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## COMMUNICATION

## Synthesis of microsphere-loaded porous polymers by combining emulsion and dispersion polymerisations in supercritical carbon dioxide†

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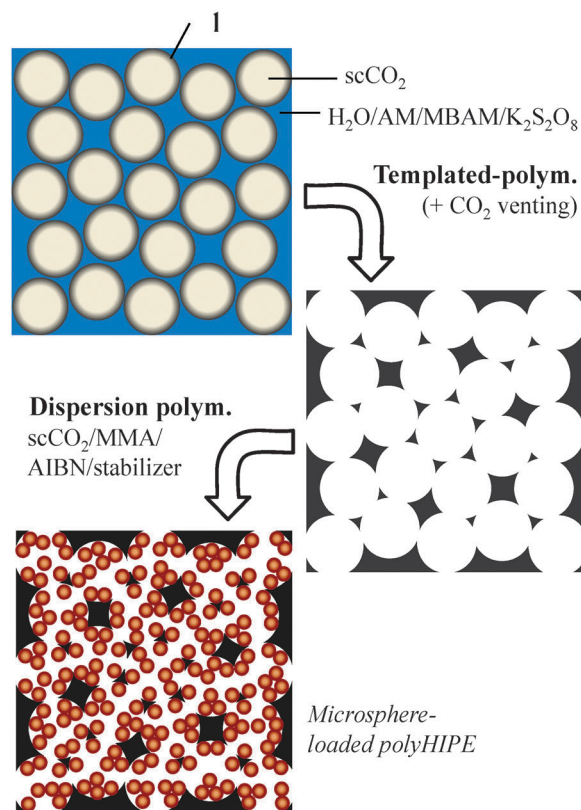
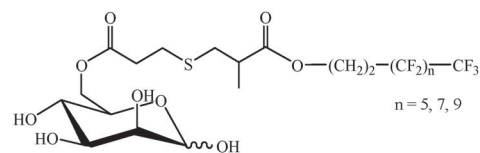
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Highly porous materials were produced by acrylamide polymerisation templated by supercritical CO<sub>2</sub>-in-water emulsions using new fluorinated glycosurfactants. Properties of the resulting polymer scaffolds were tuned by performing dispersion polymerisations within their cavities filled with supercritical CO<sub>2</sub>.

Supercritical carbon dioxide (scCO<sub>2</sub>) has been used as an alternative to organic solvents in a range of polymerisation processes in order to reduce their environmental impact.<sup>1</sup> Supercritical CO<sub>2</sub>-mediated polymerisation also benefits from straightforward product recovery and purification by venting of CO<sub>2</sub>. Dispersion polymerisations in scCO<sub>2</sub> are common due to the solubility of most industrially important monomers in the medium in contrast to the resulting polymers. Well-defined particles with standard particle diameters of 0.1 to 10 μm are usually obtained if a stabiliser is used to prevent their aggregation.<sup>2</sup> Emulsion polymerisation in scCO<sub>2</sub> is a heterogeneous process where scCO<sub>2</sub> serves as either the continuous<sup>3</sup> or the dispersed phase.<sup>4</sup> High internal phase emulsion (HIPE) (scCO<sub>2</sub>-in-water) can also be used as template for polymerisations.<sup>4</sup> In this case, the monomer is polymerised in the continuous aqueous phase before removal of CO<sub>2</sub> by venting (Scheme 1, step 1). The result is a porous polymer, referred to as a polyHIPE, with interconnected voids, where the sum of the pore volume is commonly greater than 74% of the structure's total volume. Porous polyHIPE materials have a variety of applications,<sup>5</sup> including scaffolds for tissue engineering,<sup>6</sup> supports for catalysts<sup>7</sup> and immobilisation of proteins.<sup>8</sup>

In this study, we demonstrate the efficiency of a novel class of non-ionic surface active agents, fluorinated glycosurfactants (**1**), for the stabilisation of scCO<sub>2</sub>-in-water HIPE emulsions used as

Scheme 1 Synthesis of microsphere-loaded polyHIPE in scCO<sub>2</sub>.

templates for the synthesis of porous polymers (step 1, Scheme 1). We also report for the first time the chemical modification of polyHIPEs by performing a methyl methacrylate (MMA) dispersion polymerisation in scCO<sub>2</sub> within the voids of the polymer scaffold, leading to hydrophilic porous materials loaded with hydrophobic polymer microspheres (step 2, Scheme 1). In this strategy, we took advantage of the high diffusivity and mass transfer capacity of scCO<sub>2</sub> to help the diffusion of the monomer, the initiator and the dispersion

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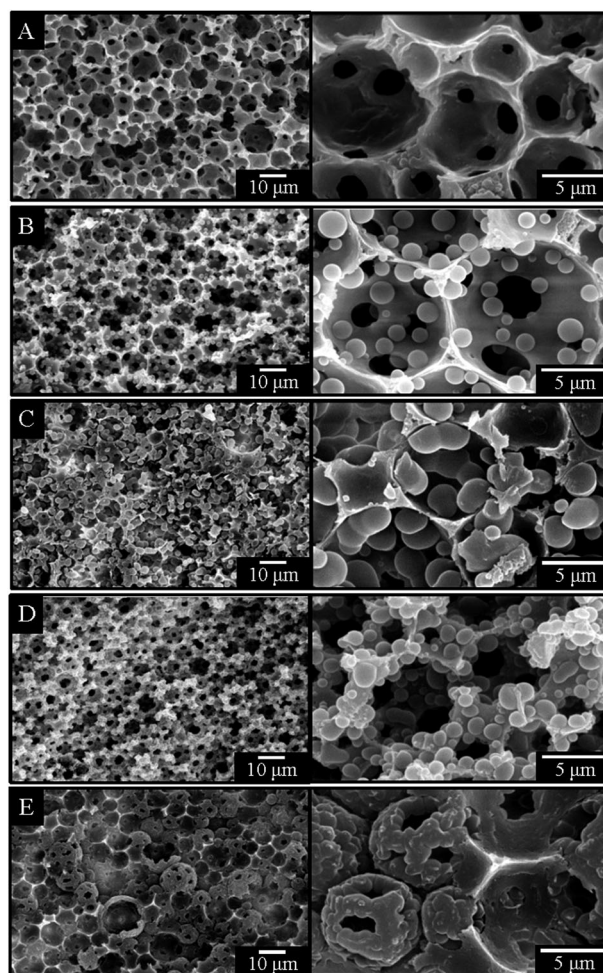
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stabiliser throughout the porous matrix prior to polymerisation, so that a homogeneous microsphere-distribution is obtained. This novel strategy offers the unique opportunity to tune the properties of preformed porous scaffolds, namely pore size, bulk density, specific surface area and mechanical properties, in order to meet the requirements of their applications. Reported examples of polymer-loaded polyHIPEs are rare and obtained by simultaneous polymerisation of different monomers located in both phases of a HIPE.<sup>9</sup> This last approach is thus not suitable for the modification of existing polyHIPEs in contrast to our strategy assisted by the scCO<sub>2</sub> technology.

In line with our recent work on the enzymatic modification of carbohydrates,<sup>10</sup> we have developed a novel fluorinated glycosurfactant (**1**) composed of a hydrophilic sugar head and a CO<sub>2</sub>-philic fluorinated tail. The synthetic procedure (see Fig. S1 in ESI†) consists of the selective enzymatic esterification of mannose with 3-mercaptopropionic acid (isolated yield = 48%) followed by a near-quantitative Michael addition of the thiol-containing sugar intermediate to Zonyl<sup>®</sup> (isolated yield = 84%), an inexpensive methacrylate mixture bearing fluorinated chains of different lengths (for MS analyses see Fig. S2 in ESI†). To help solubility, Zonyl<sup>®</sup> was distilled in order to remove the highest molecular weight methacrylates prior to the addition of the thiol.

Mixture **1** was tested as a surfactant for scCO<sub>2</sub>-in-water high internal phase emulsion polymerisations and the preparation of acrylamide polyHIPEs. Inspired by the work of Cooper *et al.*,<sup>4a,b</sup> an aqueous solution of acrylamide (AM) and *N,N'*-methylene bisacrylamide (MBAM) (8:2 w/w) was emulsified with scCO<sub>2</sub> at 250 bar in the presence of 5 wt% of **1** (conditions are detailed in the footnotes of Table 1). The polymerisation was then performed at 60 °C using potassium persulfate (K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>) as initiator (step 1, Scheme 1). After 16 h, the reactor was vented to leave a porous polymer matrix occupying the entire reactor vessel, which was then dried by lyophilisation. The scanning electronic microscopy (SEM) analyses of sections of the polyacrylamide revealed a homogeneous porous morphology with highly interconnected voids characteristic of polyHIPEs (Fig. 1, sample A). The diameter of the voids ranges from 3 to 10 μm and the thin cell walls are pierced by small windows or pores. The mean pore diameter and the specific volume of voids measured by mercury intrusion porosimetry were 2.6 μm and 4.31 cm<sup>3</sup> g<sup>-1</sup> respectively (Table 1, sample A). Mercury pycnometry analyses confirmed the low bulk density of the material (0.23 g cm<sup>-3</sup>) and the Brunauer–Emmett–Teller (BET) calculation derived



**Fig. 1** SEM images of the polyHIPEs. Sample **A** was prepared by scCO<sub>2</sub>-in-water emulsion polymerisation of acrylamide stabilised by the glycosurfactant **1**. **B** and **C** were synthesized by MMA polymerisation inside **A** in the presence of the stabiliser **2** (MMA/polyHIPE = 2.5 and 5 (w/w) for **B** and **C** respectively). **D** and **E** were prepared by MMA polymerisation inside **A** without the stabiliser (MMA/polyHIPE = 2.5 and 5 (w/w) for **D** and **E**, respectively). For detailed synthesis conditions see Table 1.

from nitrogen adsorption–desorption measurement estimated a low specific surface area (<5 m<sup>2</sup> g<sup>-1</sup>), typical of polyHIPEs.<sup>11</sup>

The acrylamide polyHIPE **A** (Fig. 1A) was used as host for MMA dispersion polymerisation performed in scCO<sub>2</sub> (step 2, Scheme 1). The glycosurfactant **1** was assessed for its ability to

**Table 1** Synthesis and characterisation of PMMA-loaded polyHIPEs

Sample	MMA/polyHIPE (w/w)	Stabilizer <b>2</b> (wt% vs. MMA)	$V_{\text{pore}}^c$ (cm <sup>3</sup> g <sup>-1</sup> )	Mean pore diameter <sup>c</sup> (μm)	Bulk density <sup>d</sup> (g cm <sup>-3</sup> )	Compressive modulus <sup>e</sup> (MPa)
A <sup>a</sup>	/	/	4.31	2.6	0.23	8
B <sup>b</sup>	2.5	5	2.20	2.5	0.35	37
C <sup>b</sup>	5	5	0.81	2.3	0.58	42
D <sup>b</sup>	2.5	/	2.08	2.6	0.33	46
E <sup>b</sup>	5	/	0.60	2.3	0.78	114

<sup>a</sup> Synthesis of the empty polyHIPE **A**: AM/MBAM/H<sub>2</sub>O = 8:2:25 (w/w/w), K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> and **1** (2 and 5 wt% based on monomers, respectively), PVOH (5 wt% based on H<sub>2</sub>O), CO<sub>2</sub>/Φ<sub>aqueous</sub> = 77:23 v/v, 60 °C, 250 ± 20 bar, 300 rpm, 16 h. <sup>b</sup> Dispersion polymerisation in the polyHIPE **A**: AIBN (2 wt% based on MMA), 65 °C, 320 ± 20 bar, 300 rpm, 16 h. <sup>c</sup> Measured by mercury intrusion porosimetry from 30 μm to 7.5 nm (for porosimetry curves see Fig. S3 and S4 in ESI). <sup>d</sup> Determined by mercury pycnometry. <sup>e</sup> Determined from the compressive stress–strain diagrams (see Fig. S5 and S6 in ESI).

stabilise PMMA particles (5 wt% of **1** and 2 wt% of AIBN vs. MMA, 65 °C, 320 bar), however it was unable to prevent particles aggregation, possibly due to the insufficient length of the fluorinated tails. Another homemade dispersion stabiliser, a fluorinated polyacrylate bearing tetraethyldiethylenetriamine pendant moieties (**2**) (see structure in ESI†),<sup>12</sup> was therefore used. MMA, AIBN and **2** (5 wt% based on MMA) and a piece of the polyHIPE **A** were placed in a stainless steel reactor with a magnetic stirrer before pressurisation with CO<sub>2</sub>. The polymerisation was conducted at 320 bar and 65 °C with different amounts of MMA (samples **B** and **C** in Table 1). The significant increase in bulk density and decrease of total pore volume ( $V_{\text{pore}}$ ) observed after the MMA polymerisation confirmed the incorporation of PMMA into the polyHIPE (compare samples **A–C** in Table 1). At the low PMMA loading, spherical micro-particles were deposited on the surface of the AM polyHIPE's walls (Fig. 1, sample **B**). The particles diameters (1–3 μm) were similar to those reported for the same experiment carried out in the absence of a porous matrix.<sup>12</sup> Examination of several sections of the modified sample revealed a homogeneous distribution of the particles, even at the heart of the material; the high diffusivity and mass transfer capacity of scCO<sub>2</sub> facilitate the diffusion of the reactants throughout the polyHIPE. Additionally, membranes of the modified polyHIPE remained thin and unaffected by the PMMA inclusion.

Upon MMA polymerisation using double MMA/polyHIPE weight ratio (Fig. 1, sample **C**) the resulting PMMA particles are observed to have merged, however, pore “windows” remained unblocked. Retention of pore connectivity of the PMMA-loaded polyHIPE was illustrated by a limited reduction in mean pore diameter (2.3–2.6 μm) (compare samples **A–C** in Table 1). The specific surface area of the polyHIPEs remained less than 5 m<sup>2</sup> g<sup>-1</sup>, but a significant increase in the compressive modulus upon PMMA loading indicated an improvement of the mechanical properties (compare samples **A–C** in Table 1).

For comparison, we performed the MMA polymerisation without a stabiliser (samples **D** and **E**, Fig. 1 and Table 1). Incorporation of PMMA into polyHIPE was effective however the polymer guests were less spherical and seemed to have grown against the wall surfaces of the polyHIPE pores (Fig. 1, sample **D**). At higher PMMA loading, the contrast was even more striking (compare samples **E** and **C**, Fig. 1); PMMA completely covers the internal surface of the polyHIPE pores when no stabiliser is used during polymerisation. SEM images of sections of the modified polyHIPE showed protrusions corresponding to PMMA cages templated by the polyHIPE's cavities (Fig. 1, sample **E**). Sample **E** exhibited the highest compressive modulus of all PMMA loaded polyHIPEs (Table 1).

In summary, this work demonstrates the effectiveness of fluorinated sugars as stabilisers for emulsion polymerisation and the production of polyHIPEs in scCO<sub>2</sub>. For the first time, polymer microspheres were formed in the cavities of a porous material by dispersion polymerisation in scCO<sub>2</sub>. This chemical modification allows adjustment of the pore volume, bulk density and improvement of the mechanical properties of a polyHIPE without affecting its pore interconnectivity.

This modification strategy could potentially be applied to a large range of polyHIPEs reported in the literature, while the incorporation of polymer particles in porous scaffolds may contribute to future developments in support catalysis and release systems.

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