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Chain transfer polymerisation of poly-*N*-alkylacrylamides in superheated methanol and by microwave induction

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Abstract

The chain transfer polymerisation (telomerisation) of poly-*N*-isopropylacrylamide (PNIPAM), poly-*N,N*-dimethylacrylamide (PNDMAM) and poly-*N*-{3-(dimethylamino)propyl}acrylamide (PN3DMAPAM) as well as of co-polymers of PNIPAM and PNDMAM were studied. Reactions in superheated yet subcritical methanol (80–170 °C) and—under solvent free conditions—induced by microwave irradiation were compared in terms of product yield and quality to those obtained under standard reflux conditions (methanol reflux, ~65 °C, ambient pressure). In superheated methanol the reaction time was reduced by 66%, the average molar mass and the yield (monomer conversion) remain largely unchanged. Dielectric heating reduces the reaction time even further, i.e. to the minute range. Surprisingly, the average molar mass of the polymers dropped by 30% in these experiments, an effect that is most likely caused by the higher polarity of the reaction mixture under solvent-free conditions.

Keywords: Microwave induction; Chain transfer polymerisation; Telomerisation

1. Introduction

Poly-*N*-alkylacrylamides comprise a well-known class of polymers with properties, which make their application attractive for a wide variety of fields. Applications of such materials can, for example, be found in improved oil recovery [1], controlled drug release [2], downstream processing in biotechnology [3], homogenous catalysis [4], and optical switches [5].

Telomerisation-also known as (free radical) chain transfer polymerisation has been introduced as a means to produce polymers of narrower molar mass distribution than those obtained by conventional free radical polymerisation [6]. For many applications, especially in the life sciences, such more defined preparations are of considerable interest. In chain transfer polymerisation the radicals are transferred from one polymer chain to the next by a chain transfer agent, often a mercaptane, a group of molecules known for their excellent radical transfer abilities [7]. The chain transfer agent will also introduce a specific end group into each synthesised polymer chain. This end group may be further functionalised and can serve also for average molar mass determination, e.g. by titration, if a carboxylic function

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is chosen. In our group, 3-mercaptopropionic acid has repeatedly been used as chain transfer agent in the telomerisation of polyacrylamides, yielding the desired short oligomers with low polydispersity [3,8]. In most cases methanol was used as solvent in these experiments, typically under reflux conditions (~65 °C) and at ambient pressure. Several hours reaction time were required to reach high (>50%) monomer conversion in such cases.

In spite of the good results obtained under 'standard conditions', we were nevertheless interested to see to what extent the reaction could be improved in terms of reaction time and/or product quality. In particular we wanted to investigate, if the telomerisation process could be accelerated at higher temperatures (80–170 °C), i.e. in superheated yet subcritical methanol (the supercritical temperature of methanol is 512.6 K with a pressure of 8.1035 MPa) [9]. For this purpose the telomerisation was carried out in a sealed autoclave immersed into a hot oil bath. In addition it was of interest to see, if microwave induced dielectric heating is a feasible approach for chain transfer polymerisation for poly-*N*-alkylacrylamides. A priori, this was deemed at least possible due to the strong dipolar character of the reactants, which is a prerequisite for the absorption of microwaves. In comparison to conventional conditions we expected a much faster reaction in this case.

Synthetic organic chemistry by microwave induction is well described in several reviews [10]. Molecules with a permanent dipole moment are in particular suited for dielectric heating, because they adsorb microwaves. The dipole moments are aligned in the microwave field and by oscillating the field the molecules start to rotate. The rapid rotation is responsible for the phenomenon of instantaneous heating. The reactants employed in this study, including *N*-isopropylacrylamide, *N,N*-dimethylacrylamide and 3-mercaptopropionic acid, contain a strong intramolecular dipole moment. In addition, microwave-induced telomerisation can be carried out under solvent-free conditions, which reduces the number of potential contaminants and should simplify the subsequent purification of the material.

The application of microwaves in polymer science is described in the literature [11] for a wide range of applications. In the field of polymerisation and in particular related to telomerisation, Chia [12] have e.g. examined the conversion of methylacrylate by free radical polymerisation at variable microwave power and compared the results with conventionally heated reactions. In another study the polymerisation of ϵ-caprolactame by thermal and microwave activation were examined and compared [13]. In both studies the reaction speed was clearly higher with microwave than with conventional heating. However, a study of the telomerisation of poly-*N*-alkylacrylamide by microwave induction is at present not available.

2. Experimental

Materials: 3-Mercaptopropionic acid, *N*-isopropylacrylamide, *N,N*-dimethylacrylamide, and *N*-3(dimethylamino)propyl-acrylamide were purchased from Aldrich, Switzerland. AIBN (2,2′-azobisisobutyronitrile), NaOH, and phenolphthalein were supplied by Fluka AG, Switzerland. The solvents methanol, acetone, and hexane were of analytical grade.

Telomerisation experiments: The telomerisation experiments in superheated, subcritical methanol (80–170 °C) were carried out in an autoclave with observation windows as they are used for reactions in supercritical fluids. 350 µl (4 mmol) 3-mercaptopropionic acid, 82 mg (0.5 mmol) AIBN, 100 mmol *N*-alkylacrylamide and 15 ml methanol were placed in the autoclave, which was subsequently sealed. Around the autoclave two wires with handles were wrapped, which allowed immersing the reactor safely into a heated oil bath of the indicated temperature (80–170 °C). After 1 h the autoclave was removed and cooled by immersion into cold water. The workup procedure was the same as described for the microwave experiment, see below.

For the telomerisation in a domestic microwave oven, 50 mmol *N*-alkylacrylamide, 175 µl (2 mmol) 3-mercaptopropionic acid, and 41 mg (0.25 mmol) AIBN were weighted into a 50 ml one-neck flask. The open flask was placed in a 100 ml glass beaker installed on the rotating plate of a domestic microwave oven (Easy Tronic MO 201). The flask with the reaction mixture was preferentially placed close to the rim of the rotating plate to enhance homogenous microwave irradiation. The mixture was heated at 350 W for 30–150 s (conditions defined by the programming buttons of the instrument). The obtained very hot, transparent, yet slightly yellow gel was allowed to cool to room temperature. The then glasslike material was slowly dissolved in 50 ml acetone. The resulting pale yellow solution was transferred to a 500 ml flask and 250 ml hexane were added. The macromolecules quickly precipitated and the supernatant solution was decanted. To improve the purity, the cleaning procedure was repeated once. The remaining pure white product was redissolved in 50 ml acetone. With a rotavapor (25 mbar/50 °C) the solvent was slowly removed. During the evaporation, the product was distributed all over the inner glass wall of the flask as a white, porous foam (2–4 mm thick). With high vacuum (10^{-3} mbar/h) the polymer was dried to completeness.

Analytics: For structure elucidation of poly-*N*-alkylacrylamides ^{1}H NMR and MALDI-TOF mass spectroscopy were used. The proton spectra were recorded in $CDCl_3$ on an AC BRUKER 200 MHz Spectrometer. The MALDI-TOF mass spectra were recorded on a PerSeptive Biosystems Voyager-DE STR equipped with a 2-m ion flight tube. The number average of the molar

mass was determined by end group titration. 100 mg of the polymer were dissolved in 3 ml H_2O and cooled with an ice bath (≈3 °C). A small amount of phenolphthalein was added and the solution titrated with 0.01 M NaOH until the mixture turned purple (low speed titration).

3. Results and discussion

By carrying out the telomerisation of the acrylamides in superheated methanol and under microwave irradiation, we hoped to accelerate the reaction as a result of the higher temperature and/or a concentration effect (no dilution of the mixture in the case of the microwave irradiation), albeit without deterioration of the product quality. In the experiments employing superheated methanol, an 'elevated' reaction temperature (between 80 and 170 °C) was adjusted via the oil bath. In the case of microwave irradiation, considerable heat generation must be expected, especially in the so-called 'hot spots'. Incidentally, such a temperature increase has also consequences for the stability of the initiator, AIBN, employed to start the reaction. The half-life of AIBN in toluene at 65 °C is 10 h. By comparison, the substance decomposes almost instantaneously at 102–104 °C [14]. Larger quantities may even explode. It can therefore be expected that the initiating radicals are generated more quickly in the experiments carried out at elevated temperatures.

While the temperature induced acceleration of the telomerisation rate was desired and the influence on the initiator stability should pose no problem, a similar increase of some putative side reactions could not be a priori excluded. In particular, at higher temperature the amide function of the product molecules may be hydrolysed. To examine the speed and hence the importance of this side reaction, we conducted several hydrolysis experiment with PNDMAM. ^{1}H NMR measurements show that complete hydrolysis occurred in D_2O after 8 h at 200 °C. As a consequence, exceptionally care was taken to assure that all telomerisations included in this investigation were carried out with dry reagents to assure moisture free conditions.

The subsequent polymerisation experiments showed no indication of hydrolysis or other side reactions in the case of PNIPAM and PNDMAM, independent of whether the telomerisation was performed in superheated methanol and in the microwave oven. However, in the case of PN3DMAPAM it was found that a stable product could only be obtained in superheated methanol and then only when the reaction temperature was kept below 120 °C (in a 1-h experiment). Telomerisation by dielectric heating was not an option in this case.

One of the polymers included in this study, PNIPAM, is well known for its stimuli-responsive behaviour [15]. PNIPAM precipitates from pure water if a temperature of approximately 32 °C (lower critical solution temperature, LCST) is surpassed [16]. The exact value may vary with the size and the concentration of the PNIPAM. To date the phase transition has only been observed in aqueous solutions (including D_2O) and is not known for any other pure polar solvent. Nevertheless we were curious to know what happens in the case of superheated methanol, a solvent that has not been investigated previously in regard to its ability to support the LCST phenomenon. In order to elucidate this question, the solubility behaviour of the PNIPAM was observed through the windows in the autoclave during the 1 h

Table 1
Comparison of the telomerisation of the investigated monomers (a) under 'standard conditions' (methanol reflux, ≈65 °C, ambient pressure); (b) in superheated methanol; (c) and under solvent free conditions by microwave induction

Polymer	Reaction conditions	Reaction time	Monomer conversion (%)	Average molar mass (g/mol)
PNIPAM	~65 °C (a)	3–5 h	84	2700
	80 °C (b)	1 h	57	2733
	120 °C (b)	1 h	82	2983
	350 W (c)	60 s	78	2447
	350 W (c)	150 s	81	1938
PNDMAM	80 °C (b)	1 h	70	2266
	120 °C (b)	1 h	92	2469
	350 W (c)	30 s	66	1677
	350 W (c)	150 s	73	2036
N3DMAPAM	80 °C (b)	1 h	71	–
	120 °C (b)	1 h	87	–
Co-PNIPAM/PNDMAM	80 °C (b)	1 h	98	2561
	120 °C (b)	1 h	98	2717
	350 W	60 s	90	2080
	350 W (c)	120 s	75	2054

The average molar mass was determined by end group titration.

experiments at reaction temperatures varying between 80 and 170 °C. However, in none of these experiments did we observe a phase transition (clouding, LCST). Some water is apparently required for occurrence of an LCST in PNIPAM containing solutions.

The results of all polymerisation experiments including control experiments under 'standard conditions' (methanol reflux, ≈65 °C, ambient pressure) are compiled in Table 1. Besides the three homopolymers, we also produced co-polymers of PNIPAM and PNDMAM.

Certain trends can be observed. In superheated methanol, monomer conversions obtained after 1 h are similar or better than those obtained under standard conditions after 3–5 h. In a given series, monomer conversion tends to increase with the reaction temperature. The number average obtained for the molar mass as determined by end group titration is similar for all polymers of a given kind produced throughout the examined temperature range, i.e. 80–170 °C (Fig. 1, 1 h experiments) and comparable to the value obtained under standard conditions, see also Table 1. The average molar mass also shows a tendency to increase with the reaction temperature, but the trend becomes less clear at reaction temperatures above 120 °C. Microwave irradiation results in monomer conversions, which tend to be somewhat lower than in superheated methanol or under standard conditions and this independent of the irradiation time in the investigated range (30–150 s). In addition, the number average of the molar mass is reduced by approximately 30% in this case. On the other hand, in the investigated range the number average of the molar mass shows little dependency on the irradiation time (30–150 s, 350 W). Moreover, no consistent trend can be observed for the dependency, Fig. 2.

A direct comparison of the distribution of the molar mass for a given polymer produced in superheated methanol and by microwave irradiation under otherwise similar conditions can be made in Fig. 3, which shows the MALDI mass spectra obtained for PNIPAM produced in (a) superheated methanol at 130 °C (1 h) and (b) after microwave irradiation for 150 s (350 W). In both cases a fairly narrow mass distribution is obtained, as evidenced by the MALDI mass spectra. The relatively low polydispersity of the produced polymers is an established advantage of the telomerisation process under standard conditions. Apparently this is also true for telomerisations carried out at elevated temperatures, i.e. in superheated methanol and by microwave induction. By direct comparison, the MALDI mass spectrum of the microwave produced PNIPAM shows a more symmetrical mass distribution than the one obtained for PNIPAM telomers produced in superheated methanol. This was also observed in the case of the other polymers produced during this investigation, with the exception of

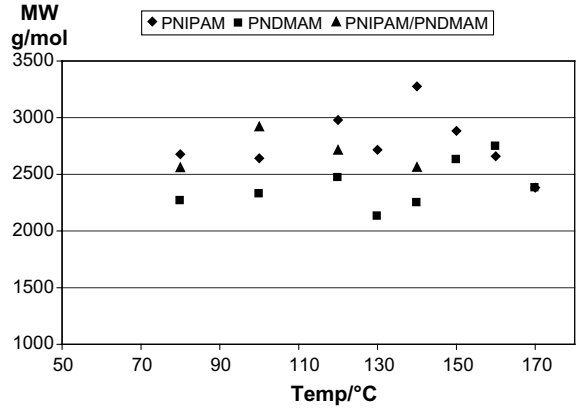

Fig. 1. Average molar mass obtained by end group titration for PNIPAM, PNDMAM and the 1:1 co-polymers thereof produced in superheated methanol of the indicated temperature and one hour of reaction time.

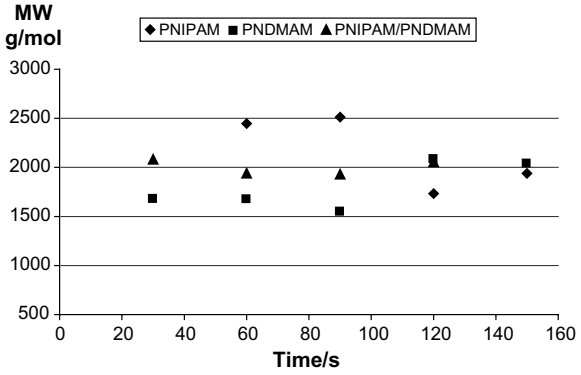

Fig. 2. Average molar mass obtained by end group titration for PNIPAM, PNDMAM and the 1:1 co-polymers thereof produced via by microwave irradiation at 350 W for different irradiation times.

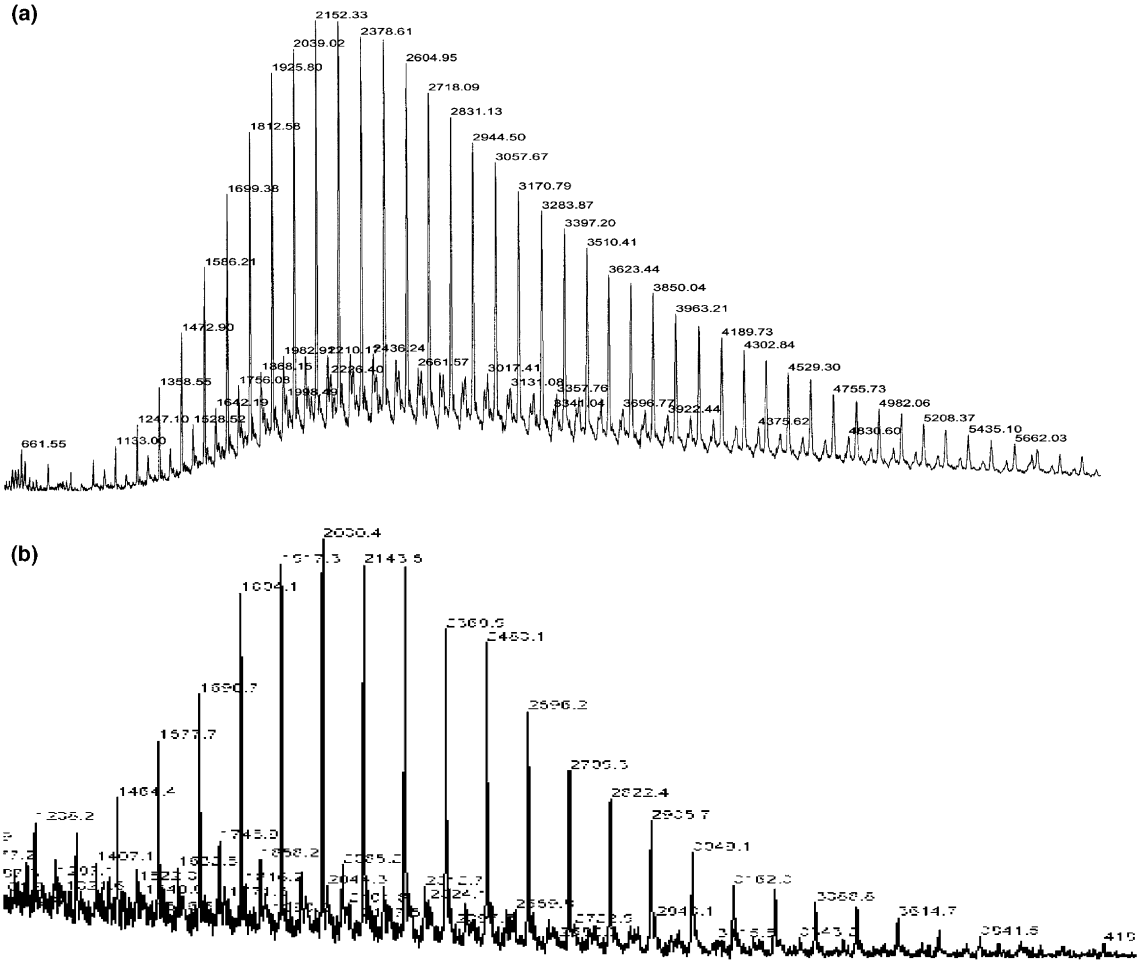

Fig. 3. MALDI mass spectra of PNIPAM telomerised with the same initial stoichiometry, (a) in superheated methanol at 130 °C/h, (b) via microwave induction at 300 W/150 s.

PN3DMAPAM that could not be produced via microwave induction.

Incidentally, we did not use the MALDI mass spectra for the determination of the mass and number average of the molar mass and the related polydispersity, as the method has in the past been found to systematically underestimate the latter parameter in the case of PNIPAM telomers. The end group titration method on the other hand has been shown to yield reliable results for the number average of the molar mass in similar cases, albeit for PNIPAM telomers produced under standard conditions [3].

The reason for the reduced average molar mass together with a more symmetrical mass distribution obtained in the microwave irradiation experiments under otherwise similar conditions (stoichiometry) can only be speculated upon. As a result of the dielectric heating, the reaction mixture is quickly transformed into a viscous mass and the diffusion of free monomer molecules may be hindered. However, this effect is less pronounced in the beginning of the reaction, when just a few polymer molecules have been formed, and becomes dominant only later on, when the polymerization is more advanced. However, such an effect is difficult to correlate with the fact that a more symmetrical mass distribution is observed in case of the telomers produced via microwave induction. Under such circumstances a more skewed distribution would have been instead expected. The hindered monomer diffusion is therefore most likely not directly accountable for the shorter average polymer length.

Different mercaptan (chain transfer agent) concentrations and the variation of the solvent's polarity are parameters, which are also known to influence the average chain length obtained in telomerisation [17]. Since the chain transfer agent was not changed in our

experiments, we focussed on solvent polarity as a possible reason for the difference in the molar mass. In particular, the transfer of the hydrogen atom from the thiol group of the chain transfer agent to the propagating chain is more likely in a polar than in a nonpolar solvent, since the transition state is more stable. As a result, under otherwise similar conditions the chain transfer rate will be higher in the more polar solvent resulting in shorter telomer chains. If we consider that the dipole moment of methanol is only 1.7 D [18] while the value, e.g., for *N,N*-dimethylacrylamide is 3.76 D [19], such a difference could very well account for the fact that the chain length produced in the microwave experiments, where the monomer co-functions as 'solvent', is reduced by 33%. The other monomers also show higher dipole moments than methanol.

4. Conclusions

Telomerisation of poly-*N*-alkylacrylamides is possible in superheated methanol and by microwave induction. Compared to 'standard conditions' (3–5 h) the reaction time is reduced to an hour in superheated methanol and to as little as 30 s in the case of microwave irradiation. A product of similar quality in terms of average molar mass and mass distribution is obtained by both methods. The consistently observed fact that smaller telomers were obtained by microwave induction is most likely related to the fact that in this case the reaction took place in a more polar 'solvent' than methanol, i.e. the monomer, which results in a higher chain transfer rate. Since side reaction and especially hydrolysis may become troublesome at elevated temperature, care must be taken to work under moisture free conditions. In one of the investigated cases, namely PN3DMAPAM, polymerisation via microwave induction was not possible for this reason.

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