ARGET ATRP of 2-(Dimethylamino)ethyl Methacrylate as an Intrinsic Reducing Agent

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Introduction. Poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA) has attracted a significant attention in recent years as a pH and temperature responsive polymer for an increasing number of applications in drug delivery, bioseparation, and microfluidic areas.[1−7] In addition, quaternized PDMAEMA (PQDMAEMA) is a good candidate for development of cationic antimicrobial surfaces.[8−10] Recently, PQDMAEMA brushes covalently attached to a range of solid surfaces have demonstrated high levels of antibacterial activity.[11,12]

The precise design of functional PDMAEMA materials requires synthesis of materials with controlled molecular weight and well-defined chain architecture as well as low molecular weight distribution. These requirements can be achieved by conducting living polymerizations, particularly controlled/living radical polymerization (CRP).[13−20] One of the most successful CRP systems is atom transfer radical polymerization (ATRP).[21−24] Well-defined PDMAEMA (co)polymers, block copolymers, and surface tethered brushes have been successfully prepared via ATRP due to its tolerance to a variety of functional groups on the monomers.[10,25−35] However, since propagating radicals are rapidly trapped by oxygen in radical-based polymerizations, small scale reaction mixtures must be rigorously deoxygenated through the freeze−pump−thaw method or bubbling with N_2.

Our group previously demonstrated that limited amounts of adventitious air can be consumed by adding a sufficient amount of an appropriate reducing agent, such as tin(II) 2-ethylhexanoate ($Sn(EH)_2$) or ascorbic acid, in the processes called activators generated by electron transfer (AGET) and activators regenerated by electron transfer (ARGET) ATRP.[36−54]The activator (Cu(I) species) is initially rapidly oxidized by oxygen to Cu(II) species, but the latter is quickly reduced to the Cu(I) state in the presence of a reducing agent. This is a repetitive process, and there is an induction period during which time aerial oxygen is consumed, and eventually the polymerization starts. Especially, in ARGET ATRP, the amount of copper catalyst can be decreased by 10^3 times from prior levels, and the procedure can tolerate a large excess of reducing agent. This new technique eliminates any requirement for the deoxygenation of reaction mixtures and greatly simplifies the ATRP process. Although ARGET ATRP has been applied to relatively nonpolar monomers (e.g., styrene, butyl acrylate, and methyl methacrylate), there are few successful examples of the novel procedure being applied to monomers containing amino or amido groups.[38,55] One of the reasons is that the large excess of monomer with a polar group may compete with a low concentration of ligand required to form the catalytic complex with ppm amount of copper species. The complex formed with monomer has insufficient activity in the ATRP process, so that polymerization does not happen.

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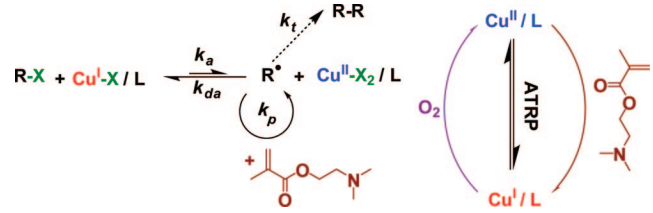
Scheme 1. ARGET ATRP of DMAEMA with Internal Reducing Agent in the Presence of Air



In this communication, we report development an ARGET ATRP of DMAEMA in the presence of limited amounts of air. Very interestingly, the polymerization proceeded smoothly without addition of any external reducing agents because DMAEMA monomer, containing tertiary amine group, served as an internal reducing agent in ARGET ATRP (Scheme 1). The polymerization was also investigated with various external reducing agents and for a surface-initiated polymerization.

Results and Discussion. ARGET ATRP of DMAEMA was initiated by ethyl 2-bromoisobutyrate (EBiB) and catalyzed by a low level (100 ppm vs monomer and 5 mol % vs initiator) of $CuCl_2$/tris[(2-pyridyl)methyl]amine (TPMA) complex under N_2 (Table 1, entry 1) and in the presence of limited air (Table 1, entries 2−6). All reactions proceeded well, indicating that TPMA formed a sufficiently stable complex and DMAEMA did not displace the ligand. No ATRP was observed without the ligand (Table 1, entry 7).

The polymerizations described in entries 1 and 2 in Table 1 were conducted without adding external reducing agents. Both of the polymerizations were well controlled, producing polymers with predictable controlled molecular weights and low polydispersities. A slight deviation from the straight line kinetic plots (Figure 1A) indicated that the number of radicals present in the system changed, to some extent, during the reaction, but control was maintained. The molecular weights obtained from size exclusion chromatography (SEC) did not vary significantly from the theoretical values (Figure 1B). The SEC traces (Figure S1 in Supporting Information) exhibited a smooth shift of the entire molecular weight distribution toward high molecular weight in both reactions. Polydispersity decreased with increase in monomer conversion.

In ARGET ATRP, a Cu^{II} deactivator resulting from radical termination needs to be continuously regenerated to a Cu^{I}

Table 1. ARGET ATRP of DMAEMA with Internal and External Reducing Agents (RA)[a]

entry	RA	$[RA]_0/[CuCl_2]_0$	volume of free space (mL)	time (h)	conv (%)	M_n[b] (theo)	M_n[c] (GPC)	PDI[c]
1			0	63.3	44	34 800	29 300	1.20
2			4	64.7	77	60 500	42 700	1.32
3[d]	$Sn(EH)_2$	100	4	18.0	90	70 600	61 500	1.35
4[e]	AA	15	4	8.7	83	64 900	61 300	1.39
5[f]	glucose	15	4	8.7	32	25 500	75 600	1.69
6	NH_2NH_2	15	4	8.7	61	47 600	43 000	2.36
7[g]			0	60.0				

[a] DMAEMA/EBiB/$CuCl_2$/TPMA = 500:1:0.05:0.25 at 30 °C in anisole. $[DMAEMA]_0 = 3.96$ M. [b] $M_n(theo) = ([DMAEMA]_0/[EBiB]_0) \times$ conversion. [c] Determined by SEC in dimethylformamide (DMF), based on polystyrene standards. [d] $Sn(EH)_2$: tin(II) 2-ethylhexanoate. [e] AA: L-ascorbic acid. [f] The reaction was conducted in dimethyl sulfoxide (DMSO). [g] No TPMA was added.

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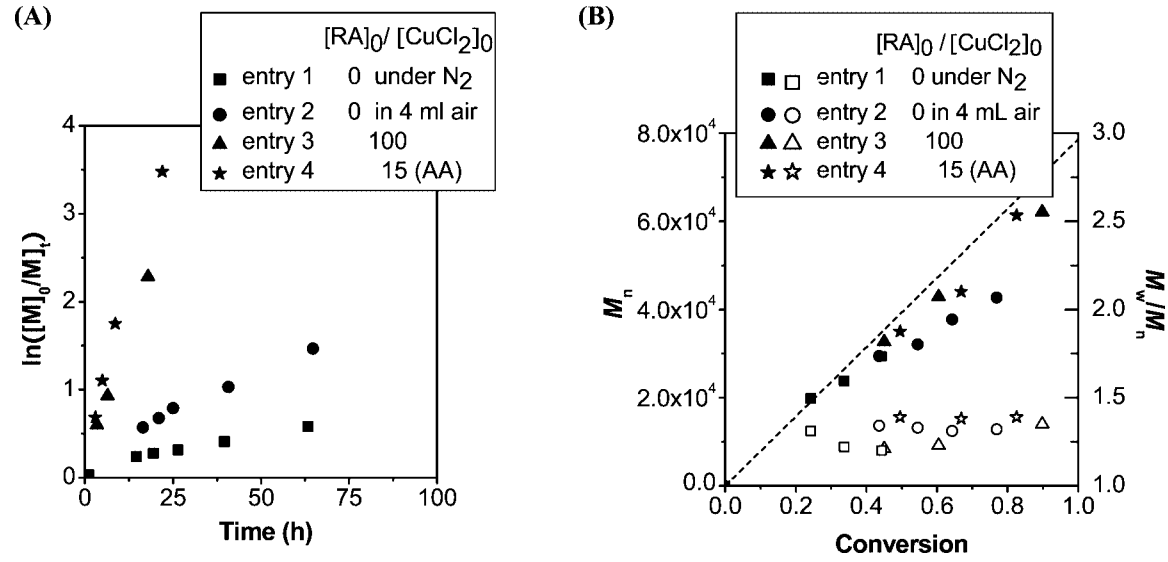

Figure 1. Kinetic plots (A) and evolution of molecular weights and M_w/M_n with monomer conversion (B) in ARGET ATRP of DMAEMA with internal and external reducing agents (Table 1, entries 1−4).

activator by an excess of reducing agents. Since no external reducing agent was added into the polymerization system (Table 1, entries 1 and 2), DMAEMA should act as an intrinsic reducing agent to reduce Cu(II) to Cu(I).

ARGET ATRP of DMAEMA in the presence of limited amount of air also proceeded with good control after the addition of an external reducing agent, $Sn(EH)_2$ (Table 1, entry 3, and Table S1 in Supporting Information), yielding PDMAEMA with controlled molecular weight and low polydispersity. When the ratio of $[Sn(EH)_2]_0/[CuCl_2]_0$ was larger than 50:1 (Figure S2 in Supporting Information), the reaction rate became faster than that relying solely on the intrinsic reducing agent (Table 1, entry 2). In addition to $Sn(EH)_2$, some external organic reducing agents including ascorbic acid, glucose, and hydrazine were examined (Table 1, entries 4−6). The best control was observed with ascorbic acid.

Surface-initiated ARGET ATRP can be carried out in sealed vials or jars without deoxygenation.[40] This new technique is especially useful for the preparation of densely grafted polymer brushes. ARGET ATRP of DMAEMA was carried out in the presence of silicon wafers functionalized with ATRP initiators (2-bromoisobutyrate groups) as well as sacrificial initiator (ethyl 2-bromoisobutyrate), under the conditions similar to those in entry 3, Table 1. The thickness of the polymer film was measured by ellipsometry on samples taken at timed intervals (Figure S3 in Supporting Information). The ultimate density of chains under highly controlled growth was 0.32 chain/nm^2.

The reduction of $CuCl_2$/TPMA to CuCl/TPMA by DMAEMA was confirmed by UV−vis spectroscopy (Figure 2). A solution of $CuCl_2$/TPMA in acetone has a characteristic absorption peak at 938 nm, while CuCl/TPMA has no absorption at this wavelength. The concentration of $CuCl_2$/TPMA was about 7 times higher than that used in the polymerization in order to get measurable absorption intensity. After the addition of DMAEMA, the color of the $CuCl_2$/TPMA solution gradually changed from green to light yellow at room temperature, and the intensity of characteristic absorption peak decreased over time. After 45 h, about 50% $CuCl_2$/TPMA was reduced in situ to CuCl/TPMA by DMAEMA. It was reported that aliphatic tertiary amines can reduce Cu(II) to Cu(I) and produce cation radicals.[56,57] Therefore, the tertiary amine group in DMAEMA monomer should also reduce Cu(II) to Cu(I) in ARGET ATRP.

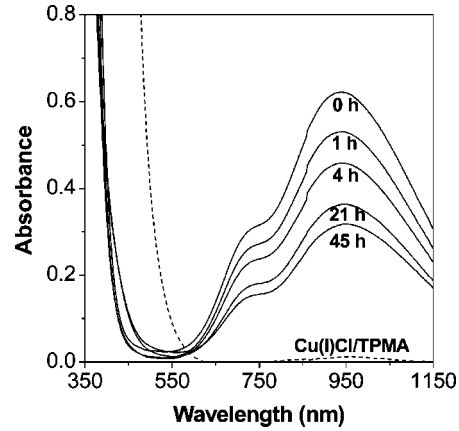

Figure 2. UV−vis spectra of $Cu(II)Cl_2$/TPMA in the presence of DMAEMA at varied time. $[Cu(II)Cl_2/TPMA]_0 = 3.00$ mM. $[Cu(I)Cl_2/TPMA]_0 = 3.00$ mM. $[DMAEMA]_0 = 3.96$ M in acetone at 30 °C.

The proposed reduction mechanism is shown in Scheme S1 in Supporting Information.

Conclusions. ARGET ATRP of DMAEMA was successfully applied for the preparation of well-defined PDMAEMA homopolymer with and without the addition of external reducing agents. The tertiary amine group in DMAEMA monomer can serve as an intrinsic reducing agent to constantly regenerate the ATRP activator, the Cu(I) species, from the Cu(II) species, but can also compensate for the presence of limited amounts of oxygen impurities. This technique can be potentially applied to other monomers containing functional reducing moieties, such as amines or phenols. In addition, ARGET ATRP was successfully applied to the synthesis of PDMAEMA brushes from the surfaces of silicon wafers with grafting density ~0.3 chains/nm^2.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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