Polyurea Microcapsules: Surface Modification and Capsule Size Control

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ABSTRACT: A postmodification method for polyurea microcapsule (PUMC) surfaces using functional polyelectrolytes is reported in this article. Fluorescein isothiocyanate (FITC) was used to probe the chemistry on PUMC surface and label nucleophilic groups on the surface, in particular amines. As well, a fluorescently labeled polyanion containing electrophilic acetoacetate groups was used to covalently react with these nucleophilic groups on the PUMC surfaces. This modification causes charge reversion of the originally cationic PUMC and enables subsequent layer-by-layer (LbL) coating using other polyelectrolytes, allowing for covalent or noncovalent modification of the capsule surface. All modification steps were monitored using either laser scanning confocal microscopy or fluorescence microscopy. Optical and fluorescence microscopy of PUMC wall cross-sections embedded in resin confirmed that the modifications were restricted to the outer surface of PUMCs, offering minimum interference of this modification method with other capsule wall properties. In addition, a simple T-junction type microfluidic device based on a commercially available Micro-TEE was designed to produce narrowdisperse PUMCs. This device was easy to set up and operate and was proved to be an useful tool for making monodisperse emulsions and narrowdisperse MCs. © 2011 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 49: 3038–3047, 2011

KEYWORDS: fluorescent labeling; functional polyelectrolytes; layer-by-layer coating; microcapsules; microfluidic device; monodisperse emulsions; narrowdisperse microcapsules; polyelectrolytes; polyurea; polyurea microcapsules; surface postmodification

INTRODUCTION Polyurea microcapsules (PUMCs) are micron-sized particles with a central cavity and a PU shell. They are typically used to protect the encapsulated materials from harsh environments and to control their release rate or mechanism. Because of their high chemical and mechanical stability, PUMCs are used in applications ranging from carbonless copy paper,[1] thermal printing paper,[2] textile,[3] to agriculture.[4] Recent studies have explored the use of PUMCs in catalysis,[5] self-healing materials,[6] and flexible displays.[7]

Since their inception, studies on PUMCs have focused on capsule properties,[8] new applications,[5–7] wall formation mechanisms,[9] creating composite capsule walls,[10] making functional capsules, and imaging capsule morphologies.[11] These studies have greatly advanced the understanding of both PUMCs and encapsulation processes, making it possible to design structured PUMCs with multiple functions.

The outer PUMC surface mediates the interaction of the capsule with the targeted substrates or surfaces and is responsible for the dispersability of capsules, their adhesion to surfaces, and their responses to environmental changes. It would thus be desirable to modify surface chemistries of PUMC independent of the wall formation, to meet the requirements of different applications and fills. So far, most studies on PUMC surface modification have been focused on in situ methods in which surface modifiers are used during encapsulation processes and, in most cases, modifiers are incorporated evenly throughout the capsule wall. Yan and coworkers[12] reported using lysine as comonomer to enhance capsule surface charge density and the resulting capsules showed improved dispersability in aqueous phases. Syngenta has used polyEPS-520 as one of the aqueous phase wall formers to react with polyisocyanates, as the incorporation of this material provides a negatively charged capsule surface, which improved the dispersability of capsules in water as well as adhesion to foliage.[13] El-Gibaly and Anwar[14] used 4,4-diaminostilbene-2,2-disulfonic acid as comonomer to introduce sulfonic groups onto capsule surfaces to improve oxygen-binding ability. These in situ approaches modified not only the capsule surfaces but also the bulk capsule walls, which, in some cases, had adverse effects on capsule wall properties and can necessitate reoptimization of capsule formulations for each new fill. Therefore, it is desirable to develop postmodifications that target the outermost surface of capsule walls to impart desirable surface properties without affecting bulk wall properties.

We describe surface modifications for PUMCs based on attaching low-molecular weight and polymeric modifiers onto preformed PUMC surfaces. Because of diffusion limits

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of high-molecular weight modifiers in dense PUMC walls, the modification is confined to the capsule surfaces, showing minimum interference with wall properties of PUMC.

A common challenge in preparing capsules with controlled adhesion and release properties lies in the wide size distribution of PUMCs prepared by classical suspension interfacial polycondensation. Such PUMCs typically have a broad distribution of diameters and wall thickness, given their wide range of surface to volume ratios. Studies of capsule properties based on such polydisperse systems can only reflect statistical averages. While broad release ranges can be beneficial in certain applications requiring long release periods, access to monodisperse or narrowdisperse PUMCs could facilitate correlations between capsule size and properties. The formation of monodisperse or narrowdisperse PUMCs is often based on monodisperse emulsions prepared using microfluidic devices. Contrary to traditional top-down methods, the microfluidic approach produces emulsion droplets individually under identical conditions to ensure their uniformity. By varying flow rates and device geometry, the droplet size can be controlled, making microfluidic devices desirable tools for fabricating monodisperse emulsions,[15] microspheres[16] and MCs.[17] However, microfluidic devices are most often fabricated by photolithography[18] and soft lithography[19] and thus not commonly accessible by chemists. In addition, isocyanates used for making PUMCs tend to hydrolyze and polymerize when in contact with water, which tends to lead to undesirable build-up in microchannel devices. To address these challenges, McQuade et al. recently designed a simple version of a microfluidic device that uses a needle inserted into poly(vinyl chloride) tubing to form an inexpensive yet functional T-junction device capable of forming narrowdisperse polyamide MCs.[20] The only drawbacks are the requirement for careful positioning of the needle within the tubing, and a typical capsule diameter of several hundreds of micrometers owing to the relatively large internal diameters of the needle and tubing, making it less practical for mimicking industrial products. We describe here a structurally robust microfluidic device built from commercially available T-junctions that is capable of producing monodisperse emulsions and MCs with diameters below 100 μm. Clogging problems can be resolved by replacing the relatively inexpensive T-junctions. We believe that these studies will lead to preparation of well-defined PUMCs with desirable functionalities on the surface, facilitating capsule property studies and wider applications of PUMCs.

RESULTS AND DISCUSSION

Surface Modifications of Aliphatic Polyurea Microcapsules

Capsules used for surface modification study were prepared by interfacial polycondensation between isophorone diisocyanate (IPDI) and diethylenetriamine (DETA) at 70 °C for 65 h to form walls thick enough for subsequent cross-sectional analysis.[9(a)] Most capsules turned out to be spherical with some dimples, characteristic for long reaction times, as shown in Figure 1.

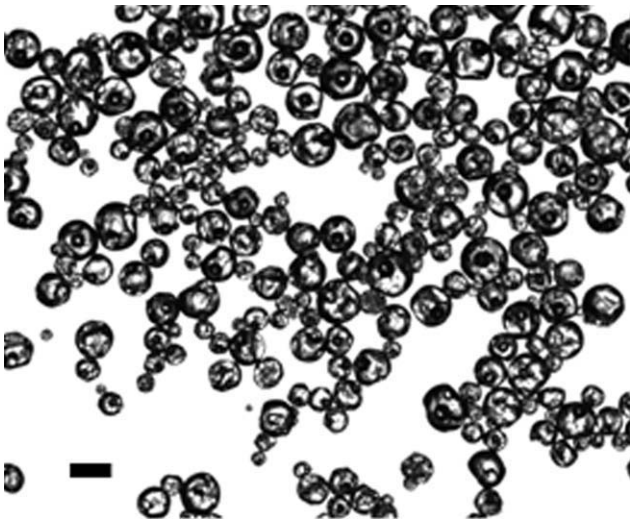


FIGURE 1 Optical micrograph of polyurea microcapsules made of IPDI and DETA. The scale bar is 100 μm.

Understanding the surface chemistry of PUMCs is the first step in designing surface postmodification methods. PUMCs are synthesized by interfacial polycondensation between polyisocyanates and polyamines. Because of the high reactivity of these comonomers, the capsule surface and wall chemistries are dominated by urea groups although one would expect some residual amine groups on the outer surface of the capsule wall, because of the use of aqueous polyamines as a wall former and also in the hydrolysis of residual isocyanate groups by way of the amic acid intermediate. The interfacial nature of the wall forming reaction might further be expected to lead to the formation of concentration gradients of both polyisocyanates and polyamines across the capsule wall during encapsulation, with more polyamines on the aqueous side and more polyisocyanates on the oil side of the interface. Both situations would lead to some residual amine groups attached to PUMC surfaces.

To probe the PUMC surface chemistry, we treated PUMCs with fluorescein isothiocyanate (FITC) in a dimethylformamide (DMF)/water mixture at pH 9. The isothiocyanate group in FITC is quite reactive toward nucleophilic groups such as amines on the capsule surface. Capsules before and after FITC treatment were subjected to confocal fluorescent microscopy. Optical sections from the capsule equator before and after FITC labeling are shown in Figure 2(a,b). Without FITC treatment, PUMC capsule walls did not show fluorescence in the FITC channel of the confocal microscope, indicating absence of PUMC autofluorescence. After FITC treatment, fluorescence signals were observed in the FITC channel, indicating the incorporation of FITC into PUMC walls. The attachment of FITC to the capsule wall indicates that there are nucleophilic groups, most likely amine groups in PUMC walls that can react with FITC to form a covalent linkage.

Further evidence of presence of amino group in the capsule wall came from capsules exposed to fluorescein-labeled

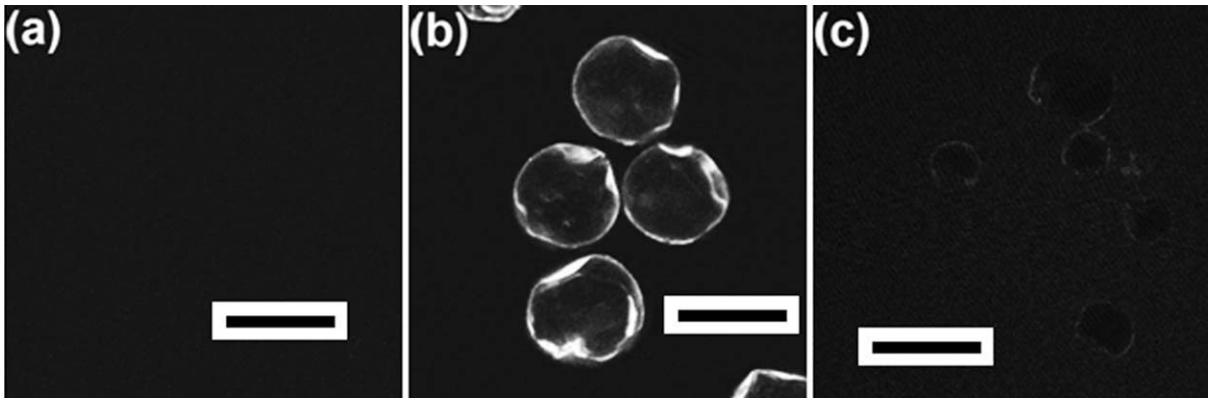


FIGURE 2 Equatorial confocal fluorescent microscope images (greyscale) of polyurea microcapsules (a) without treatment, (b) after treatment with FITC, and (c) after treatment with A100*f*. All scale bars are 50 μm.

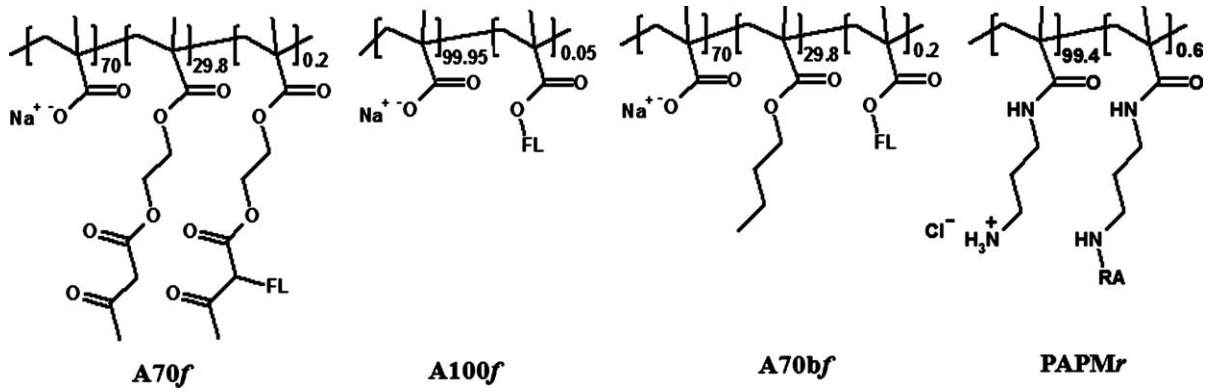
poly(sodium methacrylate) (A100*f*, Scheme 1) solution at pH 6.5. Figure 2(c) shows weak fluorescence on the capsule surface after A100*f* exposure, suggesting the attachment of A100*f* to the PUMC walls. This attachment could be attributed to the presence of amine groups in PUMC walls. At pH 6.5, most amino groups were protonated and hence able to electrostatically bind negatively charged A100*f*. Compared to FITC-treated PUMCs, A100*f*-coated PUMCs showed much weaker fluorescence probably due to both the low level of fluorescein labeling in A100*f* and inability of this polymer to penetrate into the PUMC wall. A100*f* coating was also attempted at pH 8.6 and no attachment was observed, reflecting the lower degree of ionization of amines at this pH. These observations support the presence of amine groups on PUMC surfaces that could be used for capsule surface modifications.

Polyurea Microcapsule Surface Modifications

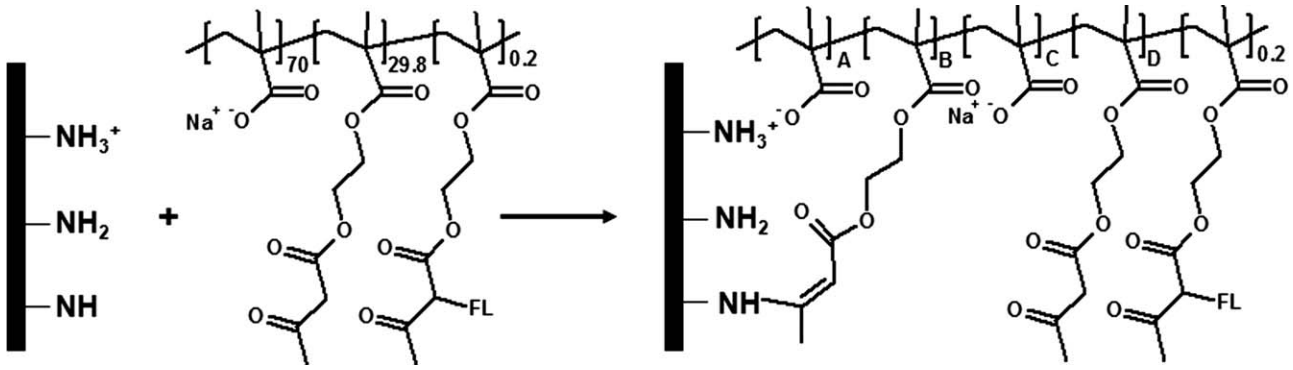
Several criteria need to be considered for designing surface modifiers for PUMCs: (1) the modifiers need to be soluble in aqueous PUMC suspensions; (2) the modifiers need to contain amine reactive groups that can help anchor modifiers to PUMC walls under mild conditions; (3) the modifiers need to carry the functional groups that needed for modification of the PUMC surfaces; (4) the modifiers need to have relatively high molecular weights to minimize their diffusion into the PUMC walls and their effect on release and other wall properties; and (5) the modifiers should contain a reporter group to allow assessing modification efficiency.

To meet these criteria, we used a fluorescein-labeled functional polyanion, poly(sodium methacrylate-*co*-2-(methacryloyloxy) ethyl acetoacetate) (A70*f*, Scheme 1) as a PUMC surface modifier. A70*f* was prepared by free radical copolymerization of methacrylic acid and methacryloyloxy ethyl acetoacetate. The presence of 70 mol % methacrylic acid provides solubility in water above pH 4.5 and electrostatic preconcentration of the modifier on the capsule surface, while the 30 mol % acetoacetyl groups were designed to react with amine groups in PUMC walls to effect covalent attachment at room temperature. The acetoacetyl groups (0.67 mol %) were labeled with FITC, to enable mapping of the polymeric modifier using conventional and confocal fluorescence microscopy. The proposed modification mechanism is shown in Scheme 2.

The PUMC surface modification was carried out at room temperature at pH 8.6. At this pH, sufficient amine groups in PUMC walls are in their free form and hence able to



SCHEME 1 Chemical structures of fluorescein-labeled poly(sodium methacrylate-*co*-2-(methacryloyloxy) ethyl acetoacetate) (A70*f*), fluorescein-labeled poly(methacrylic acid) (A100*f*), fluorescein-labeled poly(methacrylic acid-*co*-butyl methacrylate) (A70b*f*), and rhodamine-labeled poly(*N*-(3-aminopropyl) methacrylamide) (PAPM*r*). FL: fluorescein; RA: rhodamine.



SCHEME 2 The proposed mechanism for PUMC surface grafting by A70*f*. A + C = 70; B + D = 29.8.

covalently react with acetoacetyl groups in A70*f*. The confocal image of capsules after A70*f* coating, observed through the FITC channel [Fig. 3(b)], clearly shows substantial A70*f* binding, in comparison to uncoated capsules [Fig. 3(a)]. The fluorescence distribution seems heterogeneous, which is believed to reflect the irregular capsule shape (dimples) more than any inherent heterogeneity of PUMC walls.

To further explore the interactions between PUMC walls and A70*f*, we carried out two controlled experiments. In the first experiment, A70*f*-modified PUMCs were treated with 2 M NaCl solution. It is known that purely electrostatic interactions between weak polyelectrolytes can be shielded using high concentrations of small electrolytes, leading to dissociation of the polyelectrolyte complex. The dissociation of A70 from its complexes with poly(2-methacryloyloxyethyl trimethyl ammonium chloride) has been studied earlier,[21] showing that 2 M NaCl was sufficient to dissolve those complexes. In this study, we observed that A70*f*-modified PUMCs retained strong fluorescence [Fig. 3(c)] after 2 M NaCl treatment. This indicates that 2 M NaCl could not dissociate A70*f* from PUMCs walls and thus electrostatic interaction was not primarily responsible for the attachment of A70*f*. In the second experiment, the possibility of hydrophobic–hydrophobic interactions between PUMC walls and A70*f* was explored with the attempt to use fluorescein-labeled poly(methacrylic acid-*co*-butyl methacrylate; A70b*f*, Scheme 1) as a noncovalent polyanionic PUMC modifier. The butyl groups in A70b*f* were designed as hydrophobic analogs of the acetoacetyloxy ethyl groups in A70*f*, with butyl groups being slightly more hydrophobic but not reactive toward electrophiles. Studies using confocal microscope revealed that no fluorescence signal was detected after A70b*f* treatment, suggesting that no A70b*f* was attached to PUMC walls due to relatively hydrophilic PUMC surfaces. This helps to rule out hydrophobic–hydrophobic interactions between PUMC walls and A70*f* and led us to conclude that covalent reaction between amine groups on PUMC surfaces and acetoacetyl groups in A70*f* was primarily responsible for the PUMC wall modification. The covalent modification is advantageous over either electrostatic or hydrophobic–hydrophobic interaction as it is nonreversible and thus has better stability.

The successful attachment of A70*f* on PUMC walls enables further capsule surface modifications. The negative charge in PUMC walls provided by the A70*f* attachment can attract polycations while the unreacted acetoacetyl groups in A70*f* enables reactions between walls and nucleophile-containing modifiers, which provide both electrostatic and covalent modifications. To demonstrate this, we used rhodamine-labeled poly(3-aminopropyl methacrylamide) (PAPM*r*, Scheme 1) to further modify A70*f*-coated PUMCs. The resulting PUMCs showed fluorescence signals in both FITC and rhodamine channels as shown in Figure 4. This indicates

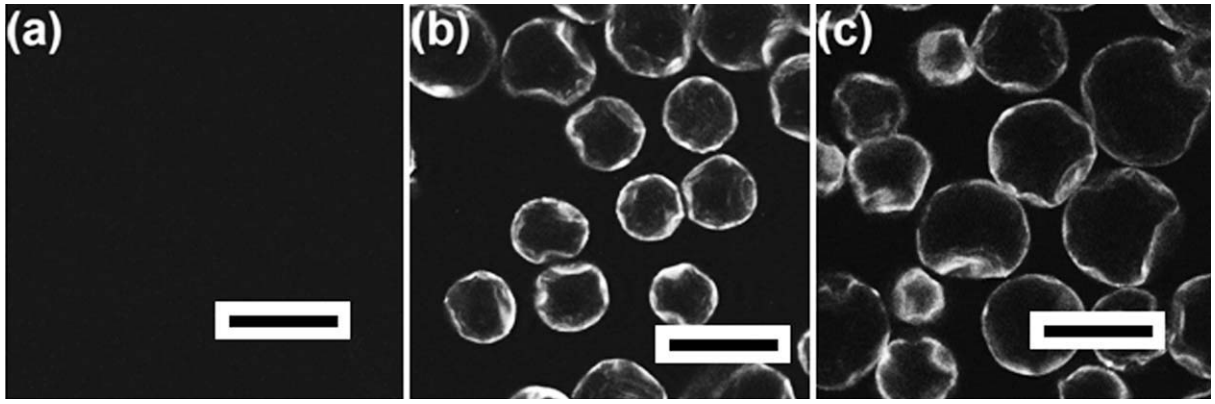


FIGURE 3 Confocal microscopy images (greyscale) of PUMCs: (a) without modification; (b) modified by A70*f*; and (c) first modified by A70*f* and then treated with 2 M NaCl solution. All scale bars stand for 50 μm.

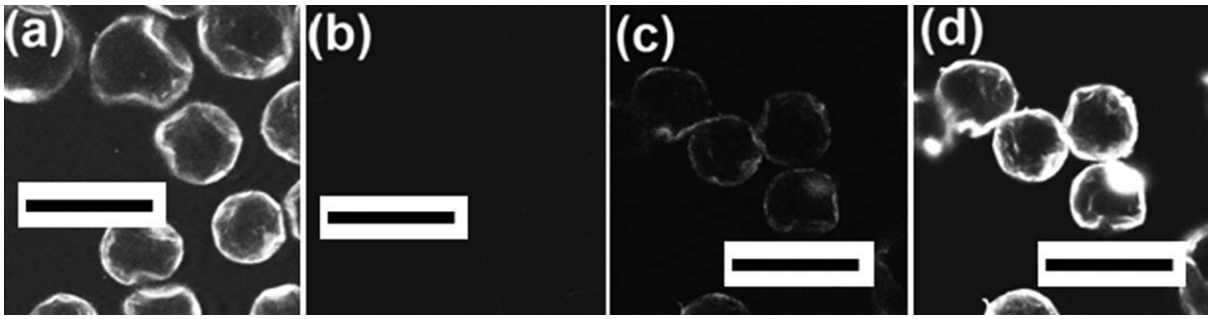


FIGURE 4 Confocal images (greyscale) of A70*f*-coated polyurea microcapsules in: (a) FITC channel (b) rhodamine channel; and A70*f*/PAPM*r* bilayer polyurea microcapsules in (c) FITC channel and (d) rhodamine channel. All scale bars denote 50 μm.

that both dyes were present in the PUMC walls, which can be attributed to the successful attachment of A70*f* and PAPM*r* to PUMC walls in two separate coating steps. It is evident that the fluorescence signal in the FITC channel became weaker on PAPM*r* coating, which is attributed to partial quenching of the fluorescein by rhodamine groups present in close proximity.[22] Modified PUMCs were further coated using A70*f* and PAPM*r* in a layer-by-layer (LbL) fashion to prepare $(A70f/PAPMr)_2$-modified capsules. The overall fluorescence intensity increased with increasing number of layers, as shown in Figure 5, confirming the successful coating of each layer.

To determine if these fluorescently labeled modifiers could penetrate the PU walls or were restricted to the wall surface, we examined the wall cross-sections of $(A70f/PAPMr)_2$-modified PUMCs using transmission electron microscopy (TEM), fluorescence and optical microscopy. This was done by embedding dried capsule samples in polystyrene and ultramicrotoming the embedded samples to about 100 nm thickness. The resulting thin sections were subjected to microscopy imaging. Figure 6(a) shows the TEM micrographs of a PUMC wall cross-section. The PUMC wall appeared delaminated into a layered structure, which could be attributed to both low cross-linking density of the PU wall chemistry and the swelling effect of styrene during embedding. Optical and fluorescence microscopes were then used to examine the same sample area, shown in Figure 6(b,c). By comparing these two images, it is evident that the fluorescence came primarily from the outer edge of capsule wall, while the rest of wall showed very little fluorescence signal. This indicates that the modification occurred almost exclusively on the PUMC surfaces and the capsule walls were not modified due to limited diffusion of the macromolecular modifiers into the relatively dense PUMC walls. The confinement of modifications to the PUMC surface is beneficial as the modification steps did not interfere with the rest of the capsule wall and thus other wall properties would remain intact.

Preparing Narrowdisperse Polyurea Microcapsules Using a Microfluidic Device

To make monodisperse or narrowdisperse PUMCs, we designed a T-junction type microfluidic device that is capable of producing monodisperse emulsions. The key part of this device is a commercial T-junction machined from polyether ether ketone (MicroTEE, P-890, Upchurch, shown in Scheme 3) with 152.4 μm diameter thru-holes, ideal for making microsized emulsions. This MicroTEE can easily be connected using standard tubing to the two pumps delivering the aqueous continuous phase (1 wt % polyvinyl alcohol, PVA) from the top, and the organic dispersed phase (xylene) through the sidearm, with the formed emulsion being collected through the bottom fitting in a collection reservoir. This setup results in a robust microfluidic devices based on shearing organic phase droplets into a high flow aqueous phase flow.

Before making PUMCs, the formation of xylene-in-water emulsions was examined using this microfluidic device.

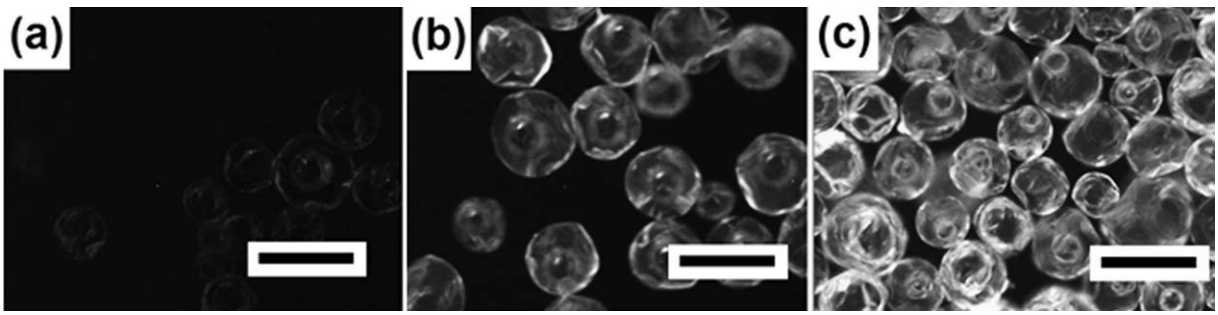


FIGURE 5 Conventional fluorescence microscope images of polyurea microcapsules using an FITC filter set (a) native capsules; (b) (A70*f*/PAPM*r*)-modified capsules; and (c) $(A70f/PAPMr)_2$-modified capsules. All scale bars denote 50 μm.

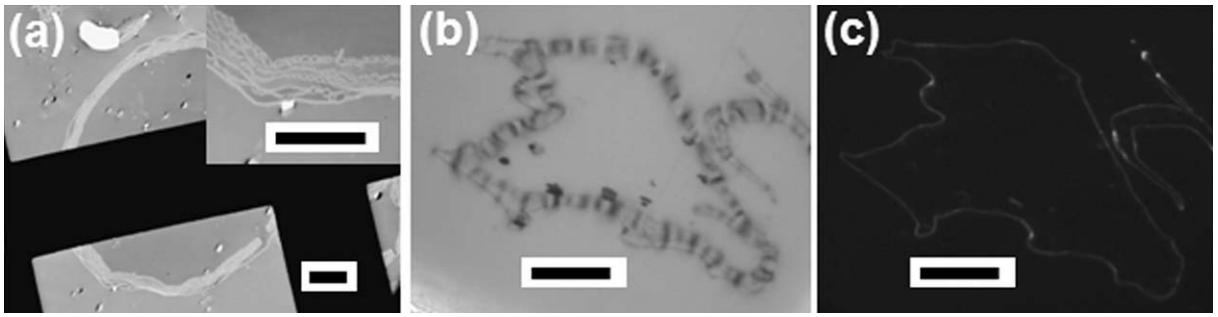
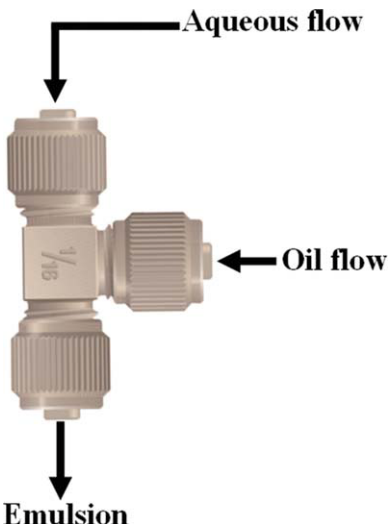


FIGURE 6 Wall cross-section of a (A70*f*/PAPM*r*)$_2$-modified polyurea microcapsule. (a) A TEM micrograph showing a capsule cross-section (the insert in the upper right hand corner is the enlarged image of the boxed area). (b) An optical microscope image and (c) A fluorescence microscope image (greyscale). (b) And (c) were taken in the same sample area. Scale bars denote 10 μm.

Figure 7 shows an optical microscope image of a xylene-in-water emulsion made using this device. Most emulsions are monodisperse with standard deviations less than 5%. Using this device, the size of the emulsion droplets can be easily tuned by varying the flow rates of either oil phase or aqueous phase (Fig. 8). Within the flow rate regimes investigated, emulsion size increases with oil phase flow rate, and decreases with increasing aqueous phase flow. Accordingly, monodisperse emulsions with the size ranging from 50 to 160 μm were successfully made.

The MicroTEE-based microfluidic device was then used to prepare narrowdisperse aromatic PUMCs. Polymethylene polyphenylene isocyanate (PMPPI, 10 wt %) was dissolved in xylene to serve as oil phase, which was then pumped into the microfluidic device along with an aqueous flow (1.0 wt % PVA) to form an oil-in-water emulsion. The resulting PMPPI containing emulsion was subsequently directed into a reservoir solution containing DETA, to start the interfacial polycondensation between PMPPI and DETA. Due to the relatively fast rate of hydrolysis of PMPPI, clogging happens on occasion due to PU build-up in the MicroTEE. To mitigate this problem, the device was flushed with neat xylene immediately after each use to remove PMPPI residues from the channels. When clogging does happen, the MicroTEE can be easily replaced and cleaned.

The narrowdisperse system allows us to precisely monitor the change of capsule size and morphology during the reaction, which is not apparent for polydisperse systems. The morphology of the narrowdisperse PUMCs formed at room temperature with different reaction time was evaluated using optical microscopy and the results are shown in Figure 9. One hour reaction at room temperature led to the formation of dimpled PUMCs with smooth surfaces, as shown in Figure 9(a). These capsules appear to be narrowdisperse with a mean diameter around 101 μm. The dimples on the surface were probably caused by collisions between capsules during the reaction. Extended reaction time (2 and 7 days) rendered rough surfaces and more deformation of those capsules, as shown in Figure 9(b,c). This suggests that the polymerization at the later stage caused stresses in the initial PU membrane, leading to the morphological change on capsule surfaces. The average diameter of these capsules did not change and stayed constant ($\sim$101 μm) during the extended reaction time.



SCHEME 3 MicroTEE (P-890, Upchurch).

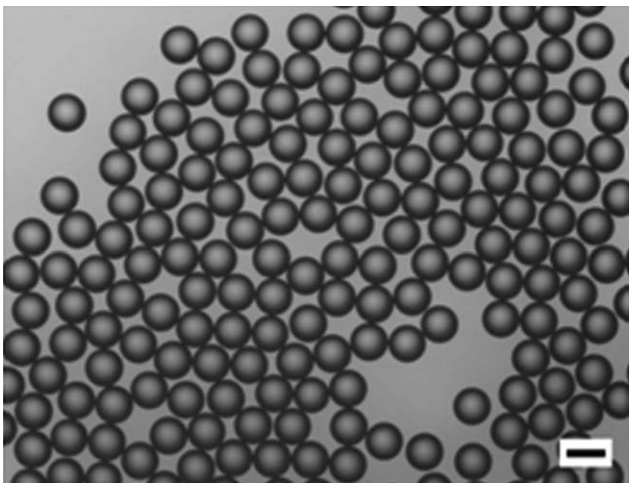


FIGURE 7 Optical micrograph of monodisperse xylene-in-water emulsion made using the microfluidic device. The scale bar is 100 μm.

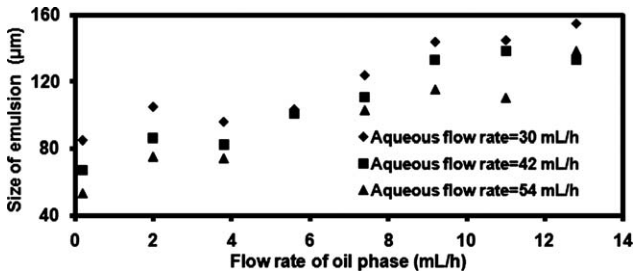


FIGURE 8 Dependence of emulsion size on the flow rates of both aqueous and oil phases.

The narrowdisperse aromatic PUMCs were then subjected to surface modification using A70*f* to test the generality of surface modification in terms of different types of PUMCs. After the surface modification, the resulting PUMCs were imaged by fluorescence microscopy. As shown in Figure 10, all PUMCs fluoresce and the modification appears to be uniform, suggesting a fairly homogeneous chemical composition of these PUMC surfaces.

EXPERIMENTAL

Materials

N-(3-Aminopropyl) methacrylamide hydrochloride was purchased from Polysciences. 2,2′-Azobis(isobutyronitrile) (AIBN) was purchased from Dupont (Mississauga, ON). All other reagents were purchased from Sigma-Aldrich and used as received. The preparation of poly(sodium methacrylate-*co*-2-(methacryloyloxy) ethyl acetoacetate) (A70*f*) and its labelling with FITC was described previously.[18] The #00 BEEM embedding capsules were purchased from Canemco.

Synthesis of Aliphatic Polyurea Microcapsules

Aqueous PVA solution (35 mL, 1 wt % PVA, MW 9000–10,000, 80% hydrolyzed) was first charged into a thermostatted Buchi suspension reactor, with an overhead three-blade stirrer driven at 1000 rpm. Isocyanate solution (2 g IPDI dissolved in 10 mL xylene) was added into the reactor, and the mixture was stirred for 15 min at room temperature. The stirring rate was reduced to 500 rpm before adding DETA solution (1 g DETA dissolved in 5 mL 1 wt % aqueous PVA solution) within 1 min. The temperature was then raised to 70 °C and maintained for 65 h. The resulting capsules were washed on filter paper with deionized water until pH 6.7.

Preparation of Narrowdisperse Aromatic Polyurea Microcapsules Using a Microfluidic Device

A microfluidic device was built based on a MicroTEE (P-890, Upchurch) to prepare monodisperse or narrowdisperse emulsions and PUMCs. The MicroTEE was placed vertically as shown in Scheme 3. The oil phase flow containing xylene and isocyanates was pumped into the side arm of the MicroTEE using a N-1600 multiple syringe pump (New Era Pump Systems), while the aqueous phase flow (1.0 wt % PVA in water) was introduced to the top arm of the MicroTEE by a Waters 590 programmable high-performance liquid chromatography (HPLC) pump. The formed emulsion came out of the bottom arm and was directed into a reservoir solution in a centrifuge tube containing 1.0 wt % PVA solution that was placed directly underneath the MicroTEE. The connections between the MicroTEE and the pumps and the reservoir solution were made using Teflon FEP tubings (1476, Upchurch). In the case of emulsion visualization, the emulsion formed was directly deposited onto a microscope slide and then imaged using an optical microscope. For making PUMCs, the oil phase containing 10.0 wt % PMPPI in xylene was pumped into the MicroTEE at a flow rate of 0.020 mL/min, while the flow rate of aqueous phase was set to 0.463 mL/min. The formed emulsion was then directed into a 10 mL reservoir solution containing 5.0 wt % DETA and 1.0 wt % PVA to facilitate the interfacial polymerization. The emulsion was collected for 5 min and then the tube was capped and placed on a rotator (Glas-Col) and rotated at a rate of 30 rpm for various lengths of time. The resulting MCs were washed four times with deionized water in the centrifuge tube to remove unreacted DETA and PVA. To avoid clogging by hydrolysis and polymerization of the isocyanate inside the MicroTEE, the system was flushed with neat xylene immediately after use.

Synthesis of Fluorescein-Labeled Poly(methacrylic acid) (A100*f*)

Methacrylic acid 1.91 g (22.19 mmol), *O*-fluorescein methacrylate 89.7 mg (0.22 mmol), and AIBN 73.6 mg (0.45 mmol) were dissolved in 18 mL of ethanol in a high density polyethylene (HDPE) bottle. The solution was gently bubbled with dry N_2 for 10 min, placed in an HB-1000 hybridizer at 60 °C for 21 h, and rotated at ~10 rpm. After reaction, the formed polymer was precipitated in 200 mL of diethyl ether and washed three times with 50 mL of diethyl ether. The solid product was dried under vacuum at 60 °C until constant

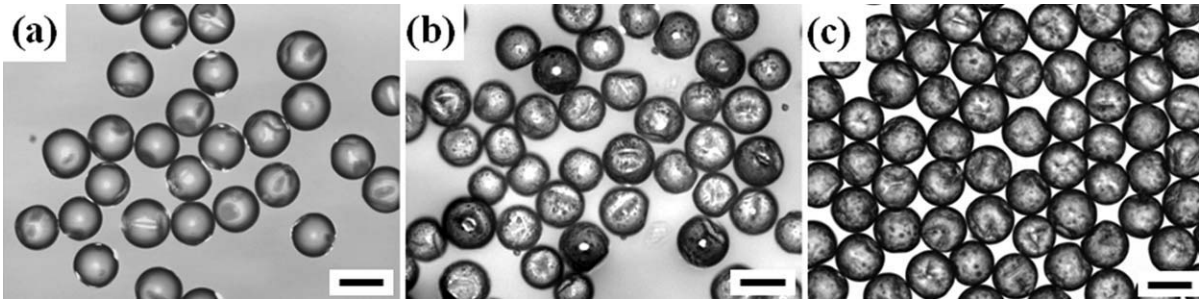


FIGURE 9 Optical micrographs of narrowdisperse aromatic polyurea microcapsules made using the microfluidic device at room temperature with different reaction time: (a) 1 hour; (b) 2 days; and (c) 7 days. The scale bars are 100 μm.

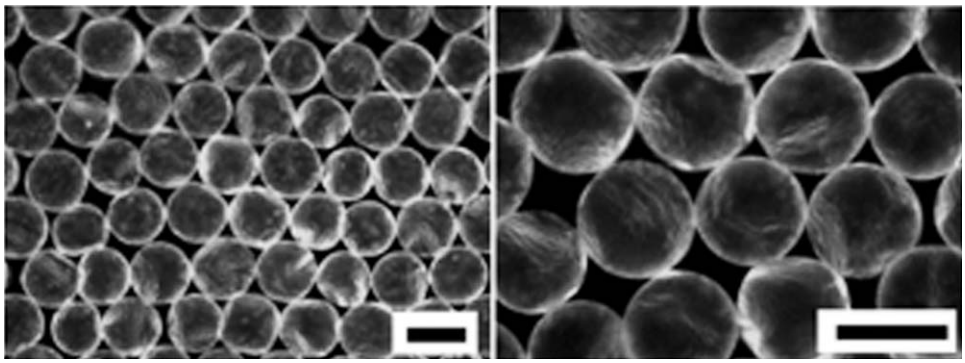


FIGURE 10 Fluorescence micrographs of narrowdisperse aromatic polyurea microcapsules surface modified with A70*f*. The scale bars are 100 μm.

weight. Yield: 1.69 g (84.5%). M_n determined using gel permeation chromatography (GPC) was 35,100 Da, with a polydispersity index (PDI) of 2.65. The fluorescence label content measured using UV–Vis was 0.05 mol % of total monomer units.

Synthesis of Fluorescein-Labeled Poly(methacrylic acid-*co*-butyl methacrylate) (A70b*f*)

Methacrylic acid 0.5 g (5.8 mmol), butyl methacrylate 0.33 g (2.32 mmol), *O*-fluorescein methacrylate 65 mg (0.162 mmol), and 14 mg AIBN (0.085 mmol) were dissolved in 9 mL of ethanol in a 20-mL glass vial. The solution was gently bubbled with dry N_2 for 10 min and then heated to 70 °C for 30 h in a HB-1000 hybridizer at 15 rpm rotation. After reaction, the solution was precipitated twice into 100 mL of cold diethyl ether, and dried under vacuum at 60 °C until constant weight. Yield: 0.634 g. The ratio of methacrylic acid to butyl methacrylate in the polymer determined by nuclear magnetic resonance (NMR) was 70:30. M_n determined using GPC was 29,700 Da with a PDI of 2.45. The fluorescence label content was measured using UV–Vis was found to be 0.2 mol % of total monomer units.

Synthesis of Poly(*N*-(3-aminopropyl) methacrylamide)

N-(3-Aminopropyl) methacrylamide hydrochloride (5.24 g, 29.3 mmol) and 2,2′-azobis (*2*-methyl propionamidine) dihydrochloride (0.159 g, 0.59 mmol, 2 mol % relative to monomer) were dissolved in 50 mL of water in a 60-mL HDPE bottle. The solution was bubbled with N_2 for 10 min. The sealed bottle was placed in an HB-1000 hybridizer and heated at 60 °C for 24 h while being rotated at 15 rpm. After reaction, the polymer was purified by dialysis in cellulose tubing (12 kDa MW cut-off, Spectrum Laboratories) against deionized water for 5 days, with daily changes of water, followed by freeze drying. Yield: 4.29 g. Molecular weight of PAPM determined using viscometry was found to be 260 kDa.

Synthesis of Rhodamine-Labeled Poly(*N*-(3-aminopropyl) methacrylamide)

Rhodamine isothiocyanate (12 mg, 0.224 mmol) was dissolved in 2 mL of DMF and added over 1 min to a solution of PAPM (0.2 g, 1.12 mmol) in 10 mL of 0.1 M $NaHCO_3$ buffer (pH = 9), and the mixture was stirred at room temperature for 2.5 h. Dialysis and freeze drying yielded a reddish solid in 83% yield. The degree of rhodamine labeling determined using UV–Vis was found to be 0.6 mol % of total monomer units.

Fluorescein Isothiocyanate Treatment on Polyurea Microcapsules

FITC solution (1 mL) at a concentration of 1 mg/mL in DMF was added to 10 mL of $NaHCO_3$-buffered (pH = 9) PUMC suspension in a glass vial. The vial was rotated at ~15 rpm at room temperature for 20 h. The resulting capsules were washed using 10 % DMF–water solution twice to remove unreacted FITC.

Polyurea Microcapsule Surface Modification Using A70*f*, A100*f*, and A70b*f*

A70*f* (5 mg) was added to 10 mL of PUMC suspension and the pH was adjusted to 8.6. After 30 min of gentle stirring, the resulting capsules were washed on a filter paper until no fluorescence could be detected in the supernatant by UV–Vis. Surface modifications using A100*f* (coating pH 6.8) and A70b*f* (coating pH 8.6) were similar to that of A70*f*.

Layer-by-Layer Coating on Polyurea Microcapsule Surfaces

A70*f*-coated PUMCs were treated in sequence with PAPM*r*, A70*f*, and PAPM*r* to form $(A70f/PAPMr)_2$-modified capsules. For each coating step, 5 mg of PAPM*r* or A70*f* was added to 10 mL of capsule suspension, and the pH was adjusted to 7. The suspension was then gently rotated at room temperature for 30 min, and the resulting capsules were washed on a filter paper to remove unattached polyelectrolyte and redispersed in 10 mL of distilled water for the next coating step.

Microcapsule Embedding and Microtoming

$(A70f/PAPMr)_2$-modified PUMCs were washed on a filter paper with tetrahydrofuran three times to extract xylene from the core. A small amount of capsules (2–3 mg) was then added to a BEEM embedding capsule and mixed with ~2 mL of styrene containing 10 wt % benzoyl peroxide. The capsule was sealed and heated at 70 °C for 24 h to complete the embedding. Thin sections of the resulting PS embedding blocks were cut with a Leica Ultracut UCT ultramicrotome and picked up onto Formvar-coated Cu TEM grids.

Characterization

The composition of A70bf was determined by proton NMR using a Bruker AV 200 spectrometer for samples dissolved

in dimethylsulfoxide-d_6. Size exclusion chromatography was conducted using a system consisting of a Waters 515 HPLC pump, Waters 717 plus Autosampler, three columns (Waters Ultrahydrogel-120, −250, −500; 30 cm by 7.8 mm, 6 micrometer particles) and a Waters 2414 refractive index detector, calibrated with narrow molecular weight poly(ethylene glycol) standards (Waters). Samples were eluted at a flow rate of 0.80 mL/min with a mobile phase consisting of 0.3 M sodium nitrate in phosphate buffer (pH = 7) prepared by dissolving 27.6 g of monosodium phosphate, 101.98 g of sodium nitrate, and 4.66 g of sodium hydroxide in 4.0 L of HPLC-grade water. The pH was adjusted to 7 with 1 M NaOH. Solutions of 1% A100*f* or A70b*f* for injection were prepared by adding a stoichiometric amount of 1 M NaOH to the corresponding copolymer dissolved in the mobile phase. The degree of labeling with FITC was measured by UV–Vis spectrophotometry, using a Varian Cary 50 BIO UV–Vis Spectrophotometer. Optical microscope images of capsules were taken using an Olympus BX51 optical microscope fitted with a Q-Imaging Retiga EXi digital camera and ImagePro software. A confocal laser scanning imaging system equipped with an Argon-ion laser and a Nikon microscope using EZ-C1 software, version 1.50, was used to investigate the coatings on PUMC surfaces and all the confocal images were acquired using the same parameter settings. TEM images were recorded using a JEOL JEM 1200 EX TEMSCAN TEM (JEOL, Peabody, MA) operated at an accelerating voltage of 80 kV.

CONCLUSIONS

In conclusion, a postmodification method was developed to change surface chemistry of PUMC using an acetoacetyl functional polyanion. The acetoacetyl groups could react with amino groups on PUMC surfaces to achieve covalent tethering. Further modifications by LbL coating were performed to demonstrate the versatility of this method. Fluorescent labeling was used throughout to provide visual detection of modifications on the capsule surface. This method can be readily extended to introduce other desirable functional groups onto PUMC surfaces for different applications by designing corresponding polyelectrolyte modifiers. This method has several advantages over in situ modification methods as the wall formation and surface modification are well separated and other wall properties can be kept intact due to the confinement of modifications only to PUMC surfaces.

To control the size distribution of PUMCs, a T-junction type microfluidic device was constructed based on commercially available MicroTEEs. The device is easy to set up and operate. Monodisperse emulsions and narrowdisperse PUMCs can be made using this microfluidic device with their sizes easily tuned by the flow rates of either oil phase or aqueous phase.

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REFERENCES AND NOTES

1 Horiike, T.; Kuroda, T.; Shiozaki, T. French Patent Fr 2498474 1982.

2 Usami, T; Tanaka, T; Ishige, S. Electrophotography 1987, 26, 115–119.

3 (a) Giraud, S.; Bourbigot, S.; Rochery, M.; Vrornan, I.; Tighzert, L.; Delobel, R.; Poutch, F. Polym Degrad Stab 2005, 88, 106–113; (b) Sarier, N.; Onder, E. Thermochim Acta 2007, 452, 149–160; (c) Zhong, Y.; Feng, J. H.; Chen, S. L. Coloration Technol 2005, 121, 76–80.

4 (a) Hashemi, S. A.; Zandi, M. Iranian Polym J 2001, 10, 265–270; (b) Schwartz, L.; Wolf, D.; Markus, A.; Wybraniec, S.; Wiesman, Z. J Agric Food Chem 2003, 51, 5972–5976; (c) Muro-Sune, N.; Gani, R.; Bell, G.; Shirley, I. Comput Chem Eng 2005, 30, 28–41; (d) Zhang, Q.; Zhang, P. P.; Jiao, Q. Z. Chem Res Chin Univ 2006, 22, 379–382; (e) Scarfato, P.; Avallone, E.; Iannelli, P.; De Feo, V.; Acierno, D. J Appl Polym Sci 2007, 105, 3568–3577; (f) Mihou, A. P.; Michaelakis, A.; Krokos, F. D.; Mazomenos, B. E.; Couladouros, E. A. J Appl Entomol 2007, 131, 128–133.

5 (a) Bremeyer, N.; Ley, S. V.; Ramarao, C.; Shirley, I. M.; Smith, S. C. Synlett 2002, 11, 1843–1844; (b) Ramarao, C.; Ley, S. V.; Smith, S. C.; Shirley, I. M.; DeAlmeida, N. Chem Commun 2002, 1132–1133; (c) Ley, S. V.; Ramarao, C.; Lee, A. L.; Ostergaard, N.; Smith, S. C.; Shirley, I. M. Org Lett 2003, 5, 185–187; (d) Yu, J. Q.; Wu, H. C.; Ramarao, C.; Spencer, J. B.; Ley, S. V. Chem Commun 2003, 678–679; (e) Siu, J.; Baxendale, I. R.; Ley, S. V. Org Biomol Chem 2004, 2, 160–167; (f) Baxendale, I. R.; Griffiths-Jones, C. M.; Ley, S. V.; Tranmer, G. K. Chem-A Eur J 2006, 12, 4407–4416; (g) Broadwater, S. J.; McQuade, D. T. J Org Chem 2006, 71, 2131–2134; (h) Price, K. E.; Broadwater, S. J.; Bogdan, A. R.; Keresztes, I.; Steinbacher, J. L.; McQuade, D. T. Macromolecules 2006, 39, 7681–7685; (i) Screen, T.; Pears, D. Chim Oggi-Chem Today 2006, 24, 33–34; (j) Mason, B. P.; Bogdan, A. R.; Goswami, A.; McQuade, D. T. Org Lett 2007, 9, 3449–3451; (k) Ji, H. B.; Li, J. L.; Pei, L. X.; Gao, J. R. Chin J Chem Eng 2008, 16, 119–123.

6 Yang, J. L.; Keller, M. W.; Moore, J. S.; White, S. R.; Sottos, N. R. Macromolecules 2008, 41, 9650–9655.

7 (a) Chen, Y.; Au, J.; Kazlas, P.; Ritenour, A.; Gates, H.; McCreary, M. Nature 2003, 423, 136; (b) Li, G.; Feng, Y. Q.; Li, X. G.; Gao, P.; Wang, J.; Xie, J. Y. J Mater Sci 2007, 42, 4838–4844.

8 (a) Hong, K.; Park, S. J Mater Sci 1999, 34, 3161–3164; (b) Hong, K.; Park, S. Mater Sci Eng A-Struct Mater Prop Microstruct Process 1999, 272, 418–421.

9 (a) Li, J.; Hitchcock, A. P.; Stöver, H. D. H.; Shirley, I. Macromolecules 2009, 42, 2428–2432; (b) Dhumal, S. S.; Wagh, S. J.; Suresh, A. K. J Membr Sci 2008, 325, 758–771.

10 (a) Croll, L. M.; Stöver, H. D. H.; Hitchcock, A. P. Macromolecules 2005, 38, 2903–2910; (b) Croll, L. M.; Stöver, H. D. H. Pure Appl Chem 2004, 76, 1365–1374.

11 (a) Hitchcock, A. P.; Li, J.; Reijerkerk, S. R.; Foley, P.; Stöver, H. D. H.; Shirley, I. J Electr Spectrosc Relat Phenom 2007, 156, 467–471; (b) Hong, K. J.; Park, S. M. Mater Res Bull 1999, 34, 963–969; (c) Jabbari, E. Iranian Polym J 2001, 10, 33–43; (d) Lan, X. Z.; Yang, C. G.; Tan, Z. C.; Sun, L. X.; Xu, F. Acta Physico-Chim Sin 2007, 23, 581–584.

12 Ni, P. H.; Zhang, M. Z.; Yan, N. X. J Membr Sci 1995, 103, 51–55.

13 Scher, H. B.; Shirley, I. M.; Chen, J.; Mazeaud, I.; Kanne, D. B.; Padget, J. C.; Wade, P.; Waller, A. WO 01/94001 A2, 2001.

14 El-Gibaly, I.; Anwar, A. Int J Pharm 2004, 278, 25–40.

15 Xu, J. H.; Li, S. W.; Tan, J.; Wang, Y. J.; Luo, G. S. Langmuir 2000, 19, 7943–7946.

16 Nisisako, T.; Torii, T.; Higuchi, T. Chem Eng J 2004, 101, 23–29.

17 Steinbacher, J. L.; McQuade, D. T. J Polym Sci: Part A: Polym Chem 2006, 44, 6505–6533.

18 Qin, D.; Xia, Y. N.; Whitesides, G. M. Adv Mater 1996, 8, 917–919.

19 (a) Xia, Y. N.; Whitesides, G. M. Angew Chem Int Ed 1998, 37, 551–575; (b) Quevedo, E.; Steinbacher, J. McQuade, D. T. JACS 2005, 127, 10498–10499.

20 Burke, N. A. D.; Mazumder, M. A. J.; Hanna, M.; Stöver, H. D. H. J Polym Sci Part A: Polym Chem 2007, 45, 4129–4143.

21 (a) Mossberg, K.; Ericsson, M. J Microsc 1990, 158, 215–224; (b) Carlsson, K.; Mossberg, K. J Microsc 1992, 167, 23–37.