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Sono-RAFT Polymerization in Aqueous Medium

T.G. McKenzie, E. Colombo, Q. Fu, M. Ashokkumar, G.G. Qiao**

Abstract

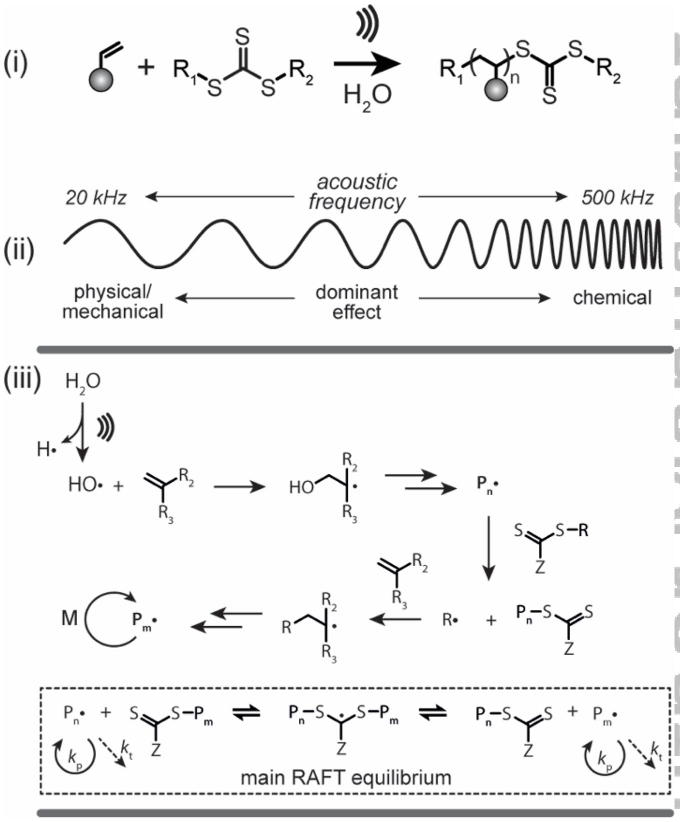
The ultrasonic irradiation of aqueous solution is demonstrated to be a suitable source of initiating radicals for a controlled radical polymerization when conducted in the presence of a thiocarbonylthio-containing reversible addition-fragmentation chain transfer (RAFT) agent. This allows for a highly "green" method of externally-regulated/controlled polymerization with a potentially broad scope for polymerizable monomers and/or polymer structures.

Introduction

Sono-/Mechano-chemistry is arguably under-investigated currently given its vast potential in a diverse range of applications, including drug delivery, organic synthesis, and polymer chemistry.[1] The use of ultrasound to degrade synthetic and bio-polymers has been known for over half a century,[1d] although it has not been applied to the construction of polymers in a controlled fashion until much more recently.[2]

Taking inspiration from these reports, and given our recent investigations into the use of hydroxyl radicals generated from a Fenton reaction to initiate RAFT polymerization,[3] we set out to determine whether radicals generated ultrasonically could also lead to a controlled chain-growth polymerization. This would provide a catalyst-free, "green"[4] polymerization technique with the potential for external regulation under ambient conditions.[5] Additionally, unlike photo-mediated polymerizations, sonochemically-generated radicals are formed uniformly throughout the reaction mixture, avoiding problematic concentration gradients caused by light penetration profiles.[6] Moreover, similar to *iniferter* polymerizations,[7] exogenous radical initiators can be omitted entirely (**Scheme 1**).

Unlike previous examples of ultrasound-assisted controlled polymerization, where low frequencies were employed to generate strong physical (shear) forces to act upon a mechano-responsive reagent,[2] the current work demonstrates that high frequencies can also be utilised, with a strong chemical effect (the generation of radical species) and negligible shear force creating a unique sonochemical environment. Given the long history of free radical polymerizations initiated via the chemical effects of ultrasound[1d, 1e, 8] it was surprising to us that attempts to control the chain-growth process were quite limited.[9] We have previously investigated the use of ultrasound for the synthesis of polymer latexes via both low frequency[10] (20 kHz) and high frequency[11] (213 kHz) irradiation in micro/miniemulsion systems.[12] Herein, we report our initial investigations into a homogeneous, sonochemically-induced RAFT polymerization (sonoRAFT) under high frequency (~400 kHz) ultrasound. Radicals generated from acoustic cavitation are shown to drive a well-controlled polymerization even up to relatively high molecular weights (> 50 kDa). Moreover, temporal control is achieved by switching the ultrasound on and off, with a rapid response time observed.



Scheme 1. (i) Schematic of sonochemically-induced RAFT polymerization (sonoRAFT); (ii) Representation of forces generated under different ultrasonic frequencies; (iii) Proposed mechanism for sonochemical initiation of RAFT process.

The formation of radical species under ultrasonic conditions occurs from the vaporization of liquid molecules into cavitation bubbles, followed by their growth and, eventually, spontaneous collapse.[1d] This generates extreme localized heats and pressures that can pyrolytically degrade the vaporized molecules into a variety of radical species. In the case of water, these are primarily hydroxyl radicals

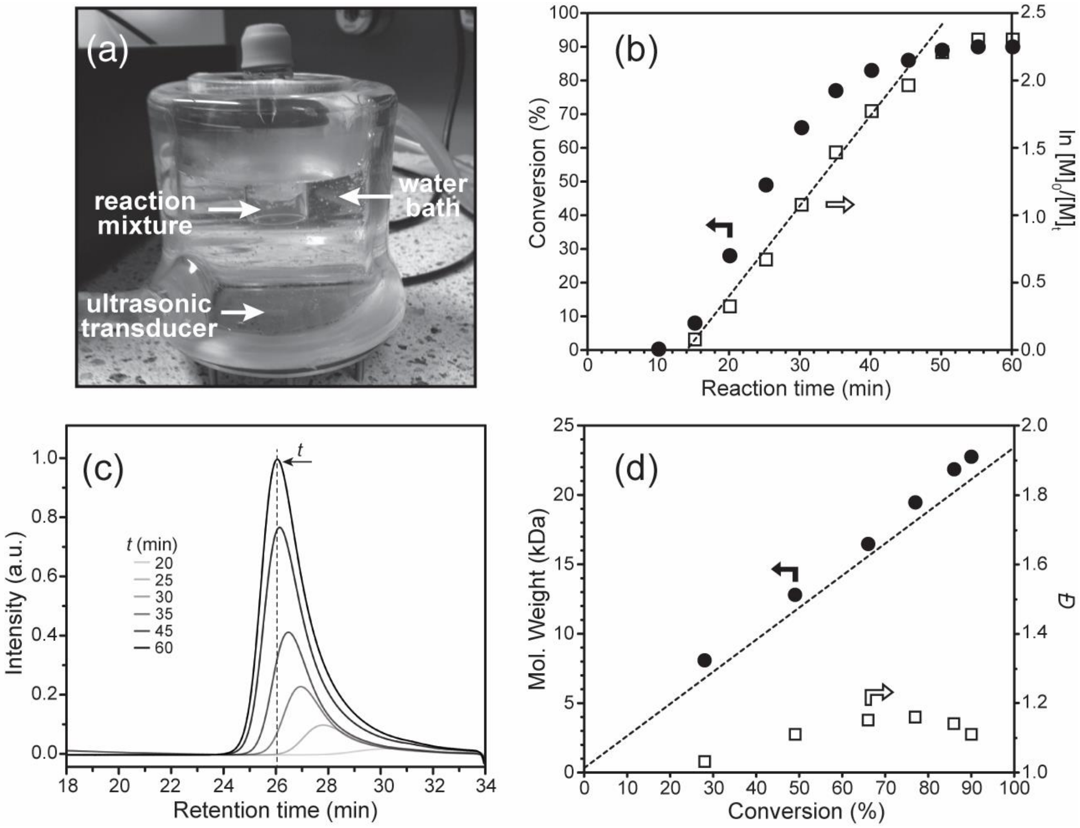


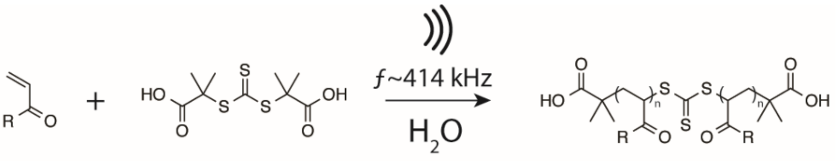
Figure 1. (a) Experimental setup for typical sonoRAFT experiment (note: power supply and water circulation pump not shown); (b) Reaction kinetics under continuous ultrasonic irradiation (f = 414 kHz, power = 40 W) of HEA (200 eq. per TTC, $[HEA]_0$ = 0.75 M); (c) GPC chromatograms showing polymer growth with time of applied ultrasound; (d) Molecular weight characterization data of formed poly(HEA) (dotted line represents theoretical molecular weight).

and hydrogen atoms. The component with the highest vapour pressure will be preferentially vaporized into the cavitating bubble, and therefore care must to be taken when designing the experiments. Generally, two primary effects can stem from ultrasonic irradiation: physical forces (i.e. high shear), and chemical effects (i.e. radical formation). The extent of each is highly dependent on the irradiating frequency. At low frequencies (~20 kHz) physical forces are dominant with minimal chemical effects, while at higher frequencies (>200 kHz) the situation is reversed (**Scheme 1**).[13]

Previously, Liu et al. reported on the ultrasonic irradiation of polystyrene with a dithiocarbamate ‘iniferter’ (initiator-terminator-transfer agent[14]) at the chain end.[9a] The authors postulate that selective C-S bond dissociation occurs under ultrasound, leading to block copolymer formation in the presence of styrene. However, low monomer conversions were obtained with relatively broad polymer dispersities. More recently, silica-tethered RAFT agents were used for a ‘grafting-from’ polymerization under ultrasonic irradiation.[9b] The polymerization was performed under anhydrous conditions using a low frequency (59 kHz). Despite promising preliminary results, the report does not attempt to describe the system in detail, particularly regarding the mechanisms of initiation and control. For our investigations, we chose to use a model water-soluble acrylate monomer, 2-hydroxyethylacrylate (HEA), and a suitable thiocarbonylthio RAFT agent (S,S’-α, α’ -methyl-)α’’-acetic acid)-trithiocarbonate, TTC)[15]. Therefore, the reaction mixture consisted of a homogeneous mixture of monomer and RAFT agent dissolved in water.

The formation of radicals using our ultrasonic setup was quantified via a hydrogen peroxide (H_2O_2) assay, where it is assumed that hydroxyl radical combination lead directly to the formation of H_2O_2. The rate of H_2O_2 formation at an ultrasonic frequency of 414 kHz initially increased, before plateauing at moderate to high power levels (Figure S1), as is typical for such systems.[16] A maximum radical generation rate was observed at an applied power of 40 W. Delivered powers were determined calorimetrically (Table S1), however, for simplicity, powers reported in the manuscript are the applied/set values. The optimum conditions (i.e. frequency (f) = 414 Hz, applied power (P) = 40 W) were selected for our investigations into the ultrasonic polymerization reaction. For all experiments,

Table 1. Characterization data for various polymers synthesized via sonoRAFT polymerization.



Entry	*monomer*	*[monomer] (M)*	*DP_n*	*t (min)*	*Conv. (%)*[a]	*$M_{n,GPC}$ (Da)*[b]	*$M_{n,th}$ (Da)*[c]	*Đ*[b]
1	HEA	5	200	60	0	-	-	-
2	HEA	2.5	200	60	51	10 200	12 120	1.01
3	HEA	1.5	200	60	90	20 100	21 180	1.01
4	HEA	0.75	200	60	92	23 500	21 650	1.04
5	HEA	0.5	200	60	93	18 700	21 890	1.01
6	HEA	0.1	200	60	56	†	13 270	†
7	HEA	0.75	400	60	80	42 700	37 440	1.02
8	HEA	0.75	800	60	76	72 000	70 880	1.03
9	HEA	0.75	1000	60	81	75 700	94 340	1.03
10	OEGA	0.5	200	60	0	-	-	-
11	OEGA	0.15	200	60	79	76 400	75 120	1.29
12	DMA	0.75	200	60	46	9 800	8 200	1.03
13	NAM	0.75	200	60	72	18 900	20 500	1.02
14	OEGMA	0.15	200	60	94	199 000‡	89 500	1.20

[a] Determined via ^{1}H NMR spectroscopy. [b] Calculated via GPC-MALS using ASTRA software. [c] Defined as: $M_{n,th}$ = (conv. x DP_n) x MW_{mon} + MW_{TTC}, where $DP_n = [M]_0/[TTC]_0$. All reactions conducted under an argon atmosphere with *f* = 414 kHz and P = 40 W. † Insufficient sample for GPC analysis. ‡ Discrepancy between observed and theoretical M_n values is thought to be due to the use of a single dn/dc for both OEG-based monomers.

the ultrasonic reactor was jacketed with a water circulation system maintained at 21°C, the reaction vessel was placed at a depth of ca. 2 cm with a working distance from the transducer plate of ca. 3 cm (**Figure 1a**).

As the range of ultrasonically-generated radicals is wider for air-saturated liquids,[13] all reaction mixtures were thoroughly degassed with argon prior to irradiation.

Initially, relatively high monomer concentrations (ca. 5 M) were attempted; however, minimal polymerization was observed (Figure S2). The monomer concentration was then reduced, and the reaction repeated. Interestingly, for moderate concentrations polymerization plateaued, while lower concentrations displayed excellent monomer conversion up to 90% in less than 60 minutes (**Figure 1b** and Figure S2). The sonochemical generation of radicals is strongly dependent on a number of factors. Among them, the volume fraction, vapour pressure, and surface activity of the monomer can cause changes in cavitation events, directly influencing the formation of radicals.[8a] At the lowest concentration attempted (0.1 M) the rate of polymerization was slow, but did not appear to plateau on the timescale investigated (Figure S2). The optimal monomer concentration was therefore found to be in the range 0.5 – 1.5 M, for which the gel permeation chromatography (GPC) chromatograms of the resulting polymers show narrow monomodal peaks that shift to higher molecular weights with increasing monomer conversion, with observed molecular weight values close to their theoretical ones (**Figure 1c-d**, **Table 1, Figure S3**). These results strongly indicate that the polymerization proceeds via the RAFT mechanism following initiation by sonochemically-generated radicals,[17] while the narrow dispersities observed are in line with our previous studies of hydroxyl radical initiation achieved via Fenton catalysis.[3] Applying the same conditions to polymerization mixtures in organic solvents (*N,N*-dimethylformamide or acetonitrile) showed no polymerization after 80 minutes (Figure S4). However, with 20 vol% water added, polymerization was observed after a prolonged induction period. This indicates the important role of water in generating the initiating radical species.

Having established efficient working conditions, the reaction was then investigated in more detail. Temporal control over the activation of polymerization was assessed via an experiment in which the ultrasonic irradiation was turned off for given time intervals, with samples extracted periodically for characterization. As shown in **Figure 2**, monomer conversion stopped completely in the absence of ultrasound, while restarting efficiently when it was turned back on. The fast cycling

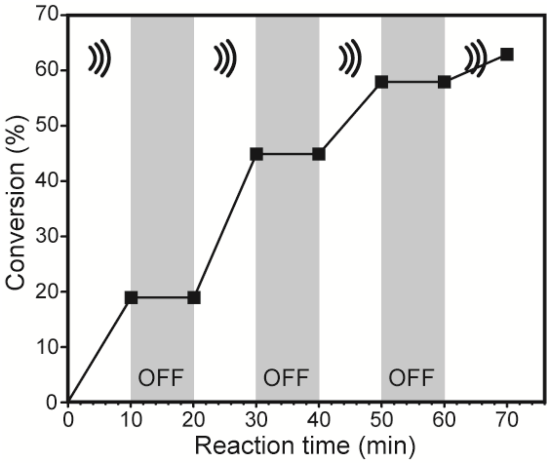


Figure 2. Monomer conversion with alternating on/off periods of applied ultrasound ([HEA]/[TTC-1] = 200/1, $[HEA]_0$ = 0.75 M, *f* = 414 kHz, P = 40 W).

time indicates the rapid switchability of this activation/deactivation, and is thought to be the result of the short lifetime of the active hydroxyl radicals as well as the rapid timescale of sonochemical events.[1a] GPC analysis of the polymers formed during this experiment clearly show no polymer growth during the dormant periods (Figure S5). Interestingly, unlike in an *iniferter* polymerization,[7] for RAFT polymerization there is no mechanism for the re-initiation of terminated polymer chains following halted chain growth.[18] However, this switchability is commonly observed for analogous photo-initiated RAFT polymerizations.[19]

One of the key features of any controlled polymerization is the ability to pre-determine the polymer chain length by adjusting the monomer-to-initiator ratio. We therefore conducted sonoRAFT with a range of different targeted degrees of polymerization (DP_n), with high monomer conversions obtained (>75%) after 60 min and GPC chromatograms that increase with increasing targeted DP_n (**Figure 3**). Additionally, when the experiment was performed in the absence of the chain transfer agent, a polymer of high molecular weight at a low monomer conversion was obtained as per a free radical polymerization process (Figure S6). These experiments confirm the participation of the RAFT agent in controlling the chain-growth process.

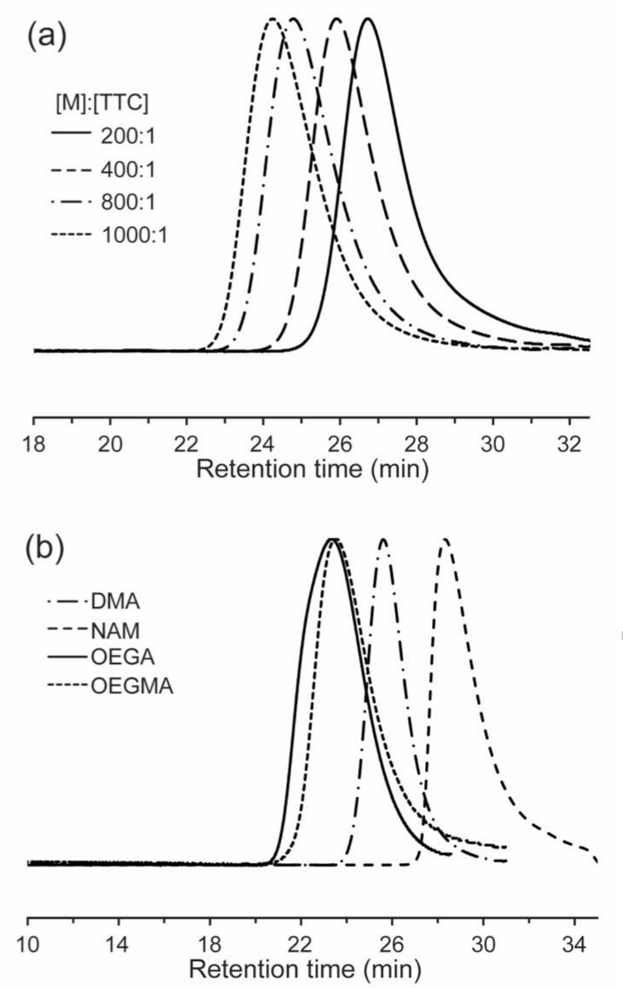


Figure 3. (a) Different chain lengths of P(HEA) formed via sonoRAFT; (b) Different monomers polymerized (DMA = *N,N′*-dimethyl acrylamide, NAM = *N*-acryloylmorpholine, OEGA = oligo(ethylene glycol) methyl ether acrylate), OEGMA = oligo(ethylene glycol) methyl ether methacrylate).

The polymerization of different monomers was also attempted. While excellent results were observed for most of the monomers attempted, the bulky monomer oligo(ethylene glycol) acrylate (OEGA, M_w = 480 g mol^{-1}) showed no polymerization when conducted at a similar molar concentration (0.5 M). The concentration was lowered to 0.15 M (giving a more similar volume fraction to the others), achieving 79% conversion (Figure 3b). This further implicates the importance of monomer-dependent factors in the ability for ultrasonic irradiation to successfully generate radicals. A methacrylate-type monomer (OEGMA) was also polymerized effectively (94% conversion in 60 mins), indicating the versatility of this technique.

Lastly, the effect of applied power was investigated. The results observed are in excellent agreement with the initial radical formation assay (Figure S1): the observed rate of polymerization (k_p^{app}) increased in accordance with the increase in H_2O_2 formation observed at various applied powers (Figure S7 and

Figure S8). This shows the potential for reaction rates to be additionally controlled via the applied power.

In conclusion, a sonochemically-induced RAFT polymerization with efficient temporal control is demonstrated using high frequency ultrasound. Unlike the low frequencies used in mechanically-induced controlled polymerizations,[2a, 9b] the high frequency employed in this study produces very little shear force, potentially avoiding chain-breaking ‘depolymerization’ events[1c] that may limit the attainable molecular weights. Scaling-up sonochemical reactors is also foreseeable, with several examples of large-scale reactors capable of delivering uniform ultrasonic irradiation.[20] This technique represents a promising advance in the “green” synthesis of controlled polymers, and further studies are ongoing in our lab.

Acknowledgements

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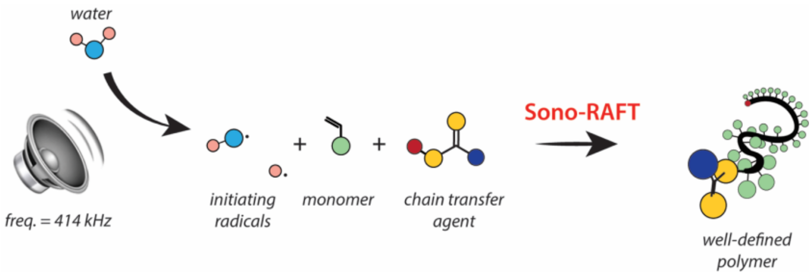
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