Polym. Bull. (2010) 64:107–114
DOI 10.1007/s00289-009-0134-z

Room temperature preparation of highly crosslinked microgels

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Received: 5 June 2009 / Revised: 3 July 2009 / Accepted: 7 July 2009 /
Published online: 21 July 2009

Abstract A series of highly crosslinked microgels has been prepared at room temperature via photoinitiated polymerisation in dilute solution using methyl methacrylate (MMA) and ethylene dimethacrylate (EDMA), respectively as non-functional monomer and crosslinker in *N*,*N*-dimethylformamide (DMF) as a solvent. The effect of monomer concentration and EDMA/MMA ratio on the yield, molecular weight and microgel size was studied and the data were compared to those previously obtained for microgels of similar composition prepared by thermal initiation. This mild polymerisation method yields better results compared to the more conventional thermal method, since it allows higher monomer concentrations to be employed as well as a better microgel size control. Consequently, the method can be advantageously used for the preparation of highly crosslinked microgels with improved properties, particularly useful, e.g. for molecular imprinting applications.

Keywords Microgels · Photoinitiation · Free radical polymerisation · Molecular imprinting

Introduction

The term "microgel" [1] defines unimolecular, crosslinked polymer particles possessing a size comparable to the statistical dimensions of uncrosslinked macromolecules (10^1–10^2 nm), which give rise to stable, low-viscosity solutions in appropriate solvents. These materials, first described by Staudinger [2] in the 1930s, can be considered as an intermediate category of polymers, which combine the characteristics of both linear macromolecules and three-dimensional networks [3–5]. For a proper understanding of microgel structure, it may be helpful to remark

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that such macromolecules closely resemble in their structure and behaviour soluble, crosslinked biological macromolecules such as proteins.

Microgels have found wide technological application as additives with binding or stabilising properties in the industrial manufacture of coatings [6]. Furthermore, in recent years the recognition of their unique characteristics has stimulated considerable research on their use as soluble supports for low molecular weight reagents, scavenging agents or (bio)catalysts [7–14], drug-delivery systems [5, 15, 16], organic and hybrid nanocomposites [17–20], responsive assemblies [21, 22] and as biomimetic receptors/catalysts [23–28]. The latter application involves use of the technique known as "molecular imprinting", in which a target molecule acts as a template around which interacting and cross-linking monomers are arranged and copolymerised to form binding sites complementary to the template and held in place by the cross-linked structure [29, 30]. Molecularly imprinted microgels are comparable in size to natural systems capable of molecular recognition and catalysis such as antibodies or enzymes, hence their successful preparation represents a major step towards the development of "plastic analoga" of these biomolecules.

Microgels are most conveniently prepared by polymerisation in dilute solution, where intramolecular crosslinking becomes favoured compared to intermolecular crosslinking for entropic reasons; moreover, the growing microgels become stabilised towards macrogelation by the osmotic repulsion forces generated by the interaction of solvated polymer chains and loops at the periphery of the microgel particles (steric stabilisation) [31]. Clearly, to achieve steric stabilisation the microgel chains must be efficiently solvated by the polymerisation solvent, so that the growing microgels can be considered to be in swelling equilibrium with the surrounding medium.

Steric stabilisation is sufficient to stabilise the growing microgels against macrogelation if the monomer concentration is reduced below a critical value (critical monomer concentration, C_m). This value is dependent on many factors such as the polymerisation methodology and conditions and especially the crosslinking monomer content. In particular, a high content of crosslinking monomer has a detrimental effect on the stability of the growing microgels, since it reduces the length of solvated polymer chains and loops making out the stabilising shell at the periphery of the microgel particles. This represents the major drawback in the preparation of molecularly imprinted microgels, since a high crosslinking degree is mandatory in order to have stable imprinted cavities within the polymer network: while it is still possible to prepare highly crosslinked microgels by lowering the concentration of the monomer mixture down to a few % by weight [2, 32], such a high dilution shifts the association equilibria that characterise the formation of the template–monomer assembly towards the free template and monomers, thereby negatively affecting the stability of the assembly and consequently the efficiency of the imprinting procedure. This problem may be overcome by a careful choice of sufficiently strong binding interactions between template and monomers or, more simply, by lowering the polymerisation temperature. It is in fact predicted that lower temperatures improve the stability of the template–monomer assembly and consequently the imprinting effect; indeed, when comparing traditional MIPs

prepared by thermally initiated polymerization or by photopolymerization at lower temperature, the latter showed better selectivity [33].

Whereas quite a number of different crosslinked polymer formats (bulk polymers, micro- and nano-spheres, films, membranes) have been prepared by radical polymerisation at low temperature, highly crosslinked microgels have been up to now exclusively prepared via conventional thermally promoted free radical polymerization with azo- and per-oxide initiatiors, which usually require temperatures in the range 60–80 °C. Therefore, we started an investigation aimed at developing polymerisation procedures for the synthesis of highly crosslinked microgels at low temperature which could be subsequently applicable for the preparation of molecularly imprinted polymers.

Experimental section

Chemicals

Monomers ethylene glycol dimethacrylate (EDMA) (Aldrich, 98%) and methyl methacrylate (MMA) (Aldrich, 99%) were freshly distilled to remove inhibitors prior to use. Radical initiator 2,2′-azobisisobutyronitrile (AIBN) was re-crystallized from ethanol. Other chemicals and solvents were of reagent grade and were used as received.

Microgel preparation

Monomers were mixed in the desired weight ratios in a glass reactor. The required amount of monomer mixture was weighted in the polymerisation reactor equipped with a magnetic stirring bar and diluted with 100 mL DMF. AIBN (3% w/w with respect to the monomer mixture) was then added and the resulting solution was purged with argon for 5 min. Finally, the polymerisation was started by switching on the immersion UV lamp (low-pressure mercury lamp, wavelength 254 nm) and the magnetic stirrer. Polymerisation was carried out at room temperature for 24 h.

Critical monomer concentrations (C_m) were determined for each composition of the monomer mixture by performing a series of polymerisation experiments with increasing concentration of monomer mixture and recording the highest monomer concentration which could be employed without sample gelation.

The polymerisation solution was concentrated to about one-third of the original volume and subsequently added dropwise to the fivefold volume of diethylether under efficient stirring. The precipitated solid was collected by centrifugation (10 min at 4,000 rpm), repeatedly washed with diethylether and finally dried in air to constant weight.

Characterisation of microgels

Gel permeation chromatography (GPC) measurements were performed on an apparatus consisting of a Shimadzu 10AD solvent delivery system, four Waters

Styragel linear columns, a Shimadzu SPD-10A UV–vis detector and a Shimadzu RID-10A RI detector using tetrahydrofurane (THF) as the mobile phase with a flux of 0.7 ml min^{-1}. Poly(methylmethacrylate) standards were used for the calibration.

Dynamic light scattering (DLS) measurements were obtained with a Particle Sizing Systems Nicomp model 370 correlator equipped with a thermostated cell holder and a Spectra Physics series 2016 Ar laser operating at 488 nm. Hydrodynamic particle diameters were obtained from cumulant fits of the autocorrelation functions at 90° scattering angle.

Probes for GPC and DLS measurements were prepared by dispersing microgel samples in THF (10 mg ml^{-1}, 20 min sonication) followed by prefiltration on a 0.45 μm membrane filters.

Results and discussion

At the outset of our investigation, we chose to deal initially with a well-established technique for room temperature polymerisation, namely photoinitiated radical polymerisation of monomer mixtures containing a free radical initiator such as azobis(isobutyronitrile) (AIBN).

We investigated the polymerisation of standard monomer mixtures comprising the nonfunctional monomer methyl methacrylate (MMA) and the crosslinker ethylene dimethacrylate (EDMA) with a crosslinker content of 70, 80 and 90% w/w. The choice of the chemical initiator and of the polymerisation solvent was made according to our previous experience with the thermal polymerisation of these mixtures [23]: consequently, we employed 3% w/w (with respect to the monomer mixture) AIBN and *N*,*N*-dimethylformamide (DMF) as the polymerisation solvent.

Photoinitiated polymerisation was carried out in a stirred reactor with an immersion UV lamp irradiating at 254 nm. First of all, the critical monomer concentration C_m for each of the monomer mixtures under investigation was determined. Interestingly, the recorded values were found to be significantly higher than in the case of thermal polymerisation. For the three crosslinker contents employed (70, 80 and 90% w/w) C_m of 7, 5, and 3% w/w were established under the above mentioned reaction conditions; for comparison, thermal initiation of the polymerisation mixture with 70% crosslinker content in DMF yields a C_m of only 3% [23].

The microgels could be conveniently isolated by precipitation as white powders, readily redispersable in many different organic solvents such as dialkylamides, nitriles, ketones, dichloromethane, dimethylsulfoxide and THF. Polymerisation yields were found to be lower than in the case of thermal initiation, especially for the synthesis run with the highest dilution (Table 1). However, it must be remarked that yields were not optimised and that photoinitiated polymerisation was run for only 24 h while thermally initiated polymerisation was carried out for 4 days [23]. We have experimentally verified in one case (microgel with 70% w/w crosslinker at 3% w/w concentration) that doubling the polymerisation time leads indeed to a markedly higher yield (50%), although we have also observed that even longer reaction times cause the phase separation of significant quantities of macroscopic gel.

Table 1 Synthesis and GPC characterisation of highly crosslinked microgels via room temperature photoinitiated polymerisation

Crosslinker (% w/w)	Monomer conc. (% w/w)	Yield (%)	M_w	M_n	M_w/M_n
70	1	34	2.7×10^3	1.6×10^3	1.7
70	3	30	2.1×10^4	1.2×10^4	1.8
70	5	60	2.4×10^4	7.4×10^3	3.2
70	7	62	nd	nd	nd
80	1	31	3.6×10^3	2.2×10^3	1.7
80	3	55	1.6×10^4	4.2×10^3	3.9
80	5	63	nd	nd	nd
90	1	36	4.1×10^3	2.4×10^3	1.7
90	3	60	nd	nd	nd
70[a]	1	78	1.5×10^4	3.3×10^3	4.7
70[a]	3	97	5.1×10^5	8.6×10^3	59
80[b]	1	66	3.4×10^4	1.0×10^4	3.4

nd Not determined

[a] Microgel prepared by thermal initiation, see Ref. [23]

[b] Microgel prepared by thermal initiation, see Ref. [34]

The isolated microgels were redispersed in THF and characterised by gel permeation chromatography (GPC). When applied to microgels, GPC yields as a rule only apparent molecular weight data since the calibration has to be performed with linear polymers, no microgel standards being available. In particular, highly crosslinked microgel particles possess a much more densely packed structure than statistical coils of linear polymer molecules of the same molecular weight, hence they are significantly heavier (10–20 times) than linear polymer standards with the same hydrodynamic radius, as the ones used as standards in GPC [23]. In spite of this, important information on the polydispersivity of the sample are obtained from the chromatograms, and the molecular weight data can be used for internal comparison within the same microgel set.

It was soon found out that the microgels prepared at a concentration equal to the C_m could not be measured because although they were apparently soluble they turned out to contain large aggregates that prevented solution prefiltration prior to injection in the GPC apparatus. For the other microgels, remarkably small molecular weights and narrow molecular weight distributions were recorded (Table 1). GPC characterisation data of microgels obtained by thermal polymerisation of the same monomer mixtures in DMF are reported at the bottom of the Table for comparison. However, it must be remarked that these data were obtained with a different GPC apparatus and, most notably, with a calibration set of different nature [polystyrene standards instead of poly(methylmethacrylate)]. Nevertheless, it is notable that, although with both synthetic methods the molecular weights and the polydispersivities increase with increasing monomer concentration (and, to a lesser extent, with increasing crosslinking degree), such increase is far less marked in microgels

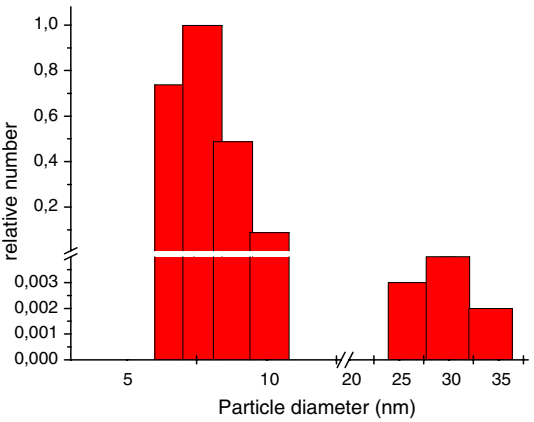

Fig. 1 Size distribution diagram for the microgel with 70% w/w crosslinking prepared at 5% w/w concentration according to DLS

prepared by photopolymerisation. This highlights the fact that the incidence of the intermolecular reaction with increasing monomer concentration, which leads to microgel agglomeration, hence to higher molecular weights and broader molecular weight distributions, is less marked in the case of the photointiated polymerisation, which is also confirmed by the higher C_m attainable with this method.

The microgel solutions were also subjected to analysis by dynamic light scattering (DLS). The samples were found to be invariably bidisperse, with a numerically predominant fraction of particles of small diameter (sometimes close to the detection limit of the DLS apparatus) and a much smaller fraction of higher diameter. This is not entirely surprising, since studies on microgel formation by radical polymerisation of MMA/EDMA solutions have shown that a bidispersion in the microgel product is characteristical of the system and is invariably present already in the initial stages of the reaction [35, 36]. A typical size distribution diagram is reported in Fig. 1 for the microgel with 70% w/w crosslinking prepared at 5% w/w concentration.

The size of the microgels (Table 2) was found to depend heavily on the concentration of the starting monomer mixture, whereas it was much less dependent on the crosslinking degree. For example, moving from 3 to 5% monomer concentration in the polymerisation of the monomer mixture with 70% crosslinking degree produced an increase in the average size of the predominant fraction from 2.1 to 8 nm, whereas increasing the crosslinker to 80% while

Table 2 DLS characterisation of highly crosslinked MMA/EDMA microgels prepared by photoinitiated solution polymerisation at room temperature

Crosslinker (% w/w)	Monomer conc. (% w/w)	Average size (nm) (small/large particles)
70	1	nd
70	3	2.1/6.5
70	5	7.7/30
80	1	nd
80	3	2.4/10

nd Not determined

keeping the monomer concentration at 3% produced only an increase in size from 2.1 to 2.4 nm.

In conclusion, we have been able to demonstrate that photoinitiated radical solution polymerisation at room temperature is a viable technique for the preparation of highly crosslinked microgels. In comparison to the thermally initiated procedure, the polymer product is characterised by smaller molecular weights and narrower molecular weight distributions, and it can be obtained using higher monomer concentrations, which overcompensates the lower polymerisation yields. Remarkably, the comparatively high employable monomer concentration as well as the low polymerisation temperature are beneficial for the envisaged application of this polymerisation method, namely the preparation of molecularly imprinted microgels, since both ensure an enhanced stability of the template–monomer assembly and consequently a higher imprinting efficiency.

We are currently carrying out further optimisation of the method from the point of view of the polymerisation yield. Furthermore, application of this procedure to the preparation of molecularly imprinted microgels is currently underway.

Acknowledgments Financial support from European Community through the Marie Curie RTN "NASCENT" (contract no. MRTN-CT-2006-033873) is most gratefully acknowledged.

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