Macromolecules **2002,** *35,* 8271−8280

Study of the RAFT Polymerization of a Water-Soluble Bisubstituted Acrylamide Derivative. 1. Influence of the Dithioester Structure

Arnaud Favier, Marie-Thérèse Charreyre,* Philippe Chaumont,† and Christian Pichot

Unité Mixte CNRS-bioMérieux, École Normale Supérieure de Lyon, 46 allée d'Italie, 69364 Lyon Cedex 07, France

Received April 5, 2002; Revised Manuscript Received August 15, 2002

ABSTRACT: Homopolymers of *N*-acryloylmorpholine (NAM), a water-soluble bisubstituted acrylamide derivative, have been synthesized by reversible addition-fragmentation chain transfer polymerization (RAFT). Several dithioesters were used as chain transfer agents: carboxymethyl dithiobenzoate (CMDB), *tert*-butyl dithiobenzoate (tBDB), menthonyl dithiobenzoate (MDB), and a bifunctional dithiobenzoate, 1,3-bis(2-(thiobenzoylthio)prop-2-yl)benzene (TPB). Whereas CMDB is a commercial reagent, tBDB and MDB were synthesized by a novel biphasic process based on a thioacylation reaction and leading to very high yields. The performances of the four dithiobenzoates were compared in term of kinetics and molecular weight distribution control. Very good control of NAM polymerization was obtained with tBDB and MDB, with a linear increase of M_n vs conversion over the whole conversion range and with polydispersity indices (PDI) below 1.1, as determined by aqueous size exclusion chromatography with on-line light scattering detection. In addition, a degradation phenomenon of the dithioester functions was evidenced during the course of the polymerization, correlated with a M_n vs conversion curve leveling off and even sometimes decreasing above 80% conversion. Such observations were assumed to be the consequence of the formation of side products in the polymerization media, subsequently acting as nondegradative irreversible transfer agents.

Introduction

In the past decade, controlled radical polymerization (CRP) has been applied to a wide variety of monomers out of the application field of living anionic (or cationic) polymerization. However, most of the research reported in the literature has focused on well-known monomers, like styrene, methyl methacrylate, and butyl acrylate. In fact, very few studies have considered CRP of acrylamide type monomers because of several problems regarding both characterization and synthesis.

First, from the standpoint of characterization, when dealing with acrylamide type polymers, it is often a challenge to get “real” molecular weight values. In the case of water-soluble polymers, analyses are performed using aqueous size exclusion chromatography (SEC) generally equipped with a refractometer and/or a UV−vis detector where molecular weight (MW) values are typically relative to PEO or polysaccharide standards, both being inadequate for polyacrylamide samples. On the other hand, on-line detection with a light scattering apparatus (providing absolute molecular weight values) is not widely used when dealing with aqueous SEC. Finally, characterization of acrylamide type polymers is a limitation to the study of their controlled polymerization.

Second, from the standpoint of synthesis, several difficulties referring to CRP of acrylamide derivatives have been pointed out, whatever the chosen technique. Concerning nitroxide-mediated polymerization (stable free radical polymerization, SFRP technique), very few studies were carried out. They indeed concern only one acrylamide derivative, a bisubstituted one, *N*,*N*-dimethylacrylamide (DMA), using TEMPO[1] or *N*-*tert*-butyl-2-methyl-1-phenylpropyl nitroxide (TIPNO)[2] as the controlling agent. The use of TEMPO led to large PDI, contrary to TIPNO, which provided polymers with PDI of 1.1−1.2 but with rather low M_n values, below 20 000 g mol^{-1}.

Concerning atom transfer radical polymerization (ATRP technique), very few acrylamide derivatives were studied again, although the application field of this technique is wider. Using a copper-based catalyst, the polymerization of DMA and *tert*-butylacrylamide (*t*BuA) was attempted;[3] however, only low molecular weights were obtained. Using a ruthenium-based catalyst, the polymerization of DMA, diethylacrylamide (DEA), and *N*-isopropylacrylamide (NIPAM) was investigated.[4] Results indicated a controlled process for the bisubstituted acrylamides, DMA and DEA (however with M_n values below 20 000 g mol^{-1} and PDI around 1.6), but an uncontrolled process for the monosubstituted acrylamide, NIPAM. In fact, acrylamide derivatives might play the role of ligand via their nitrogen atom, leading to a decrease of the available catalyst concentration, which constitutes the main limitation of ATRP regarding acrylamide type monomers.

Contrary to the above-mentioned CRP techniques, reversible addition−fragmentation chain transfer (RAFT technique)[5−7] seems well suited for the polymerization of acrylamide derivatives, even to high M_n values. This technique is based on the use of a dithioester compound (Figure 1) acting as reversible chain transfer agent (CTA). The first example[6] is related to the polymerization of DMA in the presence of benzyl dithiobenzoate; a PDI lower than 1.2 was obtained for MW exceeding 100 000 g mol^{-1}. The second example[8] concerns NIPAM, which was polymerized in benzene and 1,4-dioxane in the presence of either benzyl or cumyl dithiobenzoate.

[†] UMR CNRS No. 5627, LMPB, Bâtiment de l'ISTIL, Université Claude Bernard-Lyon 1, 43 Bd du 11 Novembre 1918, 69622 Villeurbanne Cedex, France.

[*] Corresponding author: Tel 00 33 4 72 72 83 60; e-mail mtcharre@ens-lyon.fr.

10.1021/ma020550c CCC: $22.00

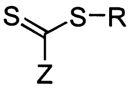


Figure 1. Dithioester general structure.

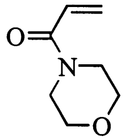


Figure 2. *N*-Acryloylmorpholine (NAM) monomer.

In this case, however, PDI was larger than 1.2 for MW above 20 000 g mol^{-1}. Recently, a third study[9] reported the polymerization in aqueous media of two other monosubstituted acrylamide derivatives, sodium 2-acrylamido-2-methylpropanesulfonate (AMPS) and sodium 3-acrylamido-3-methyl butanoate (AMBA), in the presence of 4-cyanopentanoic acid dithiobenzoate. Here, the PDI remained lower than 1.3 for MW until 30 000 g mol^{-1}. Finally, these different results confirm the ability of the RAFT technique to produce well-controlled polymer chains either from monosubstituted or bisubstituted acrylamide derivatives.

N-Acryloylmorpholine (NAM, Figure 2) is another bisubstituted acrylamide derivative exhibiting several outstanding features:[10–14] solubility in a wide range of organic and aqueous solvents; the ability to yield high molecular weight polymers that are soluble both in water and in polar or low-polar solvents. *N*-Acryloylmorpholine was used for many years to synthesize cross-linked networks for gel-phase synthesis of peptides,[15,16] semipermeable membranes for plasma separation,[17–19] polymeric supports for gel chromatography[20] and capillary electrophoresis,[21] and drug delivery applications.[22–25]

Recently, we reported a kinetic study concerning the free radical solution homopolymerization of NAM and its copolymerization with an activated ester type monomer.[26] Copolymers of various compositions were synthesized, with molecular weights ranging from 7000 to 110 000 g mol^{-1}, as determined by aqueous SEC with an on-line light scattering detector.[27] As part of a wide program to synthesize hydrosoluble polymers of controlled chain length for diagnostic and therapeutic applications, it appeared particularly challenging to evaluate the potential of RAFT to polymerize NAM in order to yield acrylamide derivative polymers with controlled MW and architecture. To our knowledge, NAM monomer has not been polymerized by the RAFT process so far or by any other controlled radical polymerization technique.

This paper first describes a novel biphasic process to synthesize dithioester compounds, based on a thioacylation reaction, with a particular emphasis on the synthesis of *tert*-butyl dithiobenzoate (tBDB). Then, performance of tBDB to control RAFT polymerization of NAM was compared with that of several other dithioesters: (i) carboxymethyl dithiobenzoate (CMDB), a commercially available dithiobenzoate; (ii) (1-(4-methylcyclohexan-2-onyl)-1-methyl)ethyl dithiobenzoate (menthonyl dithiobenzoate, MDB), synthesized by the same method as tBDB and bearing a more bulky R substituent (Figure 3); (iii) a bifunctional dithiobenzoate, 1,3-bis(2-(thiobenzoylthio)prop-2-yl)benzene (TPB). In each case, the polymerization experiments were compared in terms of kinetic and molecular weight distributions of the obtained polymer samples, and the results were related to the nature and/or to the structure of the dithioester substituent. In addition, side reactions concerning the degradation of dithioester functions during polymerization were reported with tentative explanations.

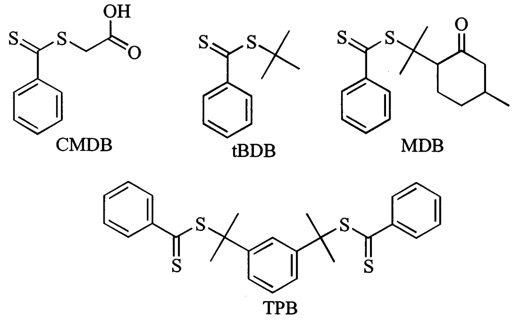


Figure 3. Structure of the used dithiobenzoates.

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. 1,4-Dioxane (Acros, 99%) was distilled over $LiAlH_4$ (110 °C).

Carboxymethyl dithiobenzoate (Aldrich, 99%), sodium 2-methyl-2-propanethiolate (Aldrich, 90%), 2-(1-mercapto-1-methylethyl)-5-methylcyclohexanone (mercaptomenthone) (Aldrich, 80%, mixture of isomers), trioxane (Acros, 99%), *tert*-butyl sulfide (tBS) (Acros, 98%), and other materials were all used without further purification.

1,3-Bis(2-(thiobenzoylthio) prop-2-yl)benzene (TPB) synthesis has been described recently.[28]

Synthesis of *tert*-Butyl Dithiobenzoate (tBDB). In a 500 mL round-bottomed flask equipped with a magnetic stirrer, 150 mL of a diethyl ether solution of carboxymethyl dithiobenzoate (1.6×10^{-2} mol L^{-1}) was added to 100 mL of an aqueous basic solution (NaOH, 1 mol L^{-1}) of *tert*-butyl thiolate (2.9×10^{-2} mol L^{-1}, 1.2 equiv). This biphasic mixture was vigorously stirred at room temperature for 5 h. Then, the purple ether phase was removed and washed twice with 500 mL of an aqueous basic solution (NaOH 1 mol L^{-1}) and twice with 500 mL of a 10% NaCl aqueous solution and dried over anhydrous magnesium sulfate. Purification by silica gel chromatography (Kiesegel-60) with petroleum ether/ethyl acetate (99/1:v/v) as eluent gave *tert*-butyl dithiobenzoate as a dark purple oil (90% yield).

The ^{1}H NMR spectrum corresponded with literature data.[6]

Fast atom bombardment (FAB) mass spectrometry [$C_{11}H_{14}S_2$ (210.0615)]: characteristic ion $[M + H]^+ = 211.0609$. Calculated: C, 62.80; H, 6.71; S, 30.49. Found: C, 63.08; H, 6.83; S, 30.29.

Synthesis of (1-(4-Methylcyclohexan-2-onyl)-1-methyl)ethyl Dithiobenzoate (MDB). MDB was synthesized from 2-(1-mercapto-1-methylethyl)-5-methylcyclohexanone (mercaptomenthone) and purified according to the same procedure as described for tBDB (80% yield).

Fast atom bombardment (FAB) mass spectrometry [$C_{17}H_{22}O_1S_2$ (306.1190)]: characteristic ion $[M + H]^+ = 307.1172$. Calculated: C, 66.62; H, 7.24; S, 20.92. Found: C, 65.79; H, 7.38; S, 19.90.

Polymerization General Procedure. NAM, dithioester (CTA), AIBN, dioxane (solvent), and trioxane (internal reference for ^{1}H NMR determination of monomer consumption) were introduced in a Schlenk tube equipped with a magnetic stirrer. The mixture was degassed by five freeze–evacuate–thaw cycles and then heated under nitrogen in a thermostated oil bath. Periodically, samples were withdrawn from the polymerization medium for analyses.

For kinetic study, monomer conversion was determined by ^{1}H NMR using a Bruker AC 200 spectrometer (200 MHz). Trioxane, which has no influence on the free radical process,[26] was used as internal reference. Typically, 500 μL of deuterated

Table 1. RAFT Polymerization of NAM in Dioxane (Initial Concentrations)[a]

expt	temp (°C)	[M] (mol L^{-1})	[M]/ [CTA]	[AIBN] × 10^3 (mol L^{-1})	[CTA]/ [AIBN]	CTA
1	60	3.75	350	3.2	3.3	CMDB
2	60	3.75	350	3.2	3.3	tBDB
3	90	1.6	350	1.4	3.3	tBDB
4	90	1.6	350	1.4	3.3	MDB
5	60	3.75	350	3.2	3.3	TPB
6[b]	90	1.6		1.4		
7	90	1.6	350[c]	1.4	3.3[c]	tBDB
8	90	1.6	350[d]	1.4	3.3[d]	tBDB

[a] [M] = [NAM]; CMBD = carboxymethyl dithiobenzoate; tBDB = *tert*-butyl dithiobenzoate; MDB = (1-(4-methylcyclohexan-3-onyl)-1-methyl)ethyl dithiobenzoate; TPB = 1,3-bis(2-(thiobenzoylthio)prop-2-yl)benzene. [b] Experiment performed without any dithioester. [c] These values do not take into account that 10 mol % of tBDB is substituted by *tert*-butyl sulfide (tBS). [d] These values do not take into account that 30 mol % of tBDB is substituted by *tert*-butyl sulfide (tBS).

chloroform, $CDCl_3$, was added to 120 μL of each sample. The theoretical M_n is defined as follows:

$$\text{theoretical } M_n = \frac{[\text{NAM}]_0}{[\text{CTA}]_0 + 2f\,[\text{AIBN}]_0(1 - e^{-k_d t})} \times M_{\text{NAM}} \times \text{conversion} \quad (1)$$

where M_{NAM} is the molecular weight of NAM monomer and f is the initiator efficiency factor.

Generally, f values range between 0.5 and 0.6 for AIBN at 60 °C in conventional free radical polymerization,[29] but it is unknown considering the RAFT process (especially above 60 °C).[30] Moreover, high viscosity associated with high monomer concentration tends to reduce f (the cage effect is indeed found to increase).[31] Consequently, the value of f is probably below 0.5, and we decided to use a "calculated M_n" equation by neglecting the chains initiated by AIBN.

$$\text{calculated } M_n = \frac{[\text{NAM}]_0}{[\text{CTA}]_0} \times M_{\text{NAM}} \times \text{conversion} \quad (2)$$

For all experiments, the predicted M_n was about 50 000 g mol^{-1} at 100% conversion; thus, the $[\text{NAM}]_0/[\text{CTA}]_0$ molar ratio was kept equal to 350.

Characterization of Dithioesters and of Polymer Samples. Elemental analyses and mass spectrometry were carried out by the "Service Central d'Analyses du CNRS" (Solaize, France). The mass spectra were obtained on a ZAB2-SEQ spectrometer (VG, Manchester, UK) using fast atom bombardment ionization.

Polymers were precipitated in a large volume of diethyl ether, recovered by filtration, washed several times with the same solvent, and finally dried under vacuum up to constant weight. The complete elimination of residual monomers was confirmed by ^{1}H NMR analysis.

Molecular weight distributions were determined by size exclusion chromatography (SEC) coupled to a light scattering detection (LSD). Aqueous SEC was performed using a Waters 510 pump, two Waters Ultrahydrogel columns (2000 and 500 Å), and a differential refractometer (DRI Waters 410). 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 (dn/dc) for poly(NAM) in the same eluent (0.163) has been 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.

Results and Discussion

RAFT controlled radical polymerization is based on an equilibrium between active and dormant species generated by a reversible addition−fragmentation process (Scheme 1). The chain transfer agent (CTA) is typically a dithioester (DT) whose efficiency depends on the nature of the substituents R and Z (Figure 1) as well as on the type of monomer.[7] The addition step is mainly Z group related, which governs the C=S double-bond reactivity. On the other hand, the R group mainly affects the fragmentation step. It must be a good leaving group (favored by steric hindrance and radical stability); i.e., the S−R bond must be weakened. Moreover, the corresponding expelled R$^\bullet$ radical must be a good reinitiator.

Considering that a phenyl Z group ensures a high addition rate[7] due to extensive intermediate radical stabilization, only dithiobenzoates were compared in this study for the polymerization of *N*-acryloylmorpholine, with the aim of determining the influence of the dithiobenzoate structure (Figure 3) both on the polymerization kinetics and on the control of the molecular weight distribution. Therefore, the results will mainly reflect the effects of the R substituent.

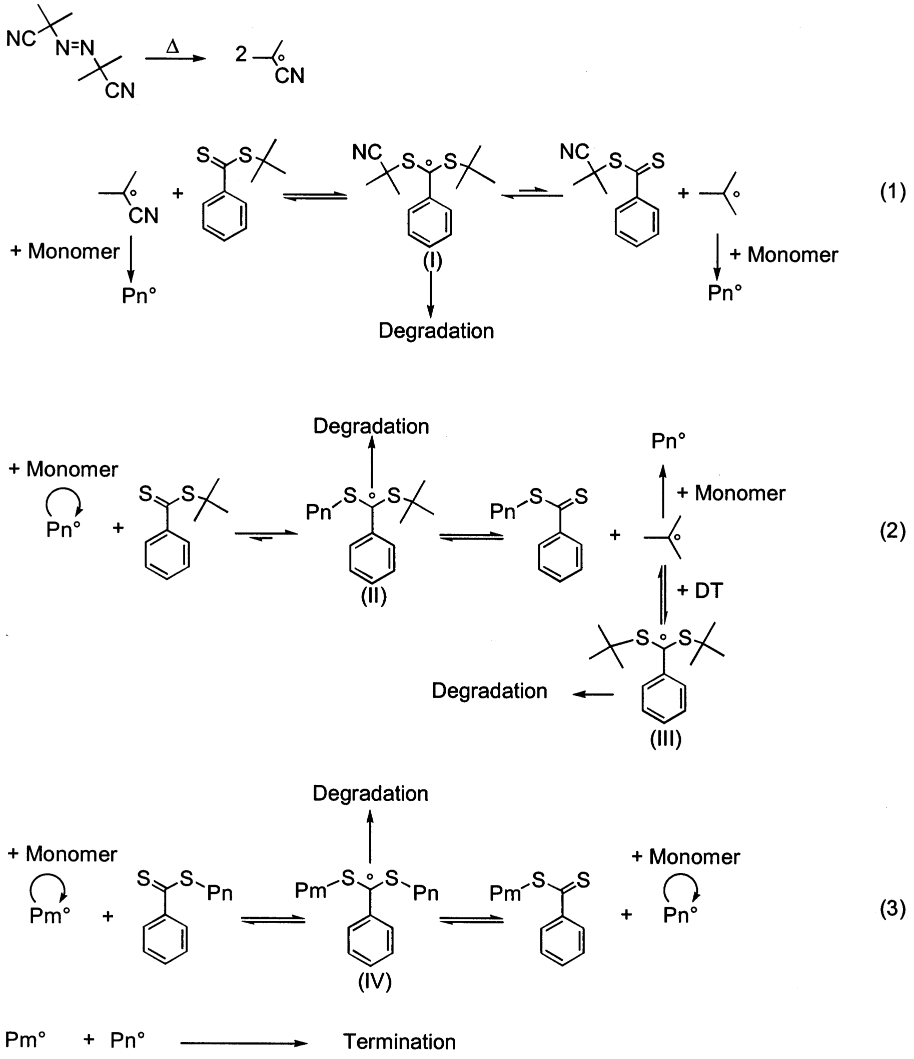
Dithioester Synthesis. Since carboxymethyl dithiobenzoate (CMDB) is to date the only commercially available dithioester, we decided to explore the synthesis of new dithioesters by thioacylation (Scheme 2) based on the procedure described by Leon et al.[32] The other generally used techniques[33] involving, among other reagents, dithiobenzoic acid[34] or bis(thiobenzoyl) disulfide[35] require tricky conditions and lead to moderate yields (<70%). The synthesis of dithioesters via reaction between carboxylic acids and thiols in the presence of phosphorus pentasulfide[33] seems to provide better results (96% yield for benzyl dithiobenzoate), even if important variations are noticed depending on the thiol nature (for instance, 45% yield for *tert*-butyl dithiobenzoate).

The procedure described by Leon et al. consists of mixing the commercially available carboxymethyl dithioester and a mercaptan in an aqueous alkaline solution at room temperature. Then, the expected dithioester separates out either as an oil or as a crystalline solid and is recovered by successive extractions. This method leads to moderate yields and has already been used to synthesize *tert*-butyl dithiobenzoate.[36,37] Here, we have developed an original biphasic (basic water/diethyl ether) process for the thioacylation reaction.[38] Then, *tert*-butyl and menthonyl dithiobenzoates were obtained at room temperature with a very high yield (90% and 80%, respectively). The expected tBDB and MDB structures were confirmed by elementary microanalysis and mass spectrometry.

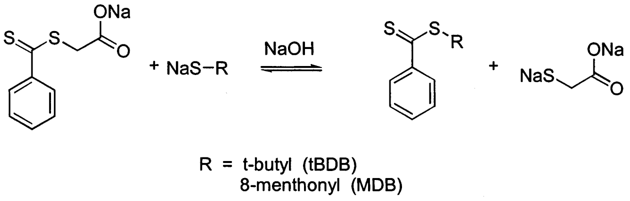
In fact, CMDB has a higher affinity for the basic aqueous phase than for the diethyl ether phase. As the mercaptan is also soluble in basic water, the thioacylation takes place in the aqueous phase. Moreover, as the resulting dithioester (tBDB or MDB) has a better affinity for the organic phase, the equilibrium is shifted toward the dithioester formation. As the reaction proceeds, the orange/red aqueous phase is discharged, and the colorless organic phase becomes rapidly purple.

However, this biphasic process exhibits some limitations which restrict its application field. The thiol must be soluble in basic water whereas the expected dithioester must have a preferential organic solubility. Thus, it is

Scheme 1. RAFT General Mechanism Including the Hypothesis of Intermediate Radical Degradation



Scheme 2. Thioacylation of Carboxymethyl Dithiobenzoate



well suited for thiols or thiolates having an appropriate structure.

Comparison between CMBD and tBDB. First, the CMDB and tBDB dithioesters were used as RAFT transfer agents in the polymerization of NAM at 60 °C (entries 1 and 2, respectively, in Table 1). The comparison of the kinetics shows that 65% conversion could be reached in 3 h with tBDB instead of 30 h with CMDB (Figure 4). Such a high polymerization rate with tBDB, which contains a better leaving group (*tert*-butyl) than CMDB (carboxymethyl), can be explained by a faster fragmentation of the corresponding adduct II (as well as adducts I and III) due to a better *tert*-butyl radical stability and to steric factors[7,39] which weaken the S−C bond.

However, in comparison with a conventional free radical process, RAFT polymerization of NAM is quite slow.[26] This retardation is due to a reduced active species concentration, [P•]. In fact, assuming that—to simplify the explanation—intermediate radicals (I, II, III, and IV in Scheme 1) are only involved in fragmentation reactions, the addition−fragmentation equilibrium can be simplified to Scheme 3.

The expression of the polymerization rate, R_p, is similar to that of conventional free radical polymerization (eq 3). However, the variation of [P•] with time is different,[40] as detailed in eq 4:

$$R_p = k_p \times [M] \times [P^\bullet] \tag{3}$$

$$\frac{d[P^\bullet]}{dt} = 2f\,[AIBN]_0 k_d e^{(-k_d t)} - k_t[P^\bullet]^2 - k_{addition}[DS][P^\bullet] + k_{fragmentation}[IR] \tag{4}$$

where k_p is the propagation rate constant, [M] the monomer concentration, [P•] the active species concentration, k_d the AIBN decomposition rate constant, k_t the termination rate constant, $k_{addition}$ the addition rate constant, $k_{fragmentation}$ the fragmentation rate constant, [DS] the dormant species concentration, and [IR] the intermediate radical concentration.

The whole radical species are divided among the propagating radicals, P•, and the intermediate radicals, IR, leading to a reduced [P•]. As a consequence, there are less termination reactions in a RAFT polymerization

Scheme 3. Simplified Addition−Fragmentation Equilibrium

$$P^\circ + DS \underset{k_{fragmentation}}{\overset{k_{addition}}{\rightleftharpoons}} IR$$

Active species (propagating radical)
Dormant species
intermediate radical

than in a conventional one. Moreover, because of the presence of the IR species acting as “propagating radical reservoir”, the extent of [P$^\bullet$] variation with time along the different stages of the polymerization is lower in the RAFT process than in a conventional one or equal if a pseudo stationary state is reached (eq 5).

$$\left|\left(\frac{d[P^\bullet]}{dt}\right)_{RAFT}\right| \leq \left|\left(\frac{d[P^\bullet]}{dt}\right)_{conventional\ process}\right| \qquad (5)$$

In the beginning of the polymerization, d[P°]/dt > 0, and consequently according to eq 5, the polymerization rate is slower in the RAFT process than in a conventional one, which will significantly influence the rest of the polymerization.

Then, when the production of new radicals from AIBN is balanced with termination reactions, d[P°]/dt = 0, and the equilibrium between P$^\bullet$ and IR species reaches a pseudo stationary state, although different from the one generally obtained in conventional radical polymerization.

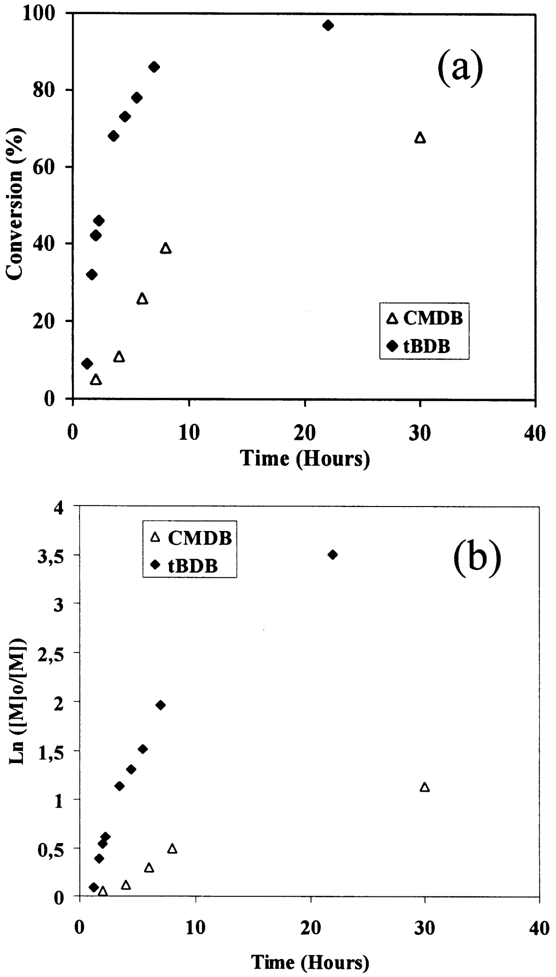


Figure 4. Monomer conversion (a) and ln([NAM]$_0$/[NAM]) (b) vs time plots for NAM polymerization at 60 °C in the presence of CMBD (experiment 1) and tBDB (experiment 2). [NAM]$_0$ = 3.75 mol L^{-1}; [NAM]$_0$/[CTA]$_0$ = 350; [CTA]$_0$/[AIBN]$_0$ = 3.3.

Finally, at high conversion, d[P°]/dt < 0. At this final stage of the polymerization, RAFT and conventional processes cannot be compared. In an unrealistic case where the amount of P$^\bullet$ would be identical, the polymerization rate would less decrease in the RAFT process than in a conventional one. In fact, because of the reduced [P$^\bullet$], the polymerization rate is very slow.

In the polymerization medium, the amount of IR species depends on the equilibrium constant,[41−44] $K_{eq} = k_{add}/k_{frag}$ (Scheme 3), and determines the magnitude of the retardation. To minimize the retardation, k_{frag} should be increased or k_{add} be decreased. k_{frag} is dependent on the R substituent[7] of the dithioester (or of the macrodithioester (Scheme 1)), and its value is mainly related to the nature of the propagating radical, i.e., of the monomer. The choice of a dithioester having a good R leaving group[7] will favor a faster fragmentation rate during equilibria 1 and 2 (Scheme 1) and therefore a decrease of the intermediate radical lifetime. Moreover, a less stabilizing Z group will additionally increase the fragmentation rate.[45] Concerning k_{add}, as it is dependent on Z substituent,[7] the choice of a less stabilizing Z group will make it to decrease. Of course, it will be necessary to make sure that the corresponding dithioester still keep a sufficient transfer activity. In conclusion, for a given monomer, the choice of the dithioester structure is preponderant to reduce the IR species lifetime and concentration and hence the retardation. Similar conclusions were given by Barner-Kowollik et al.[44] by combining experimental and simulation results concerning styrene and methyl methacrylate polymerization in the presence of cumyl phenyldithioacetate.

The ln([M]$_0$/[M]) vs time plot is expected to be linear only if the kinetics are first order with respect to the monomer and if the concentration of active species remains constant (then, the slope is equal to k_p[P$^\bullet$]). In fact, from the experimental data (Figure 4) several features appear: (i) an induction period is visible[46] (around 1 h); (ii) a straight line can be obtained at low conversion, but the whole data are curving downward; (iii) the initial slope is lower in the case of CMDB than in the case of tBDB. Consequently, it is clear that [P$^\bullet$] does not remain constant over the whole polymerization time and is significantly smaller in the case of CMDB, already at very low conversion (<5%).

Similar to the kinetic results, marked differences are also observed for the control of the molecular weight and molecular weight distribution. In both cases, as shown in Figure 5a, M_n increases linearly with conversion. However, for CMDB, the values are significantly different from the calculated ones, and the plot does not go through the origin. Moreover, the polydispersity indices (PDI) are much higher (Figure 5b). These various features can be explained by the difference of preferential fragmentation pathway between the two intermediate radicals II involved in the second equilibrium (Figure 6).

In the case of CMDB, the NAM propagating radical is more bulky and more stabilized than the carboxy-

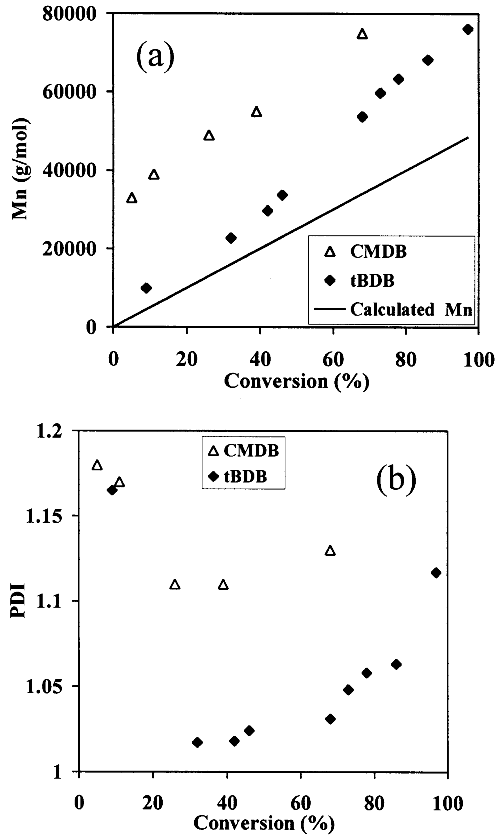
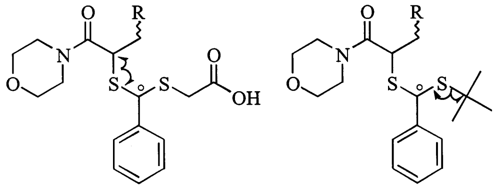


Figure 5. Number-average molecular weight M_n (a) and polydispersity index PDI (b) vs monomer conversion plots for NAM polymerization at 60 °C in the presence of CMBD (experiment **1**) and tBDB (experiment **2**). $[NAM]_0 = 3.75$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$.



From CMDB From tBDB

Figure 6. Preferential fragmentation pathway of intermediate radical II in the case of CMDB and tBDB during NAM polymerization.

methyl radical. Therefore, the fragmentation equilibrium of the intermediate radical II will be displaced such as to yield CMBD and a NAM propagating radical rather than lead to the formation of a dormant chain and a carboxymethyl radical. Then, dithioester consumption, and consequently formation of new chains, is slow. During this consumption period, the first initiated chains exhibit a higher molecular weight than the last ones, since at the beginning of the polymerization they add many monomer units whereas other chains are not initiated yet. This slow chain initiation explains the high polydispersity below 20% conversion, the experimental M_n values much higher than the calculated ones, and the nonzero intercept (30 000 g mol^{-1}).

In the case of tBDB, the NAM propagating radical is not as good a leaving group as the *tert*-butyl radical, which favors fast dithioester consumption. Consequently, the control of molecular weight distribution is more effective. Nevertheless, althougth the line goes through the origin, experimental M_n values are higher than the calculated ones, which implies that the true number of polymer chains is lower than the calculated one. This difference suggests the occurrence of termination reactions involving I$^•$ and R$^•$ radicals and/or degradation reactions involving the dithioester molecules, leading to the decrease in the number of R$^•$. Thus, these side reactions induce a decrease of AIBN efficiency factor, f.[47] By analogy, the dithioester may also be affected by an "efficiency factor", f_{DT}, reflecting that not every dithioester molecule leads to a chain.

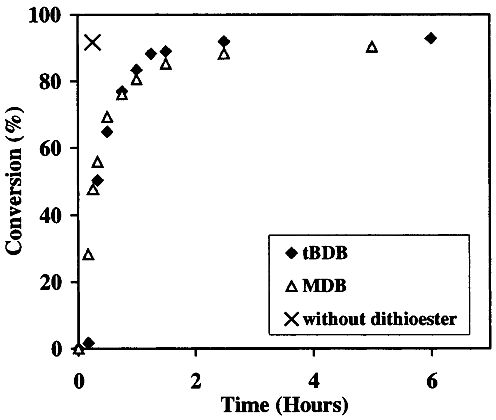


Figure 7. Monomer conversion vs time plot for the polymerization of NAM at 90 °C in the presence of tBDB (experiment 3) and MDB (experiment 4); $[NAM]_0 = 1.6$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$ and in the absence of dithioester (experiment 6); $[NAM]_0 = 1.6$ mol L^{-1}; $[AIBN]_0 = 1.4$ mol L^{-1}.

Once all the dithioester is consumed, the only intermediate radical present in the medium is radical IV, which is identical for both dithioesters. Then, M_n vs conversion curve proceeds linearly in each case. Finally, whatever the dithioester considered, it is indeed the dithioester consumption period which affects the whole polymerization (kinetics and MW control).

As shown in Figure 5b, PDI first decreases with conversion in accordance with theory[48] to reach very low values (1.02 at 30−60% conversion). Then, above 70% conversion, PDI begins to increase, since, on one hand, the probability of termination reactions increases when [M] decreases[46] and, on the other hand, the viscosity of the medium favors a heterogeneous growth of polymer chains.

The comparison between CMDB- and tBDB-mediated polymerizations highlighted the different performances obtained with two dithioesters having R substituents corresponding to primary and tertiary carbon centered radicals. In a second step, it was interesting to compare two dithioesters leading to tertiary carbon centered radicals, one being more bulky than the other (MDB vs tBDB).

Comparison between MDB and tBDB. The experiments with MDB and tBDB (entries 4 and 3, respectively, in Table 1) were performed at 1.6 mol L^{-1} and 90 °C to reduce viscosity and polymerization duration (in comparison with entries 1 and 2) conditions which, in addition, have been found to improve the control of molecular weights.[46] Also, a control experiment (6, Table 1) was carried out under the same conditions but without dithioester in order to compare the RAFT runs with conventional polymerization.

MDB- and tBDB-mediated polymerizations exhibited very similar kinetics (Figure 7). In the control experiment, 90% conversion were reached within 15 min

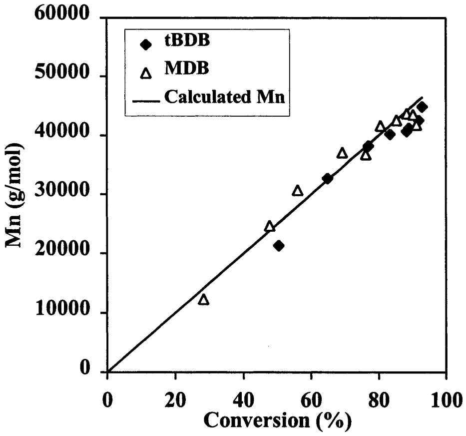


Figure 8. Number-average molecular weight M_n vs monomer conversion plot for NAM polymerization at 90 °C in the presence of tBDB (experiment 3) and MDB (experiment 4); $[NAM]_0 = 1.6$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$.

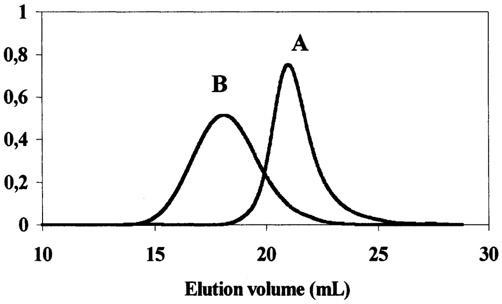


Figure 9. Comparison of the SEC chromatograms corresponding to RAFT and conventional free radical polymerization of NAM at 90 °C; $[NAM]_0 = 1.6$ mol L^{-1}; $[AIBN] = 1.4 \times 10^{-3}$ mol L^{-1}. (A) RAFT polymerization in the presence of tBDB (experiment **3**); $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$; M_n = 38 000 g mol^{-1}; PDI = 1.05; 77% conversion. (B) Conventional free radical polymerization (experiment **6**); M_n = 90 000 g mol^{-1}; PDI = 1.70; 75% conversion.

instead of 90 min for tBDB and MDB. This test illustrates that the presence of the RAFT agent induces a reduced polymerization rate in comparison with a conventional process, as explained previously.

From a general point of view, steric hindrance contributes to the $R^{\bullet}$ radical stability and plays a major role in dithioester efficiency.[7] Thus, MDB is expected to exhibit a slightly higher fragmentation rate constant and a slightly lower reinitiation efficiency (bulky menthonyl radical) than tBDB. Nevertheless, menthonyl and *tert*-butyl radicals being both tertiary carbon centered radicals are much better leaving groups than NAM propagating radical (secondary radical), which explains that the kinetics are similar. In addition, M_n values are very close to the calculated ones (Figure 8) and MWD are narrow (PDI below 1.1). In the control experiment, **6**, a M_n value of 90 000 g mol^{-1} (PDI = 1.70) was obtained in comparison with 38 000 g mol^{-1} (PDI = 1.05) in the RAFT polymerizations at the same conversion. The corresponding SEC chromatograms are given in Figure 9.

These two latter examples mainly illustrate that, to be efficient, a dithioester must have a better leaving group than the propagating radical.[7] Finally, tBDB ensures a very good MW control of poly(NAM) chains at 90 °C.[46] No significant improvement would probably be observed using a more efficient CTA. However, for other kinds of monomer, corresponding to more stabilized propagating radicals, significant differences might be observed.

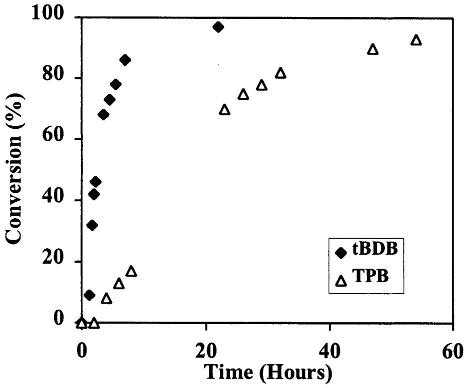


Figure 10. Monomer conversion vs time plot for the polymerization of NAM at 60 °C in the presence of tBDB (experiment 2) and TPB (experiment 5); $[NAM]_0 = 3.75$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$.

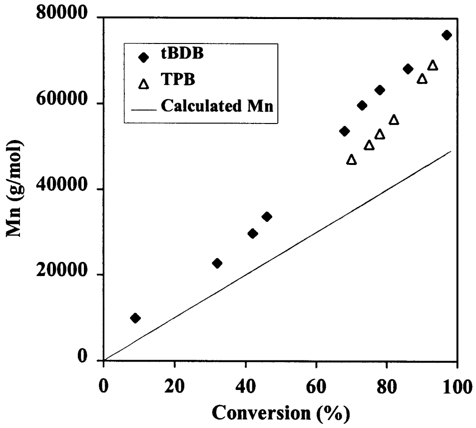


Figure 11. Number-average molecular weight M_n vs monomer conversion plot for NAM polymerization at 60 °C in the presence of tBDB (experiment 2) and TPB (experiment 5); $[NAM]_0 = 3.75$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$.

Comparison between TPB and tBDB. Finally, a bifunctional dithioester 1,3-bis(2-(thiobenzoylthio)prop-2-yl)benzene (TPB) (Figure 3) was compared to tBDB at 60 °C (entries 5 and 2, respectively, in Table 1). This comparison underscores that a distinction must be made between chain transfer agent concentration, [CTA], and dithioester function concentration, [DT].

In fact, in experiments 2 and 5, a constant [CTA] was used, corresponding to a double [DT] in the case of the bifunctional dithioester (TPB), which partly explains the decrease of R_p (Figure 10). In addition, TPB leads to a substituted cumyl radical, and it is known that cumyl dithiobenzoate induces retardation.[7,44,47] As reported in another paper,[46] more similar polymerization kinetics would have been obtained with a constant [DT]/[AIBN] ratio.

Although the TPB fragment radical is probably not as an efficient reinitiator than the tBDB one, it is a better leaving group which can explain the slightly better MW control (Figure 11) (PDI are similar in both cases). For TPB-mediated polymerization, the M_n values were not available at low conversion (10−20%) since the polymer samples were not soluble in the aqueous SEC buffer, probably due to the presence of three aromatic rings on each short chain.

Influence of Dithioester Degradation. While performing the previous experiments, several observations

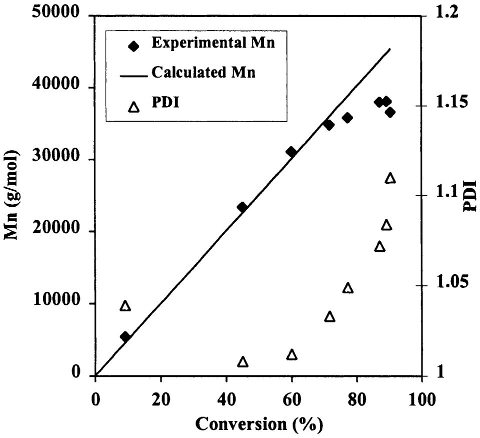


Figure 12. Number-average molecular weight M_n and polydispersity index PDI vs monomer conversion plot for NAM polymerization at 90 °C in the presence of tBDB; $[NAM]_0 = 1$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$.

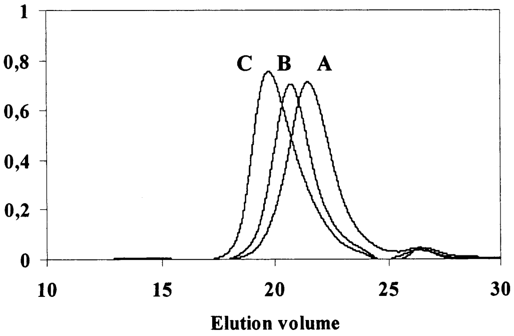


Figure 13. Evolution of SEC chromatograms with conversion for RAFT polymerization of NAM at 90 °C in the presence of tBDB; $[NAM]_0 = 1$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$. (A) 45% conversion, (B) 60% conversion, and (C) 91% conversion.

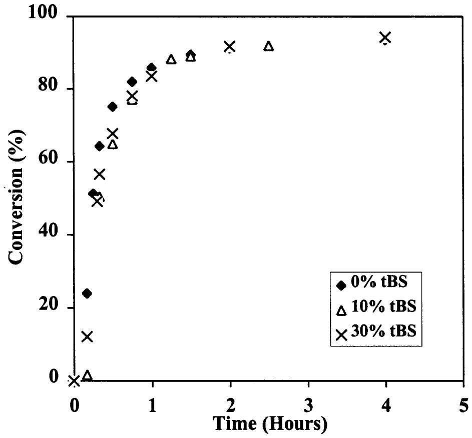


Figure 14. Monomer conversion vs time plot for the polymerization of NAM at 90 °C in the presence of tBDB (experiment 3); $[NAM]_0 = 1.6$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$. In experiments 7 and 8, respectively 10% and 30% of tBDB were substituted by *tert*-butyl sulfide (tBS).

suggested the occurrence of some dithioester degradation during polymerization. In fact, a slow discoloration of the polymerization medium (decrease of the orange color intensity) was usually observed, sometimes very significant above 80% conversion. In this latter case, the M_n vs conversion curve was no longer linear, with M_n values leveling off or even decreasing. At the same time, PDI was significantly increasing. An example of the M_n vs conversion plot for a polymerization with significant degradation is given in Figure 12, with the corresponding SEC chromatograms (Figure 13) showing a broadening of the low MW side of the peaks.

As thiocarbonylthio moieties are highly colored (purple to pink in the case of dithiobenzoates), this discoloration was directly related to a progressive disappearance of the chromophoric dithioester chain ends. Then, we proposed the hypothesis of dithioester degradation based on a radical process.

A test experiment was carried out with a dioxane solution of CMDB at 60 °C under nitrogen in the presence of an excess of AIBN (3 equiv in comparison with CMDB). The red color of the solution was discharged in less than 8 h. On the contrary, when the same experiment was performed without AIBN, the red color was maintained, and the CMBD was not degraded at all. Thus, although the conditions used in this test favor termination onto intermediate radicals, it is an indication for a radical degradation mechanism.

In fact, the fragmentation of the intermediate radical is in competition with several side reactions, i.e., termination and/or propagation reactions.[49] Obviously, the bulky structure of this intermediate radical should favor fragmentation. However, the occurrence of termination reactions by combination with a propagating radical has already been evidenced in a particular case (after induced fragmentation of a dormant chain by UV irradiation)[50] and is also expected during polymerization. Such a reaction would lead to the loss of one dithioester molecule and two active species (Scheme 1), both phenomena having an opposite effect on the polymerization rate. Finally, a resulting decrease of the polymerization rate is expected as well as a loss of MW control. Moreover, these termination reactions would lead to an additional increase of the retardation.[41,51] For instance, such termination reactions would be more numerous for CMDB- than for tBDB-mediated polymerization (intermediate radical II lifetime), which would be an additional explanation for the enhanced retardation observed in the former case (Figure 4).

In addition, the probability for the intermediate radical to undergo propagation reactions should not be discarded (although quite unlikely), since the monomer is present at high concentration and possesses a higher mobility than the propagating radicals.[52] In any case, these two kinds of side reactions induce the loss of dithioesters (i.e., can be considered as dithioester degradation reactions) and the formation of sulfides, known as irreversible transfer agents.[53]

Note that such reactions could in principle occur on each kind of intermediate radicals present in the polymerization medium (I, II, III, and IV). However, it is expected that, among the resulting sulfides, the smallest ones mainly would act as irreversible transfer agents during polymerization.

To investigate the influence of a sulfide compound on the RAFT process, two additional experiments were carried out in the same conditions as entry 3, but with substituting 10% and 30% of tBDB by a model sulfide, *tert*-butyl sulfide (tBS) (entries 7 and 8, respectively, in Table 1). Very similar kinetic results were obtained (Figure 14), although the polymerization should be faster with a lower dithioester concentration.

Concerning the evolution of M_n with conversion (Figure 15), the experimental slope was, as expected, higher than the calculated one (corresponding to 100% tBDB), this phenomenon being more significant when

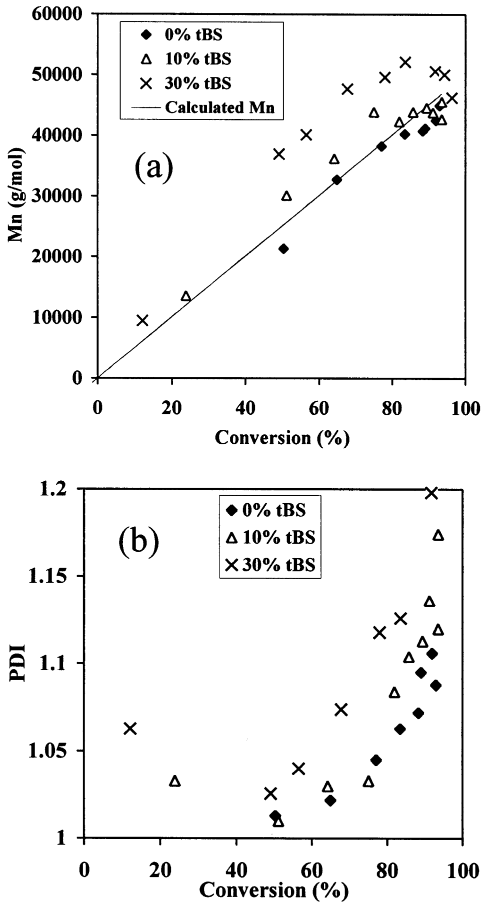


Figure 15. Number-average molecular weight M_n (a) and polydispersity index PDI (b) vs monomer conversion plots for the polymerization of NAM at 90 °C, in the presence of tBDB (experiment 3); $[NAM]_0 = 1.6$ mol L^{-1}; $[NAM]_0/[CTA]_0 = 350$; $[CTA]_0/[AIBN]_0 = 3.3$. In experiments 7 and 8, respectively 10% and 30% of tBDB were substituted by *tert*-butyl sulfide (tBS).

the proportion of tBS was increased to 30% (entry 8). However, below 70% conversion, the presence of sulfide had a limited influence on the linear evolution of M_n with conversion. On the contrary, at higher conversion, a decrease of M_n values was observed, all the more important since the proportion of sulfide increased. Moreover, it was accompanied by an increase of the polydispersity (Figure 15).

Therefore, the effects of the presence of a sulfide were mainly visible at high conversion. In fact, the probability of irreversible nondegrading transfer reactions is low as long as [M] remains high, because of the low concentration of the transferring species as well as their low transfer constants in comparison with the dithioester.[54,55] Favored reactions are addition−fragmentation and propagation. Then, when [M] decreases, this probability increases although the addition−fragmentation reactions remain preponderant. Consequently, creation of new chains is no longer negligible which influences M_n values.

Finally, these RAFT polymerization experiments in the presence of a model sulfide show similar consequences on M_n and PDI values than that observed in the case of a significant discoloration of the polymerization medium. Then, it is suspected that some sulfide species appear in the medium during polymerization (via termination reactions onto intermediate radicals) and play the role of irreversible nondegrading transfer agents at high conversion, this phenomenon being kinetically controlled.

Conclusions

This article reports the first study of controlled radical polymerization of *N*-acryloylmorpholine, a water-soluble bisubstituted acrylamide derivative. These polymerizations were achieved using the RAFT technique with several dithiobenzoates as transfer agents, namely carboxymethyl dithiobenzoate (CMDB), *tert*-butyl dithiobenzoate (tBDB), menthonyl dithiobenzoate (MDB), and thiobenzoylthiopropylbenzene (TPB). The comparison of the polymerization experiments in terms of kinetics, molecular weights, and molecular weight distributions of the obtained polymers shows that these four dithiobenzoates lead to a linear increase of MW with conversion, although in the case of the less efficient CTA, CMDB, the line lies far from the origin at zero conversion. Below 80% conversion, polydispersity indices range between 1.02 and 1.10 for tBDB, MDB, and TPB and between 1.10 and 1.20 for CMDB.

Among these four dithiobenzoates, tBDB appears to be the best suited for NAM polymerization, in terms of both synthesis versatility and MW control. Polydispersity indices were very low, and when using a temperature of 90 °C, an excellent agreement between calculated and experimental MW was obtained. The influence of other experimental parameters has been further investigated and will be presented in a following paper.[46] Finally, water-soluble homopolymers with low polydispersity indices (<1.1) were obtained over a wide range of molecular weights, i.e., between 5000 and 80 000 g mol^{-1}, these values being exactly representative of the actual MW of the polymer chains since determined with a light-scattering detector.

In some cases, side reactions were evidenced during polymerization with a surprising decrease of M_n and a simultaneous increase of PDI values above 70% conversion. These side reactions were related to some degradation of the dithioester moieties since an unusual discoloration of the reaction mixture was observed. A test reaction, with substituting 10 and 30% of dithiobenzoate by some *tert*-butyl sulfide, showed identical consequences on MWD. Such sulfide is known to behave as nondegradative irreversible transfer agent. Consequently, it is suggested that during RAFT polymerization, degradation of the dithioester functions might occur via termination reactions onto the intermediate radicals, such reactions leading to the presence of sulfide species in the polymerization medium, acting then as nondegradative irreversible transfer agents. Moreover, this termination phenomenon would lead to an additional increase of the redardation observed during the RAFT process in comparison with a conventional free radical polymerization.

Acknowledgment. The authors thank F. Asgarzadeh for TPB dithioester synthesis and J. M. Lucas (LMPB, Villeurbanne, France) for the use of the interferometer equipment.

References and Notes

(1) Li, D.; Brittain, W. J. *Macromolecules* **1998**, *31*, 3852−3855.
(2) Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904−3920.
(3) Teodorescu, M.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2000**, *21*, 190−194.

(4) Senoo, M.; Kotani, Y.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1999**, *32*, 8005−8009.

(5) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559−5562.

(6) Le, T. P.; Moad, G.; Rizzardo, E.; Thang, S. H. PCT Int. Appl. WO 9801478 A1 980115; *Chem. Abstr.* **1998**, *128*, 115390.

(7) Moad, G.; Chiefari, J.; Chong, B. Y. K.; Krstina, J.; Mayadunne, R. T. A.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polym. Int.* **2000**, *49*, 993−1001.

(8) Ganachaud, F.; Monteiro, M. J.; Gilbert, R. G.; Dourges, M.-A.; Thang, S. H.; Rizzardo, E. *Macromolecules* **2000**, *33*, 6738−6745.

(9) Sumerlin, B. S.; Donovan, M. S.; Mitsukami, Y.; Lowe, A. B.; McCormick, C. L. *Macromolecules* **2001**, *34*, 6561−6564.

(10) Parrod, J.; Jelles, J. *C. R. Hebd. Seances Acad. Sci.* **1956**, *243*, 1040.

(11) Ham, G. E. U.S. 2,683,703, 1954, Monsanto Chemical Co.; *Chem. Abstr.* **1954**, *48*, 1184.

(12) Elles, J. *Chim. Med.* **1959**, *4*, 26.

(13) Thomas, P. R.; Attfield, D. J. Brit. 914,780, 1963; British Nylon Spinners Ltd. *Chem. Abstr.* **1964**, *58*, P5810c.

(14) Lim, D.; Kopeck, J.; Bazhilova, H.; Vacik, J. Ger. Offen. 2,151,909,27, 1972; Ceskoslovenka Adademie Ved, *Chem. Abstr.* **1972**, *77*, 49139f.

(15) Narang Chander, K.; Brunfeldt, K.; Kjeld, E. *Tetrahedron Lett.* **1977**, *18* (21), 1819−1822.

(16) Epton, R.; Goddard, P.; Ivin, K. J. *Polymer* **1980**, *21*, 1367.

(17) Apte, P.; Fries, R.; Neel, J. *Membr. Permeabilite Sel. Colloq.* **1967**, *11*, 9.

(18) Ishii, K.; Honda, Z. Ger. Offen 2,414,795,27, 1973; Daicel Ltd. *Chem. Abstr* **1973**, *82*, 58534.

(19) Onishi, M.; Fujii, T. PCT Int. Appl. WO 8900,878, 1989; Terumo Corp. *Chem. Abstr.* **1990**, *110*, 194367h.

(20) Epton, R.; Holding, S. R.; McLaren, J. V. *J. Chromatogr.* **1975**, *110*, 327−334.

(21) Gelfi, C.; de Besi, P.; Alloni, A.; Righetti, P. G. *J. Chromatogr.* **1992**, *608*, 333−341.

(22) Torchilin, V. P.; Trubetskoy, V. S.; Whiteman, K. R.; Caliceti, P.; Ferruti, P.; Veronese, F. M. *J. Pharm. Sci.* **1995**, *84*, 1049−1053.

(23) Veronese, F. M.; Schiavon, O.; Calceti, P.; Sartore, L.; Ranucci, E.; Ferruti, P. U.S. 5,629,384, 1994.

(24) Ranucci, E.; Spagnoli, G.; Ferruti, P. *Macromol. Chem. Phys.* **1994**, 195, 3469−3479.

(25) Ranucci, E.; Bignotti, F.; Ferruti, P. *Macromol. Chem. Phys.* **1995**, 196, 2927−2939.

(26) D'Agosto, F.; Charreyre, M.-T.; Véron, L.; Llauro M.-F.; Pichot, C. *Macromol. Chem. Phys.* **2001**, *202*, 1689−1699.

(27) D'Agosto, F.; Charreyre, M.-T.; Mélis, F.; Pichot, C.; Mandrand, B. *J. Appl. Polym. Sci.*, in press.

(28) Asgarzadeh, F.; Beyou, E.; Chaumont, P. *Polym. Prepr. (Am. Chem. Soc., Polym. Div.)* **1999**, *40*, 899−900.

(29) Kulkarni, M. G.; Mashellkar, R. A.; Doraiswamy, L. K. *J. Polym. Lett. Ed.* **1979**, *17*, 713.

(30) Buback, M.; Huckestein, B.; Kuchta, F.-D.; Russell, G. T.; Schmid, E. *Macromol. Chem. Phys.* **1994**, *195*, 2117−2140.

(31) Moad, G.; Solomon, D. H. *The Chemistry of Free Radical Polymerization*; Pergamon Press: New York, 1995; p 51.

(32) Leon, N. H.; Asquith, R. S. *Tetrahedron* **1970**, *26*, 1719−1725.

(33) Sudalai, A.; Kanagasabapathy, S.; Benicewicz, B. C. *Org. Lett.* **2000**, *2*, 3213−3216.

(34) Meijer, J.; Vermeer, P.; Brandsma, L. *Recueil* **1973**, *92*, 601.

(35) Thang, S. H.; Chong, Y. K.; Mayadunne, T. A.; Moad, G.; Rizzardo, E. *Tetrahedron Lett.* **1999**, *40*, 2435−2438.

(36) Drosten, G.; Mischke, P.; Voss, J. *Chem. Ber.* **1987**, *120*, 1757−1761.

(37) Butté, A.; Storti, G.; Morbidelli, M. *Macromolecules* **2001**, *34*, 5885−5896.

(38) Charreyre, M.-T.; D'Agosto, F.; Favier, A.; Pichot, C.; Mandrand, B. PCT Int. Appl. WO 01/92361 A1.

(39) Mitsukami, Y.; Donovan, M. S.; Lowe, A. B.; McCormick, C. L. *Macromolecules* **2001**, *34*, 2248−2256.

(40) In particular, because termination reactions occur, the RAFT technique cannot be considered as a living polymerization according to Szwarc's criteria (*Nature (London)* **1956**, *178*, 1168) or IUPAC recommendations (*Pure Appl. Chem.* **1996**, *68*, 2287). However, recent discussions tend to introduce moderation to this definition (Darling, T. R.; Davis, T. P.; Fryd, M.; Gridnev, A. A.; Haddleton, D. M.; Ittel, S. D.; Matheson, Jr., R. R.; Moad, G.; Rizzardo, E. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 1706).

(41) Monteiro, M. J.; de Brouwer, H. *Macromolecules* **2001**, *34*, 349−352.

(42) Barner-Kowollik, C.; Quinn, J. F.; Morsley, D. R.; Davis, T. P *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 1353−1365.

(43) Goto, A.; Sato, K.; Tsujii, Y.; Fukuda, T.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **2001**, *34*, 402−408.

(44) Barner-Kowollik, C.; Quinn, J. F.; Uyen Nguyen, T. L.; Heuts, J. P. A.; Davis, T. P. *Macromolecules* **2001**, *34*, 7849−7857.

(45) Quinn, J. F.; Rizzardo, E.; Davis, T. P. *Chem. Commun.* **2001**, 1044−1045.

(46) Favier, A.; Charreyre, M.-T.; Pichot, C., submitted to *Macromolecules*.

(47) Moad, G.; Chiefari, J.; Mayadunne, R. T. A.; Moad, C. L.; Postma, A.; Rizzardo, E.; Thang, S. H. *Macromol. Symp.* **2002**, *182*, 65−80.

(48) Matyjaszewski, K. *Controlled/Living Radical Polymerization*; ACS Symposium Series 768; American Chemical Society: Washington, DC, 2000; p 7.

(49) Colombani, D. *Prog. Polym. Sci.* **1999**, *24*, 425−480.

(50) de Brouwer, H.; Schellekens, M. A. J.; Klumperman, B.; Monteiro, M. J.; German, A. L. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 3596−3603.

(51) Kwak, Y.; Goto, A.; Tsujii, Y.; Murata, Y.; Komatsu, K.; Fukuda, T. *Macromolecules* **2002**, *35*, 3026−3029.

(52) The more efficient the dithioester, the faster the fragmentation reaction and the less probable the side reactions on intermediate radicals II and III. Moreover, considering the macrodithioesters, the more stable the propagating radical, the faster the fragmentation reaction and the less probable the side reactions on intermediate radicals IV.

(53) Bamford, C. H.; Tipper, C. F. H. *Free Radical Polymerization*; Comprehensive Chemical Kinetics; Elsevier Scientific Publishing Co.: Amsterdam, 1976; p 127.

(54) Bamford, C. H.; Tipper, C. F. H. *Free Radical Polymerization*; Comprehensive Chemical Kinetics; Elsevier Scientific Publishing Co.: Amsterdam, 1976; p 169.

(55) Moad, G.; Solomon, D. H. *The Chemistry of Free Radical Polymerization*; Pergamon Press: New York, 1995; p 243.

MA020550C