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SET-LRP in biphasic mixtures of the non-disproportionating solvent hexafluoroisopropanol with water

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ABSTRACT: The fluorinated alcohol 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) is an especially effective solvent for solubilizing a wide range of polymers. However, the performance of HFIP as SET-LRP solvent has classically been questioned due to its poor Cu(I)X disproportionating properties. Taking advantage of the fast and quantitative disproportionation of Cu(I)X in water, SET-LRP in organic solvent/water mixtures rids the organic solvent of mediating this fundamental event. Here, the Cu(0) wire-catalyzed SET-LRP synthesis of well-defined poly(methyl acrylate)s and poly(butyl acrylate)s with narrow molecular weight distribution and near perfect bromine chain end functionality is reported in HFIP/water mixtures. The results reported here support the potential of HFIP/water mixtures in the preparation of more complex architectures including polymers with dual control over molecular weight and tacticity. Since HFIP is also a classic solvent for the denaturation of proteins this SER-LRP system is also expected to find applications in the grafting of protein.

INTRODUCTION

The interest for synthetic macromolecular architectures with increasing degree of complexity has growth unceasingly due to the development of living radical polymerization techniques.[1,2,3,4,5,6,7, 8,9] Amongst them, single-electron transfer radical polymerization (SET-LRP) using Cu(0)-wire has become one of the most popular due to its operational simplicity and high versatility.2,3,[10,11,12] Since its discovery in 2002, SET-LRP has been successfully applied to the polymerization of a wide range of monomers such as vinyl chloride,[13,14,15] acrylates,[16,17,18,19,20,21,22,23,24,25,26,27,28,29] methacrylates,[30] ,[31,32,33,34] methacrylamides[35,36,37] as well as other vinylic monomers.[38,39,40,41,42] The popularity of SET-LRP is mainly based on its compatibility with commercial grade monomers and high tolerance to aerobic and aqueous environments as well as the suitability to use inexpensive and air-stable Cu(0) wire.[43,44,45,46] The mechanistic framework proposed for SET-LRP relies on an activation step mediated by SET from the Cu(0) electron donor to the alkyl halide electron acceptor and the N-ligand/solvent-dependent disproportionation of the generated Cu(I)X into "nascent" Cu(0) and Cu(II)X_2. This redox reaction provides to the system the regeneration of the main activator Cu(0) in a much more active form and the build up of the necessary amount of Cu(II)X_2 to regulate the reversible deactivation step. 2,3,10,11,12,[47] A major drawback of SET-LRP is the dependence of the disproportionation step to the selection of solvent.[48,49,50,51] In this context, diverse polar solvents such as water,[52,53,54]dipolar aprotic,14,23,[55,56] fluorinated 16,17,31, [57,58] and hydrogenated alcohols,35,44,[59,60,61] cyclic carbonates and cyclic ethers 48,[62] among others [63,64] have allowed to enjoy most of the advantages of this LRP technique. However, the use of poor disproportionation solvents such as acetonitrile or solvents in which Cu(I)X does not dissolve even in the presence of N-ligands such as toluene and acetone have not been used for a long time since their use compromise chain-end functionality of the targeted polymers.50 [65] To overcome this limitation, our group recently elaborated a library of bi(multi)phasic SET-LRP systems by combination of organic solvents with water.[66,67,68,69,70,71,72,73,74,75] This fundamental approach is underpinned by the quantitative disproportionation of Cu(I)X into Cu(0) and Cu(II)X_2 species in water (K_{disp} = $1 \cdot 10^6$ - $6 \cdot 10^7$ M^{-1})51 and the unexpected immiscibility of water containing Cu(II)X_2 and ligand with water miscible organic solvents containing monomer and polymer. So far, SET-LRP "programmed" biphasic systems have been demonstrated to be compatible with acetonitrile, acetone, long chain alcohols, hexanes, toluene and other apolar solvents.66,67,69,70 Note that applying this concept to solvents with good disproportionating capability results in enhanced reaction rates without compromising the livingness of polymerization.68,71

In this contribution we report the incorporation non-disproportionating hexafluoroisopropanol (HFIP) solvent as an organic solvent in biphasic SET-LRP mixtures. The attractiveness of this specialty fluorinated organic solvent lies in its ability to provide simultaneous control of the molecular weight and tacticity and to its ability to dissolve short peptide sequences and proteins. This study is focused on the study of Cu(0)-wire SET-LRP polymerization of hydrophobic acrylates in various HFIP/water mixtures and the rigorous study of the chain-end functionality of the synthesized polymers by a combination of ^{1}H-NMR spectroscopy and MALDI-TOF.

Experimental Section

Materials

MA (99%) and BA (99%) (from Acros) were filtered trough a short column of basic alumina column (Al_2O_3) prior to use in order to remove the radical inhibitor. Cu(0) wire (20 gauge wire, 0.812mm diameter from Fischer), Tris(2-aminoethyl)amine (TREN) (98%, Acros), $CuBr_2$ (99%, Alfa Aesar), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (SynQuest Laboratories), methyl 2-bromopropionate (MBP) (99% Acros) and thiphenol (99%, Acros) were used as received. Triethylamine (99.9% Chemimpex) was freshly distilled over CaH_2. Tris-[2-(dimethylamino)ethyl]amine (Me_6-TREN) was synthetized according to a literature procedure.[76]

Techniques

500 MHz ^{1}H-NMR spectra were recorded on Bruker UNI500 NMR instrument at 25 ºC in $CDCl_3$ containing tretamethylsilane (TMS) as internal standard. For the chain end evolution analysis of PMA, the delay time (D1) was set 10 s and the number of scans (nt) was set to 80. Size exclusion chromatography (SEC) analysis of the polymer samples were carried out using a Shimadzu LC-20AD high-performance liquid chromatograph pump, a PE Nelson Analytical 900 Series integrationdata station, a Shimadzu RID-10A refractive index (RI)detector, and three AM gel columns (a guard column, 500 Å,10 µm, and 10^4 Å, 10 µm). THF (Fischer, HPLC grade) was used as eluent at a flow rate of 1 mL min^{-1} in all the analysis. The number-average (Mn) and weight-average (Mw) molecular weights of PMA and PBA samples were determined using poly(methyl methacrylate) (PMMA) samples as standards pruchased from American Polymer Standards. MALDI-TOF analysis was carried out in a Voyager DE (Applied Biosystems) equipped with a 337 nm nitrogen laser (3 ns pulse width). The accelerating potential was 25 kV, the grid was 88%, the laser power was 1950 arbitrary units, and a positive ionization mode was employed. The sample analysis was carried out using 2-(4-hydroxyphenylazo)benzoic acid as matrix.

The representative solutions for the MALDI-TOF analysis were prepares by mixing different solutions of matrix (30 mg mL-1), NaCl (10 mg mL-1) and polymer sample (10 mg mL-1) in THF as solvent and in a 9/1/1 volumeric ratio. Finally, 1μL of the solution mixture were deposited onto of sample plate and dried in air at room temperature before being subjected to the MALDI-TOF analysis.

Typical procedure for TREN and Me$_6$-TREN-mediated SET-LRP in biphasic HFIP/water mixtures. HFIP, acrylate monomer (MA or BA), water (containing the ligand (TREN) and $CuBr_2$ previously mixed) and the initiator (MBP) were added to a 25 mL Schlenk in the order mentioned. When Me$_6$-TREN was used as ligand, water and ligand were added separately and $CuBr_2$ was not necessary, following the order: HFIP, monomer, water, ligand and initiator. After that, in both cases the reaction mixture was degassed by six freeze-pump-thaw cycles. After these cycles the Schlenk tube was opened under a positive flow of nitrogen and the Cu(0) wire wrapped around a Teflon-coated stir bar was introduced and held above with the help of an external magnet. Two more freeze-pump-thaw cycles were then carried out. After that, the Schlenk tube was filled with nitrogen and the reaction mixture was placed in a water bath thermostated at 25 ºC. Finally, the stir bar wrapped with the Cu(0) wire, was introduced gently into the reaction mixture. The introduction of the Cu(0) wire was considered *t* = 0. Aliquots were withdrawn from the polymerization mixture through a side arm equipped in the Schlenk tube. The collected samples were exposed to air to be quenched and dissolved to $CDCl_3$ and the conversion of the monomer was determinted by ^{1}H-NMR spectroscopy. After that, in order to determine the molecular weight and polydispersity of obtained polymers, samples were evaporated under vacuum, redisolved in THF and filtered troughs a small basic Al_2O_3 column in order to remove possible residual copper traces and were analyzed by GPC. The resulting PMA was precipitated in cold methanol and dried under vacuum until constant weight to perform chain end analysis by ^{1}H-NMR spectroscopy, before and after thioeterification reaction.

General procedure for the chain-end modification via "thio-bromo" click reaction. In a 10 mL vial equipped with a rubber septum, the polymer (0.01 equiv) was dissolved in 1 mL of acetonitrile. After that, thiophenol (0.05 equiv) and freshly distilled triethylamine (NEt_3, 0.05 equiv) were added under argon atmosphere. The reaction mixture was stirred at room temperature for the next 3h. The resulting modified PMA was purified through a precipitation in cold methanol and dried under vacuum until constant weight.

RESULTS AND DISCUSSION

The importance of validating HFIP as solvent for SET-LRP. Alcohols are widely used as reaction media in monophasic SET-LRP because they ensure high levels of disproportionation of Cu(I)X. [35] [44] [59] [60] [61] In addition, they are considered to be less toxic in comparison with dipolar aprotic solvents. Fluorinated alcohols containing both fluorinated-hydrophobic and hydroxyl-hydrophilic sites deserve a special mention. Alcohols such as 2,2,2-trifluoroethanol (TFP) and 2,2,3,3-tetrafluoro-1-propanol (TFP) in combination with N-ligands such as Me_6-TREN and TREN mediate acceptable levels of disproportionation of Cu(I)X. Moreover, they are able to dissolve monomers and polymers in a wide polarity range and consequently have been considered as "privileged" solvents for SET-LRP.[16,17,31,57,58] HFIP has the additional feature of offering dual control over molecular weight and tacticity of the generated polymer. [77,78] [79,80,81,82,83,84] This is because HFIP can interact with the polar substituents of the vinyl monomer units such as methacrylate's *via* hydrogen bonding to induce stereospecific radical polymerization based in steric repulsion and afford polymers with a predetermined tacticity.[85] However, qualitative visualization experiments reported by our laboratory demonstrated that disproportionation in HFIP is practically nonexistent,48 even in the presence of N-ligands. Thus, the development of programmed" biphasic SET-LRP systems based on HFIP/water mixtures is justified.

SET-LRP of MA catalyzed by non-activated Cu(0) wire/Me$_6$-TREN in HFIP/water mixtures. We previously reported the Cu(0) wire-catalyzed SET-LRP of MA in biphasic mixtures of TFE/water and TFP/water mixtures with excellent results.73 However, HFIP/water mixtures were not previously investigated. The first series of experiments reported here focus on the HFIP/water biphasic SET-LRP of MA mediated by Me$_6$-TREN using the monofunctional initiator 2-bromopropionate (MBP) and 4.5 cm of non-activated Cu(0) wire as catalyst (Scheme 1a) under the following conditions: [MA]/[MBP]/[Me$_6$-TREN] = 222/1/0.1. The ratio of HFIP/water in the mixtures was varied from 10/0 to 9/1 to 8/2 to 7/3 to maintain comparable conditions to TFE and TFP-based biphasic systems. 73 (Figure 1 and Table 1, entries 1-4).

The first experiment was carried out in pure HFIP. Kinetic data are depicted in Figure 1a and data summarized in Table 1, entry 1. The kinetic plot shows some living features as linear increase of molecular weight with monomer conversion and relatively low dispersity throughout the process. However, high discrepancy between theoretical and experimental molecular weight at low conversion and low initiator efficiency (I_{eff} = 84%) was also observed. This fact is related to the non-disproportionating behavior of HFIP. The accumulation of Cu(I)Br during the reaction can produce a change in the mechanism from SET-LRP to ATRP with the consequent loss of chain end functionality. Next experiments were performed in HFIP containing 10%, 20% and 30% water. Kinetic plots can be found in Figure 1b-d respectively. In those cases, all the kinetic experiments show an excellent living behavior with a linear increase of molecular weight together with the monomer conversion. Moreover, narrow dispersities were obtained for all compositions with excellent initiator values (I_{eff} >98%) and also excellent agreement between the theoretical and experimental molecular weights were observed. As we previously observed in other “programmed” biphasic multiphasic systems, higher water contents in the reaction mixture furnish faster polymerizations.[71,72,73,74,75]

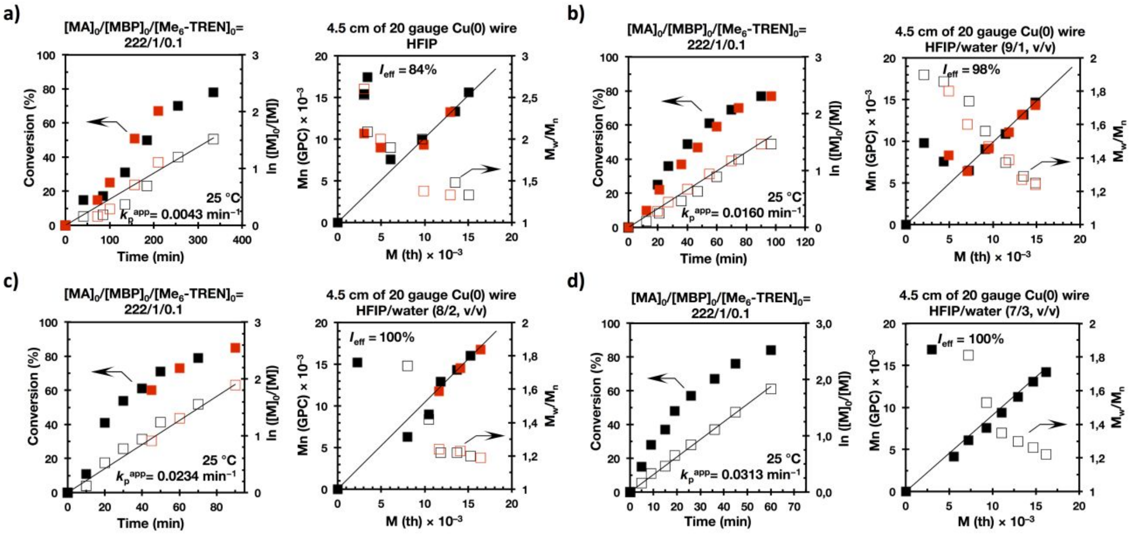
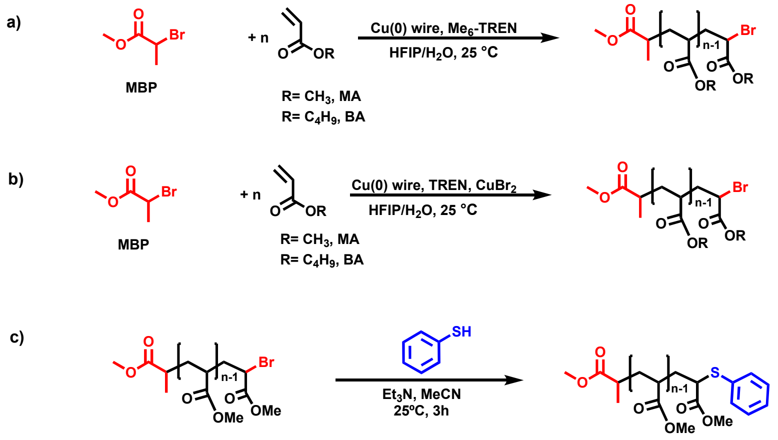


Figure 1. Kinetic plots, molecular weight and dispersity evolutions for the SET-LRP of MA (a, b, c, d) in HFIP and HFIP/water mixtures initiated with MBP and catalyzed by nonactivated Cu(0) wire at 25 °C. (a) HFIP; (b) HFIP /water (9/1, v/v); (c) HFIP /water (8/2, v/v) and (d,) HFIP /water (7/3, v/v). The v/v ratio must be multiplied by 10 to obtain % solvent/ % water. The value of v+v must be divided by 10 to obtain the total volume of solvents, 1mL. Reaction conditions: MA = 1 mL, (a) HFIP =0.5 mL, (b, c, d) HFIP + water = 0.5 mL, (a, b, c, d) $[MA]_0/[MBP]_0/[Me_6\text{-}TREN]_0$= 222/1/0.1. Experimental data in different colors were obtained from different kinetics experiments



Scheme 1. (a) Me_6-TREN and (b) TREN-mediated SET-LRP of MA and BA in HFIP/water mixtures in the presence of non-activated Cu(0) wire. (c) “thio-bromo click” modification of PMA with thiophenol.

This series of experiments show also the same trend. The addition of only 10% of water to pure HFIP increases the rate constant by factor of 4 (see Table 1, entries, 1 and 2). Next experiments corresponding to 20% and 30% also showed a very clear increase in the value of rate constant of a factor of 6 and 8 by comparison with experiments carried out in pure HFIP (see Table 1, entries, 1-4). The biphasic nature of the HFIP/water systems is supported by a series of digital images Fig 2. a-d. The transition from pure HFIP to systems containing water produces an increase of turbidity of the solution. This turbidity in the solution was more clear at 8/2, v/v and 7/3, v/v and can be associated to the presence of micro-droplets of water phase containing mainly the Cu(II)Br_2-Me_6-TREN complexes. While the influence of the amount of water on the k_p was investigated, no detailed analysis of water on the rest of the SET-LRP was discussed at this time since it will represent the main topic of a future publication. The role of water on chain end functionality, tacticity and other reaction parameters will be presented in a different publication.

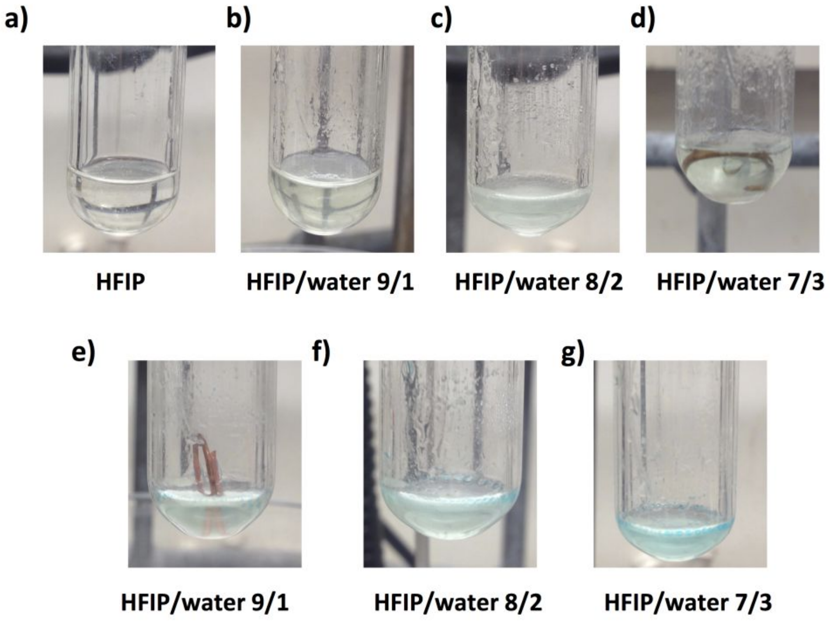


Figure. 2 Visualization of the reaction mixture after SET-LRP of MA initiated with MBP and catalyzed by the non-activated Cu(0) wire at 25 ºC in (a) HFIP, (b, e) HFIP/water (9/1, v/v), (c, f) HFIP/water (8/2, v/v), (d, g) HFIP/water (7/3, v/v). Reaction conditions: (a, b, c, d) $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0$= 200/1/0.1, (e, f, g) $[MA]_0/[MBP]_0/[TREN]_0/[CuBr_2]_0$ = 200/1/0.2/0.1.

Table 1 SET-LRP of MA and BA in biphasic mixtures of water with 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) mediated with Me_6-TREN or TREN/$CuBr_2$ and catalyzed by non-activated 4.5 cm of 20 gauge Cu(0) wire. Reaction conditions: monomer = 1 mL; solvent + water = 0.5 ml. The v/v ratio must be multiplied by 10 to obtain % solvent/% water. The value of v+v must be divided by 20 to obtain the total volume of solvents, 0.5 mL.

[a] Correspond to the k_p^{app} of (9/1 v/v) of SET-LRP experiments mediated by TREN. [b] The reaction time to the monomer conversion (%) is reported in the next column. [c] Initiator efficiency.

Entry	Reaction medium	Reactions conditions	k_p^{app} (min^{-1})	$k_{p\,(s+w)}^{app}$ / $k_{p\,(s)}^{app}$	Reaction time [b] (min)	Conv. (%)	(M_w/M_n)	I_{eff} [c](%)
1	HFIP	[MA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.004	-	335	78	1.32	84
2	HFIP/H_2O (9/1, v/v)	[MA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.016	4.00	97	77	1.24	98
3	HFIP/H_2O (8/2, v/v)	[MA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.023	5.75	90	85	1.19	100
4	HFIP/H_2O (7/3, v/v)	[MA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.031	7.75	60	84	1.22	100
5	HFIP/H_2O (9/1, v/v)	[MA]/[MBP]/[TREN]/[$CuBr_2$] 222/1/0.2/0.1	0.008	-	135	62	1.13	100
6	HFIP/H_2O (8/2, v/v)	[MA]/[MBP]/[TREN]/[$CuBr_2$] 222/1/0.2/0.1	0.022	2.75[a]	80	79	1.19	100
7	HFIP/H_2O (7/3, v/v)	[MA]/[MBP]/[TREN]/[$CuBr_2$] 222/1/0.2/0.1	0.023	2.90[a]	80	82	1.13	100
8	HFIP/H_2O (9/1, v/v)	[BA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.008	-	178	78	1.07	99
9	HFIP/H_2O (8/2, v/v)	[BA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.011	1.40[a]	120	76	1.21	94
10	HFIP/H_2O (7/3, v/v)	[BA]/[MBP]/[Me_6-TREN] 222/1/0.1	0.016	2.00[a]	100	79	1.30	98
11	HFIP/H_2O (7/3, v/v)	[BA]/[MBP]/[TREN]/[$CuBr_2$] 222/1/0.2/0.1	0.020	-	150	80	1.07	100

SET-LRP of MA catalyzed by non-activated Cu(0) wire/TREN in HFIP/water mixtures. Recently our laboratory, reported that Me_6-TREN can be replaced by TREN as ligand in biphasic SET-LRP systems.72 The results obtained were comparable to those obtained with Me_6-TREN with the only requirement of the addition of a small amount of Cu(II)Br_2 to obtain well-defined polymers. The use of TREN instead of Me_6-TREN is more economically attractive from an industrial viewpoint. In this context, the next series of experiments were carried out switching Me_6-TREN for TREN as ligand. The reactions were performed using 4.5 cm of non-activated copper wire, MBP as initiator and mediated by TREN and $CuBr_2$ (Scheme 1b) under the following conditions: [MA]/[MBP]/[TREN]/[$CuBr_2$]= 222/1/0.2/0.1 at 25 ºC. Kinetic data can be observed in the Fig. 3 and Table 1, entries 5-7.

Kinetics experiments show living features in all compositions, e.g. linear dependence of ln$[M]_0/[M]$ with time demonstrating a first order kinetics in monomer concentration and linear evolution of molecular weight during the process. Under the studied conditions narrow distributions and excellent initiator efficiency (100%) were obtained indicating the high chain growth efficiency. Also in this system, the rate constant values increase with the small addition of water. However, it only increases up to 20% water (K_p^{app} = 0.0219 min^{-1}) and reaches a plateau. (See Fig. 3 and Table 1, entries 5-7).

The biphasic nature of the reaction mixtures in these polymerizations is shown in the digital images from Figure 2e-g. In this case a better separation of water phase can be observed, especially in the image Figure 2d, in which small blue water droplets can be clearly seen supporting unequivocally that SET-LRP proceed in a biphasic regime.

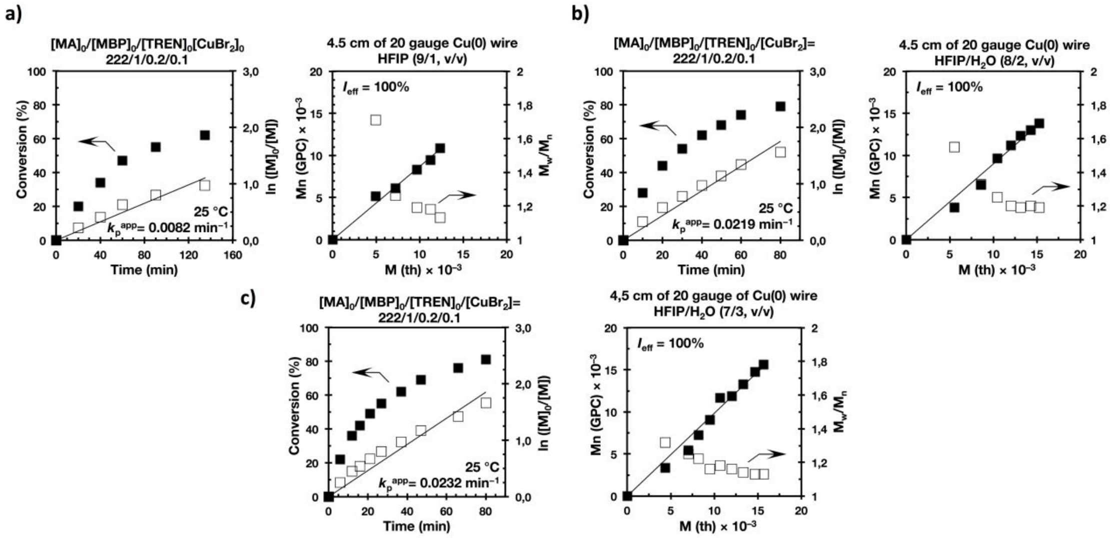


Figure 3. Kinetic plots, molecular weight and dispersity evolutions for the SET-LRP of MA (a, b, c,) in HFIP/water mixtures initiated with MBP and catalyzed by non-activated Cu(0) wire at 25 °C. (a) HFIP /water (9/1, v/v); (b) HFIP /water (8/2, v/v) and (c) HFIP /water (7/3, v/v). The v/v ratio must be multiplied by 10 to obtain % solvent/ % water. The value of v+v must be divided by 10 to obtain the total volume of solvents, 1mL. Reaction conditions: MA = 1 mL, (a, b, c) HFIP + water = 0.5 mL, (a, b, c,) $[MA]_0/[MBP]_0/[Me_6\text{-}TREN]_0[CuBr_2]_0$= 222/1/0.2/0.1.

SET-LRP of BA catalyzed by non-activated Cu(0) wire/TREN in HFIP/water mixtures.

Butyl acrylate (BA) was selected for the next series of experiments to expand the monomer scope of this system. Both Me_6-TREN and TREN were tested as ligands (Scheme 1a and b) under the following conditions: [BA]/[MBP]/[Me_6-TREN] = 222/1/0.1 and [BA]/[MBP]/[TREN]/[$CuBr_2$] = 222/1/0.2/0.1 at 25 ºC. The kinetic plots of the BA polymerization in various HFIP/water mixtures give a linear variation of the ln$[M]_0$/[M] with time, a good agreement between theoretical and experimental molecular weight as well as narrow molecular weight distribution at high conversion (Figure 4). Kinetic plots depicted in Figure 4c and d perfectly exemplifies the successful replacement of Me_6-TREN by TREN. Both kinetics show clear LRP features and comparable polymerization rate constants (K_p^{app} = 0.0163 min^{-1} and 0.0118 min^{-1} for Me_6-TREN and TREN respectively). Note also that when polymerization is mediated by TREN in combination with Cu(II)Br_2 dispersity value and I_{eff} is even better (compare entries 10 and 11, Table 1).

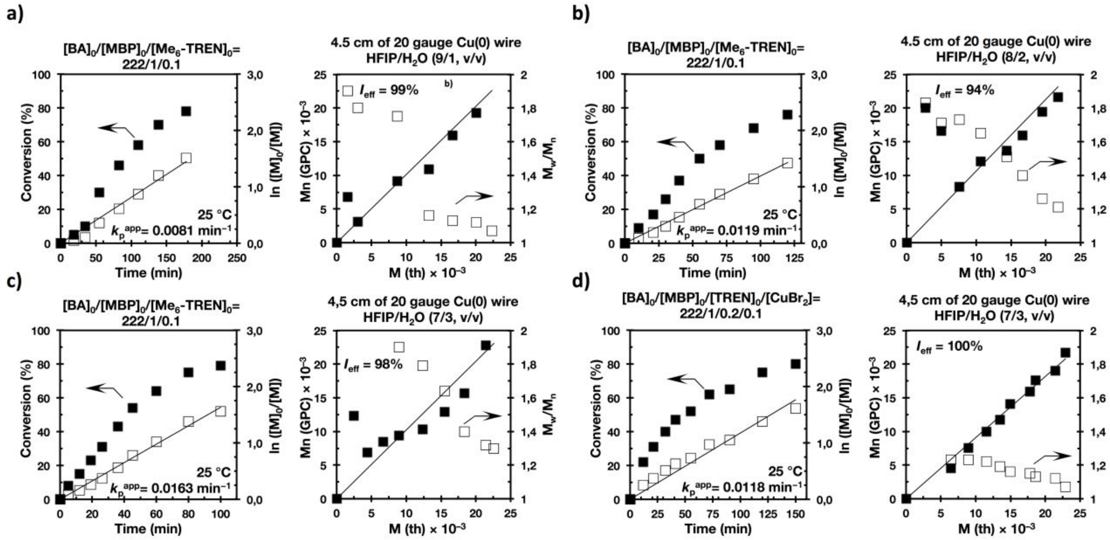


Figure 4. Kinetic plots, molecular weight and dispersity evolutions for the SET-LRP of BA in HFIP/water mixtures initiated with MBP and catalyzed by non-activated Cu(0) wire at 25 °C. (a) HFIP /water (9/1, v/v); (b, d) HFIP /water (8/2, v/v) and (c) HFIP /water (7/3, v/v). The v/v ratio must be multiplied by 10 to obtain % solvent/ % water. The value of v+v must be divided by 10 to obtain the total volume of solvents, 1mL. Reaction conditions: BA = 1 mL, (a, b, c) HFIP + water = 0.5 mL, (a, b, c,) $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0$= 222/1/0.1. (d) $[BA]_0/[MBP]_0/[TREN]_0[CuBr_2]_0$= 222/1/0.2/0.1.

Chain end analysis of PMA obtained by the SET-LRP process catalyzed by non-activated Cu(0) wire mediated by Me$_6$-TREN and TREN in pure HFIP and HFIP/water mixtures. The analysis of the chain end functionality of polymers prepared by LRP techniques is crucial to determine further applications. SET-LRP has attracted attention as it can retain extremely high bromine chain-end functionality at near-complete conversion.[3,10,11] Some of the above described experiments were selected to target low molecular weight PMA ([MA]$_0$/[MBP]$_0$=30/1). Thus, Cu(0) wire-catalyzed SET-LRP was performed in pure HFIP and a 8/2, v/v HFIP/water mixture using Me$_6$-TREN as ligand and in a 7/3, v/v HFIP/water mixture using TREN. The evolution of the chain end functionality (*f*) was monitored at different conversions during the polymerization withdrawing samples from the polymerization mixtures followed by 500 MHz ^{1}H-NMR analysis (Figure 5). Chain end functionality was determined by the direct comparison between the integrated areas of the signals Hc, corresponding to the initiator –CH$_3$ group, and Hk, corresponding to the protons of α-bromo position in the chain end (Figure 6). The fraction of these two signals represents the polymer chains initiated that remain functionalized with bromine atom. Figure 5 red squares shows that near perfect chain end functionality of PMA is retained throughout the polymerization mediated by Me$_6$-TREN in a HFIP/water mixture. High level of chain end functionality is also retained using TREN (green triangles in Figure 5). However, when HFIP is used in absence of water (blue circles) chain end functionality progressively decreases and falls below 80% at high conversion and therefore no MALDI-TOF analysis was performed on the resulting polymers. These results can be attributed to the non-disproportionating character of HFIP favoring bimolecular termination events when the polymerization is performed in a classic monophasic system. Conversely, the fast disproportionation of Cu(I)Br in HFIP/water mixtures provides excellent conditions to perform SET-LRP and emphasize the relevance of the "programmed" organic/aqueous biphasic systems to expand the table of solvents for SET-LRP.

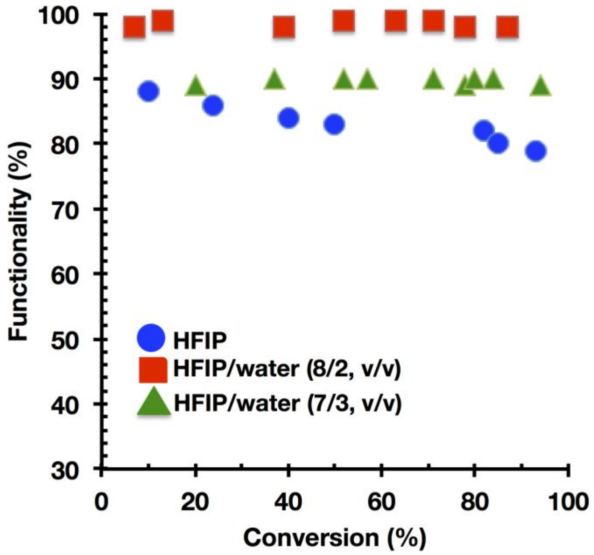


Figure 5. Evolution of bromine chain-end functionality with conversion in HFIP (blue circles), HFIP/water mixtures (8/2, v/v) (red squares) and HFIP/water mixtures (7/3, v/v) (green triangles). Reaction conditions: (blue circles), MA = 1mL, HFIP = 0.5 mL, $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0 = 222/1/0.1$ and (red squares), MA = 1mL, HFIP + water = 0.5 mL, $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0 = 222/1/0.1$. (green triangles), MA = 1mL, HFIP + water = 0.5 mL, $[MA]_0/[MBP]_0/[TREN]_0[CuBr_2]_0 = 222/1/0.2/0.1$.

Low molar mass PMAs were isolated at around 90% monomer conversion from the same series of experiments described above and characterized by ^{1}H-NMR spectroscopy and MALDI-TOF. Figures 6 and 7 shows the high resolution NMR spectra of PMA before and after the modification of bromine chain-ends via "thio-bromo click" thioeterification reaction. (Scheme 1c)[86,87] Taking into account the experimental error, near perfect chain-end functionality was determined for the PMAs prepared in HFIP/water mixture using Me_6-TREN as ligand (Figures 7b and 8b). The replacement of Me_6-TREN by TREN also furnished PMA with chain end functionality as high as 90% (Figure 6c and 7c). However, HFIP as unique solvent compromised the functionality of the synthesized polymer as previously discussed (Figure 6a and 7a). The MALDI-TOF analysis of PMAs synthesized in HFIP/water mixtures is consistent with NMR data (Figures 8 and 9). The presence of only one distribution both using Me$_6$-TREN and TREN, before and after thioetherification which appears 29 mass shifted *vs* the originals series of brominated end caped polymer supports the high chain end functionality achieved for both systems and suggest low levels of bimolecular termination. These results are in agreement with the previous data reported by our laboratory using both disproportionating and non-disproportionating organic solvents/water mixtures[66,67,68,69,70,71,72,73] and emphasize the importance of using mixtures of HFIP and water to ensure the delivery of polymers with high chain end functionality.

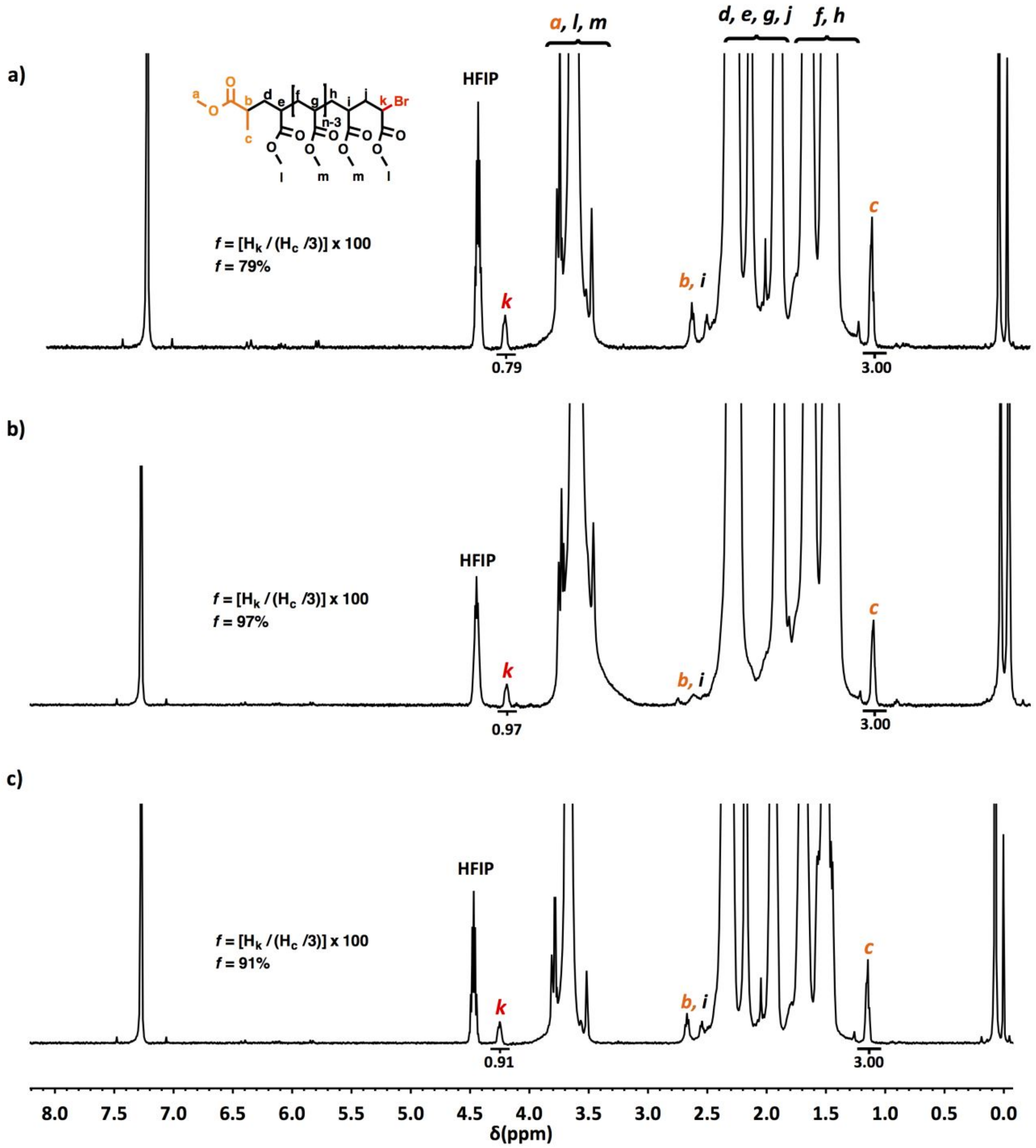


Figure 6. ^{1}H-NMR (500 MHz) recorded in $CDCl_3$, of PMA-Br isolated at (a) 95%, (b) 90% and (c) 89% conversion from SET-LRP of MA in (a) HFIP and (b, c) HFIP/water (8/2, v/v) mixtures initiated with MBP and catalyzed by non-activated Cu(0) wire at 25 ºC. Reaction conditions: (a) MA = 1mL, HFIP = 0.5 mL, $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0 = 30/1/0.1$, (b) MA = 1mL, HFIP + water = 0.5 mL, $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0 = 30/1/0.1$ and (c) MA = 1mL, HFIP + water = 0.5 mL, $[MA]_0/[MBP]_0/[TREN]_0[CuBr_2] = 30/1/0.2/0.1$, 4.5 cm of 20 gauge Cu(0) wire.

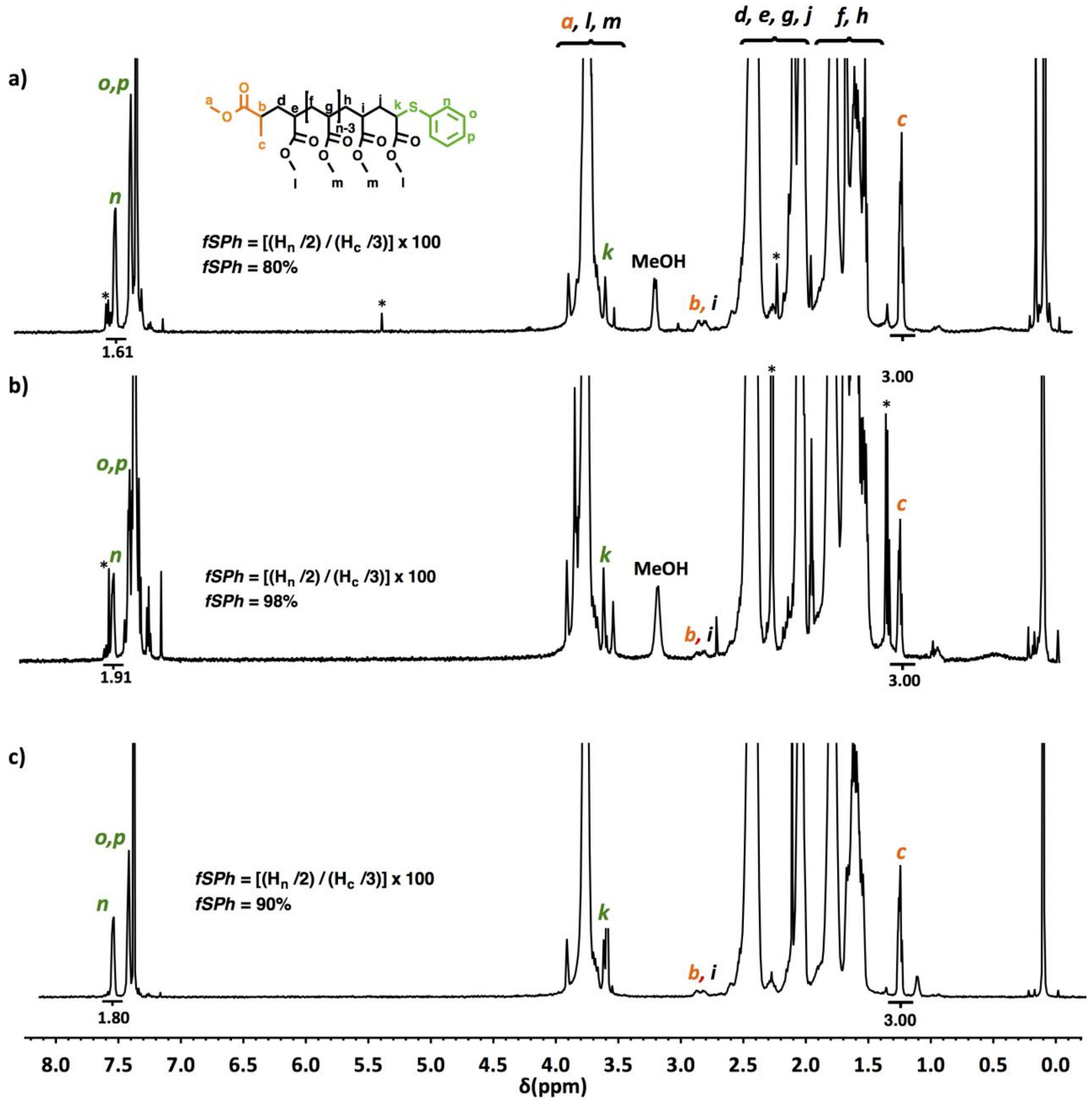


Figure 7. ^{1}H-NMR (500 MHz) recorded in $CDCl_3$, of PMA-Br after thio-bromo "click" reaction isolated at (a) 95%, (b) 90% and (c) 89% conversion from SET-LRP of MA in (a) HFIP and (b, c) HFIP/water (8/2, v/v) mixtures initiated with MBP and catalyzed by non-activated Cu(0) wire at 25 ºC. Reaction conditions: (a) MA = 1mL, HFIP = 0.5 mL, $[MA]_0/[MBP]_0/[Me_6\text{-}TREN]_0 = 30/1/0.1$, (b) MA = 1mL, HFIP + water = 0.5 mL, $[MA]_0/[MBP]_0/[Me_6\text{-}TREN]_0 = 30/1/0.1$ and (c) MA = 1mL, HFIP + water = 0.5 mL, $[MA]_0/[MBP]_0/[TREN]_0[CuBr_2] = 30/1/0.2/0.1$, 4.5 cm of 20 gauge Cu(0) wire. *Impurity peaks: triethylamine, thiophenol and acetone.

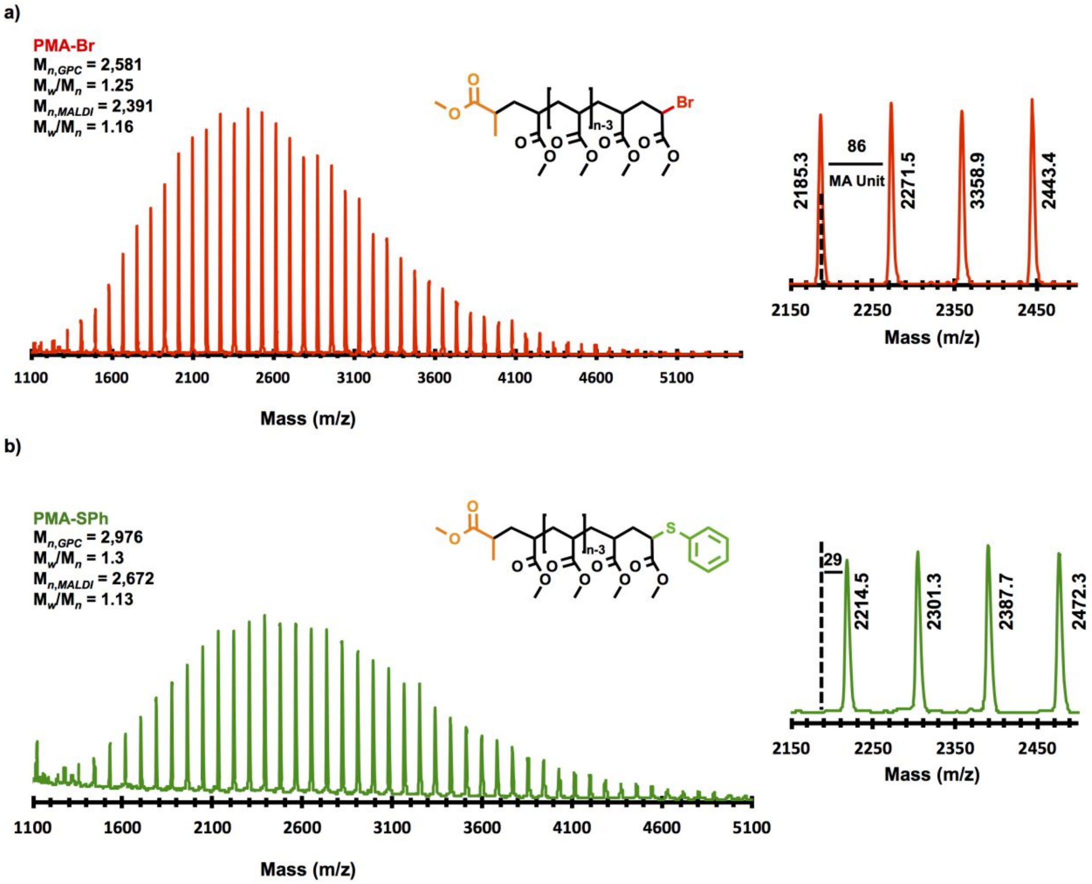


Figure 8. MALDI-TOF of (a) PMA-Br isolated at 90% conversion from biphasic SET-LRP of MA in HFIP/water (8/2, v/v) mixtures initiated with MBP and catalyzed by nonactivated Cu(0) wire at 25 ºC (b) PMA-Br after thio-bromo "click" reaction. Reaction conditions: $[MA]_0/[MBP]_0/[Me_6\text{-TREN}]_0$= 30/1/0.1 MA = 1 mL, HFIP/water (8/2, v/v), HFIP+ water = 0.5 mL, 4.5 cm of 20 gauge Cu(0) wire at 25 ºC.

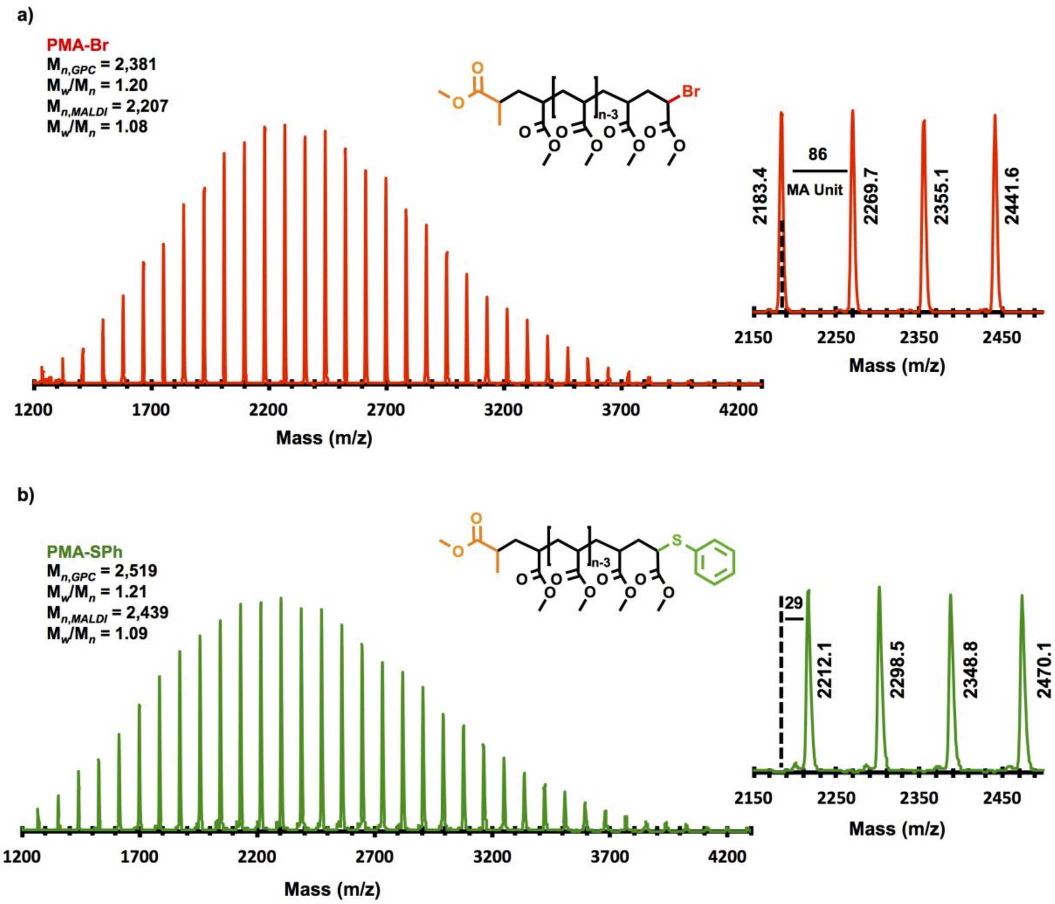


Figure 9. MALDI-TOF of (a) PMA-Br isolated at 89% conversion from biphasic SET-LRP of MA in HFIP/water (8/2, v/v) mixtures initiated with MBP and catalyzed by nonactivated Cu(0) wire at 25 ºC (b) PMA-Br after thio-bromo "click" reaction. Reaction conditions: $[MA]_0/[MBP]_0/[TREN]_0/[CuBr_2]_0$ = 30/1/0.2/0.1, MA = 1 mL, HFIP/water (8/2, v/v), HFIP + water = 0.5 mL, 4.5 cm of 20 gauge Cu(0) wire at 25 ºC.

CONCLUSIONS

HFIP is a fluorinated alcohol that does not mediate the disproportionation of Cu(I)Br into Cu(0) and Cu(II)Br$_2$. SET-LRP of MA in pure HFIP shows an incomplete monomer conversion and low polymer chain-end functionality. SET-LRP of MA and BA in biphasic HFIP/water mixtures mediated by TREN or Me$_6$-TREN allows the synthesis of near perfect chain-end functionality for both polyacrylates. All these results were validated through the kinetics experiments showing linear evolution of monomer concentration and molecular weight with narrow dispersities. An exhaustive chain-end analysis by combination of ^{1}H-NMR spectroscopy and MALDI-TOF were also provided to determine the degree of functionality of the obtained polymers. The results reported in this report support the utility of HFIP as solvent in biphasic SET-LRP and therefore expand the scope of suitable solvents for SET-LRP, including this unique fluorinated alcohol[88,89] that can be used for the synthesis of polymers with dual control over molecular weight and tacticity. Since HFIP is also a classic solvent for the denaturation of proteins this SER-LRP system will find applications in the grafting of protein.[90,91,92] Research on these two lines will be reported in due time. The interfacial[67] biphasic experiments reported here can be performed with Cu(0) generated in situ,[66-70] powder or wire and will broaden the scope of SET-LRP with complementary capabilities.[2,3,10,11,12,93,94,95,96,97,98,99,100,101,102,103]

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Notes

The authors declare no competing financial interest.

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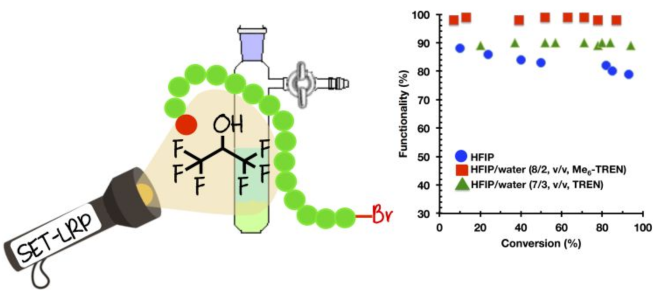

SET-LRP of Acrylates in Biphasic HFIP/Water Mixtures