Polymerization-Induced Self-Assembly of All-Acrylic Diblock Copolymers via RAFT Dispersion Polymerization in Alkanes

Liam P. D. Ratcliffe,‡ Beulah E. McKenzie,‡ Gaëlle M. D. Le Bouëdec,‡ Clive N. Williams,‡ Steven L. Brown,* and Steven P. Armes‡*†

†Dainton Building, Department of Chemistry, The University of Sheffield, Brook Hill, Sheffield, South Yorkshire S3 7HF, U.K.
‡Scott Bader Company Ltd., Wollaston, Wellingborough, Northants NN29 7RL, U.K.

Supporting Information

ABSTRACT: A series of all-acrylic poly(lauryl acrylate)—poly(benzyl acrylate) (PLA–PBzA) diblock copolymer nanoparticles are prepared by reversible addition–fragmentation chain transfer (RAFT) dispersion polymerization of benzyl acrylate in n-heptane, n-dodecane, or isohexadecane. As the PBzA block grows from the soluble PLA block it eventually becomes insoluble, which drives in situ polymerization-induced self-assembly (PISA). High monomer conversions (>99%) can be achieved and high blocking efficiencies are observed using 1H NMR spectroscopy and gel permeation chromatography, respectively. However, final Mn/Mw values range from 1.36 to 2.10, which suggests that chain transfer to polymer occurs in these all-acrylic PISA formulations. The soft, film-forming nature of these all-acrylic nanoparticles makes conventional TEM studies problematic. However, inspecting the visual appearance of these dispersions combined with DLS studies allows the construction of a phase diagram, which has been validated by cryo-TEM studies of selected copolymers. The latter technique confirms that spherical, worm-like or vesicular morphologies can be obtained depending on the copolymer concentration, mean degree of polymerization of the core and stabilizer blocks, and choice of solvent. Oscillatory rheology studies indicate that PLA–PBzA worms form free-standing worm gels at 20 °C with relatively low moduli (G’ ~ 20 Pa). Moreover, reversible thermal transitions are observed below ~15 °C and above ~67 °C. Finally, worm gels that exhibit critical gelation concentrations as low as 2.5% w/w at 20 °C can be prepared at up to 40% w/w solids using a convenient one-pot protocol. In summary, this new PISA formulation represents a cost-effective, facile synthesis route to all-acrylic nano-objects in non-polar solvents.

INTRODUCTION

Traditionally, dispersion polymerization has provided a facile route to well-defined, colloidal stable latexes in non-polar solvents via addition of a suitable steric stabilizer—usually an adsorbed homopolymer, block copolymer, or graft copolymer.1 In contrast to emulsion polymerization, the monomer is soluble in the solvent and the initial reaction mixture is homogeneous: polymerization leads to the formation of an insoluble polymer, which nucleates and ultimately to sterically stabilized latex particles (usually in the 0.1–10 μm size range).2–6 Dispersion polymerization was originally developed for paints and coatings applications,7 but the relatively narrow particle size distributions8 led to a broader range of applications ranging from biomedical assays to particulate modeling.9–13 It is well-known that AB diblock copolymers can self-assemble to form micelles in a solvent that is selective for one of the blocks.14–22 A wide range of copolymer morphologies are known,23 but post-polymerization processing (such as a solvent or pH switch,27 thin film rehydration,27–29 or electroformation30) is usually required, with this additional step normally being conducted at relatively high dilution (typically <5% solids).

The development of controlled radical polymerization (CRP) techniques such as nitroxide-mediated polymerization (NMP),24,25 atom transfer radical polymerization (ATRP),25,30 or reversible addition-fragmentation chain transfer (RAFT)34 has led to the synthesis of many well-defined, functional block copolymers over the past two decades.35–45 By utilizing the latter technique in a suitable selective solvent, a wide range of diblock copolymer nano-objects can be formed directly in situ at high copolymer concentrations (up to 50% solids) by polymerization-induced self-assembly (PISA).46,47 The copolymer morphology is dictated by the relative volume fractions of each block, with spheres, worms or vesicles being obtained as the proportion of the core-forming block is gradually increased.48 Various potential applications have been explored49–51 and this efficient new approach has sparked renewed interest in conducting dispersion polymerizations in non-polar solvents, which may be useful in areas such as inkjet printing or electronic displays.52
Many PISA syntheses are described in the literature: such formulations are commonly conducted via emulsion or dispersion polymerization in either aqueous or alcoholic media. However, there are rather few examples of PISA syntheses in non-polar media. Early examples include poly(4-vinylpyridine)-poly(styrene diblock copolymers prepared in cyclohexane and poly(styrene-alt-maleic anhydride)-based copolymers in chloroform. More recently, Armes and co-workers reported the preparation of a series of poly(lauryl methacrylate)-poly(benzyl methacrylate) (PLMA-PBzMA) diblock copolymers in n-heptane. A detailed phase diagram was constructed, which proved to be essential for the reproducible production of spherical, worm-like, or vesicular morphologies. Interestingly, PLMA-PBzMA worms undergo a worm-to-sphere transition on heating, which leads to in situ degelation. This is complementary behavior to that reported previously for aqueous methacrylic copolymer worms, which undergo a worm-to-sphere transition on cooling to sub-ambient temperatures. Subsequently, Pei et al. reported similar thermoresponsive behavior for poly(stearyl methacrylate)-poly(3-phenylpropyl methacrylate) prepared in n-tetradecane as well as related copolymers in alcoholic media. In each case, surface plasticization of the worms by solvent molecules drives the morphological transition.

Despite the growing interest in RAFT-mediated PISA, there have been very few studies of all-acrylic formulations. This is perhaps surprising since, along with methacrylates and styrenes, acrylates have historically been among the most important monomer classes, especially for dispersion polymerization in non-polar solvents. Poly(acrylates) have lower glass transition temperatures (30 or 40 °C) than their methacrylate counterparts and hence are useful for the production of polymeric films and adhesives at lower temperatures. A range of applications are being explored for self-assembled nanoparticles, including films and coatings and drug delivery. However, the paucity of all-acrylic PISA formulations in the literature could in part be related to the difficulty of investigating the copolymer morphology for such soft, film-forming copolymers. Furthermore, acrylic polymerizations have a well-documented propensity to undergo branching via chain transfer to polymer (CTP). This side reaction is mitigated by the use of CRP, but not eradicated, thus a significant broadening of the molecular weight distribution is often observed. There are a handful of acrylic macromolecular chain transfer agents (macro-CTAs), such as poly(acrylic acid) (PAA) or PAA-co-PDEMA macro-CTA (poly(poly(ethylene oxide) methyl ether acrylate)) as steric stabilizers for the RAFT aqueous emulsion polymerization of styrene. Similarly, PAA has been employed as a stabilizer for the emulsion polymerization of 4-vinylpyridine (4VP) using NMP. These formulations afforded a range of copolymer morphologies, but low dispersities could not be achieved at high monomer conversions.

In contrast, RAFT formulations utilizing poly(methacrylic acid) (PMAA), PAA, poly(N,N-dimethylacrylamide) (PDMAAm), or poly(ethylene oxide) (PEO) as steric stabilizers in conjunction with acrylic core-forming blocks such as poly(n-butyl acrylate) have invariably produced kinetically trapped spheres. Moreover, cryo-TEM was required for particle imaging, because of the low Tg of the PBA core. Block copolymer dispersities were typically greater than 1.40, with significantly higher Mw/Mn values generally being reported at high monomer conversions.

An et al. utilized RAFT aqueous dispersion polymerization to prepare cross-linked nanogels. More specifically, either a PDMAAm or poly(poly(ethylene glycol) methyl ether methacrylate) (PPEGMA) stabilizer was combined with a 2-methoxyethyl acrylate-based core-forming block. This work is particularly noteworthy because relatively low dispersities were consistently obtained using a potassium persulfate/sodium ascorbate redox initiator at relatively low polymerization temperatures (30 or 40 °C). However, only spherical morphologies were reported for such formulations.

Pan and co-workers prepared poly(acrylic acid)-b-polystyrene (PAA–PS) diblock copolymers in the form of spheres, worms or vesicles via RAFT dispersion polymerization in methanol. However, such polymerizations were relatively slow, with significant amounts of unreacted styrene monomer still present in the formulation (conversions varied between 15 and 79%). D’Agosto and co-workers chain-extended a poly(N-acryloylmorpholine) macro-CTA with n-butyl acrylate in ethanol/water mixtures using RAFT, while Charleux et al. reported the preparation of highly anisotropic worms using an all-acrylic formulation. However, this required the synthesis of a bespoke cholesteryl-based monomer for the core-forming block and dispersities were relatively high (Mw/Mn = 1.3–2.0).

To date, very little work has focused on PISA using acrylic monomers in non-polar solvents. Charbonnier and co-workers utilized several monomers (4VP, and a mixture of MMA with MAA, AA or styrene) to form core-forming blocks for dispersion polymerizations in octane or toluene using NMP, where either PLA or poly(2-ethylhexyl acrylate) (PEHA) was employed as the steric stabilizer. A range of spherical particles were obtained with the aim of producing electrophoretic ink but copolymer dispersities were often relatively high. There appears to be only one literature example of an all-acrylic RAFT PISA dispersion formulation in non-polar media. The Charleux group used a poly(2-ethylhexyl methacrylate) macro-CTA to polymerize methyl acrylate in isododecane. However, only spherical particles could be obtained, while control over the copolymer molecular weight distribution was rather poor (e.g., Mw/Mn = 1.76 at 48% conversion).

Herein an all-acrylic RAFT dispersion polymerization formulation is examined for the preparation of poly(lauryl acrylate)-poly(benzyl acrylate) (PLA–PBzA) nanoparticles in n-heptane, n-dodecane or isohexadecane. The copolymer morphology could be adjusted by varying the target degree of polymerization (DP) of the PBzA block, the copolymer concentration, and the solvent type. A phase diagram was constructed for the n-heptane formulation based on the visual appearance of the samples, dynamic light scattering (DLS) data, and our prior experience of related methacrylic PISA formulations. Selected copolymers were also characterized by cryo-TEM, which confirmed our morphology assignments. In particular, a soft, free-standing gel phase was identified that proved to be thermoresponsive. Finally, these all-acrylic copolymer dispersions can be conveniently prepared via a one-pot protocol at 40% w/w solids.

**EXPERIMENTAL SECTION**

**Materials.** Lauryl acrylate (LA, 98%) was purchased from Tokyo Chemical Industry UK Ltd., and benzyl acrylate (BzA, 97%) was purchased from Alfa Aesar; both were used as received. 2,2'-Azoisobutyronitrile (AIBN, 98%), 2-(dodecylthiocarbonothioylthio)-2-methylpropanoic acid (DDMAT, 98%) and deuterated chloroform (CDCl3) were purchased from Sigma-Aldrich (UK) and were used as purchased from Sigma-Aldrich (UK) and were used as
received. tert-Butylperoxy-2-ethylhexanoate (Trigonox 21S or T21s) initiator was supplied by AkzoNobel (The Netherlands). All other reagents were purchased from Sigma-Aldrich (UK) and were used as received, unless otherwise noted. n-Heptane (≥96%) and n-dodecane (≥99%) were purchased from Fisher Scientific (UK). Isohexadecane (main constituent of a 97% w/w mix of C16 isoparaffins) was donated by Scott Bader (Wollaston, UK) and used without further purification. All other solvents were of HPLC quality and were purchased from Fisher Scientific (Loughborough, UK).

**Synthesis of PLA macro-CTA.** A typical protocol for the synthesis of a PLA macro-CTA was as follows. LA monomer (0.32 mol, 76,922 g), DDMAT RAFT agent (12.8 mmol, 4.667 g), and acetone (1.41 mol, 82,009 g) were added to a round-bottomed flask in order to target a mean degree of polymerization (DP) of 25. AIBN initiator (2.56 mmol, 0.420 g, CTA/AIBN molar ratio = 5.0) was then added to this mixture, and the resulting yellow solution was cooled in an ice bath while sparging with N2 for 25 min. The immersed in an oil bath set at 80 °C followed by BzA monomer (0.6457 g, 3.98 mmol) and DDMAT RAFT agent (0.66 mmol, 0.2430 g) in order to target a mean DP of 14 for this PLA macro-CTA. This suggests a CTA efficiency of 98%. THF GPC analysis indicated Mₙ and Mₙ/Mₚ values of 3,700 g mol⁻¹ and 1.12, respectively.

**Synthesis of PBzA-DPLA15**. A typical protocol for the synthesis of PLA₁₅−PBzA₂ diblock copolymer was as follows: PLA₁₅ macro-CTA (0.165 g, 0.04 mmol) was added to a 25 mL round-bottomed flask (or a glass vial), followed by BzA monomer (0.06457 g, 3.98 mmol) and n-heptane (3.0959 g). T21S initiator was then added (1.9 mg, 0.009 mmol), as a 1.0% solution in n-heptane to make up a 20% w/w solution (CTA/T21S molar ratio = 5.0). This flask was stirred for 16 h to ensure high monomer conversion (98% by ¹H NMR analysis) and subsequently quenched by cooling followed by exposure to air. THF GPC analysis indicated Mₙ and Mₙ/Mₚ values of 14,000 g mol⁻¹ and 1.89, respectively.

**One-Pot Synthesis of PBzA−DPLA₁₅**. A typical protocol for the synthesis of PLA₁₅−PBzA₂ diblock copolymer nanoparticles viaRAFT dispersion polymerization. LA monomer (0.01 mol, 24.038 g) was added to a round-bottomed flask containing DDMA TRAF agent (0.66 mmol, 0.2430 g) in order to target a mean degree of polymerization (DP) of 15. AIBN initiator (0.013 mmol, 0.0219 g, CTA/AIBN molar ratio = 5.0) was then added to this flask, and the resulting yellow solution was cooled in ice prior to N₂ sparging for 30 min, before the sealed flask was immersed into an oil bath set at 70 °C. After 105 min (97% conversion, determined by ¹H NMR analysis) and subsequently quenched by cooling followed by exposure to air. THF GPC analysis indicated Mₙ and Mₙ/Mₚ values of 14,000 g mol⁻¹ and 1.89, respectively.
RESULTS AND DISCUSSION

Homopolymerization of LA. In 2013, Fielding et al. published an example of an all-methacrylic RAFT PISA formulation based on a PLMA−PBzMA diblock copolymer formulation in n-heptane. They were able to prepare a range of well-defined nano-objects, including a pure worm phase that formed relatively transparent free-standing gels. In the present work, an analogous all-acrylic formulation has been developed via chain extension of a PLA macro-CTA using benzyl acrylate (BzA) in a range of non-polar solvents.

The RAFT solution polymerization of LA (target DP = 25) was conducted in acetone at 70 °C using an AIBN initiator (see Figure 1). DDMAT was selected for this synthesis as trithiocarbonates are known to efficiently control the polymerization of acrylic monomers. A conversion of 94% was obtained after ~3 h, determined by 1H NMR (see Figure 2a,b), and the linear semilogarithmic plot indicated first-order kinetics with respect to LA. The THF GPC data shown in Figure 2b confirm the unimodal nature of the PLA molecular weight distribution over the course of the reaction. The molecular weight increases linearly with conversion and low dispersities (below 1.12) are observed throughout. Subsequently, a large batch of PLA (target DP = 25) was prepared and the polymerization quenched after 65 min (55% conversion, determined by 1H NMR). The crude PLA was then precipitated twice into a 10-fold excess of cold methanol and washed in this non-solvent, before being placed under high vacuum for 3 days at 20 °C. 1H NMR analysis indicated a mean DP of 14 for this PLA macro-CTA, which corresponds to a relatively high CTA efficiency of 98%. This was calculated by comparing the DP of the polymer after purification by precipitation with the monomer conversion. In both cases this was calculated from the molar ratio of DDMAT to PLA protons (labeled “d” and “h”, respectively; see Figure 3a).

Dispersion Polymerization of BzA in n-Heptane. The synthesis conditions for a PLA_{14}−BzA_{140} diblock copolymer...
were systematically varied to identify the ideal conditions required for a well-controlled RAFT polymerization. A series of THF GPC curves for PLA$_{14}$−PBzA$_{140}$ diblock copolymers are shown in Figure 3b. The RAFT solution polymerization of BzA in toluene (which is a good solvent for both blocks) results in a slightly higher $M_w/M_n$ value than the equivalent dispersion polymerization in n-heptane (both conducted at 20% w/w total solids, 80 °C, macro-CTA/initiator = 5.0). This might be due to a
slightly less efficient chain extension in toluene, since there appears to be a larger proportion of unreacted macro-CTA in the THF GPC trace.

The chain extension in n-heptane appears to be more efficient resulting in a lower dispersity (under the equivalent conditions of 80 °C and CTA/T21S molar ratio = 5.0). However, in general, the $M_n/M_w$ values indicated in Figure 3b are significantly higher than expected for a well-controlled RAFT polymerization. Unfortunately, this is not uncommon for all-acrylic formulations and could well be due to the aforementioned and well-documented chain transfer to the polymer backbone, which inevitably leads to extensive branching. Indeed, other all-acrylic formulations such as the dispersion polymerization described by Charleux and co-workers in alcohol/water mixtures also suffer from higher than expected copolymer dispersities. When DP's greater than 40 were targeted, $M_n/M_w$ values above 1.9 were observed. Moreover, this loss of control was more pronounced when higher monomer conversions were obtained. Similar observations were also reported for an alkane-based dispersion polymerization formulation reported by the same group. However, in this case substantially higher dispersities were observed: monomer conversions above 62% resulted in $M_n/M_w$ values above 4.0. Nonetheless, in the present case high monomer conversions were still obtained in most cases as determined by $^1$H NMR (>97% at 15% w/w solids and above), with $M_n/M_w < 2.0$ in most cases (see Table 1). Monomer conversions were calculated by comparing the integrated vinyl signals in Figure 3a (labeled “o” in the case of BzA and “g” for LA monomer) to that of the polymer signals (signal “n” in the case of PBzA and “h” for PLA). $^1$H NMR spectra recorded for the respective monomers and the CTA used in this formulation are also shown, along with a representative example of the diblock copolymer. Attempts to increase the rate of polymerization by performing syntheses at 90 °C were successful but resulted in a large increase in $M_n/M_w$ even at higher macro-CTA/initiator molar ratios. Conducting the polymerizations at 70 °C did not lead to narrower molecular weight distributions but resulted in significantly slower rates of polymerization (data not shown), so it was decided to conduct all further PLA14−PBzA syntheses at 80 °C using a macro-CTA/T21S molar ratio of 5.0. The kinetics of polymerization of BzA when targeting PLA14−PBzA syntheses at 80 °C using a macro-CTA/T21S molar ratio of 5.0. The kinetics of polymerization of BzA when targeting PLA14−PBzA syntheses at 80 °C using a macro-CTA/T21S molar ratio of 5.0. The kinetics of polymerization of BzA when targeting PLA14−PBzA syntheses at 80 °C using a macro-CTA/T21S molar ratio of 5.0.

Table 1. Summary of Synthesis Conditions, Final Monomer Conversions, and GPC Data Obtained for a Series of PLA14−PBzA Diblock Copolymers Prepared via RAFT Dispersion Polymerization of BzA in n-Heptane

| entry no. | targeted diblock composition | solids content (% w/w) | conversion (%) | $M_n$ (g mol$^{-1}$) | $M_w/M_n$ | visual appearance |
|-----------|-----------------------------|------------------------|---------------|---------------------|-----------|------------------|
| 1         | PLA14−PBzA$_{10}$          | 30                     | 99            | 11 800              | 1.58      | transparent gel  |
| 2         | PLA14−PBzA$_{15}$          | 25                     | 99            | 10 600              | 1.55      | slightly turbid liquid |
| 3         | PLA14−PBzA$_{20}$          | 25                     | 99            | 10 200              | 1.53      | slightly turbid gel |
| 4         | PLA14−PBzA$_{25}$          | 25                     | 99            | 11 800              | 1.59      | slightly turbid gel |
| 5         | PLA14−PBzA$_{30}$          | 25                     | 99            | 12 900              | 1.63      | milky gel         |
| 6         | PLA14−PBzA$_{35}$          | 25                     | 99            | 13 600              | 1.67      | milky liquid      |
| 7         | PLA14−PBzA$_{40}$          | 20                     | 99            | 9 400               | 1.47      | slightly turbid liquid |
| 8         | PLA14−PBzA$_{45}$          | 20                     | 98            | 10 500              | 1.36      | slightly turbid liquid |
| 9         | PLA14−PBzA$_{50}$          | 20                     | 99            | 11 300              | 1.56      | slightly turbid liquid |
| 10        | PLA14−PBzA$_{55}$          | 20                     | 99            | 11 600              | 1.76      | slightly turbid gel |
| 11        | PLA14−PBzA$_{60}$          | 20                     | 99            | 12 200              | 1.81      | milky gel         |
| 12        | PLA14−PBzA$_{65}$          | 20                     | 98            | 14 000              | 1.89      | milky liquid      |
| 13        | PLA14−PBzA$_{70}$          | 20                     | 99            | 17 500              | 1.81      | milky liquid      |
| 14        | PLA14−PBzA$_{75}$          | 15                     | 97            | 11 200              | 1.52      | slightly turbid liquid |
| 15        | PLA14−PBzA$_{80}$          | 15                     | 98            | 11 700              | 1.65      | slightly turbid liquid |
| 16        | PLA14−PBzA$_{85}$          | 15                     | 97            | 13 700              | 1.99      | slightly turbid gel |
| 17        | PLA14−PBzA$_{90}$          | 15                     | 97            | 12 800              | 1.69      | milky gel         |
| 18        | PLA14−PBzA$_{95}$          | 15                     | 97            | 15 400              | 1.82      | milky liquid      |
| 19        | PLA14−PBzA$_{100}$         | 10                     | 90            | 12 300              | 1.62      | slightly turbid liquid |
| 20        | PLA14−PBzA$_{105}$         | 10                     | 90            | 12 300              | 1.71      | slightly turbid gel |
| 21        | PLA14−PBzA$_{110}$         | 10                     | 92            | 14 000              | 2.10      | turbid liquid     |
| 22        | PLA14−PBzA$_{115}$         | 10                     | 88            | 13 000              | 1.84      | turbid liquid     |
| 23        | PLA14−PBzA$_{120}$         | 7.5                    | 90            | 14 000              | 2.05      | turbid liquid     |
| 24        | PLA14−PBzA$_{125}$         | 7.5                    | 86            | 15 200              | 2.05      | turbid liquid     |
| 25        | PLA14−PBzA$_{130}$         | 7.5                    | 75            | 17 700              | 1.92      | turbid liquid     |
| 26        | PLA14−PBzA$_{135}$         | 5                      | 63            |                     |           | phase separation |

All polymerizations were conducted using a CTA/T21S molar ratio of 5.0 at 80 °C. Conversions were assessed using $^1$H NMR spectroscopy, and molecular weight data were obtained via THF GPC (using a series of near-monodisperse poly(methyl methacrylate) calibration standards). Partial sedimentation was observed after the initial dispersion was allowed to stand at 20 °C for several days.
allowed particle size analysis by dynamic light scattering (DLS) (see Figure 4).

DLS studies indicate an increase in the apparent sphere-equivalent hydrodynamic particle diameter with conversion, which is consistent with the observed increase in turbidity. A discernible increase in turbidity after 30 min suggested the onset of particle nucleation, with DLS indicating an intensity-average diameter of 17 nm at this time point. The mean particle diameter gradually increased up to 23 nm after 1 h. An abrupt increase in size to 104 nm occurred after 1.5 h, which was accompanied by a significant increase in turbidity. Initially, relatively narrow particle size distributions were obtained (DLS polydispersities (PDI) 0.07–0.19). However, much broader size distributions were observed after 1.5 h (PDI > 0.60). In this context, it is worth noting that similar changes in DLS particle diameter/polydispersity and physical appearance were reported by Fielding et al. for the analogous all-methacrylic PLMA−PBzMA PISA syntheses. Of course, this does not provide conclusive evidence for similar morphologies in the case of these PLA−PBzA dispersions. Nevertheless, we hypothesized that the slightly turbid dispersions observed for relatively short PBzA DPs corresponded to spherical micelles, the gel phase formed at longer PBzA DPs indicated the presence of anisotropic worms, and the relatively turbid (milky) dispersions formed when targeting the longest PBzA DPs most likely corresponded to vesicle formation. Thus, the physical appearance of the dispersions combined with our DLS observations was used to make an initial assessment of the copolymer morphology.

The effect of systematically varying the target DP of the core-forming PBzA block and copolymer concentration for a series of PLA−PBzA copolymers prepared via PISA was subsequently investigated (see Table 1).

Lower dispersities and higher blocking efficiencies (see Figure S) and higher conversions (see Table 1) are generally observed for polymerizations conducted at higher copolymer concentrations. For example, a PLA14−PBzA80 copolymer prepared at 7.5% w/w solids attained 88% conversion and exhibited a final $M_w/M_n$ of 1.84. However, targeting the same copolymer at 15% w/w solids led to a conversion of 97% and an $M_w/M_n$ of 1.69, whereas at 25% w/w solids the corresponding values were 99% and 1.63, respectively (compare entries 5, 18, and 23 in Table 1). This suggests a gradual loss of RAFT control at lower copolymer concentrations, in addition to the problem of chain transfer to polymer discussed previously. For example, Veloso et al. recently undertook a detailed study of the RAFT solution polymerization of n-butyl acrylate using a trithiocarbonate-based chain transfer agent in various solvents (e.g., ethanol, toluene, etc.). Their findings suggested that the predominant cause of dead chains in this RAFT formulation originated from chain transfer to solvent. Clearly, this side reaction is likely to become more prevalent at lower copolymer concentrations (since there is
necessarily a higher proportion of solvent). Dispersion polymerization conditions and n-alkane-based solvents were not examined by Veloso et al., but it seems likely that chain transfer to solvent would also occur in this case. However, confirming this hypothesis would require further experimental studies, which are beyond the scope of the present study. Of course, the high molecular weight shoulder that is observed in the GPC traces could also be attributed to some degree of termination by combination, which is the dominant mechanism for acrylic polymers.

At a copolymer concentration of 10% w/w solids or higher, two different types of dispersion are observed. Increasing the DP of the PBzA block results in the transformation from a weakly turbid, free-flowing liquid to a free-standing gel, which increases in turbidity until finally a milky-white free-flowing liquid is observed. Polymerizations conducted at more than 10% w/w solids also produced dispersions that were very similar in physical appearance to the copolymers obtained by the in situ sampling method described in Figure 4. A detailed phase diagram was constructed (see Figure 6), with high conversions being obtained after 16 h at 80 °C for each synthesis (see Table 1). The inset digital photographs indicate the final visual appearance of selected copolymer dispersions at 20 °C. DLS studies indicated that only relatively small particles were obtained at or below 8% w/w solids, which is consistent with the low turbidities and free-flowing nature of these dispersions. Similar observations were also made for dispersions prepared at higher copolymer concentrations when targeting shorter PBzA DPs.

The milky-white free-flowing dispersions tended to become collooidally unstable for PBzA DPs > 90 (increasing amounts of sedimentation were observed at all copolymer concentrations). Perhaps above this DP the PLA macro-CTA is no longer an efficient enough stabilizer for the PBzA core, resulting in the very large or aggregated particles observed by DLS measurements (see data in Figure S1 in the Supporting Information). The gel phase region is initially almost transparent, with only weak turbidity being observed at lower PBzA DPs, which gradually becomes milky white at the DP increases.

**Characterization of Copolymer Morphology.** Initially, conventional TEM was used to examine copolymer morphologies, as described by Fielding et al. PLA$_{14}$–PBzA$_y$ diblock copolymers (where $y = 60, 70, 80, 90$) prepared at 20% w/w solids in $n$-heptane were examined, since these dispersions represented the main classes of dispersion: free-flowing turbid liquid, gel (slightly turbid and milky), and milky liquid. However, despite examining various staining/deposition methods, only rather poorly defined agglomerated particles could be observed whose dimensions did not correspond to those indicated by DLS studies (see Figure S1). Similar problems were encountered for particles prepared in $n$-dodecane (DD) or isohexadecane (IHD) (data not shown). This is attributed to the relatively low $T_c$ of the PBzA core (literature value = 6 °C), which results in partial particle coalescence during TEM grid preparation.

Two strategies were examined to overcome this problem. First, particles were cross-linked by introducing ethylene glycol diacrylate (EGDA) as a third comonomer. In principle, intra-particle cross-linking should make the particles more robust, ideally without perturbing their copolymer morphology. Hence, EGDA was added to each dispersion at 80 °C after conducting the BzA polymerization for 7 h. $^1$H NMR analysis indicated at least 98% conversion of BzA monomer at this point in all cases. DLS studies were conducted both before EGDA addition (in $n$-dodecane) and after EGDA addition (in THF). The latter solvent is a good solvent for the PBzA core-forming block, so a comparable particle size is only expected under these conditions if cross-linking had been successful. Moreover, $^1$H NMR spectra recorded for cross-linked particles dispersed in CDCl$_3$, indicated attenuated PBzA signals and confirmed EGDA conversions of more than 85% in all cases. TEM images recorded for the cross-linked particles prepared in $n$-dodecane were much more encouraging than those obtained for the corresponding linear diblock copolymer nanoparticles (compare Figures S1 and S2).
Three dispersions were imaged that synthesized concentrated dispersions are also shown. Thus, sublimed inside the microscope by heating from around 175 °C to −95 °C in order to gradually reveal the morphology of the embedded particles. Three dispersions were imaged that corresponded to a free-flowing dispersion of relatively low turbidity, a free-standing gel, and a highly turbid free-flowing dispersion. As anticipated, the respective predominant copolymer morphologies were confirmed to be spheres, worms, and vesicles respectively (see Figure 7). However, it is worth noting that all characterization of these diblock copolymer dispersions has been conducted at 20 °C. Rheological studies of the worms (see below) suggest that they probably undergo a thermally triggered morphological transition to form spheres. However, confirmation would most likely require small-angle X-ray scattering studies, which are beyond the scope of this work.

**Dispersion Polymerization of BzA in n-Dodecane or Isohexadecane.** The use of n-heptane as a non-solvent for the PBA block is crucial for the PISA formulation. However, this solvent is relatively volatile (bp = 98 °C) which can produce large variations in dispersion concentration and hence the data obtained from rheology experiments when they are conducted at elevated temperatures.

Therefore, n-heptane was replaced with either n-dodecane (DD) or isohexadecane (IHD), which are both much less volatile (bp >200 °C). The former solvent was of high purity (≥99%; research grade), whereas the latter solvent was technical grade (the main constituent of a 97% w/w mixture of C16 isoparaffins).

| entry no. | target composition | solids (% w/w) | solvent type | conversion (%) | $M_n$ (g mol$^{-1}$) | $M_n/M_w$ | visual appearance |
|-----------|---------------------|----------------|-------------|----------------|-------------------|------------|-----------------|
| 1         | PLA$_{15}$-PBz$_{A0}$ | 40             | DD          | 99             | 11 000            | 1.44       | transparent gel |
| 2         | PLA$_{15}$-PBz$_{A0}$ | 20             | DD          | 99             | 8 900             | 1.45       | slightly turbid liquid |
| 3         | PLA$_{15}$-PBz$_{A0}$ | 20             | DD          | 99             | 10 300            | 1.49       | slightly turbid liquid |
| 4         | PLA$_{15}$-PBz$_{A0}$ | 20             | DD          | 99             | 10 800            | 1.66       | slightly turbid gel |
| 5         | PLA$_{15}$-PBz$_{A0}$ | 20             | DD          | 99             | 11 500            | 1.74       | milky gel |
| 6         | PLA$_{15}$-PBz$_{A0}$ | 20             | DD          | 99             | 13 740            | 1.66       | milky liquid |
| 7         | PLA$_{15}$-PBz$_{A0}$ | 20             | DD          | 99             | 14 500            | 1.69       | milky liquid |
| 8         | PLA$_{15}$-PBz$_{A0}$ | 15             | DD          | 98             | 11 000            | 1.69       | slightly turbid gel |
| 9         | PLA$_{15}$-PBz$_{A0}$ | 15             | DD          | 99             | 12 700            | 1.71       | milky gel |
| 10        | PLA$_{15}$-PBz$_{A0}$ | 20             | IHD         | 99             | 8 500             | 1.43       | slightly turbid liquid |
| 11        | PLA$_{15}$-PBz$_{A0}$ | 20             | IHD         | 99             | 9 900             | 1.50       | slightly turbid gel |
| 12        | PLA$_{15}$-PBz$_{A0}$ | 20             | IHD         | 99             | 11 300            | 1.41       | milky gel |
| 13        | PLA$_{15}$-PBz$_{A0}$ | 20             | IHD         | 99             | 12 900            | 1.51       | milky liquid |
| 14        | PLA$_{15}$-PBz$_{A0}$ | 15             | IHD         | 99             | 10 200            | 1.53       | slightly turbid liquid |
| 15        | PLA$_{15}$-PBz$_{A0}$ | 15             | IHD         | 99             | 11 100            | 1.44       | slightly turbid gel |

All syntheses were conducted using a CTA/T21S molar ratio of 5.0 at 80 °C. Conversions were assessed using $^1$H NMR spectroscopy, and molecular weight data were determined via THF GPC (using a series of near-monodisperse poly(methyl methacrylate) calibration standards).

Partial sedimentation was observed after several days.

**Table 2. Summary of Synthesis Conditions, Final Monomer Conversions, and GPC Data Obtained for a Series of PLA$_{14}$-PBz$_{A}$ Copolymers Prepared via RAFT Dispersion Polymerization of BzA Conducted in Either n-Dodecane (DD) or Isohexadecane (IHD)**

Relatively small, pseudospherical particles were observed for PLA$_{14}$-PBz$_{A50}$-PEGDA$_6$, worm-like clusters were obtained for PLA$_{14}$-PBz$_{A60}$-PEGDA$_6$ (resulting in a stiffer gel; see Figure S3), and relatively large vesicular structures were formed by PLA$_{14}$-PBz$_{A70}$-PEGDA$_6$. Thus, intra-particle cross-linking can to some extent alleviate the intrinsic problems associated with TEM analysis of soft film-forming particles.

Subsequently, cryo-TEM was utilized to characterize a subset of copolymer dispersions. It is well-known that this technique enables imaging of soft particles, since they are trapped within a thin vitreous film of rapidly frozen solvent. However, although cryo-TEM is widely used for imaging biological specimens and synthetic nanomaterials in aqueous media, there are very few literature reports describing cryo-TEM studies in non-polar solvents. In the present work, liquid nitrogen was used to vitrify n-heptane dispersions, since this cryogen is known to have high solubility in n-alkanes (e.g., liquid ethane). However, the relatively slow freezing rate of liquid nitrogen led to crystallization of the n-heptane phase and so reduced the electron contrast of the embedded particles. Thus, n-heptane was sublimed inside the microscope by heating from around −175 °C to −95 °C in order to gradually reveal the morphology of the embedded particles. Three dispersions were imaged that corresponded to a free-flowing dispersion of relatively low turbidity, a free-standing gel, and a highly turbid free-flowing dispersion. As anticipated, the respective predominant copolymer morphologies were confirmed to be spheres, worms, and vesicles respectively (see Figure 7). However, it is worth noting that all characterization of these diblock copolymer dispersions has been conducted at 20 °C. Rheological studies of the worms (see below) suggest that they probably undergo a thermally triggered morphological transition to form spheres. However, confirmation would most likely require small-angle X-ray scattering studies, which are beyond the scope of this work.

**Figure 7.** Selected cryo-TEM images obtained for (a) 0.75% w/w dispersion of PLA$_{14}$-PBz$_{A50}$ copolymer prepared at 15% w/w solids in n-heptane, (b) 0.20% w/w dispersion of PLA$_{14}$-PBz$_{A70}$ copolymer prepared at 20% w/w solids in n-heptane, and (c) 0.1% w/w PLA$_{14}$-PBz$_{A50}$ copolymer synthesized at 20% w/w solids in n-heptane. In each case dispersions were diluted with n-heptane at 20 °C. Digital photographs of the physical appearance of the as-synthesized concentrated dispersions are also shown.
A series of PLA-PBzA diblock copolymer dispersions were synthesized at 20% w/w solids in each solvent under the same conditions as those employed for n-heptane. Table 2 summarizes the molecular weight data, final monomer conversions, and physical appearance for the resulting dispersions, which are also compared in Figure S4. The data in Figure S4 suggest that changing the solvent leads to subtle differences in the precise copolymer composition required for gelation. For example, gels were obtained in IHD at a lower target PBzA DP than that required for n-heptane.

One-Pot Synthesis of PLA−PBzA Diblock Copolymers.

PLA−PBzA diblock copolymer nanoparticles could also be prepared using a “one-pot” protocol starting from LA monomer (see Figure 8). First, a PLA15 macro-CTA was synthesized via bulk polymerization targeting a DP of 15. A conversion of 97% was achieved within 1.25 h prior to quenching the polymerization. BzA monomer, T21S, and n-heptane were then added to this macro-CTA to produce a 20% w/w solids formulation (targeting PLA15−PBzA80), followed by deoxygenation and heating to 80 °C for 16 h. According to 1H NMR analysis, the BzA conversion was 97%, and THF GPC analysis indicated an $M_n$ of 13 800 g mol$^{-1}$ and an $M_n$/M$\bar{c}$ of 1.97. The blocking efficiency was relatively high (see Figure 8b), with minimal unreacted macro-CTA present in the final diblock copolymer. Overall, the molecular weight data were comparable to those obtained for a very similar copolymer synthesized using a purified PLA14 macro-CTA (see entry 12, Table 1). The inset digital photograph shows the turbid gel that is formed at 20 °C using the “one-pot” protocol. The analogous PLA14−PBzA80 formulation prepared by a two-step synthesis also formed a free-standing gel (see Table 1). This suggests that such “one-pot” PISA syntheses are robust and bodes well for potential industrial applications.

Rheological Characterization of PLA−PBzA Worm Gels.

We have published extensively on RAFT non-polar46,92 and aqueous46,92 dispersion polymerization formulations, and it is now well-established that the worm phase typically forms a soft, free-standing gel. Moreover, PLMA−PBzMA worms prepared in n-dodecane were transformed into spheres upon heating above 70 °C. This morphological transition was attributed to surface plasticization of the worm cores (as indicated by greater solvation of the PBzMA block) which resulted in a reduction in the packing parameter.92 A similar explanation was also proposed by Pei et al.94 for the thermoresponsive behavior of similar block copolymer worms in n-tetradecane. The worm gels reported by Fielding et al.92 were characterized by oscillatory shear rheology, which indicated storage moduli of the order of 1000 Pa, and the worm-to-sphere transition was associated with a critical gelation temperature (CGT) of around 50 °C. In the present work, rheological studies were undertaken for PLA14−PBzA80 copolymer gels prepared at 15% w/w solids in both n-dodecane and isohexadecane. Figure 5a shows the variation in gel stiffness (represented by the storage, $G'$, and loss, $G''$, moduli) with applied strain at 20 °C at a fixed angular frequency of 10 rad s$^{-1}$. Similar plateau regions are observed for both gels, which indicate the point where the moduli are independent of strain. $G'$ and $G''$ both lie within the linear viscoelastic regime under these conditions, and hence subsequent measurements were conducted at 1% strain and 10 rad s$^{-1}$. The temperature dependence of the gels were subsequently examined under these conditions from 4–80 °C (see Figure 9).

Like the PLMA−PBzMA system described by Fielding et al.,92 much lower gel moduli are observed at higher temperatures. However, an additional thermal transition is also observed at lower temperatures where the gel modulus increases. This results in $G'$ falling below $G''$, which indicates a lower and an upper critical gelation temperature (CGT) at 12–14 °C and 67–68 °C, respectively. Similar behavior was also observed for the same diblock copolymer composition prepared in IHD, but the CGT values are shifted to higher temperatures in this case (Figure S5b). The difference between the gels is likely due to the subtle difference between the particle morphology of these samples. The turbidity of these samples is different at 20 °C (the sample in IHD is slightly milkier in appearance), suggesting a more branched worm structure has been obtained in this case according to previous studies within our group.93 However,
further detailed cryo-TEM or perhaps small-angle X-ray scattering (SAXS) studies would be required to confirm this hypothesis. The PLA$_{14}$−PBzA$_{60}$ gel in $n$-dodecane was also equilibrated at four different temperatures (see inset images for Figure 9) to provide a visual representation of the various regimes observed within the rheology data. The gel becomes much more turbid and significantly stiffer at 4 °C. At 20 °C, the gel is soft and slightly turbid but still quite resistant to mechanical stress. Similar behavior was observed at 60 °C, although the gel is significantly less turbid at this temperature. Finally, the dispersion becomes a transparent, free-flowing liquid at 80 °C. In all cases, the rheological behavior was fully reversible. The morphologies revealed by cryo-TEM studies combined with DLS studies conducted at 4, 20, and 80 °C (see Figure S6) suggest that the changes in turbidity may be associated with a worm-to-sphere transition, while the above rheological data suggest that this transition most likely occurs at between 60 and 80 °C. This interpretation is consistent with results recently published by Fielding et al., who observed a similar order–order transition on heating a dispersion of PLMA−PBzMA worms. However, the reason for the additional rheological transition observed at 4 °C is as yet unclear. Cryo-TEM studies conducted at this temperature indicates the presence of a pure worm phase (see Figure S7). Thus, it is tempting to suggest that this phenomenon may be related to the $T_g$ of 6 °C for the core-forming PBzA chains. Significantly stiffer worms might be expected below this critical temperature, which might explain the rapid increase in $G'$ (and $G''$). Indeed, a similar effect was reported by Bates and co-workers, who found that core-cross-linked poly(ethylene oxide)−polybutadiene diblock copolymer worms formed stronger gels than the corresponding linear precursor worms. Alternatively, the significant increase in sphere-equivalent diameter indicated by DLS studies at 4 °C (see Figure S6) suggests either worm branching or clustering at this temperature. However, cryo-TEM appears to be too insensitive to corroborate either possibility, with little or no apparent change in copolymer morphology being observed (see Figure S7).

A PLA$_{14}$−PBzA$_{60}$ diblock copolymer was prepared at 40% w/w solids, and its rheological properties were characterized after dilution to 15% w/w solids (see Figure 9). Almost identical behavior was observed for the diluted copolymer dispersion as for the equivalent dispersion prepared at 15% w/w solids (see Figure S7).
Another important parameter is the critical gelation concentration (CGC) (see Figure 10b), which can be determined by serial dilution. At 20 °C, a free-standing gel is obtained for copolymer concentrations of ≥5% w/w solids. At 2.5% w/w solids, the suspension remained gel-like but could no longer support its own weight in a tube inversion test, while a free-flowing liquid was observed at ≤1.25% w/w solids. Thus, the CGC is estimated to be ~2.5% w/w solids, which is in good agreement with the $G'/G''$ values obtained for the time-dependent gel modulus plots in Figure 10b.

**CONCLUSIONS**

A series of PLA–PBzA diblock copolymers have been prepared via RAFT dispersion polymerization in n-alkanes, with high monomer conversions being achieved for syntheses conducted at 15–40% w/w solids. Relatively high block- efficiency were obtained along with comparable copolymer dispersions to those reported in the literature for similar formulations.

As far as we are aware, this is the first example of an all-acrylic PISA formulation conducted in a non-polar solvent for which spherical, worm-like and vesicular particles have been obtained. Systematic variation of the copolymer concentration and the DP of the core-forming block led to a gradual increase in turbidity and a range of rheological behaviors for these dispersions, including the formation of soft free-standing gels. This led to the construction of a phase diagram based on the visual appearance of the various dispersions combined with DLS data, rather than the extensive TEM studies described in earlier PISA studies. For example, observation of a gel phase was interpreted as evidence for the presence of worms, without necessarily indicating that a pure worm phase was present. This approach was adopted because the soft, film-forming nature of these low-$T_g$ all-acrylic nanoparticles prevented conventional TEM studies. In some cases, copolymer particles were cross-linked in order to increase their $T_g$ and so aid TEM analysis. Alternatively, selected dispersions were examined by vitrification of dilute dispersions in n-heptane using cryo-TEM. The latter approach confirmed the presence of sphere, worm, and vesicle copolymer morphologies within the phase diagram, with the presence of worms being strongly correlated with the gel phase. Rheological studies were undertaken on related worm gels prepared in either $n$-dodecane or isohexadecane, since these solvents are much less volatile than n-heptane. Broadly similar behavior was observed in each case but subtle differences in gel moduli and CGT were observed, which is likely due to differences in the worm contour length and degree of branching of the worm-like particles. Selected gels exhibited thermo-responsive behavior between 4 and 80 °C.

Interestingly, these all-acrylic gels exhibit lower $G'/G''$ values than the analogous all-methacrylic gels. Moreover, the former gels undergo an additional thermal transition on cooling below 15 °C which is currently believed to be related to stiffening of the worm-like particles on approaching the $T_g$ of the PBzA block. Finally, worm gels can also be conveniently prepared at 40% w/w solids using a ‘one-pot’ protocol starting from lauryl acrylate. On dilution, such worm gels behave similarly to worm gels prepared at 15% w/w solids. These gel exhibit a critical gelation concentration of approximately 2.5% w/w solids, which is significantly lower than the all-methacrylic worm gels previously prepared in n-alkanes.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.5b02119.

Conventional TEM images for linear PLA$_{14}$–PBzA diblock copolymers and cross-linked PLA$_{15}$–PBzA–PEGDA$_6$ triblock copolymers; table displaying the controllable variation in physical appearance for PLA$_{14}$–PBzA diblock copolymer upon changing the polymerization solvent from $n$-heptane to $n$-dodecane or isohexadecane; rheological characterization of gel stiffness vs strain % for PLA$_{14}$–PBzA$_{70}$ diblock copolymer synthesized at 15% w/w in isohexadecane; DLS data obtained for PLA$_{14}$–PBzA$_{60}$ diblock copolymer in n-dodecane at 4, 20, and 80 °C and cryo-TEM images obtained for PLA$_{14}$–PBzA$_{70}$ diblock copolymer prepared in n-heptane at 4 and 20 °C (PDF).

**AUTHOR INFORMATION**

Corresponding Author

E-mail s.p.armes@shef.ac.uk (S.P.A.).

Notes

The authors declare no competing financial interest.

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