Dispersion polymerisation in supercritical CO_2 using macro-RAFT agents†

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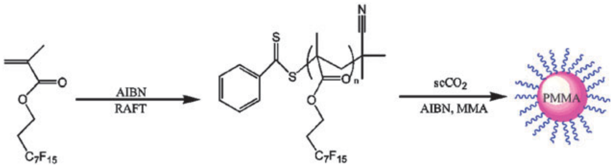
Received (in Cambridge, UK) 25th July 2008, Accepted 29th August 2008
First published as an Advance Article on the web 9th October 2008
DOI: 10.1039/b812827h

Fluorinated macro-RAFT agents can act as *in situ* stabilisers while exhibiting good control over block copolymers formed by dispersion polymerisation in supercritical CO_2 to yield well-defined spherical particles with a fluorinated "halo".

Recent advances in block copolymer self-assembly have revolutionized polymer chemistry; new applications have emerged ranging from metal sequestration, to micro-electronics and biomedicine. The driving force behind this technology has been the development of various controlled polymerisation techniques.[1] Reversible addition fragmentation chain transfer (RAFT) polymerisation has proven to be one of the most versatile of these controlled free radical methodologies.[2] RAFT is applicable to a wide range of monomers, while exhibiting exceptional control over polymerisation kinetics. Perhaps the major reason for its popularity in biomedical applications, is that the RAFT mechanism does not require toxic metal catalysts. In the general area of self-assembly, the RAFT agent is used to form living polymer chains from which amphiphilic copolymers can be synthesized. These block copolymers are then self-assembled in selective solvents or upon surfaces. In this paper, we examine a new mode of copolymer self-assembly; within polymer microparticles.

We recently demonstrated that RAFT-mediated dispersion polymerisation works effectively in supercritical carbon dioxide ($scCO_2$) to yield high quality product with low polydispersity (PDI) at high conversion. Almost all the polymer chains are living,[3,4] and molecularly well-defined block copolymer can be synthesized in the form of morphologically well-defined, spherical polymer particles.

In this paper we have developed highly soluble CO_2-philic stabilisers, which were synthesized by RAFT and can act as macro-RAFT agents in the controlled dispersion polymerisation of MMA. RAFT-terminated poly(1*H*,1*H*,2*H*,2*H*-perfluorooctyl methacrylate (PFOMA)) acts as an *in situ* stabiliser for the synthesis of block copolymers of PFOMA and PMMA by dispersion polymerisation. Normally, control in heterogeneous polymerisation is limited, but here we demonstrate excellent control over the kinetics of polymerisation arising from the exceptional mass transfer properties of the supercritical fluid, which enhances the chain transfer phenomenon in the polymer particle. Furthermore, we investigate whether these block copolymers can assemble within the microparticle in the $scCO_2$.



Scheme 1 Synthetic route for PMMA particles by macro-RAFT agent.

A fluorinated macro-RAFT agent (terminated with 2-cyanoprop-2-yl dithiobenzoate (CPDB)) was synthesized in bulk by free radical polymerisation (M_n = 15 kDa by ^1H NMR). This was then used as a macro-RAFT or reactive stabiliser in the dispersion polymerisation of MMA in $scCO_2$. Maintaining the concentration of initiator (2,2′-azobisisobutyronitrile, AIBN) to half that of the macro-RAFT agent led to well-controlled reaction kinetics. Whilst block copolymer stabilisers synthesized by RAFT have been used in the past for dispersion polymerisation in $scCO_2$,[5] this is the first time that simultaneous stabilisation and molecular weight control has been achieved (Scheme 1). All reactions reported in this paper were performed at 65 °C and 27.6 MPa (4000 psi).

A series of reactions were conducted to investigate the dispersion polymerisation kinetics. A progressive and controlled increase in molecular weight as a function of reaction time is observed (entries 1–11 in Table 1) and most importantly, a narrow PDI (1.22) was achieved in the final product. Good agreement was observed between the experimentally determined and the theoretical molecular weight. Such good control is generally limited to solution polymerisation and these data clearly show that $scCO_2$ is facilitating excellent mass transfer of reactants and good mobility of the propagating species in a heterogeneous system through the dispersed microparticles.

Monomer conversion (MMA) is almost quantitative after 20 hours and the kinetic plot (Fig. 1) follows a pseudo-first-order reaction rate at low conversion; typical for RAFT polymerisation. An inhibition period of about 1 hour is also observed in the polymerisation. This is often observed for these dithioester RAFT agents and has been ascribed to either slow fragmentation of the intermediate radical, or slow re-initiation by the leaving group of the RAFT agent.[2] Surprisingly, the inhibition period for a macro-RAFT agent is much shorter than that observed in our previous studies using a free RAFT agent (1 hour *vs.* ~10 hours).[4]

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† Electronic supplementary information (ESI) available: Experimental. See DOI: 10.1039/b812827h

Table 1 Macro-RAFT dispersion polymerisation of MMA in $scCO_2$

Entry[a]	Time/ h	Conversion (%)[b]	M_n[c]	PDI[c]	M_{nth}[d]
1	1.5	17	25 000	1.46	25 210
2	2.0	28	31 000	1.34	31 820
3	2.5	40	42 000	1.29	39 030
4	3.5	56	47 000	1.28	48 640
5	4.5	65	56 000	1.29	54 050
6	5.5	71	59 000	1.28	57 650
7	8	86	62 000	1.29	66 660
8	10	91	65 000	1.22	69 660
9	12	95	71 000	1.22	72 070
10	16	98	74 000	1.21	73 870
11	20	99	76 000	1.22	74 970

[a] Reaction performed with MMA 1.56 M, [Macro-RAFT]/[AIBN] = 2, theoretical molecular weight of 75 000 g mol^{-1} at 100% MMA conversion based on the RAFT agent concentration. [b] From ^1H NMR. [c] Determined by GPC calibrated with polystyrene standards in THF using a RI detector. [d] Theoretical molecular weight based on RAFT–monomer concentration and conversion.

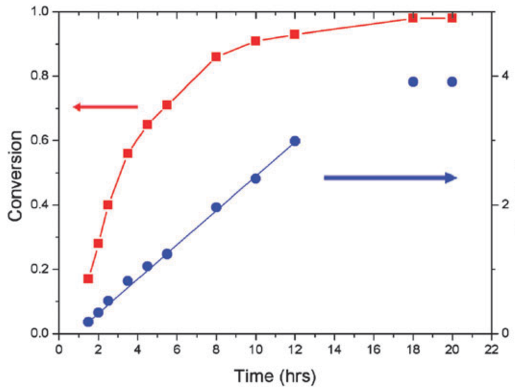

Fig. 1 Conversion as a function of polymerisation time and pseudo-first-order kinetic plot for polymerisation of MMA *via* macro-RAFT agent in $scCO_2$.

The observed linear increase in molecular weight and decrease in polydispersity with conversion (Fig. 2) are consistent with a good living/controlled process. But the key development of this work is the ability to simultaneously maintain kinetic as well as morphological control. Scanning electron microscopy (SEM) images show that well-defined spherical particles are formed (Fig. 3). These particles do have a broad size distribution compared to dispersion polymerisation in the absence of RAFT agent,[6] and this is likely caused by the known inhibiting effect that the RAFT mechanism has on the particle nucleation period in a dispersion polymerisation.[7] Nonetheless, the ability to retain the spherical morphology to this extent during a controlled dispersion polymerisation is a significant improvement on the analogous dispersion reactions in conventional media.

The ability to control, or at least direct, the self-assembly of block copolymers within polymeric microparticles could offer a unique opportunity. While the synthesis of core–shell particles from block copolymers using emulsion technology has been previously described,[8] extension of this approach to the micro-scale has not been reported. The applications of such microspheres are diverse; from core–shell particles in paints and coatings, to drug delivery applications, impact modifiers or even novel chromatographic supports. In this work we chose PMMA and PFOMA because they should require a large enthalpy of mixing and one would expect some form of phase-separation of the different blocks within the microparticles.

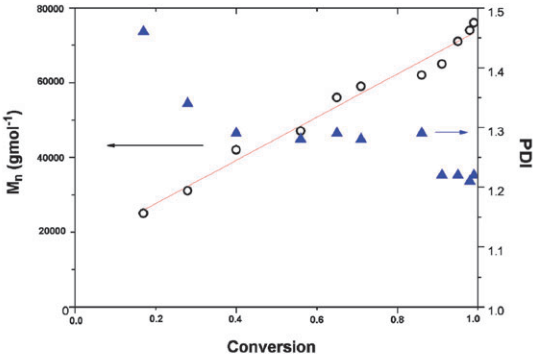

Fig. 2 Molecular weight evolution and molecular weight distribution with monomer conversion for MMA showing excellent linear evolution and the expected narrowing of the PDI at higher conversions. Note also that the plot of molecular weight with conversion intercepts the *y* abscissa at 15 kDa; the molecular weight of the PFOMA surfactant as calculated by ^1H NMR.

Focussed ion beam scanning electron microscopy has been utilised to probe and slice individual polymer particles. A 300 nm thick slice was prepared (inset Fig. 4b) and this was transferred into a transmission electron microscope for energy dispersive X-ray analysis (EDX-TEM) to produce an elemental map of the particle cross-section (Fig. 4). The imaging reveals a concentration of fluorine throughout the particle cross-section, but also clearly shows that there is a fluorine-rich halo on the extreme periphery of the polymer particle. There is no distinct phase separation within the centre of the microsphere and this is confirmed by the elemental map (Fig. 4b) in which carbon, oxygen and fluorine are mapped. This map also clearly shows the green "halo" around the periphery indicating fluorine rich areas—no such areas are observed in the inside of the particle. The fluorine density across the particle cross-section is plotted (Fig. 4) to quantify the relative concentration of PFOMA within a particle. The

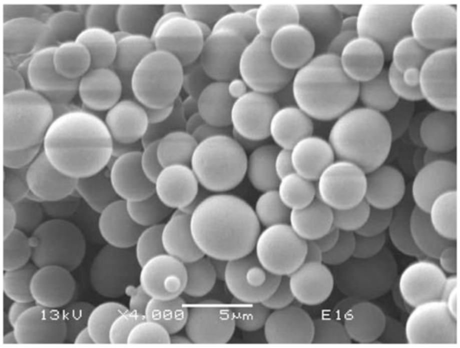

Fig. 3 SEM image of PMMA particles formed by dispersion polymerisation in $scCO_2$ using macro-RAFT agent demonstrating well-defined, discrete particles of controlled molecular weight block copolymer.

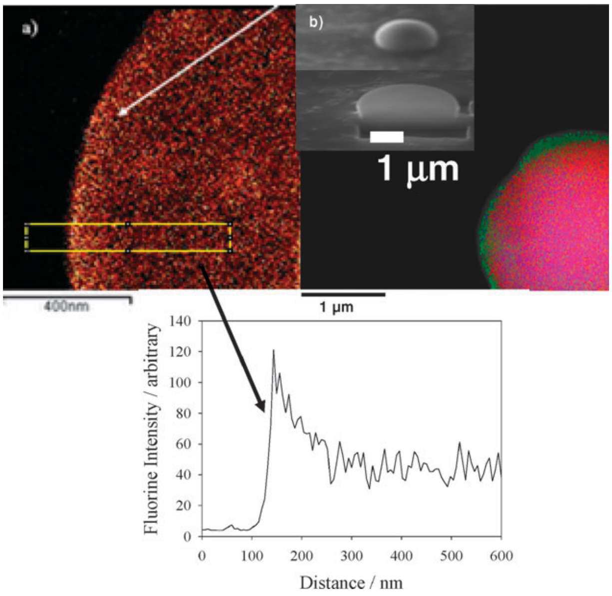

Fig. 4 TEM-EDX element map and image for polymer particles: (a) cross-sectional map showing fluoropolymer distribution (fluorine map) across a section of a particle and the subsequent histogram over the area within the yellow box; (b) showing elemental distribution around an intact particle (red—carbon, pink—oxygen, and green—fluorine). The inset shows an SEM image of a single particle before and after focussed ion beam slicing to yield ∼300 nm cross-sectioned slice. The fluorine-rich halo is present in all images.

concentration at the surface of the particle is clearly higher (up to three times) compared to the centre of the particle where the fluorine density becomes much more uniform.

A surface coating of fluorine is quite predictable for this system, since the PFOMA group acts as a stabiliser and is CO_2-philic. Thus, migration of these chains to the outside of the particle is expected and the large amount of stabiliser used in this process ensures good surface coverage of fluorinated species. But what is surprising from these maps, is the apparent lack of phase separation between the PFOMA and PMMA within the centre of the particles. We believe that $scCO_2$ acts as a compatibilizer and that under the conditions of this experiment, the PFOMA and PMMA blocks become miscible. Upon release of the $scCO_2$ at the completion of the reaction, the two blocks are kinetically trapped in this state. Thus, the $scCO_2$ acts to miscibilize the polymer blocks within the particle, whilst simultaneously producing the fluorinated "halo" around the extremity of the sphere. Enhancement of miscibility between poorly compatible polymers is a well-known phenomenon in blends formed in $scCO_2$.[9] We are currently investigating methods of enforced phase separation (*i.e.* temperature and solvent annealing) in order to further understand this phenomenon.

We have demonstrated that macro-RAFT agents in $scCO_2$ exhibit exceptionally good control over heterogeneous dispersion polymerisation and that well-defined spherical microparticles are formed. Furthermore, the particles exhibit a "core–shell" type structure with a fluorine-rich region on the periphery of the particle. The challenge now is to further develop this methodology to a wider range of block copolymers and to target specific materials for practical application.

Notes and references

1 J.-S. Wang and K. Matyjaszewski, *J. Am. Chem. Soc.*, 1995, **117**, 5614; M. Kato, M. Kamigaito, M. Sawamoto and T. Higashimura, *Macromolecules*, 1995, **28**, 1721; J. Chiefari, Y. K. Chong, F. Ercole, J. Krstina, J. Jeffery, T. P. T. Le, R. T. A. Mayadunne, G. F. Meijs, C. L. Moad, G. Moad, E. Rizzardo and S. H. Thang, *Macromolecules*, 1998, **31**, 5559; C. J. Hawker, A. W. Bosman and E. Harth, *Chem. Rev.*, 2001, **101**, 3661.
2 S. Perrier and P. Takolpuckdee, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 5347.
3 K. J. Thurecht, A. M. Gregory, W. Wang and S. M. Howdle, *Macromolecules*, 2007, **40**, 2965.
4 A. M. Gregory, K. J. Thurecht and S. M. Howdle, *Macromolecules*, 2008, **41**, 1215.
5 Z. Ma and P. Lacroix-Desmazes, *J. Polym. Sci., Part A: Polym. Chem.*, 2004, **42**, 2405; Z. Ma and P. Lacroix-Desmazes, *Polymer*, 2004, **45**, 6789.
6 H. M. Woods, M. M. C. G. Silva, C. Nouvel, K. M. Shakesheff and S. M. Howdle, *J. Mater. Chem.*, 2004, **14**, 1663; H. M. Woods, C. Nouvel, P. Licence, D. J. Irvine and S. M. Howdle, *Macromolecules*, 2005, **38**, 3271.
7 P. J. Saikia, J. M. Lee, B. H. Lee and S. Choe, *J. Polym. Sci., Part A: Polym. Chem.*, 2006, **45**, 348.
8 T. S. Wilkinson, A. Boonstra, A. Montoya-Goni, S. van Es, M. J. Monteiro and A. L. German, *J. Colloid Interface Sci.*, 2001, **237**, 21; M. J. Monteiro and J. de Barbeyrac, *Macromolecules*, 2001, **34**, 4416; C. J. Ferguson, R. J. Hughes, D. Nguyen, B. T. T. Pham, R. G. Gilbert, A. K. Serelis, C. H. Such and B. S. Hawkett, *Macromolecules*, 2005, **38**, 2191.
9 E. Kung, A. J. Lesser and T. J. McCarthy, *Macromolecules*, 1998, **31**, 4160; K. J. Thurecht, D. J. T. Hill, C. M. L. Preston, L. Rintoul, J. W. White and A. K. Whittaker, *Macromolecules*, 2004, **37**, 6019.