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# Synthesis and characterization of positively charged amphiphilic water soluble polymers based on poly(*N*-isopropylacrylamide)

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**Abstract**

The synthesis and characterization of new water-soluble shear-responsive polymers based on *N*-isopropylacrylamide (NIPAM) is reported. These copolymers are synthesized using a two-steps procedure: (a) synthesis of the precursors by radical copolymerization in aqueous solvent between NIPAM and an amine-containing monomer *N*,*N*-[(dimethylamino)propyl]methacrylamide (MADAP) and (b) modification of the macromolecular backbone by reaction between MADAP units and alkylbromide. From kinetic studies performed during copolymerization, the reactivity ratios of the two monomers were determined in media of different ionic strength ($r_{\mathrm{NIPAM}} = 0.6$ and $r_{\mathrm{MADAP}} = 0.6 - 1.3$). Under these conditions, it was shown that the composition and the distribution of NIPAM and MADAP units into the macromolecular backbone remain approximately constant until 80% of conversion. For all the copolymers, in the composition range 0–25 mol% of MADAP units, an effective control of the molar mass is reported with the concentration of the reducing agent involved in the redox initiator. Finally, a quantitative alkylation procedure of MADAP units is described in chloroform using an inactive base and a large excess of alkylbromide.

*Keywords*: *N*-isopropylacrylamide; Hydrophobically modified polymers; Copolymerization kinetics

## 1. Introduction

One of the most popular polymers, within those exhibiting Lower Critical Solution Temperature (LCST) behavior in aqueous solution, is the poly(*N*-isopropylacrylamide) (PNIPAM) [1]. This polymer, soluble in water at low temperature, phase separates from the solution at temperatures higher than ~33°C. Since 1968 when the thermosensitivity of PNIPAM was first evidenced [2] the studies based on its phase transition have exponentially increased and a large set of copolymers involving NIPAM as the main comonomer has been developed. When designing new NIPAM derivatives, the main goal is generally to control effectively the temperature of the phase transition by adding some hydrophilic or hydrophobic comonomers or to develop new stimuli responsive properties around the critical temperature (pH, mechanical, light,…) [3–5].

The introduction of hydrophobic comonomers into the PNIPAM chain enhances the amphiphilic behavior of the polymer in aqueous solution but it lowers at the same time its water-solubility. As a consequence, the hydrophobic modification of PNIPAM is most often limited by these antogonistic properties. During the last decade, Winnik [6–10], Shild [11] as well as Soutar and coworkers [12], have reported the synthesis of PNIPAM copolymers hydrophobically modified with pyrene or other fluorescent labels. Their initial goal was to probe at a molecular level the phase transition of the polymer. Depending on the nature of the comonomer and according to the required properties, the incorporation of these hydrophobic moieties into the PNIPAM chains were kept at a relatively low level (less than 5 mol% and, usually, less than 1%). Similarly the influence of small amounts of alkyl chains on the LCST behavior of PNIPAM was also reported by various authors [9,13–16], as well as trace amounts (less than 0.7 mol%) of fluorocarbons [17,18].

Recently we have designed a new family of amphiphilic polymers on the basis of a NIPAM backbone containing a relatively high amount of hydrophobic groups (5 mol% or more). In order to avoid a rapid decrease of the solubility with the hydrophobic substitution, an equivalent amount of ionic groups was introduced into the macromolecular chain.

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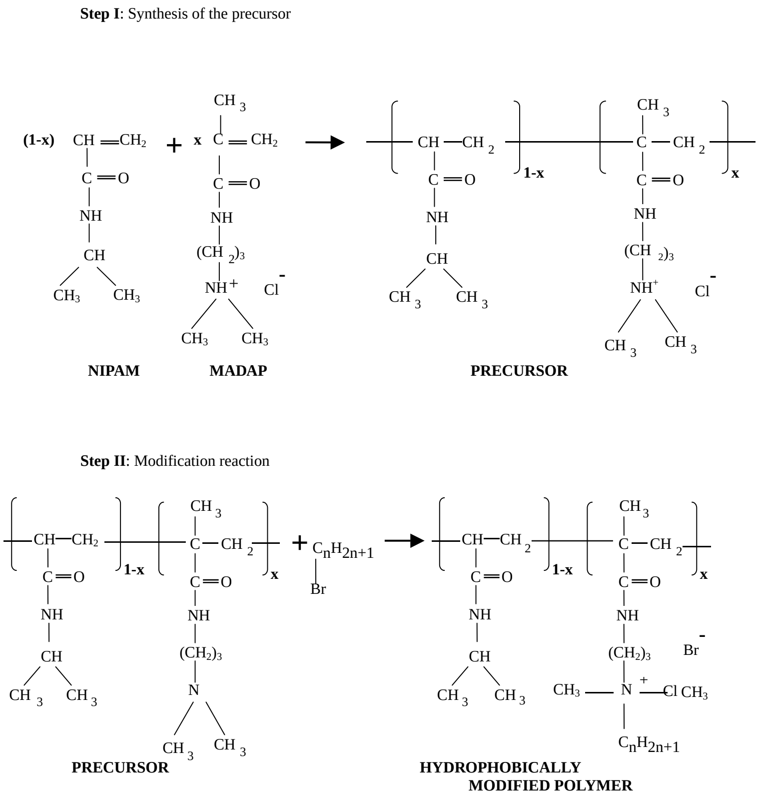

Scheme 1.

The phase behavior and mainly the rheological properties of these new polymers were shown to be particularly innovating as they exhibit a dramatic and reversible sol/gel transition upon shearing [19]. The synthesis procedure of these derivatives involves two steps (Scheme 1). The first one is the synthesis of the polymer backbone by radical copolymerization. A large amount of NIPAM is copolymerized with a smaller quantity of a comonomer (5–25% in moles): the *N*,*N*-[(dimethylamino)propyl]methacrylamide (MADAP). In the second step alkyl groups are anchored into the polymer chain by an addition reaction between MADAP units (tertiary amine) and alkylbromide. In this way, hydrophobic groups and cationic charges are introduced simultaneously into the polymer chain and this allows the maintenance of the water-solubility of the copolymer at low temperature. As the physical properties of these copolymers in aqueous solution rely on a subtle balance between thermosensitive, hydrophobic and ionic groups, the control of the primary structure is a prerequisite for the understanding of their original behavior.

In this paper, we will describe the synthesis and characterization of these copolymers during the different reaction steps. We will pay special attention to the characterization of the macromolecular precursors (control of monomers distribution and molar mass) and to the modification extent as these structural parameters strongly influence the phase behavior and the resulting shear-responsive feature of the copolymers.

## 2. Experimental

### 2.1. Materials

Monomers (NIPAM and MADAP) and alkylbromide (octyl-, dodecyl- and octadecylbromide) were obtained from Aldrich. The solvents and the salts used were of analytical grade. Water was purified with a Millipore system, combining inverse osmosis membrane (Milli-R) and ion exchange resins (Milli-Q).

### 2.2. Precursor synthesis

The synthesis of the copolymers was carried out in aqueous solution at 29°C. After neutralization of the reaction medium with HCl (final pH = 5–6), the solution was deoxygenated with argon for 2 h. Eventually, an appropriate amount of $LiNO_3$ was also added, to control the ionic strength. The syntheses were initiated with the redox couple ammonium peroxidisulfate/sodium metabisulfite, $(NH_4)_2S_2O_8/Na_2S_2O_5$, and were allowed to proceed for 24 h under an argon atmosphere. At the end of the reaction an excess of NaOH was added until a final pH of 12 was reached and the solution was dialyzed for several days against pure water (the membrane cut-off was 10,000 Dalton). The copolymer was finally recovered by freeze drying.

### *2.3. Copolymerization kinetics*

Aliquots were sampled during the synthesis from the reaction mixture and a small amount of hydroquinone was immediately added to stop the reaction. A small part of these samples was analyzed by chromatography, after an appropriate dilution with a $LiNO_3$ 0.5 M solution. The analyses were performed with a Waters chromatographic system equipped with four Shodex OH-pak columns and a differential refractometer for the detection. The system was equilibrated at 23°C and the eluent used was an aqueous solution of $LiNO_3$ 0.5 M. The rest of the aliquots were purified and the copolymer was recovered, according to the procedure described above. The composition of the copolymer recovered under basic form was determined by titration with HCl and by $^{13}C$ NMR.

### *2.4. Intrinsic viscosity*

Studies were performed with the copolymer precursors at 20°C, using an automated capillary viscometer (TI1 from SEMATech). All the measurements were carried out at high ionic strength using a 0.5 M $LiNO_3$ solution as solvent.

### *2.5. Modification reaction*

A 5% solution of the precursor, dissolved in the appropriate solvent (methanol or chloroform), was heated under reflux conditions. The required quantity of alkylbromide was then added and the reaction was left to proceed in these conditions. The kinetics of the reaction was followed by sampling aliquots from the reaction medium. The samples were cooled immediately and precipitated in diethylether. The products were finally dried under vacuum for 24 h at room temperature.

### *2.6. Characterization of the modified copolymers*

The modified copolymers were characterized mainly by combining different titration techniques, using an automated titration system from Metrohm suitable for the detection of multiple equivalent points: (a) titration of the $Br^-$ content with a solution of $AgNO_3$, after slight acidification of the solution with $HNO_3$; (b) titration of the basic MADAP units by HCl; and (c) titration of the total basic content by HCl, after addition of an excess of NaOH. For some of the samples, the $Br^-$ content was verified by elemental analysis and the alkyl content by $^1H$ NMR.

## 3. Results and discussion

### *3.1. Copolymerization kinetics*

The kinetics of copolymerization was followed by chromatography taking advantage of a dual fractionation mechanism: (1) size exclusion of the polymer chains (entropically driven process), and (2) specific interactions between monomer molecules (mainly NIPAM) and the chromatographic system (stationary phase/$LiNO_3$ 0.5 M/$T = 23$°C). In Fig. 1, we present typical chromatograms (A, B and C) obtained during the synthesis of a copolymer. In this example, the feed molar MADAP composition is $(f_{MADAP})_0 = 0.25$. The chromatograms A, B and C correspond to the same reaction medium sampled at three different times: 0, 15 and 120 min after the addition of the initiator, respectively. At $t = 0$ (chromatogram A) we clearly distinguish two narrow and well-separated peaks at $V_e = 35.5$ and 44 $cm^3$. They correspond to MADAP and NIPAM monomers, respectively. As the reaction proceeds (chromatograms B and C) a third broader peak corresponding to the copolymer appears around $V_e = 26\ cm^3$. The area of this peak increases with time, while those of the monomers decrease. After verification that all the different species (NIPAM, MADAP, copolymer) were fully eluted in these conditions, calibration curves were built by plotting the area under the chromatogram versus the injected mass of the corresponding species. This information allows a quantitative description of the copolymerization process, as reported earlier with other systems [20]. In the present case, we determine two relevant parameters: the conversion ($c$) and

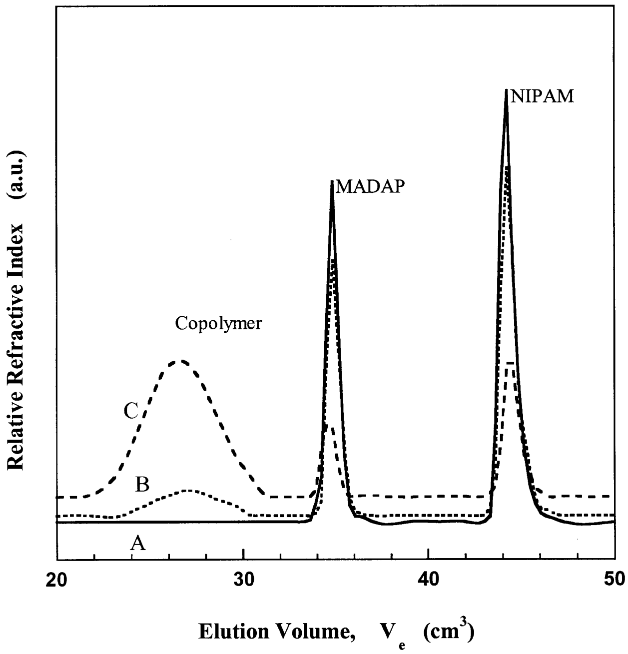

Fig. 1. Typical chromatograms of the reaction mixture during copolymerization of NIPAM with MADAP, for a feed molar composition of 25 mol% MADAP (A: $t = 0$, B: $t = 15$ min, C: $t = 120$ min).

the instantaneous monomer composition of the reaction medium as the reaction proceeds ($f_{\mathrm{MADAP}}$). The copolymer composition ($F_{\mathrm{MADAP}}$) of each aliquot was determined, after purification, by HCl titration of the basic MADAP units. For some of the copolymers, $F_{\mathrm{MADAP}}$ was also verified by $^{13}$C NMR. Note that $F_{\mathrm{MADAP}}$ is not the instantaneous copolymer composition at the reaction time $t$, but the cumulated composition of the copolymer synthesized during this period.

The dependence of the copolymer composition $[(F_{\mathrm{MADAP}})_{\mathrm{low\ conversion}}]$, measured at low conversion (below 10%), is plotted in Fig. 2 against the initial feed molar composition $(f_{\mathrm{MADAP}})_0$. The two experimental curves are related to different sets of experiments carried out either in pure water or in aqueous solution ($LiNO_3$ 1 M). For the syntheses performed in pure water, an azeotropic feed composition is observed around $(f_{\mathrm{MADAP}})_0 = 0.4$–$0.5$. On the contrary, the MADAP fraction incorporated into the copolymer chain is always higher than the MADAP content in the initial feed when the copolymerization is carried out at high ionic strength.

From these results, the reactivity ratios of the two monomers were determined using the Kelen–Tudös [21] method. We obtain (a) $r_{\mathrm{NIPAM}} = 0.62$ and $r_{\mathrm{MADAP}} = 0.59$ in pure water and (b) $r_{\mathrm{NIPAM}} = 0.59$ and $r_{\mathrm{MADAP}} = 1.31$ in 1 M $LiNO_3$ solution. One can see that the reactivity ratio of NIPAM is hardly influenced by the ionic strength, as it can be expected for a non-ionic monomer. The experimental data ($r_{\mathrm{NIPAM}} = 0.6$–$0.7$) are in agreement with the value reported by Chiklis et al. [22] ($r_{\mathrm{NIPAM}} = 0.50$), for the copolymerization of NIPAM with acrylamide (AM) in water. They can also be compared with the reactivity ratios reported for *N*,*N*-dimethylacrylamide, although these copolymerizations were performed in organic solvents [23,24].

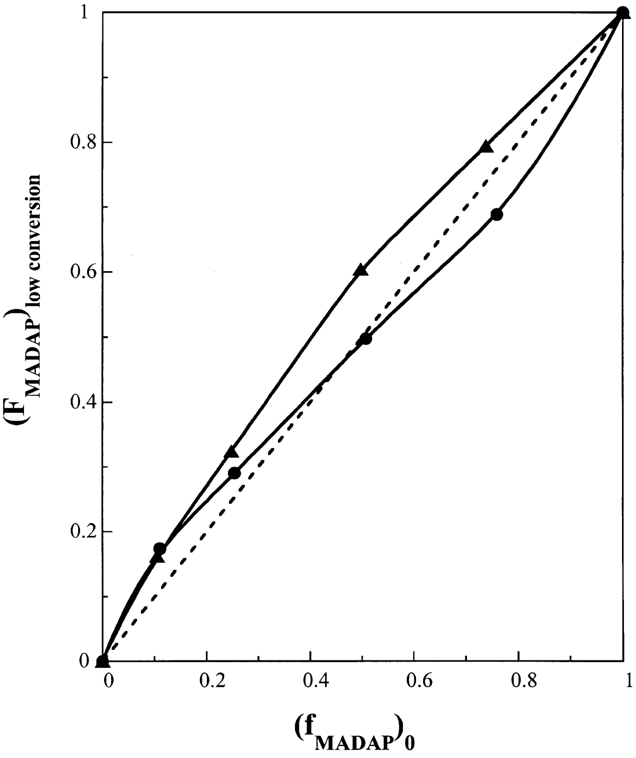

Fig. 2. The copolymer composition, $F_{\mathrm{MADAP}}$, at the beginning of the reaction as a function of feed composition $(f_{\mathrm{MADAP}})_0$ (●: pure water, ▲: 1 M $LiNO_3$ solution). The dashed line corresponds to a random copolymer.

On the other hand, the reactivity ratio of MADAP is significantly influenced by the ionic strength. At high ionic strength, where the electrostatic repulsions between the positively charged MADAP units are sufficiently screened, $r_{\mathrm{MADAP}}$ is higher than unity ($r_{\mathrm{MADAP}} \sim 1.3$). In these conditions the higher reactivity of MADAP can be attributed to the α-methyl group, following the general rule that methacrylamide or methacrylate derivatives are usually more reactive than acrylamide or acrylate monomers [25,26]. Reactivity ratios of the same order ($r_{\mathrm{MADAP}} = 1$–$2$) were also reported in similar conditions by Tanaka [25] and Baade et al. [27] for copolymerization of MADAP with AM. When the copolymerizations are performed in pure water the reactivity ratio of MADAP decreases substantially. In these conditions MADAP units prefer obviously to react with a NIPAM-terminated radical rather than with a similarly charged MADAP radical. The same tendency was also reported by Cabaness [28] for copolymerizations performed at different pH between acrylamide and acrylic acid.

As both reactivity ratios differ from unity, either in pure water or in $LiNO_3$ 1 M, a drift of the copolymer composition is expected with conversion. This is shown in Fig. 3 where the cumulated copolymer composition ($F_{\mathrm{MADAP}}$ or $F_{\mathrm{NIPAM}}$) and the instantaneous monomer composition of the reaction medium ($f_{\mathrm{MADAP}}$ or $f_{\mathrm{NIPAM}}$) are plotted as a function of the reaction conversion ($c$). These results concern two different sets of copolymerization obtained from the same initial feed monomer composition $[(f_{\mathrm{MADAP}})_0 = 0.25]$; one was performed in pure water (Fig. 3a), the other in $LiNO_3$ 1 M (Fig. 3b). From a general point of view, the experimental results observed for $f_{\mathrm{MADAP}}$ and $f_{\mathrm{NIPAM}}$ are in a rather good agreement with the theoretical ones (full lines) calculated using an alternative form of the integrated copolymerization equation [29]. The instantaneous copolymer composition (dashed line in Fig. 3), $F_1^{\mathrm{inst}}$, was calculated from the following equation:

$$F_1^{\mathrm{inst}} = \frac{r_1 f_1^2 + f_1 f_2}{r_1 f_1^2 + 2 f_1 f_2 + r_2 f_2^2}. \qquad (1)$$

A continuous drift is observed as the reaction proceeds for both the instantaneous composition ($F_{\mathrm{MADAP}}^{\mathrm{inst}}$) and the cumulated copolymer composition ($F_{\mathrm{MADAP}}$). At high ionic strength (Fig. 3b) $F_{\mathrm{MADAP}}^{\mathrm{inst}}$ is higher than the feed monomer composition $(f_{\mathrm{MADAP}})_0$ at the beginning of the reaction. As the reaction proceeds, MADAP is consumed faster than NIPAM and $f_{\mathrm{MADAP}}$ decreases, i.e. the reaction mixture

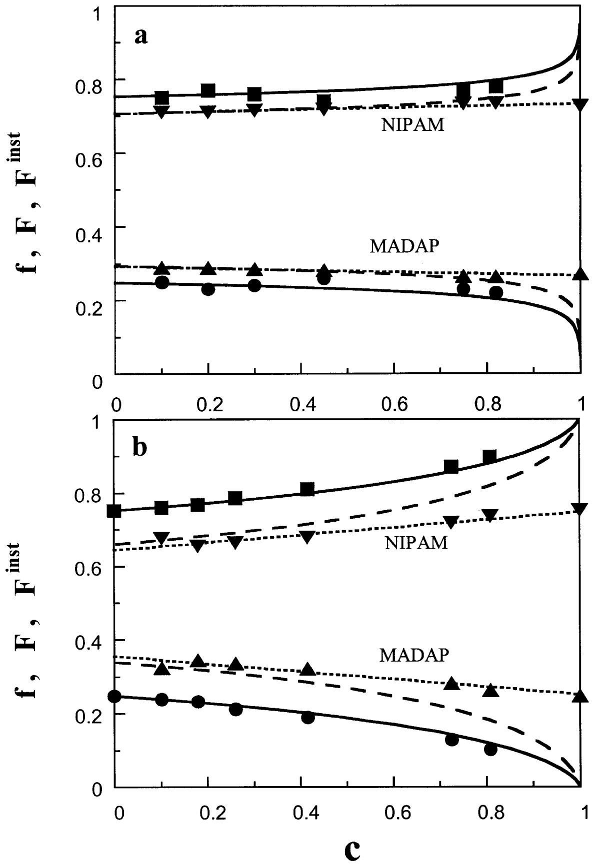

Fig. 3. Variation of the monomer composition in the reaction medium, $f$ (●: $f_{\mathrm{MADAP}}$, ■: $f_{\mathrm{NIPAM}}$), the cumulated copolymer composition, $F$ (▲: $F_{\mathrm{MADAP}}$, ▼: $F_{\mathrm{NIPAM}}$), and the instantaneous copolymer composition, $F^{\mathrm{inst}}$ of each monomer (dashed lines), as a function of the reaction conversion. Dotted straight lines correspond to the linear regressions of the corresponding experimental points. The full lines, corresponding to $f_{\mathrm{MADAP}}$ and $f_{\mathrm{NIPAM}}$ are calculated by using the integrated form of the copolymerization equation [28]. The dashed lines, corresponding to the instantaneous composition of the copolymer are calculated with the aid of Eq. (1). Experimental conditions: (a) $(f_{\mathrm{MADAP}})_0 = 0.25$, pure water and (b) $(f_{\mathrm{MADAP}})_0 = 0.25$, LiNO$_3$ 1 M).

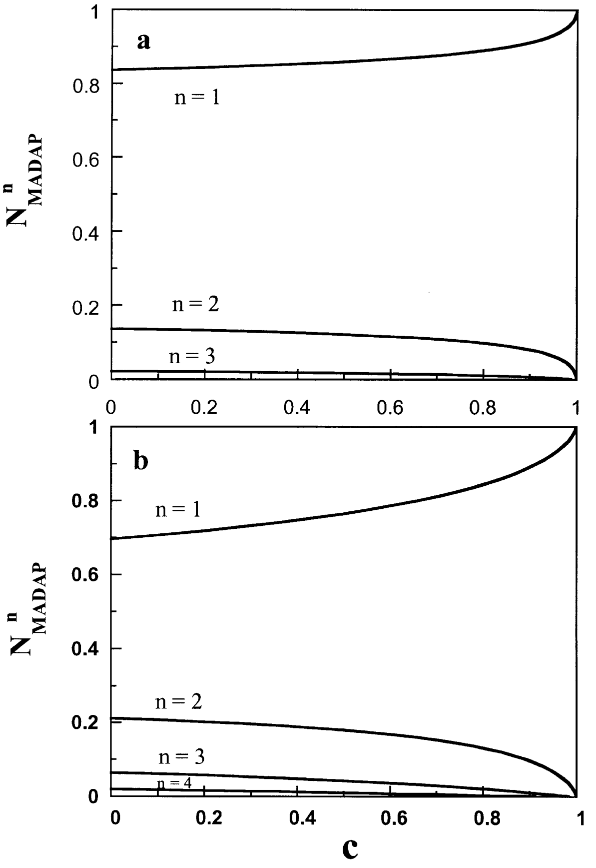

Fig. 4. Probability $N^{n}_{\mathrm{MADAP}}$ to find isolated MADAP units ($n = 1$) or longer MADAP sequences ($n = 2$, 3 or 4) with the reaction conversion ($c$) in the NIPAM–MADAP copolymers [$(f_{\mathrm{MADAP}})_0 = 0.25$] prepared: (a) in pure water and (b) in 1 M LiNO$_3$ solution.

becomes richer in NIPAM. As a result the $F^{\mathrm{inst}}_{\mathrm{MADAP}}$ also decreases. Near the end of the reaction (at $c > 0.8$), the mixture becomes very rich in NIPAM monomer and $F^{\mathrm{inst}}_{\mathrm{MADAP}}$ tends to zero.

For copolymerization performed in pure water (Fig. 3a), both reactivity ratios are lower than unity but now $r_{\mathrm{NIPAM}}$ is slightly higher than $r_{\mathrm{MADAP}}$. The drift of the copolymer composition (instantaneous or cumulated) is much smaller in that case as both monomers prefer to copolymerize rather than homopolymerize. Consequently, NIPAM-rich chains are formed only at the very end of the reaction, $c > 0.9$.[2]

An important consequence of the composition drift with conversion is the change with time of the monomer distribution in the macromolecular chain. In order to investigate this problem, we apply the statistical method to the radical copolymerization [30]. In Fig. 4, we report the probability: $N^{n}_{\mathrm{MADAP}}$ to find MADAP sequences of length $n$ in the case of copolymerizations [$(f_{\mathrm{MADAP}})_0 = 0.25$] performed either in pure water or in LiNO$_3$ 1 M. In these cases, we can see that the probability to find MADAP sequences with length higher than three (pure water) or four (LiNO$_3$ 1 M) is practically equal to zero. Moreover, as the reaction proceeds, the probability to find isolated MADAP units slightly increases and, correspondingly, we observe less and less sequences with $n \geq 2$. These drifts are very gradual with conversion and it is only at very high conversion that $N^{n}_{\mathrm{MADAP}}$ changes drastically towards one (for $n = 1$) or zero (for $n = 2$ or more). This reflects apparently the high NIPAM composition of these copolymers at the end of the reaction (see Fig. 3). These variations of $N^{n}_{\mathrm{MADAP}}$ are sharper when the copolymerization is carried out in LiNO$_3$ 1 M (Fig. 4b), as the difference between the reactivity ratios is higher. Nevertheless, the mean distribution of the MADAP sequences does not change substantially as the reaction proceeds. This can be easily calculated by integrating the

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[2] The discussion based on Fig. 3a is valid only when the initial monomer ratio is lower than the azeotropic composition. In the opposite situation, starting with $(f_{\mathrm{MADAP}})_0 > 0.5$, the general behavior will be symmetrical about the previous one with MADAP-rich chains formed at the end of the reaction.

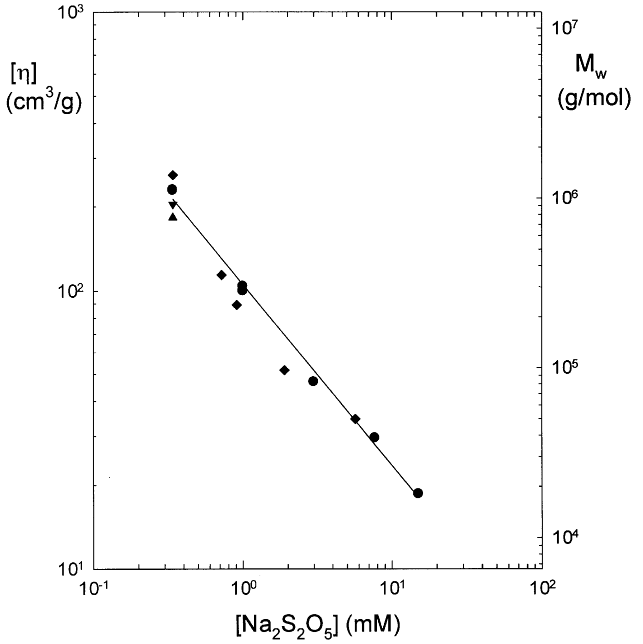

Fig. 5. The dependence of the intrinsic viscosity of PNIPAM homopolymers (●) and NIPAM–MADAP copolymers with the concentration of $Na_2S_2O_5$. The molar MADAP content of the copolymers is 10 mol% (▼), 25 mol% (◆) or 50 mol% (▲). Polymerization conditions: total monomer concentration = 1 M, $[(NH_4)_2S_2O_8] = 1$ mM, $T = 27$°C and conversion $\approx 80\%$. Intrinsic viscosities were measured in $LiNO_3$ 0.5 M at $T = 20$°C. The weight average molecular weight scale, given on the right axis, was calculated using the MHS relation established for PNIPAM homopolymer in $LiNO_3$ 0.5 M $T = 20$°C [19,31]: $[\eta] = 0.047\, M_w^{0.61}$.

curves in Fig. 4a and b. For instance, in the case of the copolymerization performed in $LiNO_3$ 1 M (Fig. 4b), the mean probability to find isolated MADAP units increases from 0.836 at the beginning of the reaction to only 0.868 at $c = 1$. At the same time, the corresponding mean probabilities to find MADAP triads in the same experiment are 0.023 (beginning of the reaction) and 0.016 ($c = 1$). Obviously, for experiments performed in pure water these mean values vary even less as $r_{MADAP}$ is lower in these conditions.

### 3.2. Molar mass control

In a previous work [31], we have reported the potentiality to control the molar mass of PNIPAM and other homopolymers, like poly(acrylic acid) and polyacrylamide, by aqueous polymerization with redox initiators containing persulfate. It was found that the oxydant concentration (ammonium persulfate in that case) had very little influence on the kinetic chain length compared to the reducing agent (sodium metabisulfite or thiol). For polymerizations performed at constant monomer concentration, a linear relationship (in a log–log scale) was found between the molar mass of the polymer and the reducing agent concentration. A similar relation is expected when using the intrinsic viscosity of PNIPAM instead of the molar mass, as the log–log dependence of the intrinsic viscosity on the molar mass is also linear according to the Mark–Houwink–Sakurada equation (MHS). Such a representation is given in Fig. 5, where the intrinsic viscosity of PNIPAM (●), determined at 20°C in a 0.5 M $LiNO_3$ solution, is plotted against the concentration of $Na_2S_2O_5$. The right *y*-axis was calculated using the MHS relation established for PNIPAM homopolymer in the same solvent conditions ($LiNO_3$ 0.5 M/$T = 20$°C) [19,31]: $[\eta] = 0.047\, M_w^{0.61}$. The intrinsic viscosity of various NIPAM–MADAP copolymers, measured under the same conditions, is also reported on this figure. Interestingly, homopolymers and copolymers follow the same straight line, suggesting that similar relations hold for PNIPAM and its copolymers under these ionic strength conditions. This is not surprising as the copolymers reported on the same figure contain a large content of NIPAM, at least 50 mol%. Finally, the most important conclusion that we can get is that, similarly to PNIPAM, the molar mass of the copolymers can be effectively controlled through the concentration of sodium metabisulfite over two decades of mass ($M_w \sim 10^4$ to $10^6$ g mol$^{-1}$).

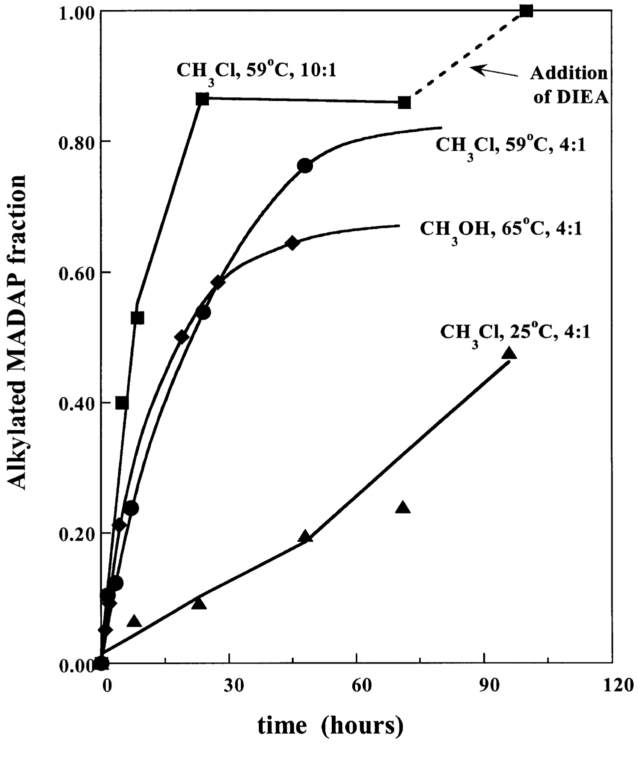

Fig. 6. Kinetic study of modification of NIPAM–MADAP copolymer with dodecylbromide. (◆): the solvent is methanol and a four times excess of dodecylbromide is used, $T = 65$°C. For the other experiments the solvent is chloroform at 25°C (▲) and 59°C (●) with a four times excess of dodecylbromide or at 59°C (■) with a tenfold excess of dodecylbromide. The dotted line represents the addition of (*N*,*N*-diisopropyl)ethylamine (DIEA).

### 3.3. Chemical modification

The quaternization of the tertiary amine of MADAP units with alkylbromide has been studied under various conditions by changing: (a) the nature of the solvent, (b) the temperature, and (c) the molar ratio between alkylbromide and MADAP units. The main results are summarized in Fig. 6, where the degree of alkylation of a NIPAM–MADAP copolymer with dodecylbromide is plotted versus the reaction time.

First of all, we can see that the reaction is not quantitative in methanol as the degree of alkylation reaches a plateau around 67 mol%. The acid–base titration of the modified copolymer shows that around 1/3 of the MADAP units remain under hydrobromide form when all the MADAP groups, quaternized or not, have a $Br^-$ as counterion. This suggests that HBr is produced during the alkylation process. HBr molecules neutralize the tertiary amines of MADAP units, which become inactive under acidic form towards dodecylbromide. Under these weakly basic conditions, such a side reaction (liberating HBr) could be attributed to the solvolysis of dodecylbromide, favored by the important autoprotolytic character of methanol. We did not confirm analytically this assumption, as this was out of the scope of this work.

When the reaction is performed in an inert solvent, like chloroform,[3] the alkylation reaches a higher level (around 90 mol%). As expected, the reaction proceeds faster when increasing the temperature or the dodecylbromide concentration but in every case a quantitative conversion cannot be achieved. Acid–base titration shows that the remaining 10 mol% unmodified MADAP units are again under protonated form. As chloroform cannot be responsible for this, one possible explanation could be the absorption of atmospheric $CO_2$ by basic MADAP units during the purification (dialysis) of the precursor. Thus, in order to complete the alkylation of the remaining groups, (*N*,*N*-diisopropyl)ethylamine (DIEA) was added at the end of the reaction. As shown in Fig. 6, deprotonation of the unmodified MADAP units by added DIEA results in total alkylation of the sample.

More evidence on the alkylation process can be obtained from $^1$H NMR. In Fig. 7, we have reported, in the region 2.6–4.2 ppm, the NMR spectra of (A) the precursor in the protonated form, (B) and (C) the modified copolymer alkylated in chloroform after and before addition of DIEA, respectively, and (D) the copolymer alkylated in methanol. As the experiments were performed in deuterated methanol, all the spectra are disturbed by the sharp peak at 3.3 ppm due to traces of hydrogenated methanol. However, we can easily attribute the other peaks observed in this region and derive some useful results. The peak centered around 3.9 ppm in all the spectra corresponds to the $-\mathrm{CH}<$ (**a**) of the isopropyl group of NIPAM units. For the protonated precursor (Fig. 7A), we observe two other broad peaks *b* (3.2 ppm) and **c** (2.95 ppm), which correspond to the *N*-methylene and *N*-methyl groups of MADAP units.

These peaks are shifted towards higher frequency when all the MADAP units are alkylated: $\mathbf{b}'$ (3.4 ppm) and $\mathbf{c}'$ (3.15 ppm). The absence in Fig. 7B of any peak **b** or **c** confirms the total alkylation of this sample. On the contrary, when DIEA is not added during the modification in chloroform (Fig. 7C), we do observe a residual peak **c** corresponding to some protonated but non-alkylated MADAP units. Finally, in the case of the modification performed in methanol (Fig. 7D), the peak **c** corresponding to the protonated units clearly appeared at 2.95 ppm. A comparison between the ratio of the peak areas (**c**)/(**a**) obtained from spectra A and D, $[(\mathbf{c})/(\mathbf{a})] = 2.2$ and 0.7, respectively, confirms once again that only 2/3 of the MADAP units have been alkylated in methanol.

Finally, we apply the formalism of a second order kinetics to the quaternization of MADAP units using the following rate equation:

$$F(t) = \frac{1}{[\mathrm{C_{12}H_{25}Br}]_0 - [\mathrm{MADAP}]_0} \times \ln \frac{1 - ([\mathrm{MADAP}]_0/[\mathrm{C_{12}H_{25}Br}]_0)\tau}{1-\tau} = kt, \qquad (2)$$

where $\tau$ is the conversion at time $t$ and $k$ is the rate constant.

In Fig. 8, the function $F(t)$ was plotted versus time, for the modification of a NIPAM–MADAP copolymer (21 mol% of MADAP units) using either (a) a four or ten times excess of dodecylbromide at 59°C or (b) a four times excess of dodecylbromide at 25°C. The straight lines obtained for the two sets of experiments, independently of the initial ratio of the reagents, confirm the second order kinetics in line with a $S_N2$ mechanism. Deviation of linearity would probably reveal neighboring effects on the reaction, as it was found in similar modification reaction with poly(vinylpyridine) [32–36]. In our case such neighboring effect is negligible due to the relatively small MADAP content and its statistic distribution along the polymer backbone (see Fig. 4). The rate constants, calculated from Fig. 8, are $2.6 \times 10^{-3}\ \mathrm{l\ mol^{-1}\ min^{-1}}$ and $3.3 \times 10^{-4}\ \mathrm{l\ mol^{-1}\ min^{-1}}$ at 59°C and 25°C, respectively, corresponding to an Arrhenius constant $A = 193.10^3\ \mathrm{l\ mol^{-1}\ min^{-1}}$ and an activation energy $\Delta H$ equal to 50 kJ mol$^{-1}$.

## 4. Conclusions

The objective of this work was to give an overall description of the synthesis of new PNIPAM derivatives characterized by a high level of hydrophobic modification.

The first step of the preparation involves the radical copolymerization between NIPAM and MADAP comonomers. The kinetic study revealed that the reactivity ratio of

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[3] The solvent used should also solubilize both reagents and products: (a) the low polar alkylbromide molecules, (b) the polar backbone, and finally (c) the resulting amphiphilic copolymer.

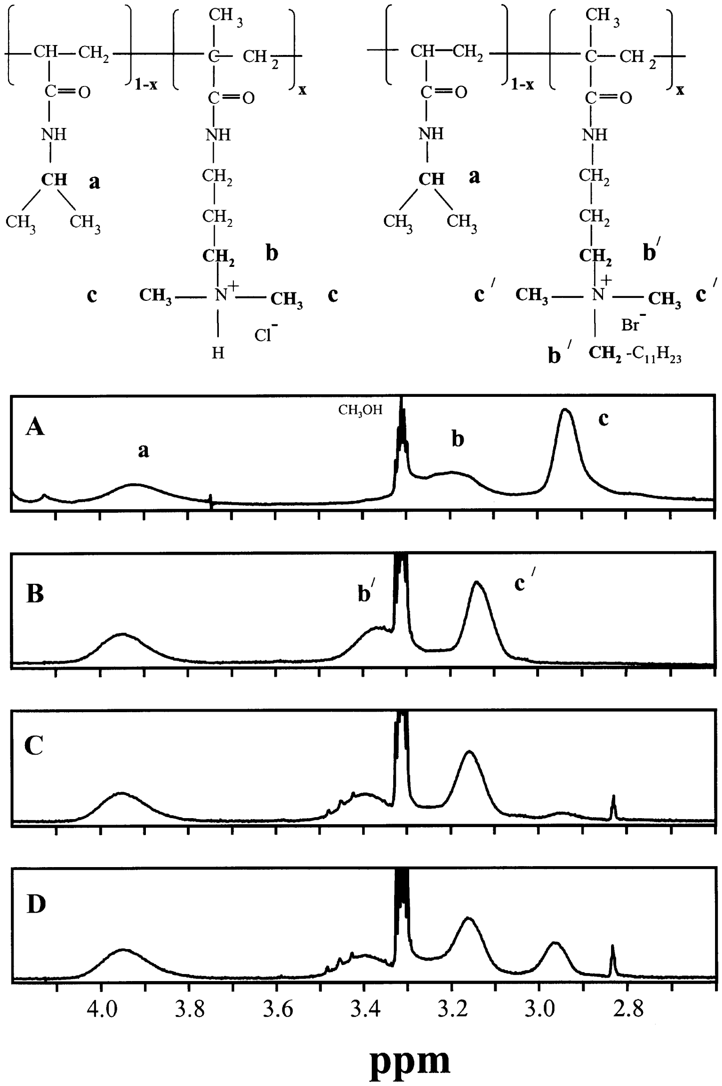

Fig. 7. $^1$H NMR spectra of solutions in $CD_3OD$ of: (A) a precursor NIPAM–MADAP copolymer containing 25 mol% of MADAP under protonated form, (B) the precursor after alkylation with dodecylbromide in chloroform and addition of (*N*,*N*-diisopropyl)ethylamine (DIEA), (C) the same before addition of DIEA, and (D) the precursor after alkylation with dodecylbromide in methanol.

MADAP (used under protonated form) depends on the ionic strength of the solution. At high salt concentration, when electrostatic interactions are screened, $r_{MADAP}$ is equal to 1.3, but it decreases with ionic strength and becomes equal to 0.6 in pure water. On the other hand, the reactivity ratio of NIPAM ($r_{NIPAM} = 0.6$) remains independent of the ionic strength. Starting with a feed molar ratio $(f_{MADAP})_0 \leq 0.25$, a composition drift is expected during the reaction. Nevertheless, the composition starts to diverge significantly only at very high conversion and finally, well defined homogeneous copolymer chains can be obtained for conversion limited below 80%. From the statistical analysis of the copolymerization we have shown that the probability of finding MADAP sequences longer than 2 is very low, especially in our situation where the initial MADAP content remains lower than 25% (in mole). This is an important argument which allows us to conclude that hydrophobically modified samples obtained after step II will not contain long hydrophobic blocks, which could later influence their macroscopic properties in water.

The variation of the molar mass of the precursors was studied as a function of the molar ratio (monomer)/(sodium metabisulfite) and a single relation was derived for all the copolymers. This is another important aspect of this work, since it provides the conditions to prepare copolymers of different composition but similar molar masses, which will be used later in a comparative study based on rheological properties.

Finally, the last part of our challenge concerned the alkylation step, where our initial goal was to define an easily handled protocol to get fully alkylated MADAP units. The results can be summarized as follows. (1) We should avoid

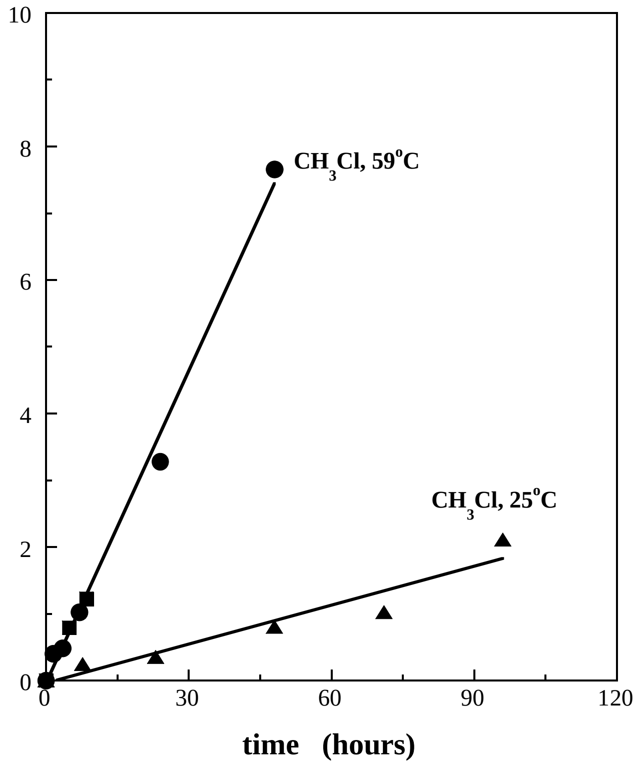

Fig. 8. The dependence of $F(\tau)$ on the reaction time for the quaternization of a NIPAM–MADAP copolymer with dodecylbromide performed in chloroform at $T = 25$°C and 59°C. The concentration of dodecylbromide is four times (●,▲) or ten times (■) that of MADAP units. $F(\tau)$ is defined in Eq. (2).

solvents, like methanol, susceptible to reaction with the alkylating agent. (2) In order to have a sufficiently high reaction rate, the reaction must be performed at the highest possible temperature and with a large excess (tenfold) of the alkylating reagent. (3) To get a complete alkylation, an inactive base must be added to ensure that all the MADAP units are under their reactive unprotonated form.

As a general conclusion, we will say that the three key points of this synthesis have been clarified: (1) the comonomer distribution, (2) the molar mass, and (3) the conversion of the hydrophobic modification. We are now able to control the primary structure of our systems and, in this way, their original properties in aqueous solution.

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