**MADIX Polymerization of Vinyl Acetate using Ethyl Acetate as a Green Solvent; Near Complete Monomer Conversion with Molecular Weight Control**

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((Additional Supporting Information may be found in the online version of this article.))

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In the past thirty years numerous Reversible Deactivation Radical Polymerization (RDRP) methods using nitroxides (NMP),1 metal catalysis (ATRP),2 iodine mediated polymerisations,3 and Reversible Addition Fragmentation Chain transfer with Macromolecular Design via Interchange of Xanthates (RAFT/MADIX)4-8 have been developed that facilitate the preparation of polymers with targeted molecular weight and narrow molecular weight distribution. Of these methods MADIX has been found to be the most effective for mediating the polymerization of vinyl acetate. Poly(vinyl acetate) (PVAc) is an industrially important polymer, forming the basis of a number of adhesives9,10 and as a precursor to poly(vinyl alcohol) (PVA) via hydrolysis of the acetate groups.11 PVA is a major component of adhesives and coatings12 and its water solubility has allowed it to find use in biomaterials and applications in FDA approved oral formulations.13 The MADIX polymerization of vinyl acetate and subsequent hydrolysis to PVA were first reported with a focus on star polymers.14,15,16 However, it currently remains a challenge to synthesize PVAc to high molecular weight with low dispersity (Ð = *Mw/Mn*) in solution polymerization.17 Chen *et al.* have shown the MADIX polymerization of vinyl acetate under 5 kBar or 1 kBar pressure with a high pressure reaction system using ethyl acetate as the solvent at 35 °C. They used a range of xanthates with differing R and Z groups in order to synthesize high molecular weight PVAc (>100,000 g mol-1),18 however, the monomer conversions were typically around 35%. Congdon *et al.* have reported the polymerization of PVAc in bulk using S-benzyl-O-ethyl dithiocarbonate as the MADIX agent, with molecular weights of up to 30,050 g mol-1 although the monomer conversions were incomplete ranging from 68% to 83% conversion.19 Gois *et al.* carried out the MADIX solution polymerization of vinyl acetate using 1,4-dioxane with near complete monomer conversion (98%).20 These articles demonstrate the promise of MADIX polymerization for producing well-defined PVAc. Emulsion polymerization has been shown to offer the green synthesis of PVAc, but it has been demonstrated that it is difficult to achieve the combination of high conversion, high molecular weight and low dispersity by this method.21-23 Therefore, there is an opportunity to develop a method for the MADIX polymerization that combines the benefits of high molecular weight, near complete conversion, simple experimental setup with the use of a green solvent such as ethyl acetate.

In the present report the MADIX polymerization of vinyl acetate in bulk, or solution polymerization (dichloromethane (DCM) or ethyl acetate) was investigated in order to optimize monomer conversion and achieve molecular weight control. All polymerization reactions were performed using a facile approach using 15 mL glass pressure tubes with Teflon screw cap. Such reactors have been demonstrated to be capable of retaining reactants such as isoprene and chloroprene and at high pressure.24-26 Ethyl acetate is an attractive solvent for solution polymerization, it has been listed as a preferred green solvent while DCM and 1,4- dioxane have been rated as undesirable.27 In all polymerizations the ratio of [CTA]0/[AIBN]0 was fixed at 1/0.2, the temperature was fixed at 70 °C and the reaction time was fixed at 48 hours. The ratio of monomer to MADIX chain transfer agent was varied, starting with 2.0 g of monomer in all polymerizations. Consequently, a process has been developed to make PVAc with molecular weight control that is simple, robust, uses a non-toxic solvent and is potentially scalable.

Firstly the MADIX agent S-benzyl-O-ethyl dithiocarbonate was prepared in a single step in 58% yield as described in Supporting Information Section 2.1 (1H NMR spectrum is shown in figure S1) and used in a range of MADIX polymerizations, Scheme 1.



SCHEME 1. MADIX agent S-benzyl-O-ethyl dithiocarbonate in the polymerization of vinyl acetate.

 Initially, bulk MADIX polymerizations were carried out. We decided to carry out our experiments with similar temperature conditions to those used by Congdon et al. who used the same CTA as in our work.19 We chose 48 hours as the reaction time for all reactions as it allows sufficient time to obtain high conversion of high DP polymers. After polymerization the product was dissolved in CDCl3 and monomer conversion was determined by 1H NMR at five different targeted number average degrees of polymerization (DPn) from 25-220. In all five polymerizations tested in bulk the monomer conversion reached a plateau of 81% to 85% with high reproducibility (Table 1 entries 1-5). This finding was in agreement with the conversion values in the literature for the polymerization performed in bulk.19 The visual observation of residual monomer on the surface of the reaction medium indicated that the bulk polymerization was as potentially limited by polymerization-induced phase separation, leading to incomplete monomer conversion. When [M]0/[CTA]0 ratios of 25, 50 and 100 were targeted in bulk, the experimentally determined number average molecular weight *Mn* of the polymer was in close agreement with the theoretical *Mn*, summarized in Figure 1A. The SEC chromatograms are narrow and symmetrical (Figure S2B&D) and the dispersities were below 1.20 indicating a well-controlled polymerization. At higher ratios of [M]0/[CTA]0 = 150 and 220 targeting of *Mn* was less precise, the dispersities were ≥1.44 and the SEC chromatograms were broader indicating a loss of control of the polymerization at these higher [M]0/[CTA]0 ratios, which is in agreement with previous reports.19 This loss of control of the polymerization was attributed to the less activated nature of the monomer resulting in “head-to-head” monomer addition, as opposed to “head-to-tail” addition, which would lead to the formation of a non-reversible chain end (and therefore a loss of control/activation).28 The SEC chromatograms (Figure 1B and Figure S3E&F) show a tailing toward lower molecular weights, indicating loss of chain transfer agent functionality or termination that is limiting controlled chain growth under these reaction conditions. In the absence of chain transfer agent an insoluble product forms with no molecular weight control.

TABLE 1 Summary of PVAc products prepared by MADIX polymerization. Reaction Conditions: VAc = 2 mL, Solvent =2 mL (0 mL in bulk) Ratio [M]0/[CTA]0 = 1/0.2 Polymerization Temperature = 70 °C

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Entry | [M]0/ [CTA]0*a* | Conditions | Time / h | % Conversionb | *Mn* (theo.)  (g mol-1)c | *Mn* (exp.) (g mol-1)d | *Mw*(exp.) (g mol-1)d | *Mw / Mn*d |
| 1 | No CTA | Bulk | 48 | - | N/A | Insoluble | Insoluble | N/A |
| 2 | 25 | Bulk | 48 | 81 | 1744 | 2100 | 2370 | 1.13 |
| 3 | 50 | Bulk | 48 | 82 | 3616 | 4250 | 4900 | 1.15 |
| 4 | 100 | Bulk | 48 | 84 | 7232 | 6800 | 7700 | 1.13 |
| 5 | 150 | Bulk | 48 | 83 | 10849 | 9350 | 13500 | 1.44 |
| 6 | 220 | Bulk | 48 | 85 | 16101 | 14100 | 22200 | 1.58 |
| 7 | No CTA | DCM | 48 | - | N/A | 18000 | 54300 | 3.01 |
| 8 | 25 | DCM | 48 | 92 | 1959 | 3060 | 3700 | 1.21 |
| 9 | 50 | DCM | 48 | 91 | 3917 | 3760 | 4420 | 1.18 |
| 10 | 100 | DCM | 48 | 91 | 7834 | 7380 | 10400 | 1.41 |
| 11 | 150 | DCM | 48 | 95 | 12268 | 9920 | 14600 | 1.47 |
| 12 | 220 | DCM | 48 | 97 | 18372 | 13500 | 19800 | 1.47 |
| 13 | 360 | DCM | 48 | 90 | 27864 | 16700 | 27300 | 1.63 |
| 14 | No CTA | Ethyl Acetate | 48 | - | N/A | 80700 | 337000 | 4.18 |
| 15 | 100 | Ethyl Acetate | 48 | 92 | 7920 | 7660 | 10600 | 1.38 |
| 16 | 150 | Ethyl Acetate | 48 | 96 | 12397 | 12800 | 18600 | 1.46 |
| 17 | 200 | Ethyl Acetate | 48 | 98 | 16700 | 18200 | 23900 | 1.32 |
| 18 | 220 | Ethyl Acetate | 48 | 97 | 18561 | 20300 | 27300 | 1.35 |
| 19 | 300 | Ethyl Acetate | 48 | 97 | 25052 | 25200 | 33100 | 1.31 |
| 20 | 400 | Ethyl Acetate | 48 | 94 | 32370 | 30100 | 46900 | 1.56 |
| 21 | 500 | Ethyl Acetate | 48 | 96 | 41323 | 37000 | 56700 | 1.53 |
| 22 | 1000 | Ethyl Acetate | 48 | 94 | 80925 | 52600 | 91000 | 1.73 |
| 23 | 1500 | Ethyl Acetate | 48 | 95 | 122678 | 65400 | 137000 | 2.10 |
| 24 | 2000 | Ethyl Acetate | 48 | 97 | 167015 | 87600 | 154000 | 1.76 |
| 25 | 3000 | Ethyl Acetate | 48 | 97 | 250522 | 104000 | 190000 | 1.83 |

a Ratio [CTA]0/[AIBN]0 =1/0.2 for all polymerizations. b Determined by 1H NMR . c *Mn* (theory) = (([M]0/[CTA]0) x (conversion/100) x 86.09). d determined by triple detection light scattering SEC in THF + 2% triethylamine eluent, using narrow poly(styrene) standard *Mw* = 105k as calibrant

When DCM was used as a solvent for the reaction near complete monomer conversion was obtained for all [M]0/[CTA]0 ratios tested (0-360). The molecular weight and distribution data for the polymerizations in DCM are summarized in Table 1, Entries 7-13 and illustrated in Figure 1C&D. These findings show that the use of the pressure tubes allows the facile solution polymerization using a low boiling point solvent like DCM (39.6 °C). When [M]0/[CTA]0 ratios of 25, 50 and 100 were targeted there was good agreement between the experimentally determined molecular weight and the theoretical molecular weight. The SEC chromatograms were narrow and symmetrical, Figure S4B&C, and the dispersities were <1.21 indicating a well-controlled polymerization at these monomer to chain transfer agent ratios. However, at higher ratios of [M]0/[CTA]0 = 150, 220 and 360 the experimental *Mn* were considerably below the theoretical *Mn*, the dispersities were greater than 1.40 (as shown in Figure 1C) and the SEC chromatograms were broader (see Figure 1D and Figure S4E&F). The ratio of [M]0/[CTA]0 seems to be a reliable indicator of the *Mw* under these conditions. These results indicate a loss of control of the polymerization at these higher [M]0/[CTA]0 ratios, although near complete monomer conversion was achieved. These findings suggest that DCM may be considered a good solvent for synthesizing poly(vinyl acetate) with low [M]0/[CTA]0 ratios. One can suggest that an increased number of secondary reactions such as head-to-head addition, loss of chain end functionality and/or transfer to the solvent may have occurred limiting the targeting of DP at high [M]0/[CTA]0 ratios.

The suitability of the green solvent ethyl acetate was also evaluated for the MADIX solution polymerization of vinyl acetate at [M]0/[CTA]0 ratios from 0-400, see Table 1, Entries 14-20. Near complete monomer conversion is obtained for all these polymerizations. At [M]0/[CTA]0 ratios ranging from 100 to 150 an excellent agreement was seen for the theoretical and observed *Mn*, summarized in Figure 1E. The dispersities were below 1.40. At higher ratios of [M]0/[CTA]0 = 200, 220, and 300 the dispersities were slightly lower than 1.35, indicating similar control over molecular weight with high conversion. The SEC chromatograms for all the samples were narrow and symmetrical, Figure 1F and Figure S5B-F. The number average degree of polymerization determined by 1H NMR analysis of the purified samples was in agreement with the targeted *DPn* and the SEC data up to chain lengths of *DPn* = 300. The higher monomer conversions for these polymers prepared by ethyl acetate solution polymerization were attributed to improved diffusion of the monomer and polymer chains through the reaction medium and are in agreement with the independent data obtained in dioxane solvent.20 These results, coupled with the ease of handling of the product, indicate that ethyl acetate may be considered an excellent and very efficient solvent for synthesizing poly(vinyl acetate) with very high monomer conversion with highly predictable molecular weight up to 30,000 g mol-1 and reasonably narrow dispersities.

FIGURE 1: Plots of experimental *Mn* and *Mw/Mn* versus theoretical *Mn* and raw GPC chromatograms at [M]0/[CTA]0 = 150 for the MADIX polymerization of vinyl acetate at 70°C in bulk (A,B) in DCM (C,D) and in ethyl acetate (E,F) Conditions: VAc = 2 mL Ratio [CTA]0 / [AIBN]0 = 1/0.2. The lines of graphs A,C and E represents the theoretical value.

The formation of very high DPn PVAc in ethyl acetate was then investigated by sequentially increasing the [M]/[CTA] ratio to 3,000. All these polymerizations obtained near complete conversion. The largest *Mn* obtained was 104,000 g mol-1 at a ratio of [M]0/[CTA]0 = 3,000/1. This result compares very favorably with literature data where a pressurized reactor and a ratio [M]0/[CTA]0 = 10,000/1 was used yielding a *Mn* of 123,000 g mol-1, a dispersity of 1.28 with a 37% conversion,18 while using our approach we obtained a much higher conversion of 97% for a polymer with a similar *Mn,* albeit with a higher dispersity of 1.83.



FIGURE 2: Plot of experimental *Mn*and *Mw/Mn* versus theoretical *Mn* for the MADIX polymerization of vinyl acetate in ethyl acetate performed at 70 °C up to [M]0 / [CTA]0 = 3000 Conditions VAc = 2 mL, Solvent = 2 mL, Ratio [CTA]0/[AIBN]0 = 1/0.2

At very high targeted degrees of polymerization (>1,000) the ability to effectively target *DPn* was somewhat lost, see Figure 2. Presumably, this was because the increased chain length affected the ability of the polymer chains to diffuse through the reaction medium, causing loss of chain end functionality which limited the polymer chains ability to grow. This also resulted in a higher dispersity value as a greater distribution. However, when compared to a free radical polymerization (i.e. in the absence of CTA) which produced a polymer with a dispersity of 4.18 (Table 1 entry 25), the use of very low amounts of CTA offers narrower distributions and some control of MW (Figure S6).

In order to demonstrate the retention of xanthate chain end functionality during the MADIX polymerizations in ethyl acetate, PVAc macromonomers prepared with [M]0/[CTA]0 = 100 in ethyl acetate were chain extended with vinyl acetate monomer under reaction conditions [M]0/[MacroCTA]0/[AIBN]0 = 300/1/0.2 or 1200/1/0.2. The SEC chromatograms from the RI detector corresponding to the macro-CTA and chain extended polymers are shown in Figure S7. The peak of the chain extended polymers shifted to earlier retention time corresponding to longer polymer chains, indicating that some dithiocarbonate moiety remained at the polymer chain end and could further mediate the MADIX polymerizations. It is important to note that the dispersity of chain extended products increases and some residual macro-CTA remains present in the chain extended product, indicating that there was incomplete functionalization of the poly(vinyl acetate) chains by the MADIX agent.

In conclusion, the MADIX polymerization of vinyl acetate in the green solvent ethyl acetate produced polymers with near complete monomer conversion, high molecular weights and allowed targeting of molecular weight. The facile polymerization system allows for ideal control of molecular weight and distribution up to 30,000 g mol-1 and can be adapted to make PVAc up to 100,000 g mol-1.

**EXPERIMENTAL**

For detailed procedural descriptions of the synthesis of the MADIX agent, MADIX polymerizations and characterization of products see the Supplementary Information.

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