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Successful Cu-Mediated Atom Transfer Radical Polymerization in the Absence of Conventional Chelating Nitrogen Ligands

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Cu-mediated atom transfer radical polymerization (ATRP) has become one of the most powerful tools for the synthesis of well-defined polymer materials. In Cu-mediated ATRP systems, the ligand plays a key role in obtaining living polymerization kinetics as well as well-controlled products.[1−4] The effect of ligand structure on Cu-mediated ATRP has been thoroughly studied.[5−8] A suitable ligand for ATRP provides a proper equilibrium constant K_{ATRP} (i.e., the ratio of rate constants for activation and deactivation) by maintaining the desired stability of the intermediate Cu species during the polymerization.[9] Although various ligands have been developed for Cu-mediated ATRP,[10−14] to date, all of the types of ligands that provide the desired stability of the intermediate Cu species are chelating molecules with strong nucleophilic N-donors. Such chelating coordination moieties usually are bipyridinyl,[15] imminopyridinyl,[16] aminopyridinyl,[17] or alkyl multiamines.[18] Without such chelating ligands, no successful Cu-mediated ATRP has been achieved.

We recently revealed that the catalytic performance as well as the stability of some transition metals (such as Pd) can be greatly enhanced by using polymer chains or polymer gels as stabilizing reagent.[19] Herein we will report that certain polymer stabilizers can also ensure the successful Cu-mediated ATRP in the absence of conventional chelating N-donor ligands.

When poly(*N*-vinylpyrrolidinone) (PVP) was used as the stabilizer, well-controlled, living polymerization of methyl methacrylate (MMA) was obtained using either CuBr or CuCl as catalyst with common ATRP initiators such as tosyl chloride (TsCl) and ethyl α-bromoisobutyrate (EBiB). CuCl gave higher initiator efficiency and narrower polydispersity index (PDI = M_w/M_n) than CuBr. CuCl/PVP in combination with EBiB as initiator gave the best control in the polymerization (for details see Supporting Information, Table S1). The kinetic curves of CuCl/PVP-mediated ATRP under different variables are shown in Figure 1.

As shown in Figure 1a, monomer conversion increased rapidly at the early stage of the polymerization. The living feature of the polymerization was demonstrated by the linear relationship of logarithmic curves vs polymerization time (Figure 1b). The first-order logarithmic kinetic curves indicated that the concentration of the propagating chain end was constant during the polymerization process, as is required in living polymerization. When EBiB was used as initiator, polymerization has the highest rate ($k_p^{app} \sim 6.5 \times 10^{-5}$ s^{-1}), and high monomer conversion (> 97%) was achieved within 5 h. However, deviation was found in the case when TsCl was used as initiator at low monomer concentration (2 mL of MMA in 5 mL of DMF). Surprisingly, the deviation in the kinetics does not imply the loss of control in the living nature of the polymerization (Figure 1c and as discussed later). In contrast, in reported cases of Cu-mediated ATRP using conventional N-ligands carried out at low monomer concentrations, the deviation in kinetics and poor control in the growth of polymer chains were usually observed.[20] In all cases studied, the molecular weight of the attained PMMA increased linearly with monomer conversion (Figure 1c). This indicated that the desired chemical equilibriums can be well maintained by PVP. The PDI of the produced PMMA decreased with the increase in the MMA conversion (Figure 1d). A fairly narrow PDI (∼1.4) was obtained after the monomer conversion reached 60% (Figure 1d). This value was slightly higher than that from CuX/chelating N-ligands system (∼1.2). This could be ascribed to the poor diffusion of the active species as constrained by the polymer stabilizer.

The relatively broad PDI of the product at the early stages of reaction was similar to that observed in the ATRP mediated by CuX/chelating N-ligands. In the latter case, the broad PDI was attributed to the persistent radical effect and reduced PDI was obtained when certain amount of CuX_2 (ca. 10% relative to CuX) was added into the system.[21] In our system, adding CuX_2 did not affect the PDI of the product. Furthermore, the k_p was reduced greatly even when 1.0% CuX_2 (relative to CuX) was used. This may be attributed to the lower concentrations of CuX_2 required to reach the equilibrium in CuX/PVP-mediated ATRP compared to the ATRP mediated by CuX/chelating ligands. The significant decrease in PDI with increasing degree of polymerization (Figure 1d) indicates that the formed polymer chains gradually grow to similar lengths during polymerization as the permanent radical termination was efficiently prevented by the in situ formed CuX_2/PVP.

It was surprising that high initiation efficiencies were observed in CuCl/PVP-mediated ATRP using EBiB as initiator, in view of the possibility that the PVP stabilizer may limit the diffusion of the molecules in the reaction system. It is apparent from Figure 1c, however, that the molecular weight of the attained PMMA was in good agreement with the theoretical value (the solid line in Figure 1c). The initiation efficiency was greater than 0.9 even in very fast ATRP (conversion/time: 97%/5 h), and the highest initiation efficiency (0.96) was obtained when the polymerization took place at a slightly slower rate (conv/time: 81%/8 h). This indicates that the probability of consumption of organic halide (either initiator or polymer chain end) through competing side reactions is very small when PVP is used as the stabilizer.

The initiation efficiency of TsCl (0.4−0.6) was lower than that of EBiB (> 0.9), but the living feature of the TsCl initiated polymerization was confirmed by the linear increase of molecular weight of the attained PMMA with monomer conversion (Figure 1c). The deviation of the $M_{n,GPC}$ from the $M_{n,theo}$ reflected the relatively low initiation efficiency. The GPC curves of the PMMA produced at different reaction times are shown in Figure 2. It can be seen that, at early stage of polymerization (0.5 h), PMMA with a broad PDI was formed. As the polymerization proceeded, the molecular weight of the attained PMMA increased and the PDI decreased. After 8 h, the monomer conversion reached 88%, and the PDI of the attained PMMA was reduced to 1.31. This indicated that PMMA chains with lower molecular weights grew faster than those with higher molecular weights at the early stage of polymerization. Eventually, a well-controlled living radical polymerization was established. The high concentration of α-chain end (stemming from the TsCl) of the attained PMMA chain was also confirmed by chain analysis

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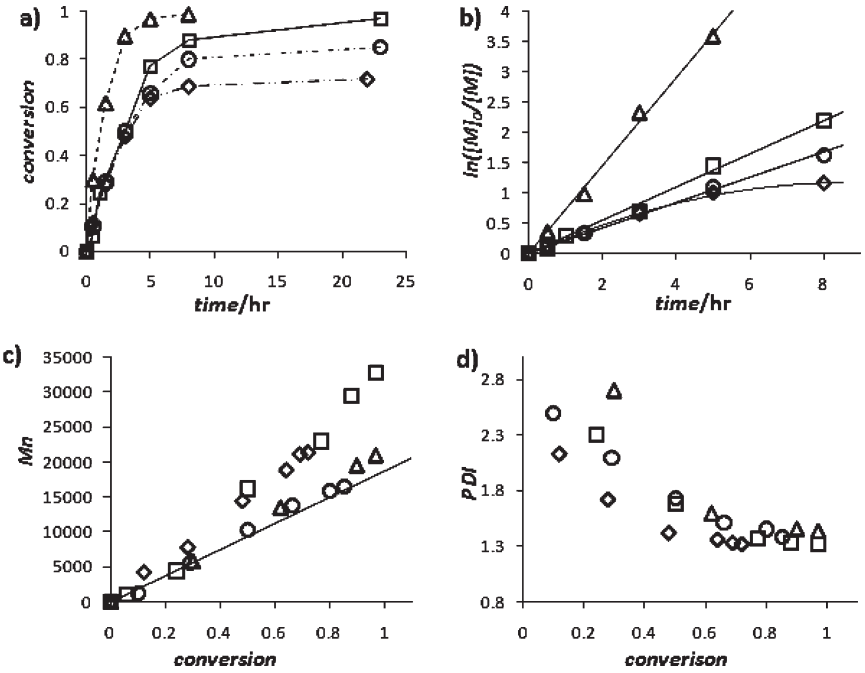

Figure 1. Kinetics of the polymerizations of MMA mediated by poly(*N*-vinylpyrrolidinone) stabilized CuCl: (a) monomer conversion vs reaction time; (b) $\ln([M]_0/[M])$ vs reaction time; (c) M_n vs monomer conversion, the solid line stands for the theoretical value of M_n; (d) polydispersity index (PDI) of products vs monomer conversion. (initiator: ◇, TsCl; □, TsCl[a]; △, EBiB; ○, EBiB[b]). Reaction was carried out in *N,N*-dimethylformamide (DMF), [MMA]:[Ini]:[CuX]:[PVP] = 187:1:4:20; MMA:DMF = 5 mL:5 mL; 80 °C. [a]2 mL of MMA; [b][MMA]:[Ini]:[CuX]:[PVP] = 187:1:2:10.

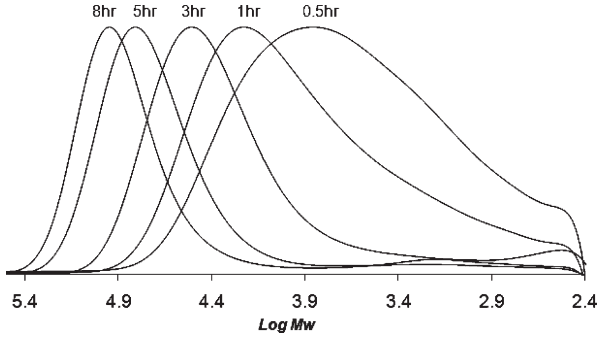

Figure 2. Gel permeation chromatograph curves of attained PMMA from tosyl chloride (TsCl) initiated CuCl/poly(*N*-vinylpyrrolidinone (PVP)-mediated atom transfer radical polymerization at various periods. Reaction was carried out in *N,N*-dimethylformamide (DMF), [MMA]:[TsCl]:[CuX]:[PVP] = 187:1:4:20; MMA:DMF = 5 mL:5 mL; 80 °C.

using ^{1}H NMR spectroscopy (for details, see Supporting Information). The molecular weight calculated from the ratio of repeat monomer units over the α-chain end closely matched the GPC-measured value, indicating that every polymer chain bore one segment from TsCl initiator. This further confirmed that the polymerization took place via a well-controlled ATRP mechanism.

As a successful ATRP should produce polymers with the reactive ω-chain end bearing organic halide functionalities, the reactivity of the ω-chain end of the product is usually treated as a criteria to confirm a well-controlled ATRP process. In CuX/PVP-mediated ATRP, the high incorporation of reactive ω-chain ends with organic halide functionality was confirmed by chain-expansion reactions. In order to confirm this, the polymerization of MMA was carried out with monomers fed in two batches (for details, see Supporting Information). After 3 h (the conversion of the first batch monomer reached 96%), the second batch of monomer solution at the same concentration was injected into the system for continuous chain growth. The polymerization results are summarized in Table 1. These studies showed that

Table 1. Chain Expansion Results of MMA Mediated by Poly(*N*-vinylpyrrolidinoe) Stabilized CuCl[a]

time[b] (h)	MMA/init	conv[c] (%)	$M_{n,theo}$	$M_{n,GPC}$	PDI	f_{ini}
0−3	100	96	9 600	10 388	1.32	0.92
3−10	200	93	18 600	20 354	1.38	0.91

[a] Theoretical molecular weight ($M_{n,theo}$ = conv × FW_{MMA} × $[MMA]_0$/[init]); initiation efficiency (f_{ini}) is derived from the theoretical molecular weight over the GPC-measured molecular weight ($M_{n,GPC}$). [b] Counted from the injection of the initiator. [c] Calculated from ^{1}H NMR of the reaction mixture. Reaction was carried out *N,N*-dimethylformamide (DMF), [MMA]:[Ini]:[CuX]:[PVP] = 187:1:4:20; 80 °C.

93% conversion of the total monomer could be reached. The molecular weight of the final product closely matched the theoretical value. The PDI remained narrow, comparable to that of the product from the first batch monomer.

In addition to the well controlled polymerization kinetics and the parameters of the product, CuX/PVP-mediated ATRP allows a facile removal of the Cu catalyst from the products. PVP showed different solubility in different solvents, and the precipitation of the PVP can be achieved by simply adding tetrahydrofuran (THF) or chloroform to the final ATRP reaction mixture; the Cu species coprecipitates with the PVP due to the latter's stabilization effect. Thus, the Cu can be easily removed from the product solution by simple filtration or centrifugation. (For the details, please see the Supporting Information.)

In order to obtain an insight into understanding the function of the polymer stabilizer, various polymers were studied as stabilizers in CuCl-mediated ATRP. The results are summarized in Table 2. Well-controlled ATRP was also obtained when the poly(dimethylacrylamide) (PDMAM) and poly(*N*-isopropylacrylamide) (PNIPAM) were used as stabilizers (Table 2, entries 1 and 2; for details please see Tables S2 and S3 in the Supporting Information). When EBiB was used as initiator, the initiation efficiency was 0.94 and 0.95 in the CuCl/PDMAM and CuCl/PNIPAM system, respectively. Furthermore, polymers bearing strong N-donor coordination moieties such as poly(4-vinylpyridine) (P4VPy) and poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA) were

Table 2. Results of Atom Transfer Radical Polymerization of MMA Mediated by CuCl with Various Stabilizers[a]

stabilizer[b]	conv[c] (%)	$M_{n,theo}$	$M_{n,GPC}$	PDI	f_{ini}
PDMAM	74.3	13 900	14 900	1.44	0.94
PNIPAM	73.2	13 700	14 400	1.48	0.95
PDMAEMA	96.4	18 042	21 232	1.76	no control
PVPy	12.9	2 418	54 635	1.55	no control
NMP	3.1	590	1 380	1.47	no control
DMF	3.0	550	855	2.93	no control
DMA	1.6	290	1 301	1.16	no control
IPGA	69.2	12 940	13 620	1.46	no control

[a] Theoretical molecular weight ($M_{n,theo} = conv \times FW_{MMA} \times [MMA]_0/[init]$); initiation efficiency (f_{ini}) is derived from the $M_{n,theo}$ over the GPC-measured molecular weight ($M_{n,GPC}$). [MMA]:[EBiB]:[CuCl] = 187:1:2, 5 mL of MMA, 80 °C. [b] For small molecules, 5 mL was used; for polymer stabilizer, [repeat unit]:[CuCl] = 5 and dissolved in 5 mL of DMF was used. [c] 8 h. Abbreviations: PDMAM: poly(dimethyl acrylamide); PNIPAM: poly(*N*-isopropylacrylamide); PDMAEMA: poly(2-(dimethylamino)ethyl methacrylate; PVPy: poly(4-vinylpyridine); NMP: *N*-methylpyrrolidinone; DMF: *N,N*-dimethylformamide; DMA: *N,N*-dimethylacetamide; IPGA: *N,N′*-diisopropylglutaramide.

also tested as stabilizers for Cu-mediated ATRP. When P4VPy was used, an insoluble complex was formed and polymerization took place slowly and stopped at low monomer conversion (12.9%) (Table 2, entry 4). When PDMAEMA was used as stabilizer, nonliving polymerization took place, and the control over parameters of attained PMMA was completely lost (Table 2, entry 3).

From the above, the efficient polymer stabilizers are those bearing amide groups, and it has been reported that amides can coordinate with Cu species.[22] Various small molecules "analogues" of the repeat units of those polymers were used as solvent cum-stabilizers/ligands (such as *N*-methylpyrrolidin-2-one (NMP), *N,N*-dimethylformamide (DMF), and *N,N*-dimethylacetamide (DMA)) in Cu-mediated ATRP. The results are summarized in Table 2 (entries 5−7). Negligible polymerization was observed in all the cases studied. This suggests that the stabilization of the monodentate amides is not sufficient for obtaining the desired control in ATRP. To investigate the stabilization effect, the bidentate diamide *N,N′*-diisopropylglutaramide (IPGA) was synthesized to mimic the diad structure of PNIPAM and used as ligand in CuCl catalyzed ATRP (Table 2, entry 8). With EBiB as initiator, the polymerization took place smoothly, and the monomer conversion of 70% was achieved after 8 h. However, poor control of polymerization resulted. High molecular weight products were formed even at very early stages of the reaction (for details please see Supporting Information, Table S4). This indicates that the diamide (IPGA) cannot provide the desired stabilization for Cu-mediated ATRP. In conventional Cu-mediated ATRP, the stability of the Cu catalyst is improved by increasing the number of donor N atoms. Analogously, the good control in polymer stabilized Cu-mediated ATRP observed in our studies is likely to originate from polymers bearing the multiple amide functionalities that may allow for ease of chelation for the Cu catalyst. Unexpectedly, P4VPy and PDMAEMA do not lead to well-controlled ATRP probably because the backbone connecting different donor functions bonded to the same Cu ion is too long or too flexible to provide the desired stability for the Cu species.[23] The structures of the polymers and small molecules that have been investigated in this paper are shown in Figure 3.

In summary, using polymer as a stabilizer, well-controlled Cu-mediated ATRP can be achieved in the absence of conventional N-donor ligands. In addition, such systems enable the efficient removal of Cu residues from the final product. This provides a promising method to carry out "green" ATRP. The investigation

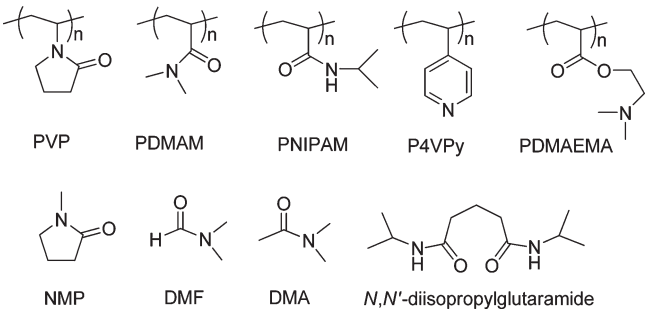

Figure 3. Structures of the molecules tested as stabilizers.

of the synthesis of various well-defined polymer structures using this new ATRP system as well as expansion of this biocompatible stabilizer to Fe-mediated ATRP is ongoing in our laboratory.

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

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