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Preparation of thermosensitive nanogels by photo-cross-linking

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Abstract A novel method to prepare thermosensitive nanogels from photocross-linkable copolymers of *N*-isopropylacrylamide and dimethyl maleinimido acrylamide (DMIAAm) was developed. The colloidal nanogels were formed by UV irradiation of solutions of thermosensitive polymers in water at 45 °C. The compositions of the photopolymer solutions were varied by changing the amount of DMIAAm in the photopolymer chains (2–10 mol%) or by varying the sodium dodecyl sulfate (SDS) concentration. The resultant nanogel particles were rather spherical and showed large changes in hydrodynamic diameters in the vicinity of the phase transition temperature of the corresponding linear photopolymers. The particle sizes of the nanogels and their swellability could be controlled through the UV irradiation time, the chromophore content and the SDS concentration. An increase in the chromophore content and the SDS concentration resulted in nanogels with smaller dimensions. The hydrodynamic diameters of the nanogels decreased significantly from 2 to 10 min UV irradiation time but not significantly after that. The phase transition of the photopolymer solutions and the respective nanogels could be adjusted by the chromophore content or the SDS concentration. An increase in the chromophore content leads to lower phase-transition temperatures, whilst an increase in the SDS concentration elevated them. Pulsed-field-gradient NMR proved a useful tool to investigate the network formation in the nanogels by determining changes in the diffusion coefficients.

Keywords Thermosensitive polymer · Microgel · Nanogel · Photo-cross-linking

Introduction

Temperature-sensitive polymers exhibit lower critical solution temperature (LCST) behaviour. The transition of sensitive soluble polymers from a homogeneous to a heterogeneous state is called the cloud point or phase-transition temperature (T_c). This behaviour is derived from changes in the balance of interactions of hydrophilic and hydrophobic groups in the polymer chains at the LCST [1–4]. These properties of the thermosensitive polymers result in interesting properties of their polymer gels, i.e., large and sharp changes in swellability upon raising the temperature above the LCST.

Among temperature-responsive polymers, poly (*N*-isopropylacrylamide) (PNIPAAm) and its copolymers have been investigated extensively theoretically and experimentally [1–15]. Much of the published work has concentrated on PNIPAAm-based hydrogels as they have potential applications in a broad range of areas, such as drug delivery systems, separation systems and controlled flocculation for enhanced oil recovery [2, 16, 17]. These applications were also found to be especially attractive with dispersions of thermosensitive gels. Colloidal gels with dimensions in the range of submicrons (namely microgels or nanogels) could be conventionally prepared by free-radical polymerization in dilute solutions or by emulsion polymerizations. Microgels were first synthesized by Staudinger and Husemann [18] in 1935. Pelton and coworkers [19–24] have systematically prepared and described PNIPAAm latex in water since the 1980s. The colloidal microgel systems were conventionally prepared using NIPAAm, with potassium persulfate as the initiator, sodium dodecyl sulfate (SDS) as the surfactant and methylene bisacrylamide as the cross-linker. The authors reported that under these conditions the microgels could only be formed above a critical temperature, i.e., 55 °C. Using similar procedures, Murray et al. [25] and Snowden et al. [26] have tailored various colloidal mircogels from NIPAAm, NIPAAm with acrylic acid (AAc) and other thermosensitive polymers. Duracher and et al. [27] prepared PNIPAAm lattices via precipitation polymerization. Jones and Lyon [28] recently developed multiresponsive core–shell microgels based on NIPAAm and AAc. The cores of multiresponsive microgels were synthesized via precipitation polymerization and then used as nuclei for shell formation.

Outstanding properties of colloidal microgels such as particle size, swellability, electromobility, rheology and colloidal stability are well described in the literature [19–31]. Such properties of microgels are significantly influenced by temperature, the presence of hydrophobic/hydrophilic groups in the polymer chains, the cross-linking density of the hydrogels or the concentration of surfactant SDS in the solution. The effects of pH, salt, surfactant and composition on the phase transition of nanoparticles of NIPAAm and methacrylic acid were systematically investigated by Huang and Wu [32].

In this work, we report a new route to prepare temperature-sensitive colloidal nanogels based on photopolymers of PNIPAAm. The photo-cross-linkable polymers described have gained considerable technological interest as the polymers exhibit many interesting properties [33–37]. In fact, hydrogel films based on photo-cross-linkable polymers of NIPAAm and dimethyl maleinimido acrylamide (DMIAAm) were successfully developed by our group for microsystem applications [38–41]. The motivation of the current work was derived from the coil–globule behaviour of thermosensitive PNIPAAm in aqueous solutions with or without SDS. By adding SDS, an interaction of polymer segments with the hydrophobic tails of the surfactant occurs. Therefore, the aggregation is suppressed by the formation of polymer globules stabilized by adsorbed surfactant [5, 6]. The solutions of photopolymers containing various amounts of chromophore were heated to a temperature higher than their phase-transition temperature, then irradiated using a UV lamp. The preparation of colloidal nanogels using the current method should minimize the differences in the cross-linking density between the core and the exterior of the nanogel particles, which were reported by Pelton's and Pichot's groups [23, 27, 28]. The statistic distribution of the comonomers in the photopolymers obtained possibly contributes to overcome this limitation. In addition, the parameters which are able to control the particle size, the swellability and the phase-transition temperatures of the resultant nanogels could be extended. The parameters include chromophore content, UV irradiation time and SDS concentration. Dynamic light scattering (DLS), scanning electron microscopy (SEM), differential scanning calometry (DSC) and pulsed-field-gradient (PFG) NMR were used in our investigation.

Experimental

Materials

Diaminoethane (Fluka), dimethyl maleic anhydride (97%, Lancaster), acryloyl chloride (Merck), di-*tert*-butyl dicarbonate (97%, Acros) were used as received. NIPAAm (Merck) was recrystallized from distilled hexane and 2,2′-azobis(isobutyronitrile) (AIBN) was recrystallized from methanol before use. SDS and the other reagents were used without further purification. The solvents were purified according to standard methods.

Synthesis of DMIAAm

DMIAAm was synthesized in four steps as outlined in Scheme 1.

tert-Butyl-N-(2-aminoethyl)carbonate

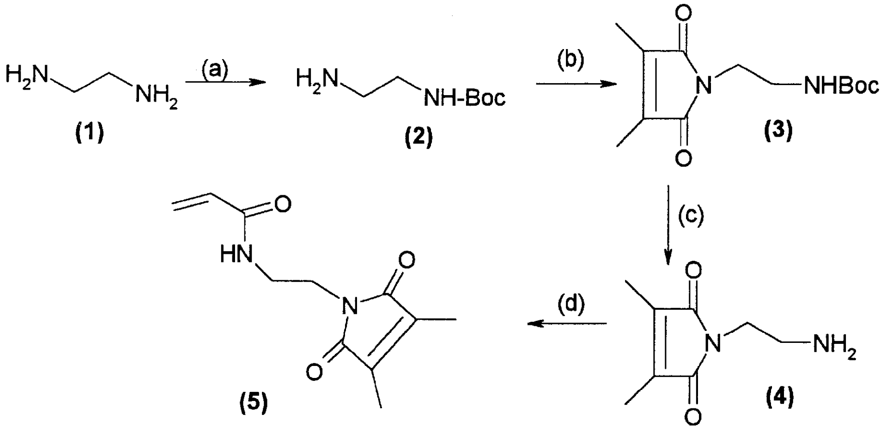
A synthesis method similar to that in the literature [42] was used. A solution of 13.10 g (0.06 mol) di-*tert*-butyl dicarbonate in 150 ml 1,4-dioxane was added slowly to a stirred solution of 27.88 g (0.464 mol) diaminoethane in 150 ml 1,4-dioxane over a period of 3 h at room temperature. After the mixture had been stirred for 2 days at 25 °C, the precipitate was filtered and the 1,4-dioxane and excess diaminoethane were removed in vacuo from the filtrate. The subsequent addition of 250 ml water precipitated bis(*N*,*N*′-*tert*-butyloxycarbonyl)-1,2-diaminoethane, which was removed by filtration. The aqueous solution was saturated with sodium chloride and extracted five times with 100 ml dichloromethane each time. The organic phase was dried with sodium sulfate and was evaporated under reduced pressure to give 8.59–9.07 g of *tert*-butyl-*N*-(2-aminoethyl)carbonate (**2**) as a colorless oil (89–94% yield).

^{1}H NMR ($CDCl_3$): δ (ppm) 1.38 (9H, $3CH_3$), 2.12 (2H, NH_2), 2.73 (2H, CH_2NH_2), 3.12 (2H, CH_2NH), 5.31 (1H, NH).

^{13}C NMR ($CDCl_3$): δ (ppm) 28.25 ($3CH_3$), 41.58 (CH_2NH_2), 43.04 (CH_2NH), 78.98 ($C(CH_3)_3$), 156.22 ($C=O$).

IR ($CHCl_3$) ν (cm^{-1}): 3,359 (NH), 2,975 (CH), 2,933 (CH), 2,871 (CH), 1,691 (amide I), 1,528 (amide II).

Scheme 1 Synthesis of the dimethyl maleinimido acrylamide chromophore



(a) $(Boc)_2O$/1,4-dioxane, 25°C, 48 h
(b) Dimethylmaleic anhydride/toluene, 130°C, 2.5 h
(c) CF_3COOH/CH_2Cl_2, RT, 1 h
(d) $CH_2 = CHCOCl$, Na_2CO_3/CH_2Cl_2, 0-5°C, 2 h

N-[2-(3,4-Dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-aminoethyl]-tert-butyl-carbonate

tert-Butyl-*N*-(2-aminoethyl)carbonate (9.00 g, 0.056 mol) was added to a stirred solution of 7.05 g (0.056 mol) dimethyl maleic anhydride in 238 ml toluene. The mixture was boiled at 130 °C for 2.5 h using a reflux condenser with a water trap to remove water. The resultant solution was evaporated under reduced pressure to give 14.73 g *N*-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-aminoethyl]-*tert*-butyl-carbonate (**3**) as a white solid (98% yield).

mp = 106 °C

^{1}H NMR ($CDCl_3$): δ (ppm) 1.38 (9H, 3 CH_3, Boc), 1.94 (6H, 2CH_3, maleic), 3.28 (2H, CH_2NH), 3.58 (2H, CH_2N), 4.83 (1H, NH).

^{13}C NMR ($CDCl_3$): δ (ppm) 8.67 (2CH_3, maleic), 28.25 (3CH_3, Boc), 37.92 (CH_2N), 39.73 (CH_2NH), 79.31 [$C(CH_3)_3$], 137.25 (2C = C), 155.87 (C = O, Boc), 172.21 (2C = O, maleic).

IR (KBr) ν (cm^{-1}): 3,389 (NH), 2,984 (CH), 2,938 (CH), 1,713 (C = O, maleic), 1,687 (amide I), 1,520 (amide II).

N-[2-(3,4-Dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)]-ethylamine

Trifluoroacetic acid (165 ml, 6.84 mol) was added to a solution of 23.05 g (0.086 mol) **3** in 69 ml dichloromethane. The mixture was stirred for 45 min at room temperature. The resulting solution was concentrated in vacuo to give 26.7 g trifluoroacetic acid salt of *N*-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)]-ethylamine (**4**) (TFA salt). Diethylamine was added to the solution of 26.7 g TFA salt in 267 ml water until neutral pH was achieved. The solution obtained was stirred for 2.5 h at room temperature then extracted with an excess of ethyl acetate. The organic phase was dried with sodium sulfate and evaporated under vacuum to give 14.0 g of **4** as a white solid (92–100% yield).

Melting point (mp) = decomposition at 210 °C

^{1}H NMR ($CDCl_3$/DMSO): δ (ppm) 1.69 (6H, 2 CH_3), 2.85 (2H, CH_2NH_2), 2.52 (2H, CH_2N), 8.41 (2H, NH_2).

^{13}C NMR ($CDCl_3$/DMSO): δ (ppm) 8.02 (2CH_3), 34.86 (CH_2NH_2), 37.80 (CH_2N), 136.85 (C = C), 171.30 (2C = O).

IR (KBr) ν (cm^{-1}): 3,462 (NH_2), 3,054 (CH), 2,925 (CH), 1,704 (C = O).

N-[2-(3,4-Dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-acrylamide

4 (14.76 g, 0.086 mol) and 9.11 g (0.086 mol) sodium carbonate were added to 147 ml dichloromethane. The mixture was cooled to 0 °C in an ice bath. Acryloyl chloride (7.78 g, 0.086 mol) was added dropwise to the stirred suspension. The suspension was stirred in the cold initially and then allowed to warm up to room temperature for 2 h. The resultant solution was filtered, dried with sodium sulfate and evaporated to give 7.26 g of *N*-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-acrylamide (**5**) as a white solid (38% yield).

mp = 125 °C.

^{1}H NMR ($CDCl_3$): δ (ppm) 1.85 (6H, 2CH_3), 3.39 (2H, CH_2NH), 3.58 (2H, CH_2N), 5.51 (1H, CH_2 =), 6.00 (1H, CH =), 6.10 (2H, CH_2 =), 6.64 (1H, NH).

^{13}C NMR ($CDCl_3$): δ (ppm) 8.46 (2CH_3), 37.12 (CH_2NH), 38.89 (CH_2N), 126.00 (CH_2 =), 130.63 (CH =), 137.16 (2C = C), 165.80 (C = O, acrylic), 172.11 (2C = O, maleic).

IR (KBr) ν (cm^{-1}): 3,307 (NH), 3,071 (CH), 2,942 (CH), 1,707 (C = O, maleic), 1,656 (amide I), 1626 (C = C), 1546 (amide II).

Synthesis of photo-cross-linkable copolymers

The photocopolymers were prepared by the following procedures (Scheme 2) [43]. AIBN was added to a solution of NIPAAm and DMIAAm in dried dioxane. After purging with argon for 20 min, the mixture was kept at 70 °C for 7 h under an argon atmosphere with stirring. After the reaction, the mixture was poured into 500 ml diethyl ether. The copolymer was washed with diethyl ether, purified through reprecipitation from dioxane solution into diethyl ether and finally dried in a vacuum for 24 h. Various feed compositions and the properties of photopolymers are given in Table 1.

Nanogel formation

Solutions of photocopolymers (5 g/l) and predetermined amounts of SDS in distilled water were prepared at room temperatures (20–25 °C) (Table 2). The mixtures were stirred to dissolve all solid components, filtered and left overnight before conducting the following steps.

Scheme 2 Synthesis of the photopolymers

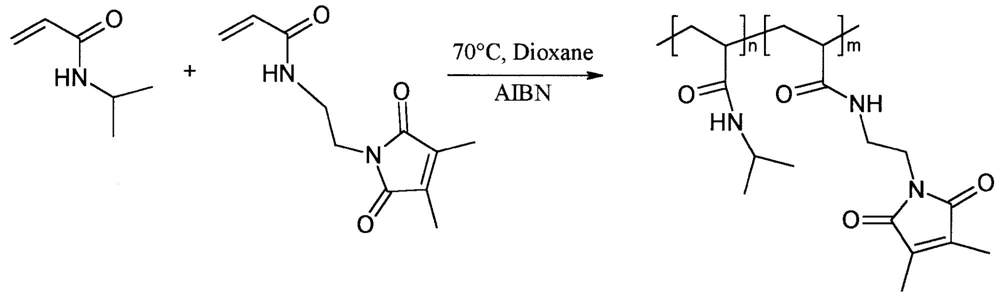


Table 1 Photopolymers and their characterization

N-Isopropylacrylamide /dimethyl maleinimido acrylamide photopolymer	Dimethyl maleinimido acrylamide composition (mol%)		Polymer yield (%)	T_g (°C)
	Feed	Polymer		
A	2	2.9	85	130
B	5	5.2	67	129
C	10	9.1	46	126

Table 2 Photopolymer solutions to prepare colloidal nanogels

Sample	Polymer concentration (g/l)	Sodium dodecyl sulfate concentration (mmol/l)	Phase-transition temperature (°C)
2-0-0	5	0.000	33
2-1-0	5	0.085	33
2-2-0	5	2.680	37
2-3-0	5	5.000	41
5-0-0	5	0.000	33
5-1-0	5	0.085	33
5-2-0	5	2.680	36
5-3-0	5	5.000	41
10-0-0	5	0.000	30
10-1-0	5	0.085	32
10-2-0	5	2.680	36
10-3-0	5	5.000	41

To make nanogels, the photopolymer solutions were heated to 45 °C under stirring in a reactor. The solutions turned turbid after a few minutes, indicating the occurrence of a phase transition of the photopolymers. Under these conditions, copolymer chains were aggregated to form particles and were stabilized by SDS molecules as illustrated in Scheme 3. After 15 min at 45 °C, the solutions were irradiated by UV light. After different periods of time, ranging from 0 to 60 min, samples were taken from the solution for characterization.

The photopolymer solutions and corresponding nanogels are abbreviated by their feed molar percentage of chromophore (2, 5 and 10), SDS concentration (0 for 0.000 mmol/l SDS, 1 for 0.085 mmol/l SDS, 2 for 2.680 mmol/l SDS, 3 for 5.000 mmol/l SDS and S as a variable) and time of UV irradiation (0–60 s and t as a variable). 10-2-0, for instance, is the solution of photopolymer containing 10% feed chromophore composition, 2.680 mmol/l SDS with no irradiation, while 10-1-30 is the nanogels from a solution of photopolymer (10% feed chromophore composition), 0.085 mmol/l SDS and 30 min of UV irradiation.

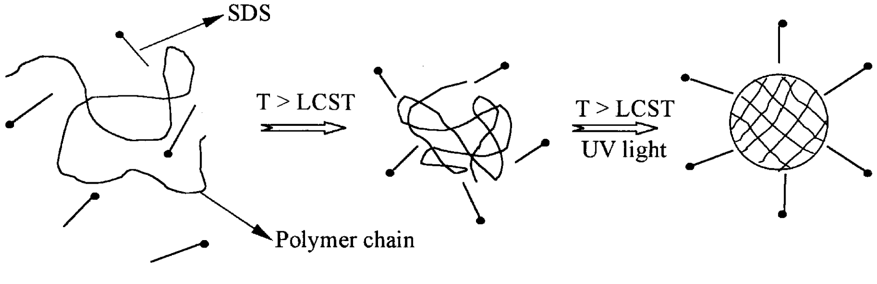
Instrumentation and characterization

The NMR spectra of the chromophores were obtained with a Bruker DRX500 NMR spectrometer. IR spectra were recorded with a UNICAM Analysis Technology (Mattson) research series Fourier transform IR spectrometer. The melting points of the substances were measured using a Büchi B-545 melting point apparatus (Switzerland). The glass-transition temperatures of the photopolymers and the phase transitions of the photopolymer solutions were determined using a 2920 modulated differential scanning calorimeter (TA Instruments). The photo-cross-linking reactions were conducted using a short-arc mercury lamp (100 W, Osram, Berlin) installed vertically to generate UV light (wavelength from 250 to 500 nm). PFG-NMR diffusion experiments were performed using a Bruker 400 MHz Avance spectrometer (DMX400) equipped with a PFG probe head (Bruker DIFF 30). Echo decays were determined by a stimulated echo sequence with gradient pulses under variation of the gradient strength. The sample temperature was set to 25 °C and controlled by the gradient cooling system, which is a suitable way to achieve a homogeneous temperature distribution and avoid convection effects, which otherwise might be induced by small temperature gradients in the sample. The signal of the CH_3 resonance at 1.2 ppm was evaluated.

Particle diameter analysis

The resultant suspension (2 ml) was transferred to a sample cell and analysed in a DLS-700 DLS spectrometer (Otsuka Electronics

Scheme 3 Formation of colloidal nanogels by photo-cross-linking



Co.). The data were taken with a He–Ne laser (633 nm) at an angle of 90° and at various temperatures (from 10 to 45 °C).

Morphology of the nanogel particles

A few droplets of the diluted suspension (0.5 g polymer/l) were dropped onto an aluminium foil and dried at 45 °C under vacuum conditions. The dried polymer was coated with gold vapour prior to observation in a GEMINI-Zeiss DMS-982.

Results and discussion

Synthesis of chromophore

N-substituted acrylamide containing dimethyl maleinimide moieties has been synthesized and used successfully in our group to prepare photo-cross-linkable polymers. The functional monomer DMIAAm was prepared via a four-step procedure using protecting *tert*-butyloxycarbonyl group (Boc) in the initial stage. The average yield of the reported route [42] was relatively high; however, it has been difficult to get pure intermediate compound in the fourth step. The amine chromophore (**4**, Scheme 1) could also be used directly in the modification of reactive polymers. In order to improve the yield of the process and to obtain pure intermediate compounds for subsequent steps, we used the synthesis route as in Scheme 1. The average yield of the current synthesis scheme was 80%, which was higher than that calculated in the previous method. It is interesting to note that by using sodium hydroxide to neutralize the TFA salt of **4**, it was difficult to extract the pure compound **4** from the reaction mixture; however, when dimethyl amine was used instead of the former base, the extraction of compound **4** by ethyl acetate was much easier.

Synthesis of photopolymers

Different photo-cross-linkable polymers with 2, 5 and 10 mol% chromophore content were prepared. As can be seen from Table 1, with increasing chromophore content the yields of the photopolymers are reduced significantly owing to the fact that the DMIAAm groups act as regulators, but no cross-linking was observed. The relative reactivity ratio values were determined to be $r_{\mathrm{NIPAAm}} = 1.45$ and $r_{\mathrm{DMIAAm}} = 1.33$ [43]. In addition, the glass-transition temperature (T_g) of the photopolymer decreases when inserting more chromophore groups in photopolymer chains. The presence of hydrophobic chromophore groups in the polymer chains possibly results in increased spacing and therefore less interaction between the polymer chains. Thus, the polymer chains are more flexible and the T_g of the respective polymers decreases.

The formation of nanogels from photopolymer solutions

Our preparation method is based on the phase-transition properties of PNIPAAm and its copolymers in dilute aqueous solution with or without the presence of SDS [11–13]. It is well known that the water solubility of PNIPAAm is controlled by the subtle balance between the favourable water interactions i.e., hydrophilic amide groups, and the unfavourable water interactions i.e., hydrophobic isopropyl groups and backbone methylenes. The phase transition occurs upon raising the temperature of the PNIPAAm solution above the critical temperature. At the phase transition, the polymer chains change from coil to globule before aggregating to form suspended particles.

The phase-transition temperatures of PNIPAAm are appreciably independent of molecular weight, polydispersities of PNIPAAm and polymer concentrations [6, 44, 45]. Meewes and coworkers have suggested that the transition temperatures are primarily governed by local interaction effects rather than by properties related to the nature of a polymer molecule in terms of statistical thermodynamics [6, 45]. However, the flexibility and high molecular weight of PNIPAAm allow large conformation changes to be influenced by small changes in the subtle balance between the repulsive forces of the adsorbed surfactant molecules and the attractive forces which occur between the polymer segments as well as between the polymers and the hydrophobic tails of the surfactants [6].

In our study, the polymer concentration was kept constant at 5 g/l. The amounts of SDS in the polymer solutions were varied and kept below the critical micelle concentration ($\mathrm{cmc_{SDS}} = 8.2$ mmol/l) in order to obtain polymer solutions with phase-transition temperatures in a convenient range. In addition, at too high SDS concentration, the phase transition would be suppressed owing to the repulsive electrostatic interactions between the ionic heads of the adsorbed surfactant molecules preventing the polymer chains from aggregating. The phase-transition temperatures of the various polymer solutions measured by DSC are listed in Table 2. As can be seen, the phase-transition temperatures of PNIPAAm copolymers increase upon increasing the SDS concentration. The same behaviour was also reported by Meewes et al. [6]. The elevation of the transition temperature might result from repulsive electrostatic interactions between the ionic heads of the adsorbed surfactant molecules.

The phase-transition temperatures of the NIPAAm copolymers could also be adjusted by insertion of hydrophobic and hydrophilic groups into the polymer chains. The introduction of hydrophobic groups in the polymer chains results in a decrease in T_c, whilst the introduction of hydrophilic moieties raises it [11]. A photopolymer solution with 10 mol% feed chromophore content shows a phase transition at 30 °C, whilst photopolymers with lower chromophore contents, for example, with 2 and 5 mol% feed chromophore contents show a phase transition at 33 °C. The influence of the chromophore on the phase-transition temperatures of polymer solutions in the present study is less significant in comparison with the influence of SDS.

The formation of PNIPAAm particles in aqueous solution is probably similar to particle formation following a nucleation mechanism in precipitation polymerization. The polymer particles with a diameter in the range of nanometres in water at 45 °C were then irradiated with UV light with or without the presence of thioxanthone as a photosensitizer. The aim of using thioxanthone was primarily to accelerate the photo-cross-linking reaction of DMIAAm in aqueous solutions; however, in the present study similar results were obtained when no photosensitizer was used, which might be due to the fact that the solubility of thioxanthone in the hydrophobic polymer domains is still low. This suggests that DMIAAm could be used as an efficient chromophore for the photo-cross-linking reaction in water. The resulting solutions are still opaque at ambient temperature (25 °C), but are not transparent as they were prior to irradiation, suggesting the formation of colloidal nanogels. Visually, the UV-irradiated solutions become opaque while the unirradiated samples or irradiated solutions of homo-PNIPAAm are still transparent.

The turbidity changes of the colloidal nanogels can be observed in Fig. 1. There is an increase in turbidity with a reduction in SDS concentration or increase in the chromophore content and/or the UV irradiation time. This is due to the influence of the nanogel dimensions on the light scattering of the dispersion systems.

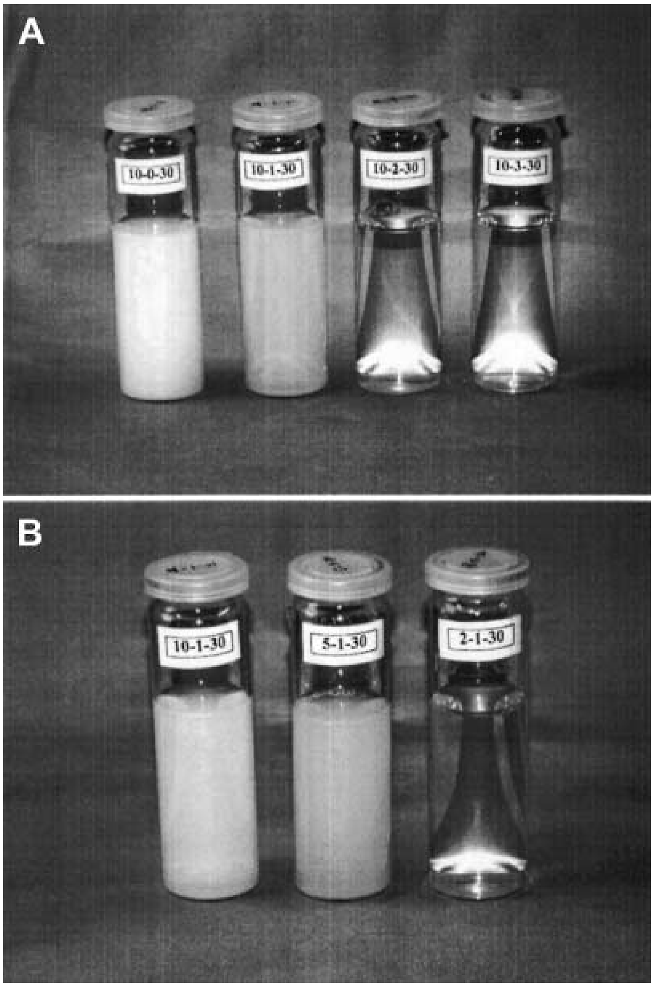


Fig. 1 Changes in turbidities of various colloidal nanogels

Influence of UV irradiation time on nanogel diameter

For the chromophore DMIAAm, the UV absorption in solution was rather weak, so it was not possible to utilize the reduction in the UV intensity of the represented peaks to evaluate the [2 + 2] cycloaddition as in the case of other chromophores, such as acrydizinium salts. Thus, in this study PFG-NMR was employed instead of UV spectroscopy to investigate the network formation. PFG techniques have been used to qualitatively follow the formation of the nanogel by measuring changes in the diffusion coefficient of nanogel particles in D_2O. With increasing UV irradiation time, the diffusion coefficient decreases, as can be seen in Fig. 2 (samples 10-1-*t*). The linear photopolymer without any irradiation showed a diffusion coefficient of 2.4×10^{-11} m^2/s, while the diffusion coefficient of the sample after 10 min

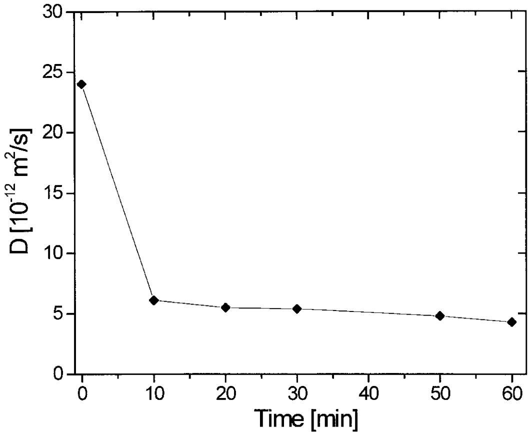


Fig. 2 Dependence of the diffusion coefficients, *D*, of colloidal nanogels on the UV irradiation time. The values were determined by pulsed-field-gradient (PFG) NMR in D_2O at 25 °C for samples (10-1-*t*)

irradiation significantly decreased to 6.0×10^{-12} m^2/s. After longer UV irradiation times, the diffusion coefficients of samples (10-1-*t*) remained constant within experimental error, suggesting the completion of the [2 + 2] cycloaddition reaction and the formation of networks via the photo-cross-linking reaction. From the diffusion coefficients, the hydrodynamic diameter is calculated, which amounts to 16 nm for the free coils in solution and 65 nm for the nanogel particles after cross-linking.

An interesting question is whether the reaction is complete, i.e., whether free chains in solution are present in addition to the nanogel particles after photo-cross-linking. In the diffusion experiment, free chains would cause an additional fast diffusing component in the echo decay. The echo decay for the sample after 10 min of UV irradiation is shown in Fig. 3. A monoexponential decay, corresponding to one monodisperse component, fits the data well, apart from a deviation at high gradient strengths, which might possibly arise from a small fraction of larger structures or a slight polydispersity of the gel particles. In particular, no fast component with diffusion coefficients similar to the linear chains is observed, i.e., the network formation was successfully achieved in all particles via the photo-cross-linking reaction of chromophores.

The influence of the UV irradiation time on the particle size and the swellability of the nanogels was also examined by DLS at 20 °C (swollen state). The results correlated well with the NMR investigation. It can be seen from Fig. 4 that there is a large decrease in the hydrodynamic diameter of the nanogel particles when the UV irradiation time varies from 2 to 10 min. This phenomenon can be explained by the formation of a network via photo-cross-linking reactions, which in turn result in more compact particles. Owing to the lower chromophore content, nanogels of photopolymers with 5 mol% chromophore were formed more slowly than that of photopolymers with 10 mol% chromophore content. It can also be seen from the DLS results that the average hydrodynamic diameters of non-cross-linking polymers varied largely with each measurement and a large distribution of hydrodynamic size was observed owing to large structure fluctuations, while for the nanogels their hydrodynamic diameters were kept almost constant. The particle size or the swellability of the nanogels could be controlled by varying the time of UV irradiation up to 10 min. Polymers with 2 mol% chromophore did not show strong nanogel formation.

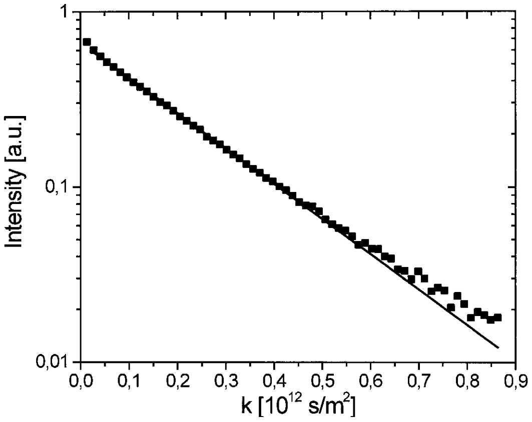


Fig. 3 Echo decay of the PFG-NMR experiment on sample (10-1-10). The data points (*squares*) and the exponential fit assuming a monodisperse size distribution (*solid line*) are in good agreement. *k*: instrumental parameter, $k \propto g^2$, *g*: gradient strength

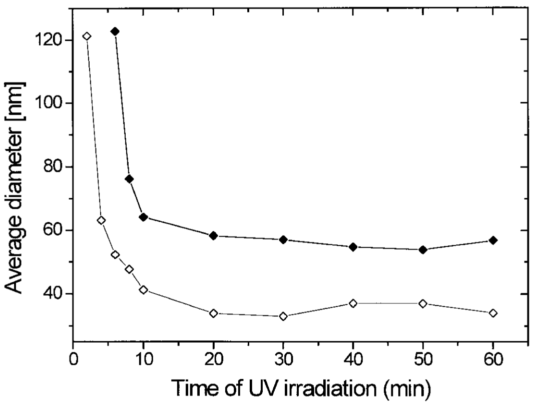


Fig. 4 The influence of the UV irradiation time on the hydrodynamic average diameters of nanogels at 20 °C (*filled diamonds*: 5-2-*t*; *open diamonds*: 10-2-*t*) determined by dynamic light scattering

Influence of SDS concentration on the nanogel diameter

The particle diameters of the nanogels were significantly influenced by SDS concentration (Fig. 5). A significant

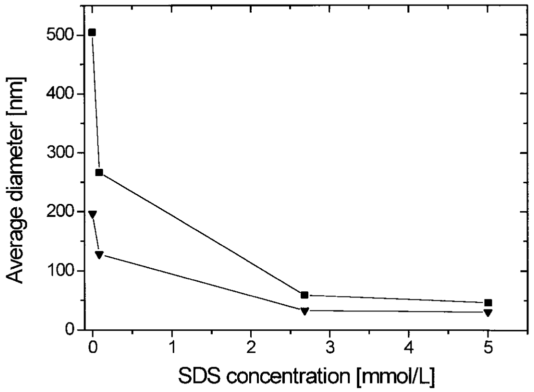


Fig. 5 Influence of sodium dodecyl sulfate (*SDS*) concentration on the nanogel diameter at 20 °C (*squares*: 5-*s*-30; *triangles*: 10-*s*-30)

decrease in the average diameters of sample 10-1-30 or 5-1-30, which contain 0.085 mmol/l SDS, and those of sample 10-3-30 or 5-3-30, which contain 5.000 mmol/l SDS, (at 20 °C) are seen, for example, about 4 and 5.7 times respectively. The higher the SDS concentration, the lower the number of photopolymer chains which aggregate to form a particle, and consequently smaller hydrodynamic diameters were observed.

Although the phase-transition temperature of the photopolymer solution increases with the increase in the SDS concentration, the hydrodynamic average diameters of samples containing 2.680 and 5.000 mmol/l SDS are insignificantly different. SDS functions as a stabilizer and contributes to the increase in the phase-transition temperature by preventing polymer chains from aggregation. It is expected that no colloidal nanogels can be formed at high SDS concentration.

Dependence of the nanogel diameter on temperature and chromophore content in the photopolymer chains

The degree of swelling or changes in the dimension of the gel particles as a function of temperature are typical properties of thermosensitive colloidal gels. DLS has been proved to be a useful technique to examine the dependence of the hydrodynamic average diameter of the nanogel particles on temperature. For the sample with 0.085 mmol/l SDS, insignificant changes in the dimension of the nanogels upon raising the temperature from 10 to 20 °C were seen (Fig. 6). However, dramatic changes in the diameter were observed in the vicinity of the phase-transition temperature (32 °C) owing to the shrinkage of the network. For the samples with 2.680 and 5.000 mmol/L SDS, the sharp changes in swellability were observed at around 36 and 41 °C respectively, which correspond to the phase-transition temperature of the linear polymers.

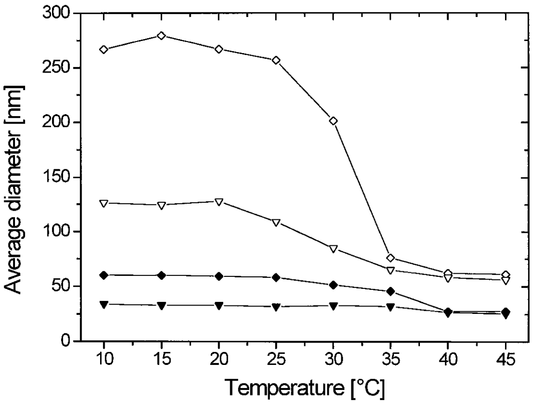


Fig. 6 Dependence of the average hydrodynamic diameter of the nanogels on temperature (*open diamonds*: 5-1-30; *open down triangles*: 10-1-30; *filled diamonds*: 5-2-30; *filled down triangles*: 10-2-30)

It should be noted that at higher chromophore contents, smaller hydrodynamic diameters and a lower swellability of the nanogels are obtained. For example, the average diameters of sample 10-1-30, which contains 10 mol% chromophore, are smaller than those of 5-1-30, which contains 5 mol% chromophore, and the ratio of the diameters at low and high temperatures is 2.2 (at 20 °C) and 4.3 (at 40 °C), respectively. This is obvious as the higher chromophore contents result in the higher cross-linking density in nanogels. Thus, one might expect the nanogels become more hard-sphere-like. The influence of the cross-linking density on the swellablity and the physical state was described by Richtering's and Wolfe's groups [29, 46, 47]. Photopolymers with 2 mol% chromophore content were not able to form well-defined nanogels but possibly weakly cross-linked gels owing to their low cross-linking density. This conclusion derives from the formation of a film rather than individual particles in SEM images and the results determined by DLS.

Morphology of nanogel particles by SEM

SEM images of different samples are shown in Figure 7. The nanogel particles are rather spherical and the particle size distributions are quite narrow. After a short time of UV irradiation, nanogel particles of photopolymers with 5 and 10 mol% feed chromophore content could retain their shape rather than form a film like the non-UV-irradiated polymer solutions or weakly cross-linked gels of 2 mol% chromophore polymers under the same experimental conditions.

The flock coaggulation as can be seen in SEM images might be due to the high concentrations of the colloidal nanogels and surface tension effects caused by the drying process. The average diameters of the nanogels determined from the SEM images are higher than those determined by DLS in which the nanogels are in the shrunken state (at 40 °C). For example, the average diameter of sample 5-1-30 determined from the SEM image is 115 nm, while by DLS at 40 °C the average diameter is 62 nm. This is unexpected as the nanogels for the SEM measurements were dried under critical conditions (heating and long vacuum) but we can explain these differences as follows. Firstly, the particles might be flattened on the supporter (aluminium foil) during the sample preparation as suggested by Jones and Lyon [28], so the apparent diameters of the particles in the SEM images were larger. Secondly, the SEM images are only locally representative and a small fraction of smaller particles, which would significantly contribute to the average diameter, might not be accounted for in the SEM images. Both these factors could cause the dimension

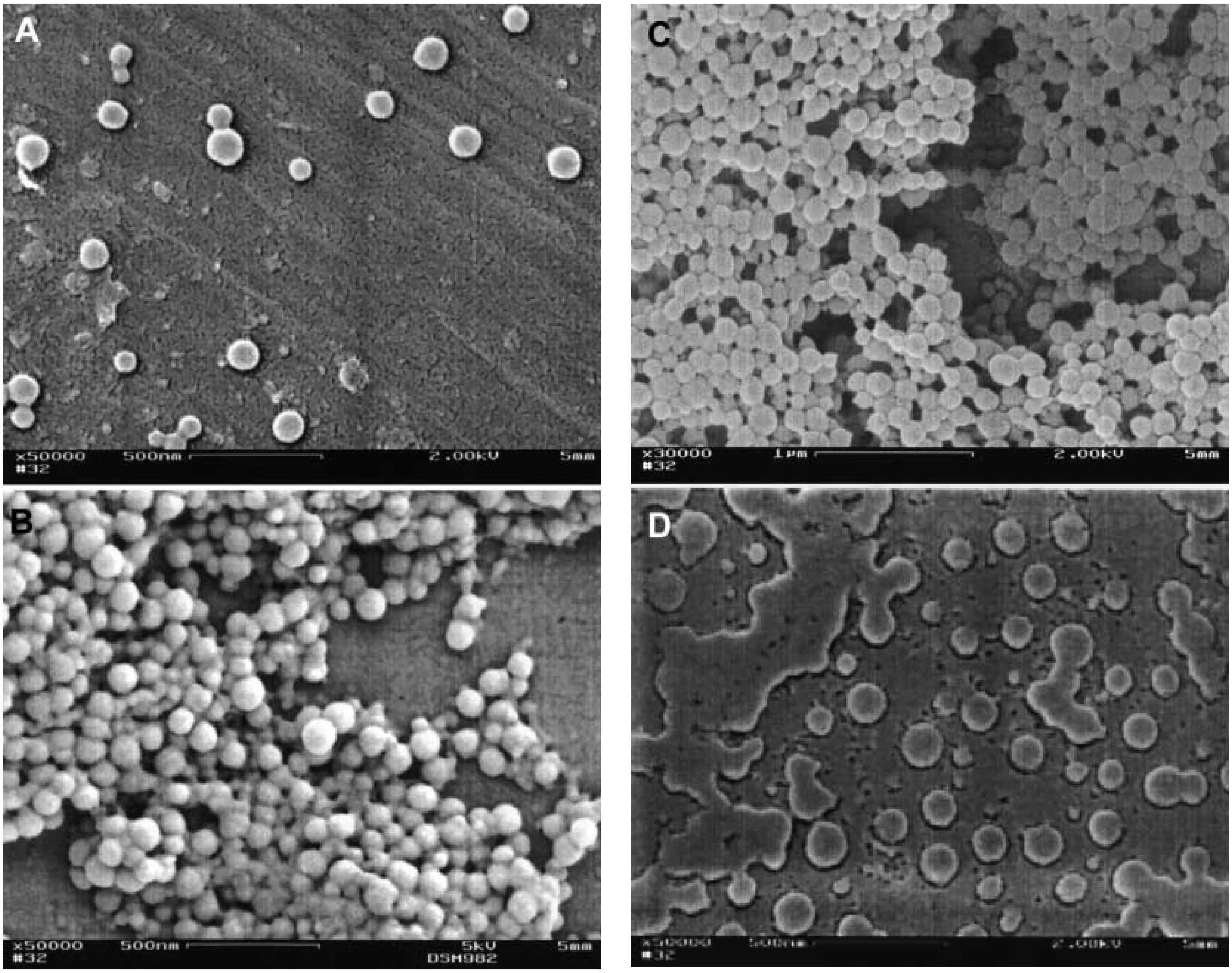


Fig. 7 Scanning electron microscopy images of the nanogels (**A**: 10-0-30; **B**: 10-1-30; **C**: 5-0-30; **D**: 5-1-30)

differences. In fact, the SEM of smaller particle sizes, for example, 10-2-30 and 10-3-30, were not imaged successfully under the scanning electron microscope. However, the dependence of the average diameter of the nanogel particles measured from the SEM images on the chromophore content is well correlated with the results determined by DLS, i.e., the higher the chromophore content, the lower the average diameter which was observed.

Conclusions

Colloidal nanogels have been successfully prepared by UV irradiation of thermosensitive photopolymers in aqueous solutions with various SDS concentration below the cmc. The phase-transition temperatures of thermosensitive photopolymers in aqueous solutions and subsequent colloidal nanogels could be controlled by varying the SDS and/or chromophore content. The dimension and the swellability of the nanogels obtained could be controlled not only by the chromophore content but also by the UV irradiation time and the SDS concentration. The colloidal nanogels could be formed with well-defined shape if the feed chromophore content in the photopolymers were high enough, for example, in our study the chromophore content must be 5 mol% or higher. The current work may open a new route to prepare colloidal nanogels and extend potential applications of photo-cross-linkable polymers.

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