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Poly(vinyl alcohol) star polymers prepared *via* MADIX/RAFT polymerisation†

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Poly(vinyl acetate) stars were prepared using MADIX/RAFT polymerisation mediated by xanthates. The polymerisation shows living characteristics with molecular weight increasing with conversion. The subsequent hydrolysis of these three and four arm stars led to the formation of poly(vinyl alcohol) stars.

Poly(vinyl alcohol) PVA is the largest volume water-soluble polymer produced commercially.[1] PVA is synthesised *via* the hydrolysis of poly(vinyl acetate) PVAc. In recent years, PVA has been utilised as a significant building block in biotechnological and biomedical applications because of its water solubility, biocompatibility and the potential for biodegradability. Hydrogels based on PVA have been investigated as carriers for the controlled delivery of hydrophilic drugs.[2,3] In addition to its attractive intrinsic properties for biomedical materials applications[4] it also confers a high functionality, allowing the potential for modification of the polymer *via* chemical transformations. For example, mono- and oligonucleodites covalently bound to PVA have been tested as primers for the enzymatic synthesis of polynucleotides.[5]

The interest in star-like polymers for biomedical applications is mainly motivated by their favourable properties, such as low solution viscosity and high functionality.[6] The latter property can be manifest as a multi-valent effect, where the higher binding affinity of end group functionalised star polymers compared to their linear counterparts results from multiple receptor–ligand interactions. Nature uses this so-called multivalency effect successfully in cell–cell interactions or in the targeting of cells by viruses.[7]

Star polymers can be synthesised using living radical polymerisation techniques. A versatile method to control molecular weight as well as the architecture of the polymer is MADIX[8]/RAFT[9] polymerisation. Using thiocarbonyl thiocompounds as the controlling agent, this method can be used for a broad range of monomers and has successfully been employed in the preparation of well-defined poly(vinylacetate). Xanthates[10,11] and dithiocarbamates[8] were both effectively used as RAFT agents.

In this communication, we would like to report initials results on the synthesis of PVAc or PVA three and four arm stars using MADIX polymerisation with xanthates as controlling agents. To our knowledge this is the first report on PVA stars generated *via* living radical polymerization.

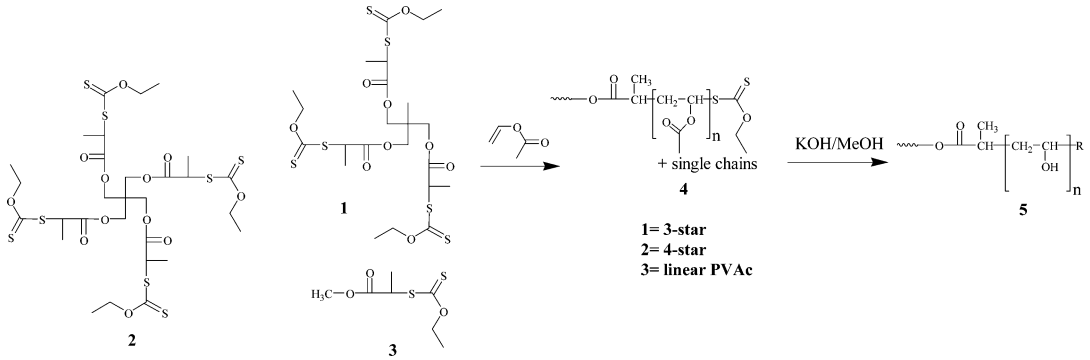
The MADIX/RAFT mechanism based upon the generally accepted addition–fragmentation mechanism was first published in 1988 by Zard *et al*.[12] and is given in detail elsewhere.[9,13] A study on the systematic variation of the xanthate structure of MADIX agents was performed to optimise the living polymerization of VAc with the result that methyl (ethoxycarbonothioyl) sulfanyl acetate proved to be an effective RAFT/MADIX agent.[11] However, VAc polymerisation using xanthates has been shown to be very sensitive towards impurities[14] inducing both inhibition periods and retardation.

In the synthesis of MADIX agents for the preparation of star polymers a xanthate group was attached to pentaerythritol or 1,1,1-tris(hydroxymethyl)propane forming the core for a four and three-arm star, respectively (Scheme 1). The polymerisation was then carried out at similar thiocarbonylthio concentrations in bulk VAc using AIBN as the initiator at 60 °C.† For comparison, the polymerisation was carried out with a mono-functional xanthate suitable for the living polymerisation of linear PVAc. The RAFT/MADIX polymerisations performed in the presence of the controlling agents (**1**), (**2**) and (**3**) proceeded with pseudo-first order kinetics with comparable rates of polymerisation and a short inhibition period of 40 minutes. After 2 hours and 3 hours, PVAc conversions of 20 % and 40 % were attained.

The GPC chromatograms show a single peak growing with reaction time and conversion (Fig. 1). The peak corresponding to the initial RAFT/MADIX agent fully disappears at a conversion of 5% indicative of its total consumption. The design of the RAFT agent involves a so-called "R-group approach" with the initial radical leaving group (R) attached to the core. As a result, linear polymers are generated in addition to the star architectures, as shown earlier for polystyrene 6-arm stars.[15] In the present work these single arms were not easily observed in the chromatograms. We hypothesise that the chromatographic separation and resolution in the case of PVAc was not sufficient to fully resolve the two individual molecular weight distributions.

The molecular weights of PVAc were measured using GPC calibrated with linear polystyrene standards together with the appropriate Mark–Houwink constants for PVAc in THF.† The molecular weight growth of linear PVAc in the presence of **3**

† Electronic Supplementary Information (ESI) available: synthesis and NMR data of MADIX agents, polymerisation and analysis technique. See http://www.rsc.org/suppdata/cc/b4/b404763j/



Scheme 1 Polymerisation of vinyl acetate VAc and hydrolysis to linear or three or four arm polyvinylalcohol PVA.

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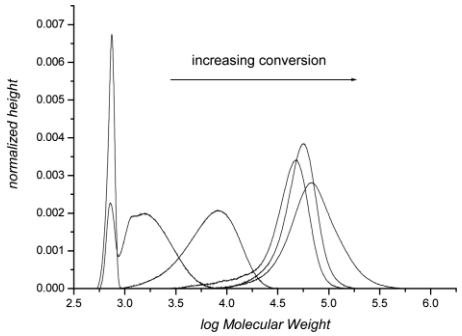

Fig. 1 Evolution of the SEC chromatograms for the RAFT bulk polymerization of VA at 60 °C in the presence of **2**. $[\mathbf{2}]_0 = 5.42 \times 10^{-3}$ mol L^{-1} = [xanthate groups]$_0$ = 2.17×10^{-3} mol L^{-1}; $[AIBN]_0 = 2.2 \times 10^{-3}$ mol L^{-1}. The conversions are 0, 1, 3, 21, 38 and 70%, respectively.

accorded to that predicted by theory (Fig. 2). In contrast, the molecular weight of the three and four arm star polymers displayed a slight deviation from the calculated molecular weight even at low conversions. This can be attributed to the altered hydrodynamic volumes of star polymers compared to linear polymers. However, there is a reasonable agreement between the theoretical and experimental molecular weight values until a conversion of about 40% is attained when the deviation becomes increasingly pronounced. The deviation at high conversions is accompanied by a strong broadening of the molecular weight distribution consistent with the (expected) occurrence of termination/transfer reactions.

The hydrolysis of PVAc in methanol using potassium hydroxide leads to PVA. The ester bond connecting the arms to the core is stable under these conditions, maintaining the integrity of the PVA stars. The molecular weights of these stars obtained *via* GPC in dimethylacetamide (DMA) as a mobile phase show a slight increase in molecular weight after hydrolysis,† which is probably caused by an altered hydrodynamic volume of PVA compared to PVAc while a polystyrene calibration is applied when DMA was used as a mobile phase. Futhermore, no evidence of star degradation was observed using this method, because only a single narrowly distributed peak was observed while low molecular weight products such as single arms were absent.

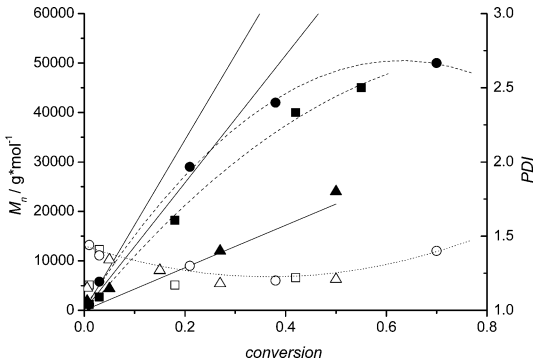

Fig. 2 Number average molecular weight M_n and polydispersity index (PDI) *vs*. conversion plot for the MADIX bulk polymerization of VAc at 60 °C in the presence of **1** (squares), **2** (circles) and **3** (triangles) [xanthate groups]$_0$ = 2.17×10^{-2} mol L^{-1}; $[AIBN]_0 = 2.17 \times 10^{-3}$ mol L^{-1}. The full line gives the theoretically expected M_n *via* M_n = $[VAc]_0$/[xanthate groups]$_0 \times M_{VA} \times$ conversion × number of arms. The dotted lines are only a guide to the eye.

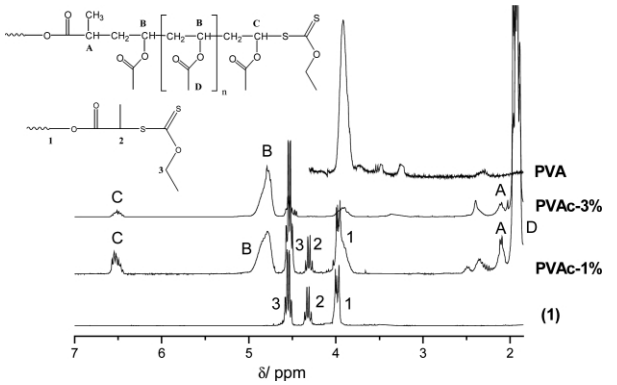

Fig. 3 ^{1}H-NMR of RAFT agent (**1**) and the corresponding polymers after 1 and 3% conversion ($CDCl_3$), PVAl (**5**) after hydrolysis of PVAc (D_2O).

As the arms of the star polymers could not be removed from the core without destruction of the polymer, ^{1}H-NMR analysis was used to verify the full consumption of xanthate groups and therefore the growth of three (**1**) or four (**2**) arms. A shift of the methine proton from 4.40 ppm to 2.1 ppm (Fig. 3) indicated the complete transfer of the growing macroradical to the thiocarbonylthio group and a subsequent reinitiation of the polymerisation by the leaving group (R-group). A signal at 6.6 ppm appears corresponding to the methine protons of the VAc unit adjacent to the xanthate group. Hydrolysis can be quantified using ^{1}H-NMR (D_2O). The methyl signal at 2.0 ppm disappears and the methine proton shifts from 4.9 ppm to 4.0 ppm confirming complete hydrolysis.

In summary, RAFT/MADIX polymerisation was used to obtain three and four arm PVAc stars with narrow polydispersities. These were subsequently hydrolysed to generate well-defined PVA stars.

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