Ultra-fast microwave enhanced reversible addition-fragmentation chain transfer (RAFT) polymerization: monomers to polymers in minutes†

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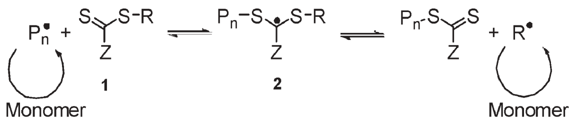
Microwave mediated RAFT polymerization leads to ultra-fast polymerizations, whilst keeping excellent control over molecular weights and molecular weight distributions; this is the first example of such a dramatic effect of microwaves on living radical polymerization kinetics, and it shows the potential for chemists to produce very well controlled polymers in a matter of minutes.

The increasing use of synthetic polymers to enable high-technology fields such as organic synthesis[1] (*e.g.* polymer supports), material science (*e.g.* polymer nanoparticles), biology (*e.g.* protein–polymer conjugation),[2] medicine (*e.g.* non-viral gene delivery)[3] and optoelectronics (*e.g.* semi-conducting polymers and photonics)[4] calls for an ever-increasing control of polymer structure and versatile synthetic methodologies that are accessible to the wider scientific community. Since their conception in the early 1990's, living radical polymerization (LRP) techniques have evolved from novel and niche polymerization routes, to become one of the most useful polymer synthetic tools. Free radical polymerizations can operate under a wide variety of reaction conditions (with or without solvent, including water; from room temperature to <150 °C), permitting the use of almost all functional vinyl monomers. Living polymerizations are often restricted to specific monomer types but lead to polymeric structures with an excellent degree of control over topology, functionality, molecular weight and molecular weight distribution. LRP techniques, such as nitroxide mediated polymerization (NMP),[5] atom transfer radical polymerization (ATRP)[6] and reversible addition fragmentation polymerization (RAFT),[7] offer a combination of these advantages. RAFT polymerization was first reported in 1998 and relies on the rapid chain transfer of thiocarbonyl thio moieties between propagating chains, Scheme 1.[7] The absence of catalysts and ease of scale-up makes RAFT one of the most versatile LRP techniques. Excellent control over polymer structures *via* a living radical process comes, however, at the expense of reaction time, with polymerizations lasting hours and sometime days.[8,9] Such lengthy reaction times, and the associated difficulty of producing RAFT transfer agents, have often discouraged scientists from this technique. Recently we addressed the issues of RAFT agent synthesis in a report outlining a facile approach that enables the formation of a wide range of RAFT agents without the need for CS_2.[10]



Scheme 1 Generally accepted reaction scheme for reversible addition fragmentation chain transfer (RAFT) and macromolecular architecture design *via* interchange of xanthate (MADIX) polymerizations.

The use of microwave reactors in synthetic chemistry has been shown to enhance reaction rates, increase yields and eliminate side products.[11] Microwave enhanced polymerizations are already well documented, and some excellent reviews are present in the literature.[12] By contrast, publications describing rate-enhanced microwave LRP are sparse and generally present conflicting results. The effects of microwave heating were measured for the atom transfer radical polymerization (ATRP) of MAA, and rate enhancements were witnessed when utilizing a modified domestic microwave oven at 450 W,[13] whilst no rate enhancement was observed when using a monomodal microwave reactor with infrared temperature probe.[14] Schubert *et al.*[15] studied the nitroxide mediated polymerizations (NMP) of methyl methacrylate and *tert*-butyl methacrylate in a monomodal microwave reactor, and obtain well controlled polymerizations, but did not observe any microwave induced acceleration. On the other hand, the NMP of styrene in a multimodal microwave reactor was recently studied by Zhu *et al.*,[16] and they reported quite significant microwave acceleration at both 100 W and 200 W with respect to that achievable under conventional heating protocols. In all these studies, rate enhancements have only been observed when employing laboratory-modified domestic multimodal microwave ovens, where the heating rate and profile are inconsistent and irreproducible. In the case of reactions performed in monomodal microwave reactors, for which the microwave power is more focused and the temperature is accurately monitored, no, or very little, rate enhancement is observed. In RAFT polymerization, Zhu *et al.*[17] observed rate enhancements when using a modified existing domestic microwave oven. In a recent publication,[18] however, we reported that the use of monomodal reactors, whilst keeping the reaction temperature at 60 °C, allowed for only a slight increase in polymerization rate. In this study, we show that the use of monomodal microwave reactors, without controlling reaction temperatures, for the polymerization of three common monomers,

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methyl acrylate (MA), vinyl acetate (VA) and styrene (STY), can lead to reactions faster than that have ever been reported, and polymers with very well controlled molecular weights.

MA polymerization, Fig. 1, mediated by ethylsulfanylthiocarbonyl sulfanyl-propionic acid ethyl ester (ETSPE) using conventional oil bath heating (50 °C) was able to achieve approximately 50% conversion in 4 h. The use of monomodal microwave irradiation however had a dramatic effect, enhancing the kinetics to allow 60% monomer conversion in just 5 min and 80% conversion in 20 min. A study of the development of number average molecular weight (M_n) and polydispersity (PDI) relative to conversion throughout the two polymerization reactions showed excellent consistency, demonstrating that although the kinetics have been significantly enhanced, this has not been at the expense of the control of molecular weight or polydispersity.

VA is a polar low-cost monomer, and poly(vinyl acetate) is known for its biodegradability and solubility in liquid and supercritical CO_2, making it very attractive for a range of applications. Previous attempts at controlling the free radical polymerization of VA either through ATRP or NMP have proven unsuccessful. To date, RAFT polymerization is the best system to control the growth of poly(vinyl acetate) chains, although it is difficult to reach low molecular weight polymers with low PDIs. Fig. 2 shows the evolution of conversion with time, and M_n/PDI with conversion for the ethoxythiocarbonylsulfanyl-propionic acid ethyl ester (EOSPE)-mediated RAFT polymerization of VA, targeting molecular weights of 1000 g mol^{-1} and 5000 g mol^{-1}.

Heating the VA polymerization in an oil bath (70 °C) led to a high conversion (85 + %) in less than 3 h with good control and low polydispersity (<1.2). The use of microwave heating again showed a significant rate increase, with near quantitative conversion (90 + %) reached in 15 min for the 1000 g mol^{-1} target polymer and in 9 min for the 5000 g mol^{-1} sample. This accounts for a respective rate increase by more than 1300% and 1100% when compared to the oil bath induced polymerization. Furthermore, the molecular weight increases linearly with monomer conversion, remaining close to the predicted values and maintaining exceptionally low polydispersities (<1.1). Such control over low molecular weight polymers at high polymerization rates and short reaction times is, to the best of our knowledge, unprecedented.

Styrene (STY) is a monomer that is known to polymerize very slowly in the presence of dithiobenzoates[8,9] (typically, conversions around 20% are reached within 16 hours at 60 °C) and attempts to increase the rate of monomer conversion either through increased temperature, pressure and initiator concentration result in a loss in molecular weight control.[8,9] The microwave enhanced RAFT polymerization of STY has been reported by Zhu *et al*[17] using a multimodal laboratory-modified domestic microwave oven. Rate enhancements of between 500% and 600% were observed compared to conventional heating methods, with excellent control and low polydispersity. We have also investigated the cyanoisopropyl dithiobenzoate (CPDB) mediated RAFT polymerization of STY. Fig. 3 shows a comparison of the use of monomodal microwave heating and the use of an oil-bath (60 °C). As seen with the other monomers, the kinetics of polymerization are accelerated to a much higher extent under monomodal microwave irradiation than when using conventional heating (approximately 1000% increase), with low polydispersity (<1.1) and good control over molecular weight.

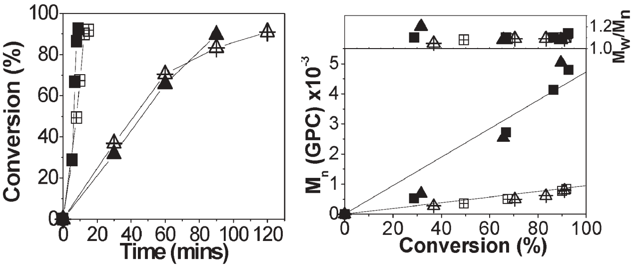

Fig. 2 Plot of monomer conversion *vs.* time and M_n and PDI *vs.* monomer conversion for the polymerization of vinyl acetate mediated by EOSPE. (Molar ratio of VA : EOSPE : AIBN = 11 : 1 : 0.10 (Open shapes) and 55 : 1 : 0.10 (Filled shapes)). (Monomodal microwave = square, Oil Bath = triangle). The line represents the theoretical molecular weight as a function of conversion (right).

The process underpinning RAFT polymerization differs greatly from ATRP or NMP techniques. Both ATRP and NMP rely on the reduction of the propagating radical concentration *via* reversible termination, leading to polymerization rate reduction when compared to conventional free radical polymerization. On the other hand, in an ideal RAFT process, the propagating radical concentration is identical to that of conventional process and the control over molecular weight and molecular weight distribution is obtained *via* the rapid degenerative chain transfer to the thiocarbonyl thio group. Monomodal microwave reactors allow

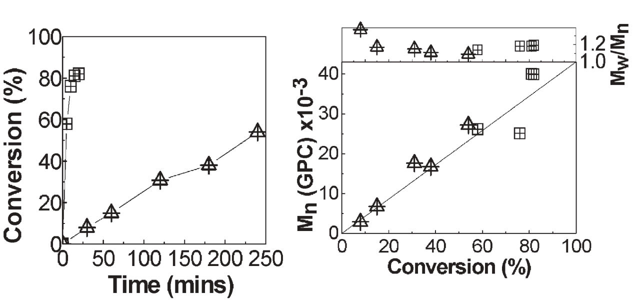

Fig. 1 Plot of monomer conversion *versus* time (left) and M_n and PDI *versus* monomer conversion (right) at 50 °C. Molar ratio of MA : ETSPE : AIBN = 500 : 1 : 0.10 (Monomodal microwave = square, Oil Bath = triangle). The line represents the theoretical molecular weight as a function of conversion (right).

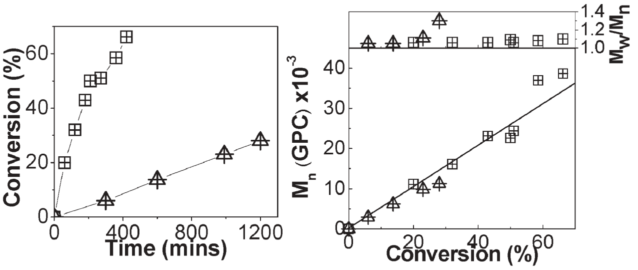

Fig. 3 Plot of monomer conversion *vs.* time and M_n and PDI *vs.* monomer conversion for the polymerization of styrene mediated by CPDB. (Molar ratio of Styrene : CPDB : AIBN = 500 : 1 : 0.25) (Monomodal microwave = square, Oil Bath = triangle). The line represents the theoretical molecular weight as a function of conversion (right).

the maintenance of a constant and uniform energy input to the polymerization reaction. For RAFT polymerization, this appears to result in an overall increase of both the propagation rate and the addition-fragmentation rates of the degenerative chain transfer reaction, therefore allowing excellent control over molecular weight.

In conclusion, we have demonstrated exceptional enhancement in the rate of RAFT polymerization of both polar and non-polar monomers *via* monomodal microwave irradiation that may not be achieved by simply increasing the heat in a conventionally heated reaction. Furthermore, we believe this increases the utility of the RAFT technique whereby well-defined and well-controlled polymers, including low molecular weight materials, can be delivered in minutes, rather than hours, through the simple application of microwave heating.

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