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Use of alcohols as reducing agents for synthesis of well-defined polymers by AGET-ATRP†

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Alcohols have been demonstrated to be efficient reducing agents for AGET-ATRP for the first time. Well-controlled polymerizations have been successfully achieved with the typical characteristics of "living"/controlled radical polymerization.

Since its discovery in 1995, atom transfer radical polymerization (ATRP) has become an efficient technique for synthesis of well-defined polymers with desired molecular weight, narrow molecular weight distribution, and various architecture.[1] Normal ATRP usually involves a combination of a relatively unstable lower oxidation state metal complex (*e.g.*, Cu(I) or Fe(II)) and an alkyl halide.[2] The transition metal complexes can be easily oxidized to a higher oxidation state, therefore, the preformed catalysts must be stored under an inert atmosphere and the process of catalyst complex handling can be challenging.[3] To perform the polymerization more conveniently, new ATRP techniques such as reverse ATRP[4] and activators (re)generated by electron transfer ATRP (A(R)GET-ATRP)[5] have been developed using more stable metal species (Cu(II) or Fe(III)). While reverse ATRP rarely allows the synthesis of pure block copolymers, the products are always contaminated with homo-polymers formed by direct initiation from the free radical initiator. A(R)GET-ATRP uses a reducing agent to react with a higher oxidation state catalyst (*i.e.*, Cu(II) complex) selectively and to generate a lower oxidation state catalyst such as Cu(I) complex *in situ*, therefore this approach has all the advantages of normal ATRP and reverse ATRP as well as additional benefits of facile preparation, storage, and handling of ATRP catalysts.

The reducing agent plays a key role in an AGET-ATRP process. In an effort to make environmentally friendly, efficient, and cost-effective A(R)GET-ATRP procedures, rigorous studies have been devoted to finding suitable reducing agents, which proceed in a manner devoid of side products, facilitate facile removal, and efficiently perform at catalytic concentrations. Various reducing agents have been reported upon the investigation of A(R)GET-ATRP, including not only such organic

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reducing agents as glucose,[5c] ascorbic acid,[6] hydrazine,[5e] phenols,[5e] amines,[7] or even excess of ligands[8] but also inorganic reducing agents such as tin(II) 2-ethylhexanoate,[5c] or zerovalent metal.[9] Since these reducing agents have some disadvantages, such as chemical instability or environmental harmfulness, we are trying to explore more practical reducing agents for AGET-ATRP.

Yamamoto and Kirai[10] found that the Cu-catalyzed homo-coupling of *p*-tolylboronic acid could be well performed in alcohol solvents instead of aprotic solvents such as tetrahydrofuran, CH_2Cl_2, and *N,N*-dimethylformamide and proposed that Cu(II) could be reduced to Cu(I) by the alcohols in 2009, and then the reduction reaction of Cu(II) by alcohols was successfully applied in the azide–alkyne cycloaddition reactions.[11]

Here we report an AGET-ATRP using alcohols as reducing agents for $CuBr_2$/bipyridine(bpy). First, we examined reduction of Cu(II)Br_2 using different alcohols such as methanol, ethanol, isopropanol, ethylene glycol (EG), glycerol, and 1,4-butanediol as reducing agents under the AGET-ATRP conditions to search for new reductants for AGET-ATRP. Reduction reactions of $CuBr_2$/bpy with the different alcohols not only can be observed with the naked eye based on the color change of the reaction solution, but also can be detected by UV-Vis spectroscopy (Fig. S1 in ESI†). The color of the solution changed gradually from blue to green when the reaction proceeded under the given conditions, indicating that Cu(II)/bpy was reduced into Cu(I)/bpy. From UV-Vis spectroscopy, it can be clearly seen that the maximum absorption of the Cu(I)/bpy solution appears at 680 nm, whereas the absorption peak of Cu(II)/bpy solution disappears. These results demonstrate that Cu(II)/bpy can be reduced into Cu(I)/bpy under the polymerization conditions.[7,12] It is worth pointing out that the reduction of Cu(II) in the presence of excess of ligands such as tris[2-(dimethylamino)-ethyl]amine and *N,N,N′,N″,N″*-pentamethyldiethylenetriamine has been reported,[8] so, in the current system, we used bipyridine as the ligand to avoid the ligand effect.

We then performed AGET-ATRP of methyl acrylate (MA) using $CuBr_2$/bpy as the catalyst precursor and different alcohols as reducing agents in anisole at 70 °C. The experimental results of the polymerization are summarized in Table S1 (ESI†), showing that the polymerizations can be well controlled with all the primary and secondary alcohols examined in the experiment. Number-average molecular weights M_n of the polymers obtained are in good agreement with the theoretical calculations,

and the polydispersities are relatively low. The AGET-ATRP in the presence of *tert*-butanol was also examined under the same conditions, however, no polymerization was observed. The polymerization results show that the primary and secondary alcohols are suitable candidates as the reducing agents for the AGET-ATRP. It is necessary to point out that no polymerization can be observed even by varying solvents or temperature for all the systems when it is performed without Na_2CO_3. A similar phenomenon was reported recently in the iron-mediated AGET-ATRP of styrene,[13] the reason could be attributed to the basicity of Na_2CO_3 leading to the decrease of the values of redox potentials. Moreover, Sheldon *et al.*[14] also observed the effect of the base as co-catalyst on the oxidation of alcohols with the $CuBr_2$/bpy catalyst system.

Using EG as reducing agent, we further investigated the AGET-ATRP in detail to understand the polymerization behavior. The results show that a higher amount of reducing agent, EG, gives rise to a higher polymerization rate, as illustrated in Table 1 (entries 1–4). When the amount of reducing agent is 5 times higher than that of the Cu(II) catalyst precursor, the conversion of the polymerization reaches over 72% MA conversion in 23 h. However, although an increase in the concentration of EG can increase the rate of the polymerization, the polydispersity becomes somewhat wider simultaneously. This phenomenon indicates that it is necessary to keep a suitable reduction rate of Cu(II) to Cu(I) for the well controlled polymerization process. Moreover, the increase of polymerization temperature can also effectively enhance the apparent polymerization rate of MA with a slight increase in the polydispersity (entries 2, 5, 6 in Table 1).

AGET-ATRP of *tert*-butyl acrylate (tBA) and styrene (St) in anisole with EG as the reducing agent have also been conducted and the results are shown in Table 1 (entries 7–9). Similar to the MA polymerization, the AGET-ATRP of tBA has been performed very well at 75 °C, while no polymer (at least very little) can be obtained for St at the same temperature. But the AGET-ATRP of St has been successfully achieved at a temperature of 110 °C. The molecular weights of both the prepared PtBA and PSt are close to their theoretical values with low polydispersities. Therefore, $CuBr_2$/bpy/EG
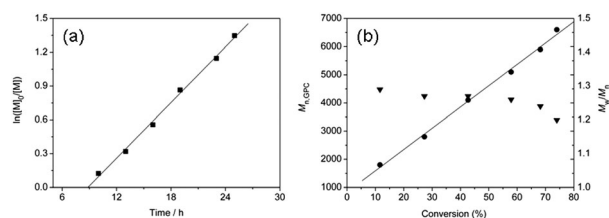

Fig. 1 (a) Kinetic plots of monomer conversion and (b) dependence of M_n and M_w/M_n *vs.* conversion for MA AGET-ATRP using EG as the reducing agent. *Reaction conditions*: MA/PEBr/$CuBr_2$/bpy/EG/Na_2CO_3 = 200/2/2/4/6/3, $[MA]_0$ = 7.4 M, temperature = 75 °C.

can be considered to be an effective catalyst system for the AGET-ATRP.

Kinetics of AGET-ATRP of MA using EG as the reducing agent was studied, and the results of the polymerization are shown in Table 1 (entries 10–14). The structure and molecular weight of the polymers were characterized by ^{1}H NMR spectroscopy and GPC (Fig. S2 and S3 in ESI†). From the data listed in Table 1, we can see that the theoretical molecular weight $M_{n,th}$ of the polymers is close to the NMR measured molecular weights $M_{n,NMR}$, this indicates that the polymers have been obtained with well-controlled molecular weight, and the molecular weight distributions are all narrow. Fig. 1(a) shows a linear relationship between $\ln([M]_0/[M])$ and the polymerization time, which demonstrates that the polymerization is a first-order reaction with respect to the monomer concentration and the number of active radicals remains constant during the polymerization. It can be seen that an induction period of 9 h exists in the early stages of the polymerization. This suggests that it needs a certain time to generate Cu(I) and establish a dynamic equilibrium between the catalyst CuBr/bpy and the catalyst precursor $CuBr_2$/bpy species in the polymerization process.[15] Fig. 1(b) describes the molecular weight and molecular weight distribution as functions of the monomer conversion for the AGET-ATRP of MA. The molecular weight of poly(methyl acrylate) (PMA) increases linearly with monomer conversion and the molecular weight distribution remains narrow (less than 1.3) throughout the polymerization.

Table 1 Polymerization of MA, tBA, and St using EG as reducing agent[a]

Entry	Monomer	EG/$CuBr_2$	Temperature/°C	Time/h	Conv.[b] (%)	$M_{n,th}$[c]/Da	$M_{n,NMR}$[d]/Da	$M_{n,GPC}$[e]/Da	PDI[e]
1	MA	2	75	23	44.7	4000	4100	4200	1.19
2	MA	3	75	23	68.2	6100	6200	5900	1.24
3	MA	4	75	23	71.0	6300	6300	6500	1.28
4	MA	5	75	23	72.6	6400	6500	6600	1.32
5	MA	3	70	23	38.4	3500	3700	3800	1.20
6	MA	3	80	23	72.6	6400	6500	6500	1.29
7	tBA	3	75	25	68.6	9000	9200	8700	1.21
8	St	3	75	25	< 5.0	—	—	—	—
9	St	3	110	25	65.5	7000	7100	7100	1.16
10	MA	3	75	10	11.6	1200	1700	1800	1.29
11	MA	3	75	13	27.3	2500	2900	2800	1.27
12	MA	3	75	16	42.7	3900	4100	4100	1.27
13	MA	3	75	19	57.9	5200	5300	5100	1.26
14	MA	3	75	25	74.0	6500	6600	6600	1.20
15[f]	MA	3	75	45	75.2	6700	6700	6800	1.12

[a] Polymerizations were carried out in anisole with monomer/1-bromoethylbenzne (PEBr)/$CuBr_2$/bpy/Na_2CO_3 = 200/2/2/4/3, $[Monomer]_0$ = 7.4 M. [b] Determined gravimetrically. [c] Calculated from the equation: $M_{n,th}$ = conversion $\times 100 \times M_{(monomer)}$ + 185. [d] Determined by ^{1}H NMR. [e] Determined by gel permeation chromatography (GPC). [f] Polymerization was performed in the presence of a limited amount of air.
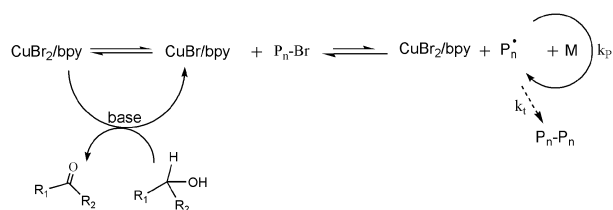
Scheme 1 A proposed mechanism for alcohol-reduced AGET-ATRP.

In order to further confirm the "living" nature of this AGET-ATRP system, chain extension polymerization of the obtained PMA was carried out with ^tBA under the AGET-ATRP conditions. The bromo-capped PMA was used as a macroinitiator (M_n, 7700; PDI, 1.19) for AGET-ATRP of ^tBA and the polymerization was performed to produce block copolymers under the same conditions as those in the polymerization of MA. GPC analysis of the resulting block copolymer reveals that the molecular weight (M_n, 11200; PDI, 1.25) obviously increases in comparison with the starting macroinitiator (M_n, 7700; PDI, 1.19) (Fig. S3 in ESI†), which indicates that the diblock copolymer, poly(methyl acrylate-b-tert-butyl acrylate) PMA-b-P^tBA, has been obtained with a relatively narrow molecular weight distribution.

It is well known that oxygen is an inhibitor of free radical polymerization, and can also oxidize Cu(I) into Cu(II) ions, therefore, usually air must be completely removed from the radical polymerization system. Herein, we examined the effect of the limited air on the polymerization. The experiment (entry 15 in Table 1) was performed without removing the air in the polymerization tube by nitrogen purging. The GPC result shown in Fig. S4 (ESI†) indicates that the polymer has been obtained with a narrow molecular weight distribution. Based on these results, we can conclude that in this AGET-ATRP system using EG as the reducing agent, existence of a limited amount of air has no detectable effect on the living nature of the polymerization, but leads to a longer induction period; this is due to the oxidation of Cu(I) by oxygen, which was well confirmed in the recent report regarding the aerobic oxidation of alcohols using CuBr$_2$/bpy as the catalyst.[16]

Based on the literature related to the CuBr$_2$/bpy-catalysed oxidation of alcohols,[14,16] we propose a possible mechanism of the polymerization as shown schematically in Scheme 1. The active CuBr/bpy species can be generated *in situ via* the reduction of the CuBr$_2$/bpy species and then primary radicals come from the reaction of alkyl halide (PEBr) with the active CuBr/bpy and subsequently initiate the polymerization of the monomers. Meanwhile, the alcohols are oxidized to aldehydes or ketones. The reduction of the Cu(II) species into the catalytic Cu(I) species by the alcohols is the key point for this AGET-ATRP process.

In conclusion, we have demonstrated that alcohols can be used as efficient reducing agents for AGET-ATRP for the first time. Well-controlled AGET-ATRP of MA, St, and ^tBA have been successfully achieved in the presence a catalytic amount of Na$_2$CO$_3$ and demonstrated having typical characteristics of "living"/controlled radical polymerization. We believe that this work is a more promising step toward the development

of practical AGET-ATRP systems because alcohols are stable, environmentally friendly, and cost-effective. The optimization of polymerization conditions to reduce the induction period and improve the rate of the polymerization is under way.

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