functionalization. The RAFT process was chosen to produce polyNAM chains of controlled chain length and end functionality. Given the structure of CTA 1 and the living behavior evidenced above, each polyNAM chain should be α- and ω-functionalized by a propanoic acid group and a phenyldithioacetate group, respectively. This last part of this study aims at characterizing the presence of these two end groups using two independent techniques: NMR and MALDI-ToF mass spectrometry.

The ^{1}H NMR spectrum of polyNAM obtained using CTA 1 is presented in Figure 11. A comparison of this spectrum with that of CTA 1 (not shown) enabled the

Scheme 3



different protons of the Z group (protons 1−5 at 7.4 ppm and proton 6 at 4.9 ppm) and the −CH of the R group (proton 7 at 4.4 ppm) to be assigned, as shown in Figure 11. Peaks corresponding to the vinylic protons between 5.6 and 6.9 ppm are evidence for the presence of a very small amount of residual monomer. The carboxylic function provided by the R group is visible (proton 8 around 12.5 ppm) but broadened by the unavoidable presence of water in DMSO, while the peak of the methyl group (proton 9), at around 1.6 ppm in CTA 1, is probably shifted downfield in the polymer and may correspond to the very small peaks around 1.1 ppm.

This NMR technique could in principle be used to determine the absolute molecular weight of the chains, by comparing the integrals of peaks for the chain-end protons to those of the main-chain protons. However, this cannot be realized in the present system because of the overlap of peaks from the deuterated solvent and water with those of the main polymer chain. To overcome this drawback, ^{1}H NMR analysis of the same polymer was carried out in D_2O, and comparison of integrations of the benzylic chain-end protons and of the −CH of the main chain gave $\bar{M}_n$ = 26 500, in good agreement with the theoretical value of 21 700.

MALDI ToF Mass Spectrometry Analyses. Characterization of the chain structure of a short-chain polyNAM was performed by MALDI−ToF mass spectrometry; three other RAFT MALDI spectra have also appeared in the literature.[31,37,38] The spectrum (reflectron mode) is given in Figure 12.

The molecular weight difference between two consecutive peaks in the MALDI−ToF mass spectrum is 141.2, which corresponds to a single NAM monomer unit. The degree of polymerization (DP) for each peak is found by taking into account the Z and R groups of the CTA 1 and the attached Na^+. This analysis confirms that each polyNAM chain is α- and ω-functionalized by a propanoic acid R group and a phenyldithioacetate Z group, respectively.

Figure 12 also shows an enlarged part of the spectrum, corresponding to the chain population centered on 1533.6 (DP = 9). The main population, P_0, is that expected from the widely accepted mechanistic scheme for RAFT polymerization. Thus, the peak at 1533.6 corresponds to a DP = 9, with the Z and R groups from CTA 1 and an Na^+. Four populations of low intensity, denoted P_1, P_2, P_3, and P_4, are present and centered respectively on 1549.4, 1587.5, 1625.7, and 1649.7. P_1 can readily be assigned to a side cationization by K^+ often observed in MALDI. Population P_4 is consistent with the structure displayed in Scheme 3. These chains, with DP = 11, may be formed from termination reactions. Two possible explanations for the formation of these chains are events (i) in the polymerization medium or (ii) in the spectrometer. In the polymerization medium, the macroradical can undergo termination by disproportionation, giving rise to an ω-unsaturated and an ω-saturated chain. Both chain populations should then be observable in the mass spectrum; however, this is not the case. The macroradical formed in the spectrometer after fragmentation of the $-CH_2-S-$ bond under the laser beam can abstract a hydrogen from the matrix and give rise to P_4. In this case, no unsaturated chains would be produced, and the only population present is P_4. However,because of the intensity and the resolution of the peaks under consideration, it is difficult to discriminate between the two possible phenomena. Note that the proportion of population P_4 corresponding to dead chains tends to be higher at low molecular weight (see starred peaks in Figure 12). In addition, we were unable to assign P_2 and P_3, for which there are many possibilities. The MALDI-ToF spectrum did not show significant peaks corresponding to chains initiated by a radical coming from the initiator, which suggests an efficient functionalization.

Conclusions

Two new RAFT chain transfer agents bearing the same functional propanoic acid group R and two different Z groups were synthesized: a benzyl (CTA 1) and a phenyl group (CTA 2). The kinetics of RAFT polymerization of NAM mediated by CTA 1 were fast and showed good molecular weight control, but those with CTA 2 were much slower and gave poorer control of molecular weight.

The living character of the process mediated by CTA 1 was confirmed by polymerizing both NAM and styrene in the presence of polyNAM, previously synthesized using CTA 1, used as a macro chain transfer agent. Second-stage polymerization with the parent NAM monomer gave the desired chain extension. The polymer synthesized by second-stage polymerization with styrene showed all the characteristics of a polyNAM-*block*-polystyrene amphiphilic block copolymer. ^{1}H NMR and MALDI-ToF mass spectrometry analyses of the α,ω-functionalized polyNAM chains were consistent with the conventionally accepted mechanism for RAFT polymerization.

The techniques developed here have application in the synthesis of functionalized latex particles.

Acknowledgment. We gratefully acknowledge the support of the Australian Research Council's Research Infrastructure Equipment and Facilities Scheme, Dulux Australia, bioMérieux S.A France, the ARC Strategic Partnerships with Industry−Research and Training Scheme (R.H.), and the International Research and Development and Technology Access Activities component of the Innovation Access Program of AusIndustry. We also thank Jelica Strauch and Dr. Christopher Ferguson (Key Centre for Polymer Colloids, University of Sydney) for the SEC analyses, Dr. Christopher Barner-Kowollik (Centre for Advanced Macromolecular Design, University of New South Wales, Australia), and Dr. Keith Fisher (School of Chemistry, University of Sydney) for MALDI-ToF mass spectrometry analyses. The Key Centre for Polymer Colloids is established and supported under the Australian Research Council's Research Centres Program.

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MA025646L