A Library of Thiol-Terminated Methacrylate Telomers Prepared by Photoinitiated Iniferter Mediated Polymerization for Use in Modifications of Chromatographic Surfaces by the "Grafting to" Approach

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ABSTRACT: A library of thiol-terminated methacrylate telomers aimed for use in surface modifications of chromatographic support materials has been prepared by iniferter mediated polymerization, using isopropylxanthic disulfide as a photoiniferter. The telomers range from hydrophobic to hydrophilic and were prepared in different lengths, with the length being adjusted by the ratio of monomer to iniferter used in the polymerization mixture. The telomers were characterized by size-exclusion chromatography and MALDI-TOF-MS. In initial surface characterization experiments, the prepared telomers were attached to the inner surface of fused silica capillaries by radical initiated addition to vinyl groups, and the electro-osmotic flow (EOF) in the prepared capillaries was determined in a capillary electrophoresis set-up. The EOF measurements verified surface grafting. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 117: 2781–2789, 2010

Key words: telomer; iniferter; living polymerization; methacrylate; thiol-terminated; grafting to

INTRODUCTION

In the preparation of new materials for separation science, both the physical properties of the support and the possibilities of dressing it with a proper surface chemistry are important for attaining useful materials. When a support material with suitable porous and mechanical properties is available, different strategies for surface modification offer ways of achieving a wide variety of selectivities from the same support substrate. One attractive strategy for surface modification is the 'grafting to' approach, in which a preprepared molecule or polymer chain is attached to anchoring points on a surface, a coupling that is initiated either from the surface, by the molecule to be attached, or by an external initiator. 'Grafting to' has the advantage of allowing the attached moieties to be fully characterized before attachment, and the thickness of the grafted layer can also be controlled by adjusting the size of the attached polymer chains.[1] The success and relative interchangeability of separation columns in high performance liquid chromatography (HPLC) based on C_{18} silica is largely due to the fact that the functional group is a monodisperse telomer, namely an ethylene nonamer terminated in a halogenated or alkoxylated silane, which yields surfaces with comparable properties on different support materials. Further, the 'grafting to' approach enables the attachment of chains with different functionalities on a single interactive surface. This can either be done in a parallel way by using a mixture of telomers,[2] or in a sequential manner provided the first functionality grafted does not occupy all attachment points.[2] This ability to create layers with more than one chemistry is a clear advantage in the design of new surfaces with controlled interaction properties and in the preparation of mixed-mode stationary phases.[3]

The ability to control the properties of the attached group or polymer chain is essential when the 'grafting to' approach is going to be used for altering the characteristics of a surface. The size of the attached chain is of importance, as well as its chemical composition, expressed by the backbone structure, the pendant chains, and the end terminal functionalities. Hence, the techniques used to synthesize such telomers need careful control of key parameters, such as overall composition, size, and terminals.

The synthesis of short polymer chains of controlled size and composition can be achieved by various living radical polymerization schemes, including anion,[4] atom transfer radical (ATRP),[5,6]

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iniferter-controlled,[7] nitroxide-mediated,[8,9] and reversible addition-fragmentation transfer (RAFT)[10,11] polymerizations, each having their advantages and limitations. Traditional free radical polymerizations suffer from lack of control over the progress, and hence the outcome, of the polymerization. Controlled radical polymerization schemes offer, on the other hand, a mechanism for controlling the molecular size as the rate of monomer incorporation in these polymerizations are controlled by the kinetics rather than by diffusion and rate of initiation.

The iniferter-concept was introduced by Otsu et al.[12] in early 1980's, and iniferters have since then been used to achieve control in thermally[13–15] as well as photoinitiated polymerization systems,[14–16] for the synthesis of both linear and branched mono- and copolymers. In iniferter mediated polymerizations, the control originates from the iniferter used and its characteristics. An iniferter combines the role of initiator, transfer agent, and chain terminator in one compound, and in a photoiniferter both the initiation and the dissociation of the reversibly terminated chain are trigged by ultraviolet (UV) light. The progress of the polymerization results in the iniferter being propagated as the terminal of the polymer chain. By careful choice of iniferter, one can therefore design a desirable end group functionality into the polymer.[7] Isopropylxanthic disulfide is an iniferter that is capable of producing polymer chains with a terminal thiol functionality (after hydrolysis or thermal decomposition[17]), which enables coupling of the prepared polymer to surface functionalities such as epoxy or vinyl groups by nucleophilic addition to epoxy groups[18,19] or (anti)-Markovnikov addition to vinyl groups.[20] The thiol end group also facilitates attachment onto gold surfaces for atomic force microscopy (AFM) or X-ray photoelectron (XPS) studies.

Verification of grafting and changes in surface characteristics can be performed in a number of ways, such as elemental analysis, XPS, or infrared (IR) spectroscopy for the verification of added functionality or atoms. Changes in surface characteristics can be investigated using AFM or scanning electron microscopy (SEM)[21] to locate structural changes. Measurements of electro-osmosis (EOF) can also be used in characterization of surfaces,[22] to assess surface charge, shielding effects, and grafting density. A particular advantage of EOF measurements is that the characteristics of the water–surface interface are probed, making the EOF approach suitable for nondestructive analysis of materials designed for use under (partly) aqueous conditions, including biocompatible medical materials and medical devices. This approach should also be well suitable for analysis of chromatographic media, were the interactions of interest take place at a solvent–surface interface.

In our on-going work aimed at preparation of new chromatographic support materials with controlled bulk and surface properties, the goal is to develop techniques that enable the preparation of a matrix of supports and surface functionalities. To facilitate this work, we decided to prepare a library of ligands, ranging from moderate to mild hydrophobicity, as well as selected hydrophilic functionalities. Mildly hydrophobic ligands could be used in the preparation of materials for hydrophobic interaction chromatography while hydrophilic ligands could be used in combination with other functionalities, thereby forming hydrophilic 'cushions', to shield the surface from amphiphilic solutes such as proteins. This work consequently describes the synthesis of a library of thiol-terminated methacrylate telomers of adjustable length made from starting monomers with different functionality and hydrophobicity, using isopropyl xanthic disulfide as a photoiniferter. The effect of some experimental parameters on the polymerization, yield, and control are investigated and discussed. The prepared telomers were characterized primarily by size-exclusion chromatography (SEC) and matrix-assisted time-of-flight mass spectrometry (MALDI-TOF MS) to yield information on progress of the reaction and the size of the resulting telomers. As the aim of preparing the telomer library is for surface modifications of chromatographic support materials, grafting the telomers onto the inner surface of fused silica capillaries was chosen as a model system, and the resulting effect of grafted chain on the electro-osmotic flow (EOF) in a capillary electrophoresis set-up was investigated for selected telomer chains.

EXPERIMENTAL

Materials

The monomers used (Fig. 1) were methyl methacrylate (MMA), ethyl methacrylate (EMA), butyl methacrylate (BMA), benzyl methacrylate (BzMA), 2-hydroxyethyl methacrylate (HEMA), and 2,3-epoxypropyl methacrylate (GMA). These, as well as the isopropylxanthic disulfide (IXD) iniferter, and the 4,4′-dithiodipyridine were from Aldrich (Schnelldorf, Germany). Tetraethylthiuram disulfide (TED) was from Sigma (St. Louis, MO). Before telomerization, the inhibitors were removed from the monomers by passing through packed beds of basic alumina, Brockman activity I, 150 mesh (Aldrich). The MALDI-matrices used were dihydroxybenzoic acid (Sigma) and trans-3-indoleacrylic acid (Aldrich). The silanization reagent, 3-(trimethoxysilyl)propyl methacrylate and the initiator 2,2′-azobis(2-methylpropionitrile) (AIBN) used in the capillary modifications were from Fluka (Buchs, Switzerland). Polyamide-

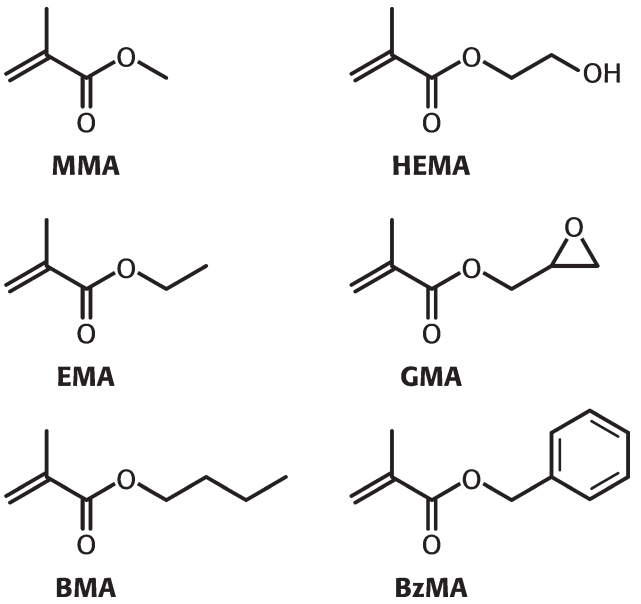

Figure 1 Structures of monomers used in the initial telomer library.

coated fused silica capillaries (50 μm i.d.) were purchased from Polymicro Technologies (Phoenix, AZ). Anhydrous sodium hydroxide (analytical grade) was from Merck (Darmstadt, Germany). The organic solvents, such as diethyl ether and methanol (Merck), acetone (Fisher Scientific, Loughborough, UK), dimethylformamide (DMF; Labscan, Dublin, Ireland), dimethylsulfoxide (DMSO; Scharlau, Sentmenat, Spain), *N*-methylpyrrolidinone (NMP; Aldrich), tetrahydrofuran (THF; J.T Baker, Deventer, Holland), toluene (Fluka, Buchs, Switzerland), were of analytical grade and used without further purification. Perdeuterated tetrahydrofuran (THF-*d8*) was from Deutero (Kastellaun, Germany) and HPLC-grade THF from VWR (Leuven, Belgium). Water was produced by a Millipore (Bedford, MA, USA) Ultra-Q system.

Methods

Photoiniferted polymerization

Controlled telomer polymerizations were performed in a CureZone (UV Process Supply, Chicago, Illinois) UV irradiation chamber equipped with a 400 W Hg lamp. A float glass sheet was placed between the lamp and the reactor inside the curing chamber, providing a wavelength cut-off at ~ 320 nm. This left the 365 nm Hg line as the most intensive UV wavelength. The polymerizations were carried out in a double-walled 100 mL Ingold vessel, thermostatted to 20°C by cooling liquid circulated by means of a Lauda (Königshofen, Germany) UKT 350 cryothermostat. In a typical polymerization experiment, the monomer and iniferter were dissolved in the reaction solvent (Table I). The polymerization solutions were degassed by purging with nitrogen gas for 10 min to remove dissolved oxygen, and thereafter transferred to the reaction vessel. Slow N_2 purging was used throughout the polymerizations to ensure

TABLE I
Selected Polymerization Mixtures

Annotation	Monomer	Solvent	Monomer mmol/mL	Monomer/IXD Molar ratio	Expected MW Da	Mp[a] Da	PDI[b]
H054	HEMA	THF	1.3	17:1	2200	2,204	1.20
H055	HEMA	THF	1.3	31:1	4000	3,010	1.14
H056	HEMA	THF	1.3	32:1[c]	4000	3,289	1.19
H057	HEMA	THF	1.3	74:1	9600	GEL[d]	N/A
H058	HEMA	THF	1.3	173:1	22,500[e]	GEL[f]	N/A
H059	HEMA	THF	1.3	12:1	1600	1,532	1.13
BZ036	BzMA	THF	1.2	24:1	4200	4,191	1.15
BZ038	BzMA	THF	1.2	9:1	1600	2,361	1.16
BZ039	BzMA	THF	1.2	56:1	9900	7,591	1.17
BZ040	BzMA	THF	1.2	132:1	23,000[e]	17,524	1.16
BZ041	BzMA	THF	1.2	26:1	4600	3,227	1.14
BZ042	BzMA	DMSO	1.2	26:1	4600	7,591	1.14
BZ043	BzMA	NMP	1.2	26:1	4600	7,232	1.10
BZ044	BzMA	DMF	1.2	26:1	4600	6,510	1.10

[a] Molecular weight determined by SEC in polystyrene equivalents.
[b] Polydispersity index.
[c] Polymerization mixture containing 1 : 1 TED : iniferter.
[d] A gel-like precipitate formed after 40 min reaction, with the preceding fraction (30 min) having reached 70% monomer conversion.
[e] Expected molecular weight outside the SEC calibration window; exclusion limit of the size-exclusion column used was 20 kDa.
[f] A gel-like precipitate formed after 30 min reaction with the preceding fraction (20 min) having reached 46% monomer conversion.

an air-free environment and continuous mixing. Aliquots were collected from the polymerization mixture at predetermined intervals to monitor the polymerization reaction. After the polymerization was completed, the polymerization mixture was poured into centrifugation tubes, precipitated by diethyl ether (HEMA) or methanol/water mixtures (MMA, EMA, BMA, GMA, and BzMA), and the produced telomers isolated by centrifugation. In parallel, polymerizations were performed in sealed 1.5 mL borosilicate glass vials instead of in the reactor, in which magnetic stirring, but no cooling was employed.

Iniferter decomposition under UV conditions

The stability of the iniferter in solution under UV light was investigated using ^{1}H-NMR spectroscopy. An approximately 2 m*M* solution of the iniferter in THF-*d8* was prepared in an NMR tube and irradiated under UV light in the curing chamber. NMR spectra were recorded at $t = 0$, and at 15 s intervals of irradiation time to monitor the stability of the iniferter and the S—S bond. ^{1}H-NMR (360 MHz) measurements were performed on a Bruker Avance DRX-360 spectrometer. The chemical shifts were determined with respect to the solvent signal.

Temperature effect

Mixtures of monomer, HEMA, and the iniferter in THF were transferred to 1.5 mL glass vials, of which two series were polymerized in the UV curing chamber, one thermostatted to 20°C and one without applied cooling. The third series was shielded from light and placed in a convection oven at 70°C, which is approximately the temperature reached inside the UV curing chamber during operation. The vials in the series were removed from the UV curing chamber, or the heating oven, respectively, after reaction times varying between 10 and 165 min for the irradiated series. An additional time point at 8 h was added in the non irradiated series. All solutions were thereafter analyzed by SEC to determine whether polymerization had taken place. The contents of the vials were precipitated by diethyl ether and the product isolated by centrifugation. The recovered polymer was thereafter dried and weighed. The weight of each precipitated fraction was compared to the expected weight, based on the amount of monomer charged.

Reducing the risk of bimolecular termination

In an additional experiment, tetraethylthiuram disulfide was added to polymerization mixtures with monomer to iniferter ratios of $\sim 30 : 1$, in a TED to iniferter ratio of 1 : 1. As in the regular experiment, the iniferter, monomer, and added reagent were dissolved in the reaction solvent, THF, and polymerization conditions were identical to the regular polymerizations performed.

Thiol-terminated telomers

Hydrolysis of the iniferter-terminated telomers was achieved by dissolving the telomers (50–100 mg/mL) in either methanol (for HEMA, MMA, and EMA) or acetone (for BzMA, BMA, and GMA), followed by addition of 5 *M* sodium hydroxide, to a total concentration of 5% v/v in the solution. This solution was thoroughly stirred for 24–48 h and the product was thereafter precipitated and isolated by centrifugation, as described for the 'raw' telomers.

Size exclusion chromatography

Characterization of the telomers by SEC was performed on a system set-up consisting of an LKB (Bromma, Sweden) model 2150 HPLC pump, a Rheodyne 7125-081 injector (loop size 5 μL), and a variable wavelength UV absorbance detector from Gamma Analysentechnik (Bremerhaven, Germany) operated at $\lambda = 254$ nm. The column used was a Shodex GPC KF402.5 HQ (4.6× 250 mm, 3 μm) from Showa Denko (Kawasaki, Japan) with a nominal exclusion limit of 20 kDa. THF was used as the eluent at a flow rate of 0.3 mL/min. Calibration was performed with narrow polydispersity polystyrene (PS) standards from Polymer Laboratories (Church Stretton, UK). A Clarity Chromatography Data Station software with GPC Extension from DataApex (Prague, Czech Republic) was used for the data analysis. Benzyl alcohol was used as a flow marker to ensure consistent calibration.

MALDI-TOF-MS

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometric analyses were carried out on a Voyager DE-STR MALDI-TOF MS instrument from Applied Biosystems (Foster City, CA). Spectra were collected in positive linear mode (25 kV acceleration voltage, 85% extraction voltage, delay time 150 ns) while maintaining a laser intensity slightly above the threshold of the individual matrix. Spectra were processed using the DATA EXPLORER software from Applied Biosystems. The sample and the matrix were dissolved separately and diluted to concentrations of approximately 2 mg/mL for the analyte, and 15–20 mg/mL for the matrix. The solvents used were either methanol (HEMA, MMA, EMA), or acetone (BzMa, BMA, GMA) for the telomers, with the same solvent used to dissolve the matrix. To slow down the drying and gain a better crystal

formation, 20% (v/v) of water was added to the final solution of the matrix. The matrix and sample solutions were mixed before placement on the MALDI plate by combining 2 μL of the sample and 10 μL of the matrix solution. The mixture was vortexed briefly and thereafter 0.5 μL was applied to the MALDI plate.

Hydrolytic end group conversion

Conversion of the end group into a thiol was verified by determination of free thiols using UV spectroscopy and 4,4′-dithiodipyridine. The procedure was adopted with modifications from Egwim and Gruber[23] and the determinations were performed on telomers that had been hydrolyzed in solution, precipitated, isolated, dried, and weighed. In addition, the thiol contents were determined in solutions of nonhydrolyzed telomers at the same concentrations. The telomers were weighed and dissolved in DMSO (for GMA and BMA), or methanol (HEMA, EMA, and MMA) to an expected thiol concentration of about 3 m*M*. A sample portion of 30 μL was added to a mixed solution of 3 mL triethylamine (0.1% v/v in DMSO) and 50 μL of 4,4′-dithiodipyridine (12 m*M* in DMSO). After 5 min, 100 μL concentrated acetic acid was added to quench the reaction and the UV absorbance measured at 360 nm. Calibration was performed by stock standards of 1-octanethiol in DMSO, and a blank was measured with the sample volume being replaced by solvent.

Attachment of telomers to the capillary wall

The inside of the fused silica capillaries was pretreated with 3-methacryloyloxypropyltrimethoxysilane (γ-MAPS) to introduce vinyl bonds to the silica surface, thereby introducing attachment points for covalent attachment of thiol telomers to the silica surface. Pretreatment was performed following a published protocol,[24] with the exception that the etching step was omitted. The capillary was briefly flushed with 1 *M* aqueous sodium hydroxide, then with water followed by acetone, and finally with toluene. The capillary was thereafter filled with a nitrogen purged (10 min) silanization mixture, consisting of 1 : 9 (v/v) γ-MAPS in toluene. The filled capillary was plugged with rubber stoppers and left to react at room temperature for 2 h. It was then rinsed with toluene and dried with a stream of nitrogen. The vinyl groups introduced onto the capillary inner wall by the γ-MAPS reagent were used for attachment of functional methacrylate telomers using a free radical initiated addition.[25] The initiator AIBN (2 mg) was dissolved in a 1 : 1 solution of telomer (200 mg/mL) and solvent, which was acetone for BzMA, BMA, and GMA, or methanol for HEMA, MMA, and EMA. Each solution was purged with nitrogen for 10 min and then a series of pretreated capillaries were filled with the solutions from 1.5 mL glass vials using nitrogen over-pressure, plugged with rubber stoppers, and placed in an oven at 80°C for 24 h. The capillaries were thereafter removed from the oven, flushed with the solvent used in the grafting solution, and plugged with rubber stoppers prior to EOF determination.

Determination of electro-osmotic flow

EOF measurements were performed for the native silica capillary, the γ-MAPS silanized capillary, and the telomer grafted capillaries, using injections of 10 m*M* thiourea as an EOF-marker. Capillary electrophoresis was run on a Beckman (Fullerton, CA) P/ACE instrument controlled by the accompanying Gold software. The background electrolyte consisted of acetate buffer (pH 6.8 or 3.9, 40 m*M*), as well as 20 : 80 mixtures of acetonitrile and the buffers, Table II. Injections were performed in pneumatic mode. The length of the tested capillaries was 27 cm, with 20 cm effective length from the inlet to the detector. Capillary electrophoresis was run in forward mode, with the cathode at the outlet, using an applied voltage of 10 kV and UV detection at 214 nm. The EOF mobility, μ_{EOF}, was determined from the migration time of the neutral marker, according to the formula $\mu_{EOF} = L \times L_t/t_m V$, where L is capillary length from the injection to the detector, L_t is the total capillary length, t_m is the migration time of a neutral marker, and V is the applied electric field.

RESULTS AND DISCUSSION

Iniferter stability

Whereas a traditional radical initiator decomposes under irradiation or heat yielding free radicals that trigger the polymerization and is consumed in the process, an iniferter will undergo reversible decomposition under irradiation or heat to yield a radical that is either recombined with its counterpart, or reacts with monomer in a polymerization. ^{1}H-NMR spectra collected from the irradiated iniferter in solution will yield information about the stability of the isopropylxanthic disulfide in solution under the irradition conditions used in these syntheses. After a UV radiation time of 1 min, a small change in the NMR spectrum was detected (spectra not shown), with a more complex pattern of the septuplet at 5.75 ppm, and a doublet emerging at 1.52 ppm. After further irradiation time the spectrum turned visibly different; after 4 min the septuplet at 5.75 ppm had been transformed to a multiplet, and a signal at 1.52 ppm had fully developed. This indicates that the

TABLE II
Determination of electro-osmotic Flow in Fused Silica Capillaries

Capillary	Water		ACN/water 20 : 80	
	pH 3.9	pH 6.8	pH 3.9	pH 6.8
Native fused silica capillary	2.9	3.6	3.1	3.9
After modification by γ-MAPS	1.6	2.5	1.5	3
After grafting by HEMA telomer	2.8	2.6	2.6	2.9
After grafting by BzMA telomer	N/D	1.3	N/D	1.6

Values listed are the electro-osmotic flow velocities, μ_{EOF}, in $m^2/Vs \times 10^{-8}$. Experiments were run on 50 μm i.e., 27 cm long (20 cm effective length) fused silica capillaries in 40 m*M* acetate buffer, with or without addition of 20% (v/v) acetonitrile (ACN). Applied electrophoretic voltage 10 kV. UV detection at 214 nm. Injected EOF-marker: 10 m*M* thiourea. N/D, no peak detected after 30 min.

S—S bond had been fully cleaved and had not recombined to the original compound. Although the stability of the iniferter is relatively high compared to, e.g., a free radical azo initiator such as AIBN under the same radiation (data not shown), the experiment verifies that the initiation phase lasts only for the first few minutes of the polymerization time.

Polymerization temperature

The activity of the photoiniferter was also investigated at elevated temperature to determine the need of temperature control during the UV-initiated polymerization. The comparison of the recovered telomers from the three different series is shown in Figure 2. The series of vials heated to 70°C without irradiation by UV light showed no signs of polymerization at all (the point at 8 h did not differ from the fraction at 165 min and is thus not shown in the Figure), whereas polymerization was seen in all the vials treated in the UV curing chamber. This confirms a purely photoreactive action of the IXD iniferter also at elevated temperature. The amount of polymer produced in the UV curing chamber in the thermostatted and unthermostatted polymerizations showed comparable trends, and the SEC traces were almost identical. Hence, we saw no signs of accelerated polymerization or breakdown due to the elevated temperature under the conditions employed.

Iniferted polymerization

All the chosen monomers polymerized under the conditions used, and the size of the resulting telomers could be adjusted by changing the concentration ratio of monomer to iniferter. By maintaining a constant monomer concentration and altering the iniferter concentration, telomers with chain lengths in the 5- to 150-mer interval were prepared. For mixtures with identical concentration of monomer but altered concentration of iniferter, it can be seen from Table I that the use of an increased iniferter concentration, translating into a lower monomer to iniferter ratio, yielded correspondingly shorter telomers. The monomer conversion typically reached between 60–100%, and higher iniferter concentrations led to lower conversion, estimated from the magnitude of the monomer peak in the SEC chromatograms. As this peak overlapped the peak of unreacted iniferter, if present, the conversion at the lowest polymerization times may be slightly underestimated, especially in polymerization mixtures with high initial iniferter concentration.

Molecular weights for selected samples as determined by size-exclusion chromatography are given in Table I. As the SEC system was calibrated with polystyrene standards, the values should not be taken as absolute, especially for telomers expected to differ from polystyrene with respect to their

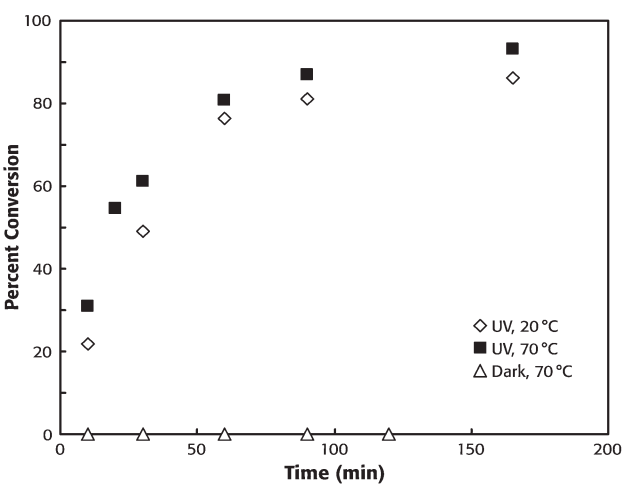

Figure 2 Iniferted polymerization of 2-hydroxyethyl methacrylate under UV irradiation at two different temperatures, and at elevated temperature without irradiation. Polymerization took place in THF, with a monomer : iniferter ratio of 15 : 1. The progress of the telomerization over time as determined by amount of precipitated telomer relative expected weight from amount of monomer charged.

solubility and hydrodynamic radius in THF. The peaks from the prepared telomers were generally broader than those obtained for the polystyrene standards, indicating that the telomers were not entirely monodisperse. In addition, the telomers with lower molecular weight slightly overlapped with the peak for remaining monomer, thereby affecting the accuracy of the molecular weight determinations.

In the polymerizations of benzyl methacrylate with monomer : iniferter ratios from 10 to 130 (Fig. 3) the conversions for the mixtures with the lowest (9 : 1) and the highest (132 : 1) monomer to iniferter ratios never reached above 80 per cent during the 2 h polymerization time, with the lowest conversion seen for the mixture with the highest monomer to iniferter ratio. The relationships between $ln[M]_0/[M]$ and polymerization time were reasonably linear, with some tendencies of leveling off at higher conversion ratios, and the molecular weight (M_p polystyrene equivalents) showed the expected increase with polymerization time. The telomers with highest molecular weight were recovered from the polymerization mixtures having the lowest iniferter concentration and thereby the highest monomer : iniferter ratio. In addition, the steepness of the M_p *versus* polymerization time relationship was highest for these mixtures.

For the polymerization of 2-hydroxyethyl methacrylate under similar conditions, with monomer to iniferter ratios between 12 and 173 at a monomer concentration of 1.3 mol/L, the mixtures with the highest monomer to iniferter ratios (74 and 173) resulted in the formation of a gel-like precipitate after polymerization times of only 30–40 min, with conversions of 77 and 46%, respectively, in the fractions preceding the precipitation. For lower monomer to iniferter ratios the polymerization proceeded in the same fashion as the other monomers, with the mixtures having the highest ratio of monomer to iniferter reaching the highest M_p.

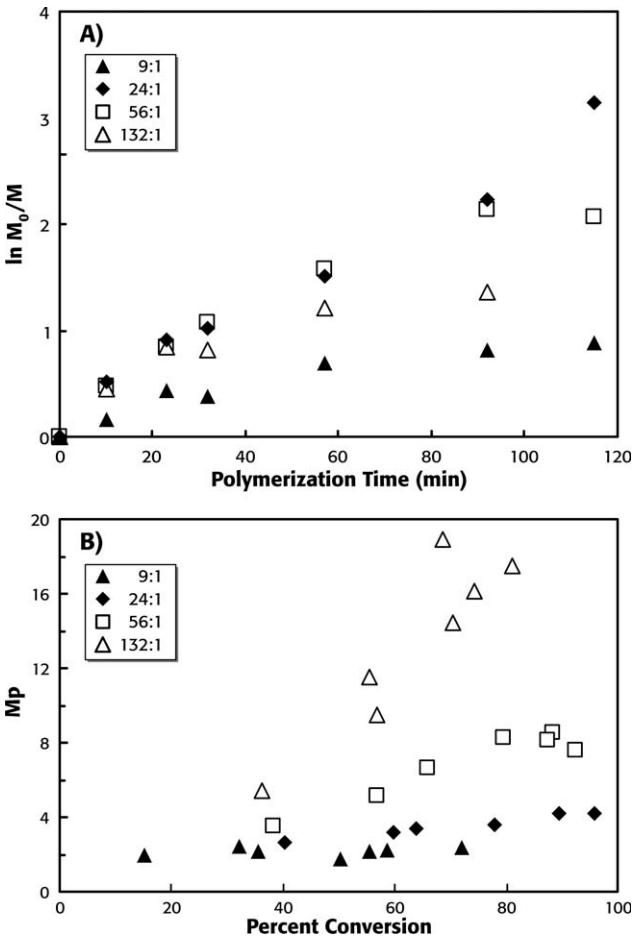

Figure 3 Iniferted polymerization of benzyl methacrylate at varied monomer to iniferter ratios (given in the graphs). Polymerization solvent THF. A) The progress of the telomerization over time as determined by SEC and monomer consumption, B) Resulting molecular weights with conversion. M_p in polystyrene equivalents as determined by size-exclusion chromatograph.

Reducing the risk of bimolecular termination

As in all controlled polymerization schemes, the risk of bimolecular termination needs to be eliminated also in iniferter polymerization, as this would destroy the living nature of the polymerization. As long as the monomer concentration is low and the iniferter is kept at a relatively high concentration, the risk of formed radicals reacting with other growing chains instead of with the monomer is low.[7] To decrease the risk of bimolecular termination, a reagent can be added, which decomposes under irradiation and reversibly generates radicals that can act as counter radicals to those originating from the iniferter.[26] The risk of free radicals being released is thereby minimized. One such reagent, tetraethylthiuram disulfide,[26] was added to polymerization mixtures with a monomer to iniferter ratio of around 30. The result for a HEMA telomer is shown in Table I. The difference in M_p between this polymerization (H056) and the corresponding experiment without TED added (H055) was hardly significant.

Solvent effect

Polymerizations were tested in four different solvents, THF, DMSO, DMF, and NMP, which were chosen based on their ability to dissolve the iniferter and all monomers. Although all solvents produced mixtures that appeared homogeneous, the solubilities of the growing polymer chains will be different in the different solvents, and the choice of solvent is thus expected to influence the polymerization. The solvent will further have an impact on the stability of the radical formed, the dormant species, and the conformations of the polymer chains during polymerization.

Apart from the precipitation discussed earlier for HEMA, the outcome of the polymerizations in the various solvents was indeed different. Benzyl methacrylate (monomer to iniferter ratio 26 : 1, monomer concentration 1.2 mol/L) showed a linear relation between $ln\ M_0/M$ and the polymerization time for all mixtures, Figure 4. However, the sizes of the resulting telomer (M_p; PS equivalents) were quite different among the solvents; the polymerizations in THF, DMSO, and DMF showed an increase in molecular weight with both polymerization time and conversion, whereas in NMP, the molecular weight remained almost constant over the course of the polymerization reaction. The increase in M_p (PS standard equivalents) with conversion was clearly linear with polymerization time in THF and in DMSO, but less linear in DMF at higher conversion. The sizes of the telomers polymerized in DMSO were equivalent to polystyrene standards of larger size than the corresponding telomers synthesized in THF.

The MALDI spectrum of a HEMA telomer with a molecular weight (M_w) of 3535 and polydispersity index of 1.2 is given in Figure 5. Signals originating from the matrix at *m/z* below 600 were omitted from the molecular weight and polydispersity determinations.

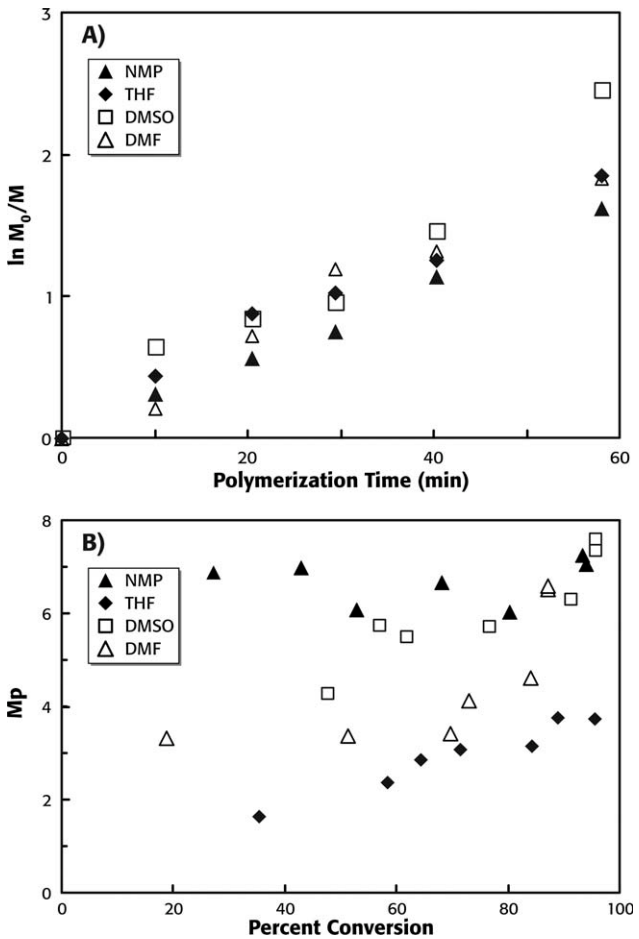

Figure 4 Iniferted polymerization of benzyl methacrylate in four different solvents, THF, DMSO, DMF, and NMP. The monomer to iniferter ratio was 26 : 1 and the total monomer concentration was 1.2 mmol/mL.

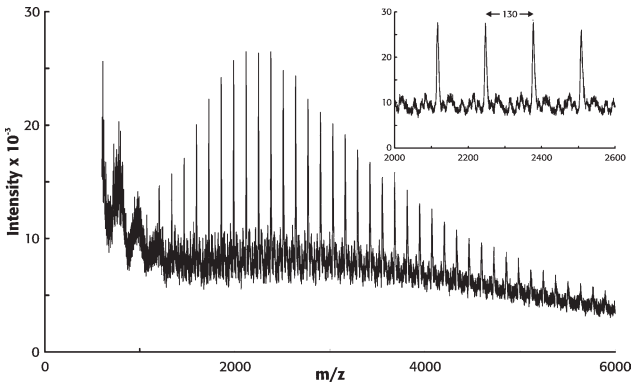

Figure 5 MALDI-TOF MS spectra of a HEMA telomer with monomer to iniferter ratio 31 : 1. Deconvolution showed M_w 3535 and polydispersity index 1.2. The corresponding molecular weight determined by SEC was 3010. The inset shows the molecular weight difference between consecutive signals, corresponding to the weight of a monomer unit. Acquisition on Voyager DE-STR, in positive linear mode.

Determination of electro-osmotic flow

The EOF is a parameter than can be used to assess properties of surfaces.[22] For this reason, an initial model system for testing grafting and the effect of surface properties by 'grafting to' of prepared telomers was investigated. The results from these EOF measurements are listed in Table II. The initial surface modification involving attachment of the silylating reagent (γ-MAPS) reduced the EOF, which was expected as the silanization reagent reacts with silanol groups and thereby reduces the density of dissociable groups at the surface. The grafting of telomer chains had an additional effect on the EOF; further reduction of EOF was seen for the capillary grafted with BzMA, which is expected as the nonpolar graft effectively shields the surface. More surprising was the enhancement of EOF seen in the capillary grafted with HEMA telomer. The HEMA telomer should ideally be noncharged and cause an increased viscosity of the double layer with a concomitant reduction in EOF. The increase in EOF therefore hints that the HEMA telomer may have been partially hydrolyzed in the telomer hydrolysis step. We are therefore investigating alternative ways for accomplishing the final step in the synthesis.

CONCLUSIONS

The synthesis of thiol-terminated telomers by controlled polymerization using isopropylxanthic

disulfide as photoiniferter enabled the adjustment of telomer size, with polymerization mixtures of higher monomer to iniferter ratio yielding longer telomer chains. The synthesis of short telomers could be readily performed in all the four solvents tested; THF, DMSO, DMF, and NMP. For mixtures with higher monomer content and monomer to iniferter ratios, polymerization of 2-hydroxyethyl methacrylate resulted in gel-like precipitates. The resulting sizes of telomer prepared in the solvents THF, DMSO, NMP, and DMF were different, with a linear increase in telomer size with reaction time for BzMA polymerized in THF, NMP and DMF. Although cooling might be beneficial depending on the solvent system, the iniferter did not decompose under heat alone and similar results were obtained when photoiniferted polymerization of 2-hydroxyethyl methacrylate was performed at 20 and 70°C. Grafting of telomers to the inside of fused silica capillaries performed via radical initiated addition to vinyl bonds introduced by the silylating reagent, γ-MAPS, had an influence on the EOF in a capillary electrophoresis set-up. The initial surface modification using the silylation reagent resulted in a reduced EOF. Subsequent grafting of 2-hydroxyethyl methacrylate telomers resulted in an increased EOF, compared to the γ-MAPS-modified surface, while grafting of benzyl methacrylate telomers resulted in further decrease in EOF. In future studies, the grafting of telomers onto chromatographic supports, and the chromatographic evaluation of single-mode and mixed-mode phases of different types will be included.

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