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MALDI-TOF MS Investigation of the RAFT Polymerization of a Water-Soluble Acrylamide Derivative

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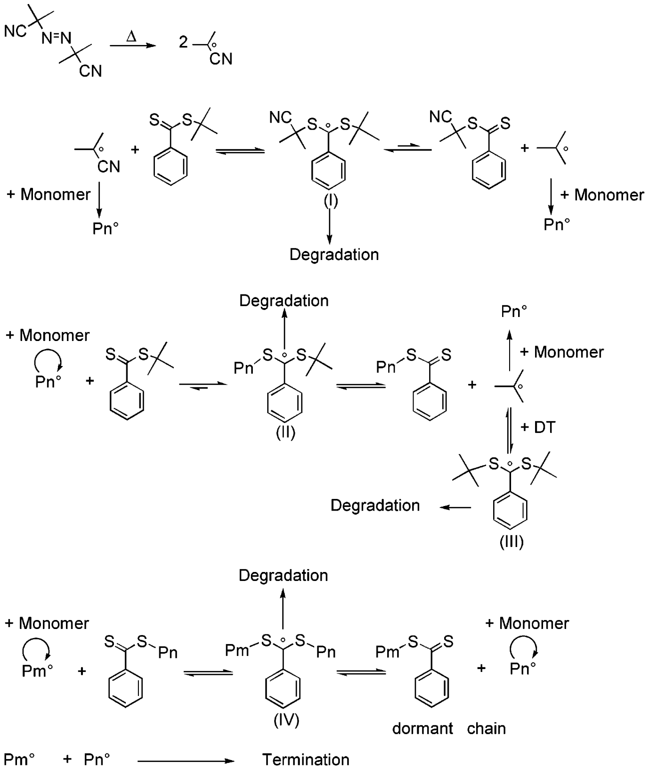
ABSTRACT: A matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI−TOF MS) study of *N*-acryloylmorpholine (NAM) homopolymers, as obtained by reversible addition−fragmentation chain transfer (RAFT) polymerization technique, is reported. Polymerization of NAM was performed in dioxane using azobis(isobutyronitrile) (AIBN) as initiator and *tert*-butyl dithiobenzoate as RAFT chain transfer agent. Polymer samples of low molecular weights ($<$10 000 g mol^{-1}) and low polydispersity indices (PDI $<$ 1.1) were obtained, which are essential requirements for such MALDI−TOF MS analysis. First, analysis of poly(NAM) samples in linear mode led to $\overline{M_n}$ values very close to both size exclusion chromatography/light scattering (SEC/LS) and ^{1}H NMR values as well as to the theoretical ones. Then, an accurate examination of chain end groups was performed using the reflectron mode. Two main chain populations were identified: (i) dormant chains (i.e., initiated by a *tert*-butyl and terminated by a dithiobenzoate group) together with sulfine and thioester-ended chains probably resulting from oxidation of dithiobenzoate chain ends during storage; (ii) proton-terminated chains mainly produced by fragmentation of the former chains in the spectrometer. In addition, some chains which could correspond to termination reactions onto the intermediate radicals involved in the RAFT equilibrium were suspected. Finally, comparison of polymer samples before and after aminolysis indicated that dithioester-ended chains constituted the majority of chains initially present in these samples. This study confirms that it is indeed possible to use MALDI−TOF MS to investigate the structure of polymer chains synthesized by the RAFT technique.

Introduction

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI−TOF MS), first developed to study peptides and proteins, has also been applied to synthetic polymers.[1] As the technique requires that the polymer is of relatively narrow molecular weight distribution (MWD), it was first used to investigate polymers synthesized by living anionic[2,3] and cationic[4−8] processes. In contrast to other analytical techniques (NMR, IR, UV) which provide an average image of a polymer sample, and to size exclusion chromatography (SEC) which gives a real image but with a low resolution, MALDI−TOF MS analysis reveals, for each individual polymer chain present in the sample, its absolute molecular weight and end group structure.

Recently, with the development of controlled radical polymerization, MALDI−TOF MS has been applied to a variety of polymers, synthesized either by nitroxide-mediated polymerization,[9−11] by transition-metal-catalyzed polymerization,[12−14] or by the RAFT technique.[15−22] Concerning the latter, an article reported that MALDI−TOF MS analysis was not suitable to study polymer chains synthesized by RAFT and recommended the use of electrospray ionization mass spectrometry (ESI-MS).[23]

Scheme 1. RAFT General Mechanism Including the Hypothesis of Intermediate Radical Degradation by Termination and/or Transfer



In fact, RAFT polymerization is based on a reversible equilibrium between a few active chains and numerous dormant ones (Scheme 1), the latter being temporarily ended by a thiocarbonylthio moiety derived from a reversible chain transfer agent (CTA).[24,25] This equilibrium results in the synthesis of chains of homogeneous size (low polydispersity index), with a molecular weight

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increasing linearly with conversion. In addition, the presence of the thiocarbonylthio chain end opens the way to the synthesis of block copolymers. To confirm the RAFT mechanism, it was first of interest to prove the presence of such dormant chains in the polymerization medium, which has been achieved by MALDI−TOF MS for several kinds of CTA like dithioesters,[15,21,22] xanthates,[16] dithiocarbamates,[17,20] disulfides,[19] and trithiocarbonates.[18] These MALDI−TOF MS studies mainly concerned poly(*N*-isopropylacrylamide),[15,20] poly(acrylic acid),[18] poly(ethyl acrylate),[16] poly(styrene),[19] and poly(vinyl acetate).[17] No report dealing with poly(methacrylates) could be found.

In this article, we investigate by MALDI−TOF MS the RAFT polymerization of a bisubstituted acrylamide derivative, *N*-acryloylmorpholine (NAM), in the presence of *tert*-butyl dithiobenzoate (tBDB). In previous articles, we reported the influence of several parameters on the RAFT polymerization of NAM, especially the nature of the used dithioester[26] and the experimental conditions (temperature, monomer concentration, dithioester to initiator mole ratio).[22] Well-controlled poly(NAM) chains were obtained in the range from 2000 to 80 000 g mol^{-1} with low polydispersity indices (PDI < 1.10). Some preliminary analyses[21,22] showed that under certain conditions MALDI−TOF MS was applicable to poly(NAM) with a fair resolution. In this article, a detailed study of MALDI−TOF MS of poly(NAM) chains is reported. Analysis of the well-resolved spectra should provide structural information about the various chain populations, bringing new insight into the RAFT mechanism.

Experimental Section

Materials. *N*-Acryloylmorpholine (NAM) (Aldrich, 97%) was distilled under reduced pressure (120 °C, 10 mmHg) to remove inhibitor. 4,4′-Azobis(isobutyronitrile) (AIBN) (Fluka, 98%) was purified by recrystallization from ethanol, and 1,4-dioxane (Acros, 99%) was distilled from $LiAlH_4$ (110 °C). Trioxane (Acros, 99%), diethyl ether (SDS, 99.5%), and hexylamine (Aldrich, 99%) were all used without purification. *tert*-Butyl dithiobenzoate (tBDB) was synthesized according to a previously published process.[26]

Polymerization General Procedure. NAM (2.5 g, 18 mmol), tBDB (35.4 mg, 0.17 mmol), AIBN (2.8 mg, 0.017 mmol), trioxane (123.7 mg, 1.37 mmol), and dioxane (solvent, 3.85 mL) were introduced in a Schlenk tube equipped with a magnetic stirrer. The mixture was degassed by five freeze−evacuate−thaw cycles and then heated at 90 °C under nitrogen in a thermostated oil bath. Samples were periodically withdrawn from the polymerization medium for analyses.

Monomer conversion was determined by ^{1}H NMR spectroscopy using a Bruker AC 200 spectrometer (200 MHz), comparing one vinylic proton (5.7 ppm) to trioxane (5.1 ppm) used as internal reference.[27] Typically, 500 μL of deuterated chloroform, $CDCl_3$, was added to 120 μL of each sample.

Aminolysis of the Polymer Chains. Poly(NAM) synthesized as described above (pink color) was dissolved in $CHCl_3$ containing hexylamine (100 equiv in comparison with the dithioester end groups). For instance, a precipitated poly(NAM) sample (100 mg, 0.04 mmol, $\overline{M}_n = 2700$ g mol^{-1}, PDI = 1.04, 12.4% conversion, 20 min polymerization time) was dissolved in $CHCl_3$ (10 mL) containing hexylamine (405 mg, 4 mmol). The mixture was stirred at room temperature for 12 h and then precipitated into a large volume of diethyl ether. The recovered polymer was white. ^{1}H NMR spectroscopy confirmed the disappearance of the dithioester end group at 7.4−8 ppm.

Characterization of the Polymer Samples. Polymer samples were precipitated into a large volume of diethyl ether, recovered by filtration, washed several times with the same solvent, and finally dried under vacuum to constant weight. The complete removal of residual monomers was confirmed by ^{1}H NMR analysis (Bruker AC 200 spectrometer, 200 MHz).

Molecular weight distributions were determined by size exclusion chromatography (SEC) coupled to a light scattering detection (LS). Aqueous SEC was performed using a Waters 510 pump, two Waters Ultrahydrogel columns (bead size 3 μm, 2000 and 500 Å), and a differential refractometer (DRI Waters 410, $\lambda = 930$ nm). On-line double detection was provided by a three-angle (47°, 90°, 130°) MiniDAWN light scattering photometer (Wyatt Technologies) operating at 690 nm. Analyses were performed by injection of 200 μL of polymer solution (5 mg mL^{-1}) in a borate buffer (pH = 9.3, 0.05 mol L^{-1}), previously filtered through a 0.22 μm Millipore filter and used as eluent at a flow rate of 0.5 mL min^{-1} (25 °C). The specific refractive index increment (d*n*/d*c*) for poly(NAM) in the same eluent (0.163) was determined with a NFT ScanRef monocolor interferometer operating at 633 nm. The molecular weight and polydispersity data were determined using the Wyatt ASTRA SEC/LS software package.

MALDI−TOF MS Analyses. The matrix-assisted laser desorption ionization time-of-flight mass spectrometer (MALDI−TOF MS) used to acquire the mass spectra was a Voyager-DE STR (Applied Biosystems, Foster City, CA). This instrument was equipped with a nitrogen laser (wavelength 337 nm) to desorb and to ionize the samples. The accelerating voltage used was 20 or 25 kV. The positive ions were detected in all cases. The spectra were the sum of 200 shots, and an external mass calibration was used (mixture of 5720 and 13 000 PMMA standards, Polymer Laboratories, Amherst, MA). This MALDI instrument used a stainless steel target, on which the samples were deposited and dried. Samples were prepared by dissolving the polymer in tetrahydrofuran (THF) at a concentration of 10 g L^{-1}. In some cases, the polymers were stirred with a strong cation-exchange resin DOWEX 50W-X8, mesh size 200−400 (Supelco, Bellefonte, PA). In only one case, some NaI was added to the sample solution. Unless stated otherwise, the matrix used for all experiments was 3-β-indoleacrylic acid (IAA, Fluka, Milwaukee, WI), used without further purification and dissolved in THF (0.25 M). In a preliminary analysis, 1,8,9-trihydroxyanthracene (dithranol), 2,5-dihydroxybenzoic acid (DHB), and α-cyano-4-hydroxycinnamic acid (CHCA) matrices were also used (Sigma-Aldrich, St. Louis, MO). Matrix and polymer solutions were mixed at a molar ratio of 500:1, and then 1 μL of the mixture was deposited onto the MALDI target before insertion into the ion source chamber.

A test analysis performed by ^{1}H NMR spectroscopy allowed us to check that there was not any reaction between the IAA matrix and the used dithioester, *tert*-butyl dithiobenzoate.

Results and Discussion

Polymerization of NAM was performed in dioxane using AIBN as initiator and *tert*-butyl dithiobenzoate as RAFT chain transfer agent according to previously optimized conditions.[22,26] Such conditions (90 °C, [NAM] = 1.6 mol L^{-1}, [CTA]/[AIBN] = 10) led to poly(NAM) samples with well-controlled molecular weight and narrow MWD (<1.10). As the targeted molecular weight was low (15 000 g mol^{-1} at 100% conversion), these samples were well-suited for MALDI−TOF MS analyses.

Optimization of Measurement Conditions. First, several matrices were tested since the matrix nature is often a key parameter when studying a polymer by MALDI−TOF MS:[4,9] 2,5-dihydroxybenzoic acid (DHB), 1,8,9-trihydroxyanthracene (dithranol), α-cyano-4-hydroxycinnamic acid (CHCA), and 3-β-indoleacrylic acid (IAA). However, only IAA and CHCA matrices led to desorption/ionization of the poly(NAM) chains. The number of significant peaks (peaks present in each repetitive sequence unit, thus corresponding to a polymer chain population) was higher on the spectrum

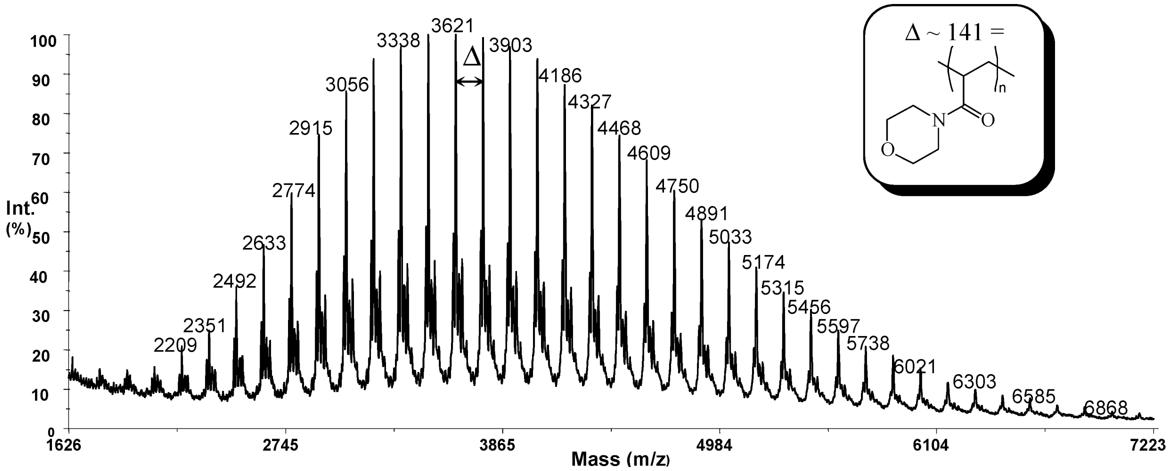


Figure 1. Positive ion MALDI−TOF mass spectrum of poly(NAM) ($\overline{M}_{n(\mathrm{MALDI-TOF\ MS})}$ = 3960 g mol^{-1}, $\overline{M}_w/\overline{M}_n$ = 1.04) obtained in linear mode (IAA matrix).

recorded from IAA matrix, providing more information. Consequently, this matrix was selected for further studies.

The poly(NAM) spectrum (in linear mode) is well-resolved (Figure 1), and the peaks are separated by 141 mass units, which corresponds to the molecular weight of NAM monomer (141.17 g mol^{-1}). The number-average molecular weight, $\overline{M}_n$, is 3960 g mol^{-1}, a value close to the one determined by SEC with a light scattering detection ($\overline{M}_{n(\mathrm{SEC-LS})}$ = 3800 g mol^{-1}) and to the calculated value (on the assumption of one polymer chain formed per dithioester molecule, $\overline{M}_{n(\mathrm{calc})}$ = 3795 g mol^{-1}).

Each main peak of the distribution corresponds to a chain with the expected structure for RAFT polymerization (dormant chains, Scheme 1). For instance, the mass of the highest peak of the distribution, 3621, corresponds to a poly(NAM) chain of 24-mer cationized with a sodium ion, possessing a *tert*-butyl fragment at the α-end and a dithiobenzoate fragment at the ω-end (expected mass: 3621.4).

Some other peaks are present on both sides of each main peak. To clarify the spectrum, some additives were introduced to the sample. In fact, the use of a cationic additive usually displaces the cationization equilibrium between the chains which help to identify them. For relatively polar polymers, proton, sodium, and/or potassium adduct ions are observed in the MALDI−TOF mass spectrum even if salts are not added to the matrix/analyte mixture.[28] These cations are present as impurities in matrix, reagents, solvents, glassware, and other sources.[1] Mixing the sample with an ion-exchange resin should enhance the protonated chains whereas addition of some NaI salt should enhance the Na$^+$ cationized chains (Figure 2).

In the spectrum recorded in the salt-free conditions (Figure 2B), it was possible (as explained above) to attribute the main peaks to the Na$^+$ cationized dormant chains. The corresponding protonated (H$^+$) and K$^+$ cationized chains were identified (peaks with a 22 lower mass units and with a 16 higher mass units, respectively, dotted lines in Figure 2). Mixing with the resin (Figure 2A) and addition of sodium salt (Figure 2C) confirmed this attribution since in the first case, the proportion of H$^+$ cationized dormant chains significantly increased, and in the second case, the H$^+$ and K$^+$ cationized chains almost disappeared. In general, addition of NaI reduces spectral complexity of the spectrum, as shown in the enlarged part of the spectrum. Attribution of the other peaks was not done here since this spectrum was recorded in the linear mode, but on the corresponding spectrum recorded in the reflectron mode which brings more resolution (see below).

This optimization confirms that it is possible to observe poly(NAM) chains synthesized by RAFT with MALDI−TOF MS using the IAA matrix without added salt. The expected dormant chains are indeed present as the main population.

Analysis of Various Molecular Weight Poly(NAM) Samples. Another criterion of a well-controlled RAFT polymerization is a linear increase of $\overline{M}_n$ with conversion. Then, MALDI−TOF MS was used to follow the evolution of $\overline{M}_n$ and PDI with conversion. Well-resolved spectra were obtained (Figure 3) with high sensitivity until masses of about 12 000 g mol^{-1}. Until now, the upper mass limit for polymer synthesized by RAFT and analyzed by MALDI−TOF MS was below 7000 g mol^{-1}.[15] In addition, poly(NAM) molecular weight increased with conversion, as indicated by higher mass signals.

Spectra D and E (Figure 3) have a tail at low molecular weights (increasing with conversion). A test experiment was performed with decreasing the laser power to check whether this tail was a result of fragmentation of the poly(NAM) chains, as reported by Martin et al.[29] for polystyrene. However, the tail was still present (data not shown). Moreover, the main peaks of this tail indeed correspond to dormant poly(NAM) chains initiated by a *tert*-butyl group and not to dead chains or to AIBN-derived chains. Consequently, this tail does not result from fragmentation and is not related to either termination reactions or progressive decomposition of initiator. The presence of these short dormant poly(NAM) chains indicates that a few initial dithioester molecules remained in the polymerization medium after the initiation period. However, as the importance of this tail was mainly due to a molar mass discrimination effect (which overestimates the low molecular weight chains),[29−33] the real proportion of these short dormant chains in the polymerization medium was very low. Indeed, the SEC trace of the same samples did not exhibit a tail at low MW.

The plot of $\overline{M}_n$ vs conversion was linear, and the values agreed very well with those determined by SEC-

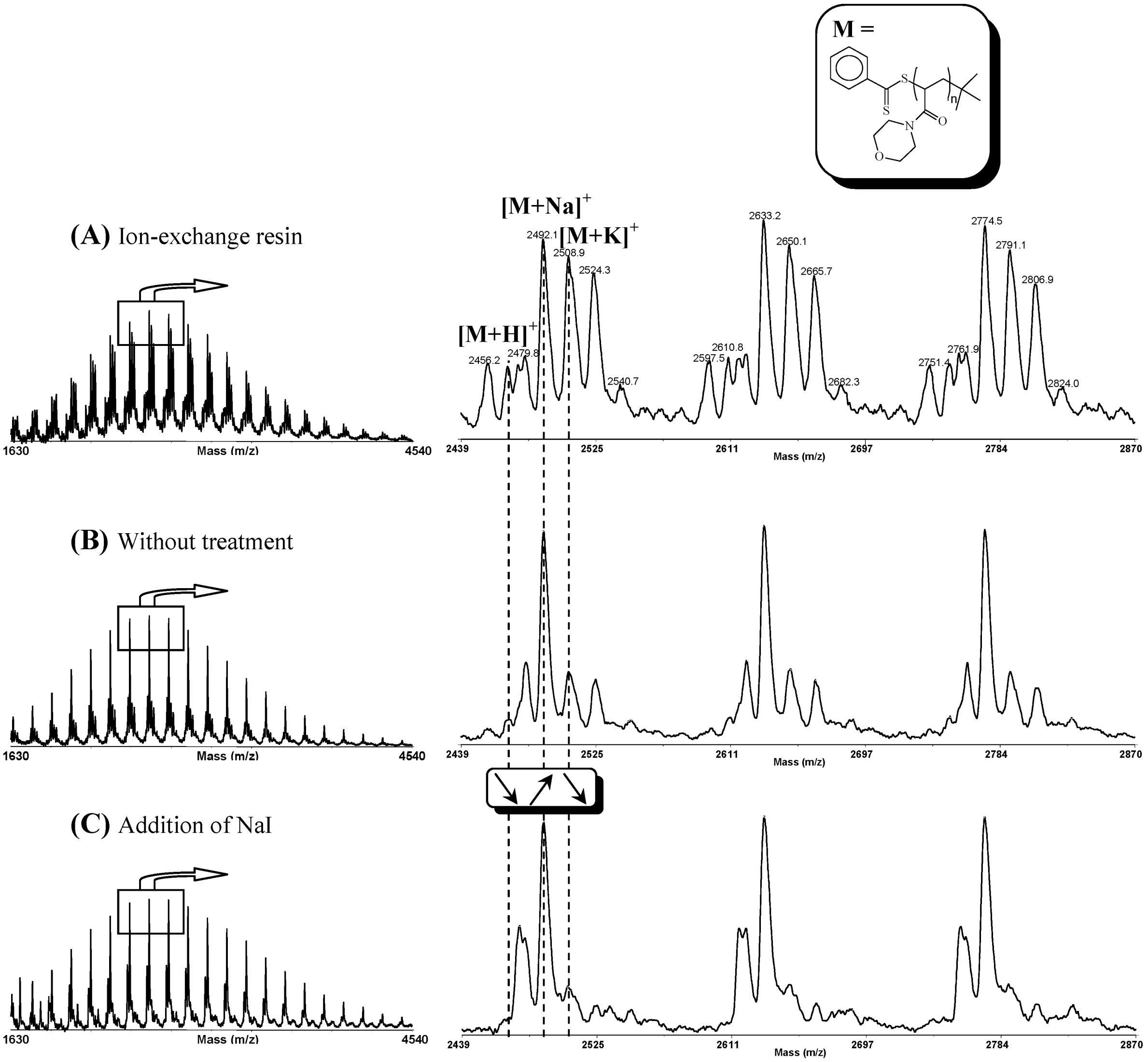


Figure 2. Effects of additives on enlarged regions of MALDI−TOF mass spectra of poly(NAM) in linear mode (IAA matrix) (**A**) after stirring with a H^+ ion-exchange resin, (**B**) without treatment, and (**C**) after addition of NaI.

LS and by ^1H NMR (see Experimental Section) as well as with the calculated values determined according to the RAFT mechanism (Figure 4).

For the higher mass sample ($\overline{M}_{n(SEC-LS)}$ = 10 300 g mol^{-1}), the corresponding MALDI−TOF MS value was underestimated ($\overline{M}_{n(MALDI-TOF\ MS)}$ = 7370 g mol^{-1}), probably due to the molar mass discrimination effect.

Analysis of Terminal Groups. The determination of end groups of poly(NAM) samples synthesized by RAFT had been previously carried out with the linear mode.[21,22] Here, a more accurate analysis was performed using the reflectron mode. This mode provides well-resolved spectra exhibiting the isotopic distribution of the peaks. The low molecular weight sample of poly(NAM) of $\overline{M}_{n(MALDI-TOF\ MS)}$ = 2700 g mol^{-1} was analyzed; each repeat sequence consists of seven peaks of various importance, as shown on an enlarged part of the spectrum (Figure 5 and Table 1).

The expected dormant chains (initiated by a *tert*-butyl group and terminated by a dithiobenzoate group) are observed as the highest peak (peak D, Na^+ cationization; peak E, K^+ cationization). The shape of the isotopic distribution exactly corresponds to the simulated one (see inset in Figure 5). For further analyses of the spectrum, peak D will be considered as the reference.

Other chains, initiated by a *tert*-butyl group and terminated by a proton (peak located at −11 mass units from each main peak), are also observed (peak C, Na^+ cationization; the K^+ cationized chains are located under the “tail” of peak D). Similar chains, terminated by a proton, were first reported by Beyou et al.[34] for polymer synthesized by another process of addition−fragmentation (nonreversible) using dithiocarbamates. They were attributed to the weakness of the chain-end C−SC(S) bond which would undergo some fragmentation in the spectrometer. Similar chains have also been observed by Destarac et al.[17] for polymers synthesized by RAFT. They were attributed to some irreversible transfer or disproportionation termination reactions during polymer synthesis.

However, in our case, no chains terminated by disproportionation (double-bond chain end) or by recombination reactions were observed on the MALDI−TOF spectra. Moreover, considering the excellent control of molecular weight (Figure 4), irreversible transfer and termination reactions were very unlikely to occur to such an extent (peak C is almost of the same height as peak D). In addition, analysis of the polymer sample by ^1H NMR allowed one to quantify the proportion of dormant chains to 96%.[22] As a consequence, it was

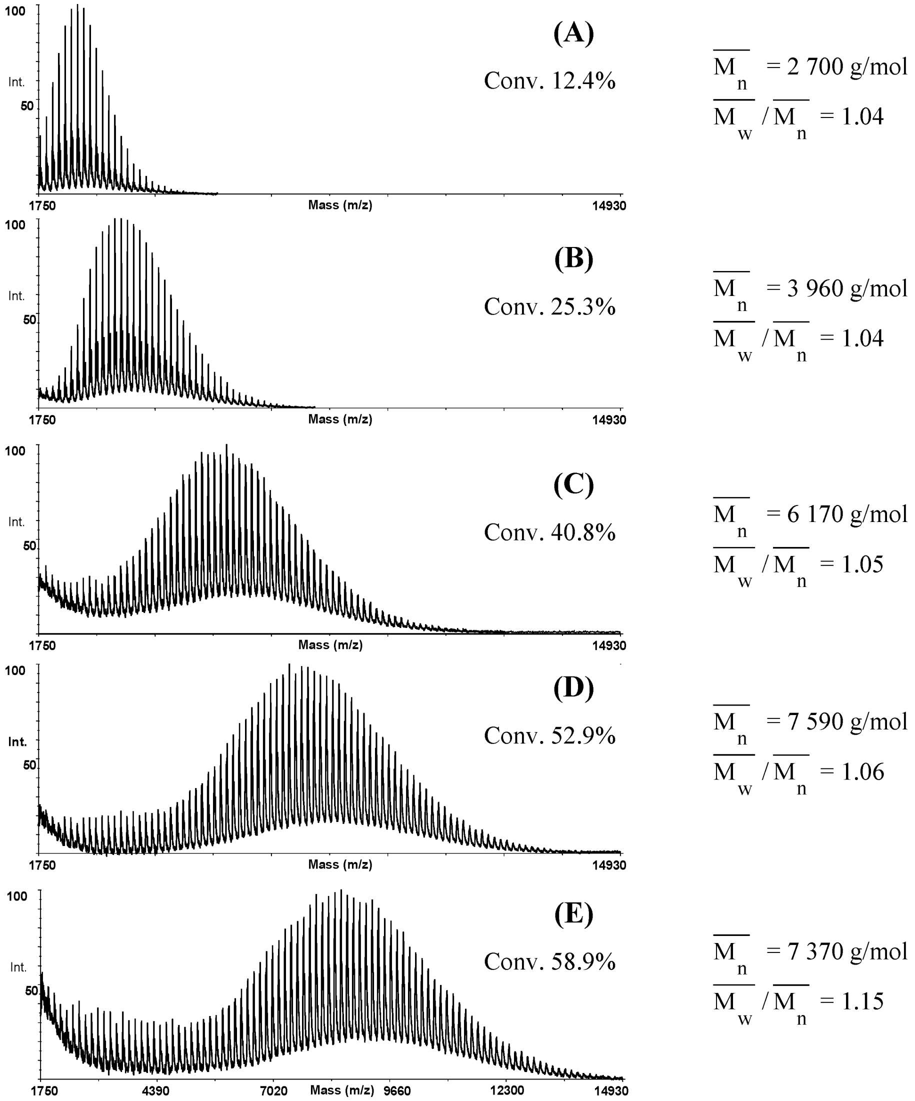


Figure 3. MALDI−TOF mass spectra (linear mode, IAA matrix) of poly(NAM) samples obtained at different conversions: (**A**) 12.4%, (**B**) 25.3%, (**C**) 40.8%, (**D**) 52.9%, and (**E**) 58.9%. Temperature = 90 °C, $[NAM]_0 = 1.6$ mol L^{-1}, $[NAM]_0/[tBDB]_0 = 105$, and $[tBDB]_0/[AIBN]_0 = 10$.

concluded that the numerous chains terminated by a proton observed on the MALDI−TOF spectrum (peak C) did not reflect the number of proton-terminated chains present in the sample but mostly resulted from fragmentation (at the dithioester site) in the spectrometer. Recently, Schilli et al.[20] confirmed (by performing some post source decay (PSD) experiments) that such kind of chains indeed arise from fragmentation inside the MALDI−TOF spectrometer.

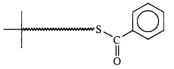
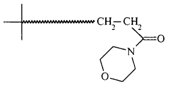
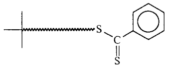
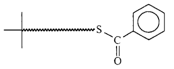
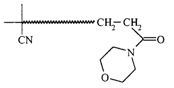
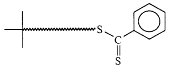
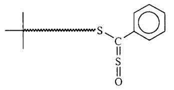
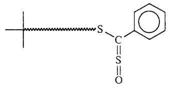
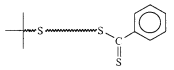
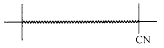
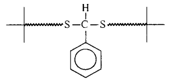
Another peak, located at −16 mass units from peak D, appears as significant (peak B). It is present on every spectrum, however, with a varying intensity. It may correspond to dormant chains which would have undergone an oxidation reaction. In fact, oxidation of a dithioester function gives rise to a sulfine which decomposes to a thioester and elemental sulfur[35,36] (Scheme 2).

Such thioester-ended chains would exactly be observed at peak B (Na^+ cationization) with the K^+ cationized chains overlapping with peak D (an analysis in the presence of added NaI confirmed the Na^+ cationization of peak B). Concerning the sulfine-ended chains, they would overlap with peak E (Na^+ cationization), and the corresponding K^+ cationized chains could explain the presence of the badly resolved peak F, although there is a difference of +2 mass units with the suggested structure. Indeed, peak F partly corresponds to K^+ cationized chains since it decreases upon addition of NaI (see Figure 2).

Now, it may be surprising to find these oxidized chains in this sample. In fact, we previously observed that *tert*-butyl dithiobenzoate could undergo some degradation (attributed after several tests to an oxidation reaction)[37] when stored several months at 4 °C in the presence of air. Then, a partial oxidation of dithiobenzoate-ended chains seems possible upon storage several weeks at room temperature under air. Recently, Vana et al.[23] reported an ESI-MS spectrum of poly(methyl acrylate) synthesized by RAFT, showing the appearance of thioester-ended chains when an oxidation reaction of the dithioester-ended chains was performed with a peroxide, the *tert*-butyl hydroperoxide, for several hours.

Peak F could also correspond to a dormant chain containing an additional sulfur atom (Table 1), although there is again a difference of +2 mass units with the suggested structure. Such structure could result from nondegrading irreversible transfer reactions due to the presence of some sulfide species in the polymerization

Table 1. Structures Corresponding to the Various Peaks in Figure 5

Peak	Monoisotopic mass		Structure	Cationization	X
	Experimental	Theoretical			
A	2440.2	NA	NA	NA	NA
B	2474.2	2474.3		Na	16
C	2479.2	2479.4		Na	17
D	2490.1	2490.3		Na	16
		2490.3		K	16
		2490.4		Na	17
E	2506.2	2506.3		K	16
		2506.3		Na	16
F	2524.2	2522.3		K	16
		2522.3		Na	16
G	2546.1	2546.4		Na	17
		2548.4		Na	16

NA = nonattributed; X = polymerization degree of the considered chain.

medium. In fact, in a previous article,[26] we already suspected the occurrence of termination reactions onto intermediate radicals (by addition of a propagating chain or of a small radical), leading to sulfide species. For instance, the termination product of an intermediate radical (II or IV in Scheme 1) by a proton could correspond to peak G (difference of −2 mass units). Then, this sulfide species could transfer onto a propagating chain, releasing a radical species of the kind $(CH_3)_3C-(NAM)_n-S°$ (with $n \geq 0$), able to initiate the polymerization of NAM, i.e., leading to dormant chains possibly corresponding to peak F. Considering that F and G peaks are small and badly resolved, the suggested structures need to be confirmed; however, the given hypotheses seem plausible since related to possible side reactions during RAFT mechanism.[26]

In fact, the study of side reactions onto intermediate radicals is an ongoing subject in several groups, whether they refer to reversible[38,39] or irreversible[40,41] termination reactions. It is worthy to note that Calitz et al.[39] recently evidenced by ESR studies the presence of an unknown radical species (exibiting a strong coupling to S nuclei) during RAFT polymerization of styrene. In addition, they observed a pronounced loss of color with increasing concentration of this unknown radical. In fact, as we already explained,[26] the formation of the above-mentioned sulfide species (responsible for the

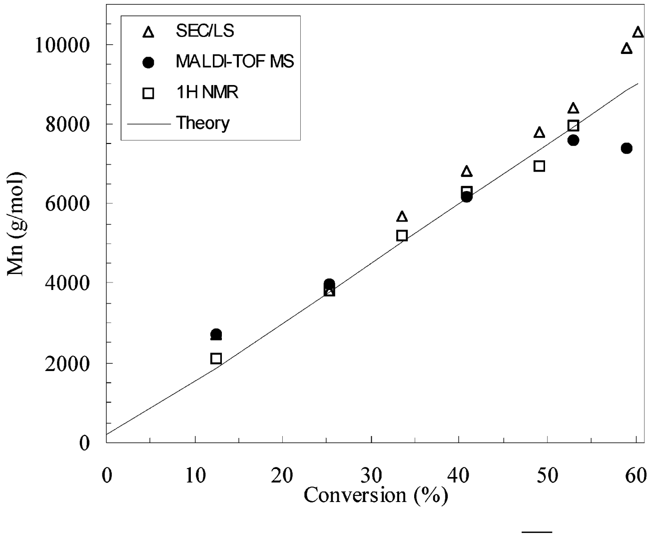


Figure 4. Number-average molecular weight, $\overline{M_n}$, vs conversion plots for poly(NAM) samples synthesized in the presence of tBDB: Temperature = 90 °C, $[NAM]_0 = 1.6$ mol L^{-1}, $[NAM]_0/[tBDB]_0 = 105$ and $[tBDB]_0/[AIBN]_0 = 10$. $\overline{M_n}$ values were determined by (circle) MALDI−TOF MS, (triangle) SEC/LS, and (square) ^1H NMR spectroscopy; the line corresponds to prediction of $\overline{M_n}$ from the following equation: calculated $\overline{M_n} = [NAM]_0/[CTA]_0 \times M_{NAM} \times \text{conversion} + M_{CTA}$, where M_{NAM} and M_{CTA} are the molecular weights of NAM monomer and chain transfer agent (*tert*-butyl dithiobenzoate), respectively.

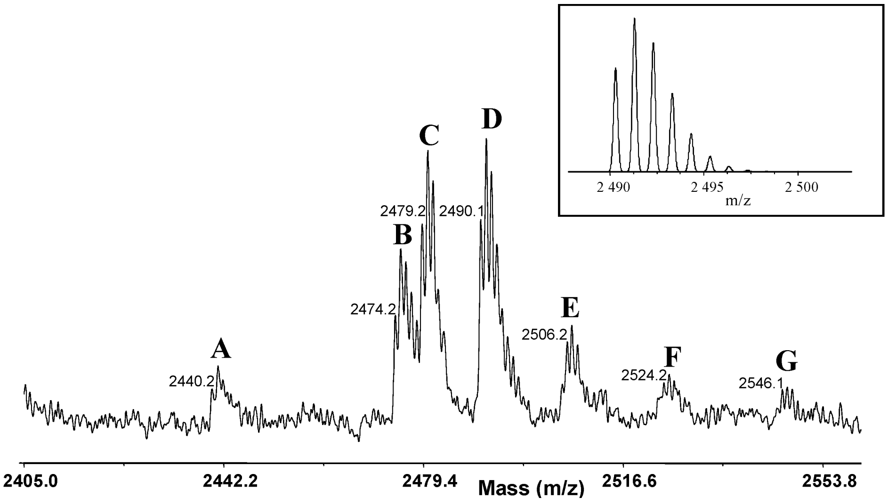
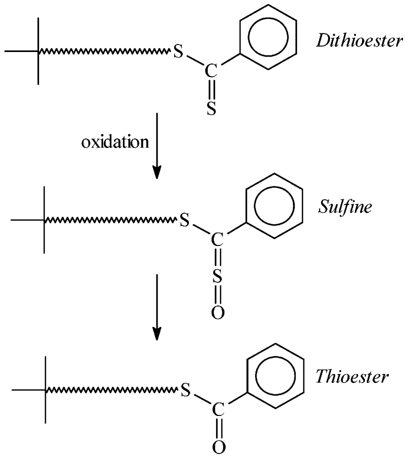


Figure 5. Enlarged region of MALDI−TOF mass spectrum of poly(NAM) sample of $\overline{M_n}$ = 2700 g mol^{-1} (Figure 3A) in reflectron mode (IAA matrix). The figure shows the labels of monoisotopic masses (Table 1). Inset: calculated isotopic pattern for peak D ($C_{123}H_{190}N_{16}O_{32}S_2Na_1$).

Scheme 2. Mechanism of Dithioester Function Oxidation



release of the S°-ended radical) indeed induces a pronounced loss of color.

Now, concerning the dormant chains initiated by AIBN, they were not observed which was often the case in previous studies.[15,16,18] Only Destarac et al.[17] and Schilli et al.[20] reported such kind of chains, although with a very low intensity. Taking into account that they were using a DT/AIBN ratio of 5 and 3, it is not surprising that, at the used ratio of 10, these chains are hardly observable. In addition, the corresponding peak would overlap with the tail of peak D (at *m*/*z* 2501.3).

Considering the low proportion of the AIBN-derived chains, it would be surprising to observe the products of the various termination reactions. The combination product between an AIBN-derived chain and a *tert*-butyl-initiated chain could correspond to peak G (Table 1). However, it would be curious that the more numerous combination products between two *tert*-butyl-initiated chains would not be observable (at *m*/*z* 2535). Consequently, it is likely that peak G would rather correspond to the first-mentioned structure, i.e., the product resulting from addition of a proton onto an intermediate radical. Finally, only peak A, at −50 from peak D, could not be attributed.

Analysis of Polymers after Aminolysis. It may be valuable to perform an aminolysis of the dithioester chain end into a potentially reactive thiol chain end, which in addition affords a white polymer. Then, aminolysis with hexylamine was carried out to several poly(NAM) samples; this reaction is fast and quantitative at room temperature.[42,43] The spectra of two samples of $\overline{M_n}$ = 2700 and 3960 g mol^{-1} are presented in Figure 6 (linear mode), before and after aminolysis.

The spectra after aminolysis exhibit a second chain distribution at a double mass from the initial distribution, especially visible for the low molecular weight sample (also visible on the corresponding SEC chromatogram, data not shown). The structure of these new chains corresponds to the formation of a disulfide bond between two thiol-ended poly(NAM) chains (Figure 7). Such reaction is generally favored in a concentrated solution and in the presence of oxygen and basic species. On the spectrum, these chains appear protonated (H^+) and cationized by Na^+ and K^+, the three corresponding peaks being quite well-resolved (see enlarged part). For the sample corresponding to longer chains, the proportion of double chains is lower, probably due to the increase of the chain length and also to the mass discrimination effect. Some recent results[44] showed that for longer polymer chains (10 000 g mol^{-1}) aminolysis did not result in the formation of double chains if the reaction was performed under nitrogen (and only to less than 10% under air, as quantified by SEC).

A fourth peak, located at +32 from the Na^+ cationized disulfide chains, is present in the second distribution (inset in Figure 7). This peak may result from a coupling between two different thiol-ended chains, one of them corresponding to the chain containing an additional S atom identified before aminolysis (peak F and Table 1).

Concerning the first chain distribution observed after aminolysis, it consists of several populations, the main one corresponding to thiol-ended chains (cationized by Na^+). There were no remaining chains terminated by a dithiobenzoate end group, confirming that aminolysis reaction is quantitative. Some proton-ended chains were also observed as well as a chain population located at +32 from the thiol-ended chains, possibly corresponding to aminolysis of peak F chains.

Comparison of the proportion of disulfide chains and thiol-ended chains with all of the other observed populations, as well as the molar mass discrimination effect,

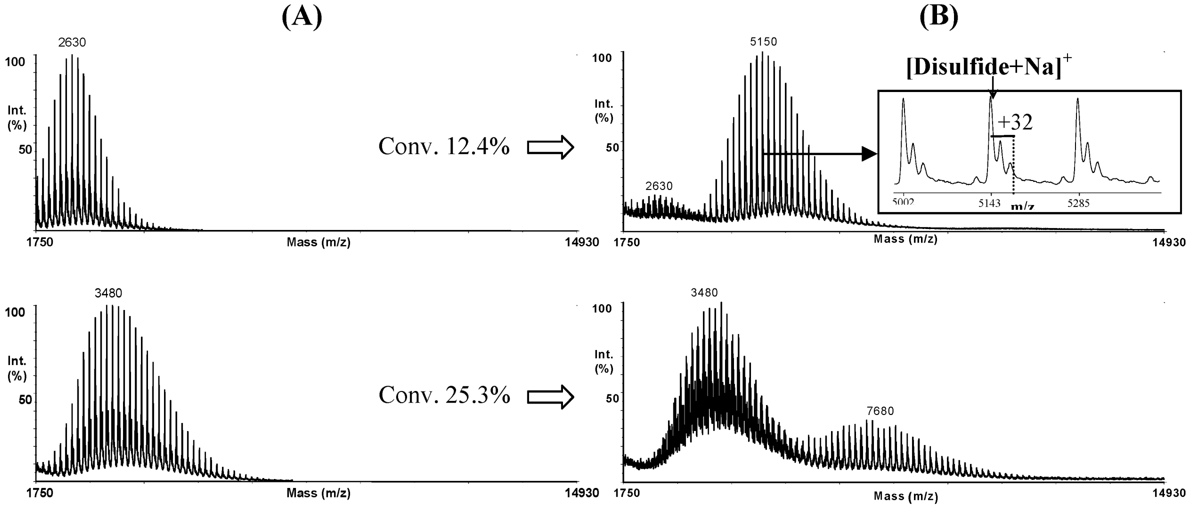


Figure 6. Positive ion MALDI−TOF mass spectra of poly(NAM) samples of $\overline{M_n}$ = 2700 and 3960 g mol^{-1} (Figure 3, A and B) in linear mode (IAA matrix) before (**A**) and after (**B**) treatment by hexylamine. Inset: zoom between *m*/*z* 5000 and 5400.

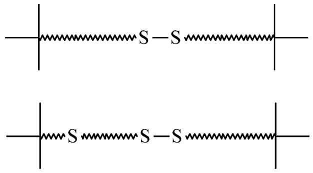


Figure 7. Possible assignments for the chains of the second distribution (Figure 6) after aminolysis.

demonstrated that the dithioester-ended chains represented a large majority of chains in the sample before aminolysis. Moreover, the presence of a very low amount of proton-ended chains after aminolysis confirmed that the observation of a large amount of this kind of chains before aminolysis (peak C, Figure 5) was mostly resulting from fragmentation of the dithioester end groups inside the spectrometer. However, the presence of these chains indicates that fragmentation is not the only explanation and that the occurrence of some transfer or disproportionation reactions during the RAFT polymerization is unavoidable.

Conclusion

Poly(*N*-acryloylmorpholine) chains synthesized by the RAFT technique in the presence of *tert*-butyl dithiobenzoate were analyzed by MALDI−TOF MS. For molecular weights below 10 000 g mol^{-1}, an excellent agreement was found between $\overline{M_n}$ values determined by three independent techniques (MALDI−TOF MS, SEC-LS, and ^{1}H NMR) as well as with the theoretical values. Moreover, the structural analysis of end groups revealed that the main chains were the expected dormant chains (initiated by a *tert*-butyl group and terminated by a dithiobenzoate group).

This study confirms that it is indeed possible to use MALDI−TOF MS to investigate the structure of polymer chains synthesized by the RAFT technique. However, it seems that the C−S bond of the chain end (close to the thiocarbonyl function) may fragment inside the spectrometer according to the nature of the propagating radical. In the case of a poly(styrene) or of a poly(methacrylate), this C−S bond strength is lower than in the case of a poly(acrylate), which could explain why dormant chains could not be observed (or with greater difficulty) by MALDI−TOF MS. In these cases, the main observed chains are proton-terminated chains.

In the MALDI−TOF MS spectrum of poly(*N*-acryloylmorpholine), some chains derived from the dormant chains were also observed, terminated by a sulfine and by a thioester end group and probably resulting from oxidation reactions upon storage of the polymer. In addition, we suspected the presence of some chains corresponding to intermediate radicals terminated by a proton (resulting from termination and/or transfer reactions), which constitutes a new experimental indication in the ongoing controversy about the possible termination reactions (whether reversible or not) onto these intermediate species.

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Note Added after ASAP Posting

This article was released ASAP on 2/17/2004 with reference 21 incorrect. References 21 and 22 have been changed to cite the correct journal. The correct version was posted on 02/27/2004.

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(37) Note: The degradation products, evidenced both by ^{1}H NMR spectroscopy and by thin layer chromatography, could not be isolated due to their too small amount. The origin of this degradation was attributed to either hydrolysis, photochemical or thermal S−C bond cleavage, or oxidation. Then, a first test experiment was carried out in order to detect a possible hydrolysis with traces of water. Water (5%) was introduced in a dioxane solution of tBDB under nitrogen, stirred at 90 °C for 1 day. Despite these conditions, no degradation was observed. Concerning a possible photochemical reaction, it was already reported that sulfur containing compounds could undergo S−C bond cleavage.[34] In addition, De Brouwer et al.[40] showed that, in the case of short polystyrene chains terminated by a dithioester end group, S−C bond cleavage was possible under UV irradiation (5 h under a broad-band high-pressure mercury lamp with a maximum intensity at a wavelength of 360 nm). Then, a test experiment was performed with a dioxane solution of tBDB maintained at 90 °C under nitrogen in daylight for several days. No significant tBDB degradation was observed, even after 3 days at this high temperature ($<$2%). Moreover, another experiment showed that tBDB alone was not able to initiate NAM polymerization at 90 °C in the absence of AIBN. Both tests excluded the possibility of a photochemical and/or thermal S−C bond homolytic cleavage at 90 °C and therefore at lower temperature. Finally, an eventual oxidation reaction was tested with a dioxane solution of tBDB kept at 90 °C during 24 h in the absence or presence of air. In this last case only, a significant tBDB degradation was noticed (by TLC and ^{1}H NMR spectroscopy), indicating a reaction involving oxygen from air, which could explain the slow degradation observed during storage under air at 4 °C.

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