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Radical Polymerization

A Green Route to Well-Defined High-Molecular-Weight (Co)polymers Using ARGET ATRP with Alkyl Pseudohalides and Copper Catalysis[**]

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Atom-transfer radical polymerization (ATRP) has emerged as one of the most robust and powerful techniques for the preparation of well-defined polymeric materials with complex architectures ranging from blocks, stars, combs, and cyclic structures to hybrids and bioconjugates.[1]

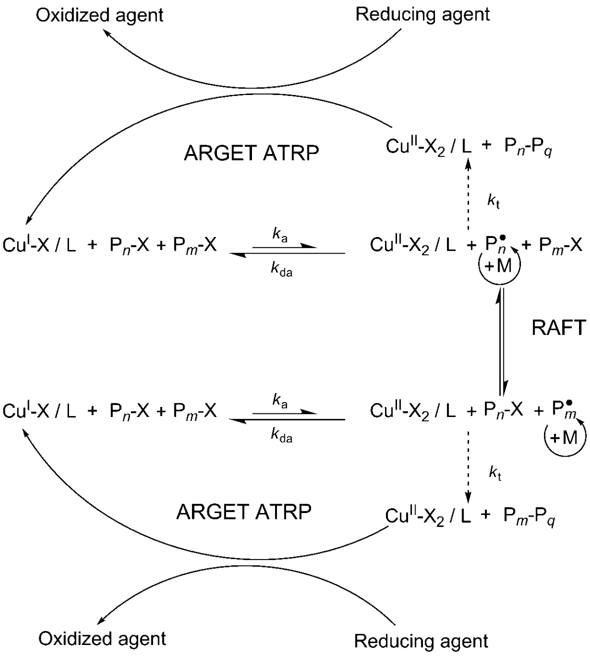
More recently, considerable effort has been devoted to decreasing the amount of catalyst used in ATRP systems.[2] The movement towards greener processes overcomes a drawback of traditional ATRP techniques that require relatively large amounts of copper catalyst (typically 0.1–1 mol% vs. monomer). Lowering the amount of catalyst would be beneficial both commercially and environmentally.

In activators regenerated by electron transfer (ARGET) ATRP,[3] an excess of reducing agent, relative to the catalyst, is used to continuously regenerate the activators by reduction of the copper(II) products that accumulate because of unavoidable radical termination. Therefore, ARGET ATRP allows the concentration of copper(I) to be at ppm (parts-per-million) levels using various reducing agents such as tin octoate, ascorbic acid, or copper(0).[4] However, the synthesis of polymers with a low polydispersity index (PDI) and predetermined molecular weight (MW) requires a deactivator concentration above a threshold value, as given by Eq. (1).

$$\frac{M_w}{M_n} = 1 + \frac{1}{\mathrm{DP}_n} + \left(\frac{[\mathrm{RX}]_0 k_p}{k_{da}[\mathrm{XCu^{II}/L}]}\left(\frac{2}{\mathrm{conv}} - 1\right)\right) \qquad (1)$$

Reversible addition–fragmentation chain-transfer (RAFT) polymerization is another efficient controlled radical polymerization (CRP) technique that affords versatility in polymerization procedures, functional-group compatibility, and good architectural and MW control.[5] The RAFT process requires a continuous supply of new initiating radicals from the decomposition of radical initiators (e.g. AIBN) to compensate for the continuous radical termination. For the synthesis of high-molecular-weight (HMW) polymers, the number of chains that result from the radical initiator, affecting both the MW and chain-end functionality cannot be neglected.

We recently demonstrated that ATRP catalysts, as well as organic radicals, can activate alkyl dithioesters (common RAFT chain transfer agents, CTAs), thus acting as alkyl pseudohalides, that is, ATRP initiators.[6] Herein, we report the synthesis of HMW (co)polymers under ambient conditions using ARGET ATRP with alkyl pseudohalides as initiators/CTAs and a $\mathrm{Cu^I/L}$ catalyst with concentrations as low as 0.01 ppm (mol vs. monomer), in the presence of copper(0) as reducing agent (Scheme 1). Process control relies on both activation/deactivation and degenerative reversible transfer between the dormant and active species. This system presents several significant advantages over both conventional RAFT polymerization and ATRP with alkyl halide initiators: 1) the initiating radicals are generated directly from the CTA, thus eliminating the formation of new chains; 2) the use of CTA as alkyl pseudohalides removes the need for a minimal amount of deactivating copper(II) complex whilst still retaining low PDI; 3) the use of ARGET ATRP allows the level of $\mathrm{Cu^I/L}$ catalyst to be lowered to below ppm levels, and 4) the use of copper wire as a solid heterogeneous reducing agent facilitates the handling of the



Scheme 1. ARGET ATRP with alkyl pseudohalide initiators/CTAs.

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reducing agent and simplifies purification of the polymer or copolymer products.

ARGET ATRP using cumyl dithiobenzoate (CDB) as the initiator/CTA, low catalyst concentrations ($[Cu^I]_0/[M]_0$ ranging from 50 to 0.33 ppm), and copper(0) powder (75 μm) as the reducing agent was initially employed to prepare HMW poly(methyl methacrylate) (PMMA; Table 1). PMMA was obtained with a low PDI and good agreement between the theoretical and experimental MWs for targeted degrees of polymerization (DP) of 2000 and 30000. For example, an unprecedented HMW PMMA was obtained that had a $M_n = 1.25 \times 10^6$ g mol^{-1} and $M_w/M_n = 1.21$ using only 0.33 ppm of CuBr.

Table 1: ARGET ATRP of MMA with CDB using copper(0) powder (75 μm) as the reducing agent, and control experiments.[a]

$[MMA]_0/[CDB]_0$	$[Cu^I]$ [ppm]	t [h]	Conv. [%]	$M_{n,th}$ [kg mol^{-1}]	$M_{n,exp}$ [kg mol^{-1}]	M_w/M_n
2000[b]	50	44	80.1	161	150	1.13
2000[b]	5	32	61.1	123	112	1.08
30000[c]	3.3	32	35.4	1060	912	1.24
30000[d]	0.33	125	43.9	1320	1250	1.21
30000[d,e]	0.33	43	29.5	887	1300	2.05
30000[d,f]	–	120	59.2	1780	1210	1.30

[a] 80 °C in anisole with ratios $[CDB]_0/[Cu^0]_0 = 1{:}5$ and $[CuBr]_0/[TPMA]_0 = 1{:}3$. [b] MMA/anisole = 1:2 (v/v). [c] MMA/anisole = 2:1 (v/v). [d] MMA/anisole = 1:1 (v/v). [e] Conventional ARGET ATRP: EBPA used instead of CDB. [f] Conventional RAFT: $[CDB]_0/[VAm\text{-}110]_0 = 1{:}1$, no $CuBr/Cu^0/$TPMA.

Two control experiments were performed to show the benefits of ARGET ATRP with alkyl pseudohalides as initiators/CTAs. A conventional ARGET ATRP was carried out by using 0.33 ppm of Cu^IBr/TPMA and ethyl α-bromophenylacetate (EBPA) as an alkyl halide initiator. In that case, the catalyst concentration was insufficient to ensure a fast equilibrium between dormant and active species, which resulted in poor initiation efficiency and a high PDI. HMW PMMA was also prepared by conventional RAFT polymerization. A significant discrepancy was observed between the theoretical and experimental MWs, although PDI values were relatively low. This difference originates from the continuous supply of initiating radicals formed by decomposition of the thermal initiator, which decreases the observed MW and chain-end functionality.

Figure 1. A photograph of the ARGET ATRP reaction of MMA with CDB and a copper wire as the reducing agent. Flask contents: $[MMA]_0/[CDB]_0/[CuBr]_0/[TPMA]_0 = 30{,}000{:}1{:}0.01{:}0.03$; MMA/anisole = 1:1 (v/v); copper(0) wire $l = 30$ cm, $d = 1$ mm.

Table 2: ARGET ATRP of MMA with CDB using copper(0) wire ($d = 1$ mm) as the reducing agent.[a]

$[MMA]_0/[CDB]_0$	$[Cu^I]$ [ppm]	t [h]	Conv. [%]	$M_{n,th}$ [kg mol^{-1}]	$M_{n,exp}$ [kg mol^{-1}]	M_w/M_n
2000[b]	5	72	80.9	162	168	1.13
2000[b]	5	72	79.4	159	157	1.12
2000[b]	5	72	75.4	151	155	1.11
30000[c]	0.33	120	44.9	1350	1170	1.26

[a] 80 °C in anisole; $[CuBr]_0/[TPMA]_0 = 1{:}3$. [b] MMA/anisole = 1/2 (v/v); copper(0) wire $l = 70$ cm. The same copper(0) wire was used for the three polymerizations without purification. [c] MMA/anisole = 1:1 (v/v); copper(0) wire $l = 30$ cm.

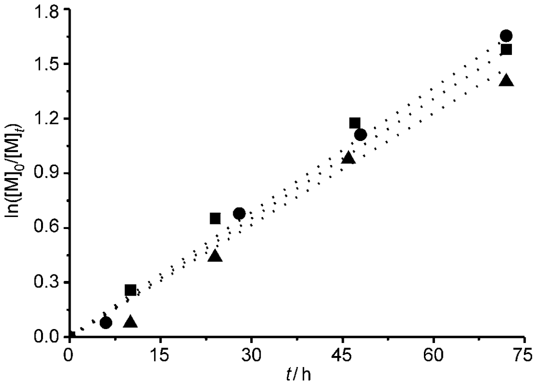

Figure 2. Kinetic plots for three consecutive polymerizations of MMA with CDB using the same copper wire as the reducing agent. 1st use ●, 2nd use ■, 3rd use ▲. Polymerization conditions: $[MMA]_0/[CDB]_0/[CuBr]_0/[TPMA]_0 = 2{,}000{:}1{:}0.01{:}0.03$; MMA/anisole = 1:2 (v/v); 72 h at 80 °C; copper(0) wire $l = 70$ cm, $d = 1$ mm.

To simplify the purification of the final (co)polymers, copper wire was used as the reducing agent (Figure 1). The use of copper wire offers several advantages; for example, ease of handling and removal and the possibility to reuse the same wire several times, which is both economically and environmentally beneficial. Three successive polymerization reactions were performed using the same wire without any treatment between the polymerizations; well-defined PMMA product was obtained from each experiment (Table 2). More importantly, the rate and control of the polymerization were very similar in each case (Figures 2 and 3). Furthermore, HMW PMMA ($M_n = 1.17 \times 10^6$ g mol^{-1}; $M_w/M_n = 1.26$) was prepared using copper(0) wire as the reducing agent (Table 2). Inductively coupled plasma mass spectrometry (ICP-MS) analyses of the polymers obtained after removal of the copper wire and evaporation of all volatile compounds showed 222 ppm and 34.6 ppm of residual copper at the end of MMA polymerizations targeting DP = 2000 and 30000, respectively. These values significantly exceeded the amount of soluble copper complex added (5 ppm and 0.33 ppm, respectively) and presumably correspond to copper(0)

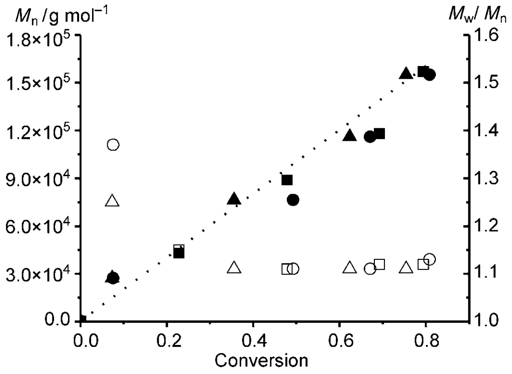

Figure 3. Plot of M_n (filled shapes) and M_w/M_n (empty shapes) versus conversion for three consecutive polymerizations of MMA with CDB using the same copper wire as the reducing agent. 1st use ●, ○, 2nd use ■, □, 3rd use ▲, △. Polymerization conditions: $[MMA]_0/[CDB]_0/[CuBr]_0/[TPMA]_0 = 2000:1:0.01:0.03$; MMA/anisole = 1:2 (v/v); 72 h at 80 °C; copper(0) wire $l = 70$ cm, $d = 1$ mm.

mechanically scrubbed from the wire during stirring, CuO leached from the oxidized surface layer and copper dithiobenzoate ($Cu^{I}DB$ and $Cu^{II}DB$), formed from radical termination. ICP-MS analyses also indicated that less than 0.01 % of the copper(0) wire was consumed during the polymerizations. These results demonstrate that a copper wire can be used successfully several times as a reducing agent for ARGET ATRP, with alkyl pseudohalides as initiators/CTAs.

The synthesis of HMW polystyrene (PSt) by ARGET ATRP using CDB at 80 °C was also attempted. Two concentrations of CuBr (1.4 and 0.01 ppm) were tested (Table 3). In each case, HMW PSt ($M_n > 200$ kg mol^{-1}) was obtained which had narrow MW distributions. However, when styrene (St) was polymerized under the same conditions in the absence of copper(0) and Cu^{I}/L, it was not possible to reach 200 kg/mol and a higher PDI value was obtained. Well-defined HMW polymers were successfully prepared even with sub-ppm Cu^{I}/L concentrations of 1.4 ppm and 0.01 ppm (ARGET ATRP of styrene with CDB and CuBr). This result contrasts with ARGET ATRP using alkyl halides as initiators, in which the PDI is dependent on the concentration of deactivator.

The retention of chain-end functionality is one of the key features of any controlled/living polymerization processes, as it is a crucial condition for the synthesis of block copolymers.

HMW PMMA-*b*-PBMA block copolymers were prepared by ARGET ATRP with CDB as the alkyl pseudohalide initiator, using either copper(0) powder or copper(0) wire as the reducing agent (Table 4). PMMA macroinitiators, with M_n values in the range 112–585 kg mol^{-1}, were used to synthesize well-defined block copolymers with M_n values of 1420–1800 kg mol^{-1} and a PDI of between 1.21 and 1.39. These results represent the first preparation of linear diblock copolymers with $M_n > 10^6$ kg mol^{-1} by CRP, and indicate the high degree of chain-end functionality of polymers synthesized by ARGET ATRP with a leaving group that can participate in degenerative transfer.

Table 3: ARGET ATRP of styrene with CDB using copper(0) powder (75 μm) as the reducing agent.[a]

$[Cu^{I}]$ [ppm]	T [°C]	t [h]	Conv. [%]	$M_{n,th}$ [kg mol^{-1}]	$M_{n,exp}$ [kg mol^{-1}]	M_w/M_n
1.4	80	92	41.1	299	222	1.26
0.01	80	92	39.2	285	203	1.25
0[b]	80	192	70.9	516	166	1.59

[a] In anisole; $[St]_0/[CDB]_0/[Cu^0]_0 = 6980:1:5$, St/anisole = 20:1 (v/v) and $[CuBr]_0/[TPMA]_0 = 1:3$. [b] No copper(0), copper(I) or TPMA.

Table 4: Synthesis of PMMA-*b*-PBMA block copolymers by ARGET ATRP with alkyl pseudohalide initiators/CTAs and copper(0) as the reducing agent.[a]

Entry	$[MMA]_0/[CDB]_0$	t [h]	Conv. [%]	$M_{n,th}$ [kg mol^{-1}]	$M_{n,exp}$ [kg mol^{-1}]	M_w/M_n
1a[b]	2000	32	61.1	123	112	1.08
2a[c]	2000	48	67.1	135	138	1.11
3a[c]	30000	48	24.8	744	585	1.24

Entry	$[BMA]_0/[PMMA]_0$	t [h]	Conv. [%]	$M_{n,th}$ [kDa]	$M_{n,exp}$ [kDa]	M_w/M_n
1b[b]	30300	92	31	1450	1420	1.21
2b[c]	30300	73	35.7	1680	1470	1.34
3b[c]	60600	75	18.9	2190	1800	1.39

[a] 80 °C in anisole; $[CDB]_0/[CuBr]_0/[TPMA]_0 = 1:0.01:0.03$ and $[PMMA]_0/[CuBr]_0/[TPMA]_0 = 1:0.01:0.03$; Entries 1a and 2a: MMA/anisole = 1:2; Entry 3a: MMA/anisole = 1:1; Entries 1b–3b: BMA/anisole = 1:1; [b] Copper(0) powder (75 μm); [c] Copper(0) wire ($d = 1$ mm).

In summary, we report the preparation of HMW PMMA ($M_n > 10^6$ g mol^{-1}) and PSt ($M_n > 200$ kg mol^{-1}) under atmospheric pressure using ppm levels of Cu^{I}/L catalyst. This process provides excellent control over MW, MW distribution, and chain-end functionality, and has afforded the first successful synthesis of HMW block copolymers ($M_n > 10^6$ g mol^{-1}) by CRP. The dual nature of control in this procedure offers advantages over both conventional RAFT and ATRP. In particular, the formation of new chains from radical initiators is suppressed, as compared to typical RAFT polymerization; furthermore, a minimal amount of deactivating copper(II) complex is not necessary for the retention of low PDI values, unlike typical ARGET ATRP techniques. We have also demonstrated that a single piece of copper wire can be reused several times, without any additional treatment, to prepare HMW (co)polymers with excellent control. This suggests that the synthesis of HMW (co)polymers using ARGET ATRP with a leaving group that can participate in degenerative transfer could be a preferred technique from both industrial and environmental viewpoints.

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