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Thermo-regulated Phase Separable Catalysis (TPSC)-Based Atom Transfer Radical Polymerization in Thermo-Regulated Ionic Liquid †

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A thermo-regulated phase separable catalysis (TPSC) system for AGET ATRP based on a thermo-regulated ionic liquid was developed for the first time. The corresponding transition metal catalysts could be easily recovered and reused for several times with negligible loss of catalytic activity.

AGET ATRP (activators generated by electron transfer for atom transfer radical polymerization) has gained much more attention since it was developed by Matyjaszewski's group in 2005.¹ It is also one of the reversible-deactivation radical polymerization (RDRP) methods, through which not only well-defined polymers² with pre-designed molecular weight and narrow molecular weight distribution but also various functional polymers with complex architectures such as block copolymers,³ star block copolymers,⁴ etc. can be conveniently prepared. Utilizing oxidative stable catalyst precursors and reducing agents, AGET ATRP has all benefits of normal ATRP plus the benefits of more facile preparation, more convenient catalyst storage and so on. Generally, AGET ATRP is carried out under heterogeneous conditions; to the contrast, homogeneous catalyst is of higher catalytic activity, but it's difficult to separate from the resultant polymers and therefore colors/pollutes the products. This further limits application of ATRP in an industrial scale.

To deal with this problem, a variety of techniques have been developed, such as solid-liquid biphasic catalysis systems (solid phase ATRP,⁵ solid-supported catalysts by physical adsorption⁶ and by covalent bonding,⁷ soluble/recoverable supported catalysts,^{7a,8} immobilized/soluble hybrid⁹ system and reversible supported catalysts¹⁰) and liquid-liquid biphasic systems (fluorocarbon-organic¹¹ solvents, water-

carried out under N₂ protection. Moreover some of these techniques were just used to separate catalysts, and still some of the others displayed either poor control over polymerization, low initiator efficiency or unsatisfying recovery.

As one of the three "green solvents", ionic liquids (ILs) have attracted increasing attentions in organic synthesis and polymer science owing to their unique properties such as negligible volatility, excellent thermal stability, high designability and good solubility to inorganic/organic substances. However, in most cases, the polymerization systems involving ionic liquids are either mono-phase allowing for fast polymerization or bi-phase facilitating separation of catalysts from products during the whole polymerization process. Therefore, to seek new catalyst systems that might combine the advantages of both homogeneous and heterogeneous catalysis will have a significant impact.

In organic synthesis, based on the critical solution temperature (CST) of nonionic phosphine ligand, a novel catalytic system termed thermo-regulated phase separable catalysis (TPSC) was proposed by Jin's group¹⁵ and applied in the hydroformylation of cyclohexene. After that, this novel catalytic system has been successfully used in various organic reactions (e.g., selective hydrogenation,¹⁶ hydroformylation,¹⁷ hydroaminomethylation,¹⁸ Heck reaction,¹⁹ Knoevenagel condensation,²⁰ and Stetter reaction²¹), which allows for an efficient homogeneous catalytic reaction, easy biphasic separation and catalyst recycle.

To solve the catalyst residue problems in ATRP and expect to reuse the catalyst in next turn, we investigated the possibility of applying TPSC catalytic system based on a thermo-regulated ionic liquid to an AGET ATRP (TPSC-based AGET ATRP) system for the first time. Herein, a Cu (II)-mediated polymerization of styrene was used to establish the concept of TPSC in AGET ATRP based on a thermo-regulated ionic liquid, [CH₃(OCH₂CH₂)_nN⁺Et₃][CH₃SO₃⁻] (MPEG₇₅₀NIL, n = 16). The general principle of TPSC-based AGET ATRP of styrene was illustrated in Scheme 1. In the polymerization, catalysts are soluble in MPEG₇₅₀NIL, which is immiscible with the mixed solvent of toluene and *n*-heptane at room temperature, while at reaction temperature (T > CST), the mixture homogenizes and the polymerization proceeds under homogeneous conditions. The system separates into a biphasic system composed of ionic liquid phase containing catalyst complex and organic phase containing polymers upon cooling to room temperature after polymerization. By simple

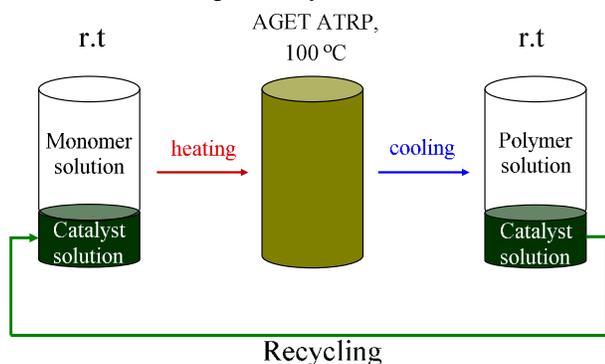
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organic¹² solvents, thermo-regulated phase transfer catalysis biphasic system¹³ and ionic liquid-organic solvents¹⁴). These techniques are mainly used in normal ATRP, which is sensitive to oxygen and the post-polymerization should be

decanting, the bottom ionic liquid phase containing catalyst complex can be recovered and reused easily. Therefore, the highlights of TPSC ATRP mainly relied on: (1) it allows highly efficient homogeneous polymerization at reaction temperature and easily remove catalyst from the resultant polymers by changing temperature without complex post-treatment and recycle the catalyst by simple decantation; (2) the catalyst could be reused for several times without the evident loss of catalytic activity; (3) it successfully combines the advantages of both homogeneous and heterogeneous catalysis and apply to AGET ATRP in the presence of a limited amount of air, which simplifies the operation procedure of ATRP significantly.



Scheme 1. General principle of thermo-regulated phase separable catalysis (TPSC) based AGET ATRP

Firstly, the ionic liquid, MPEG₇₅₀NIL was synthesized according to the literature^{17a}, the synthetic route is shown in Scheme S1 (ESI). Then, the effect of the components of AGET ATRP such as the type of catalysts (e.g., FeCl₃·6H₂O, CuBr₂ and CuCl₂·2H₂O), ligands (PPh₃, tris(3,6-dioxaheptyl)amine (TDA-1), 2,2'-dipyridyl (bpy), pentamethyldiethylene triamine (PMDETA), tris(2-pyridylmethyl)amine (TPMA)) and reducing agents (ascorbic acid (AsAc), sodium ascorbate (AsAc-Na), glucose, phenol, Sn(EH)₂ and triethyl amine) on TPSC ATRP was investigated. The results are shown in Table S1 and Table S2 (ESI). Considering the good controllability and the higher initiator efficiency of the polymerization, CuCl₂·2H₂O, TPMA and glucose were chosen as the catalyst, ligand and reducing agent, respectively. Besides, the effects of different amount of catalysts, ligands and reducing agents as well as the designed polymerization degree on polymerization were investigated and the results are in Table S3 and Table S4 (ESI), respectively. All the results indicated that the polymerization were affected mainly by the ligand but slightly by the amount of the reducing agent and the catalyst. The more the ligand used, the faster of the polymerization but the broader of the molecular weight distribution became slightly.

In order to further investigate the polymerization behaviour, polymerization kinetics of TPSC-based AGET ATRP of styrene in the ionic liquid was studied in the presence of a limited amount of air, using ethyl 2-bromoisobutyrate (EBiB) as the initiator, CuCl₂·2H₂O as the catalyst, TPMA as the ligand and glucose as the reducing agent, and the results are shown in Figure 1. Figure 1 (a) showed a linear relationship between $\ln([M]_0/[M])$ and the polymerization time, which

demonstrates the polymerization was a first order reaction with the respect to the monomer conversion, and the number of active radicals remained constant during the polymerization. An induction period of 4 h existed in the early stage of the polymerization. This suggests that it needed a certain time to generate Cu(I) species and establish a dynamic equilibrium between the catalyst CuCl/TPMA and the catalyst precursor CuCl₂/TPMA species in the process of the polymerization. Figure 1 (b) describes the molecular weight and molecular weight distribution as functions of the monomer conversion. The molecular weight of the polymers increased linearly with the conversion and the molecular weight distribution remained narrow ($M_w/M_n < 1.30$) during the polymerization; besides the molecular weights ($M_{n,GPC}$) of the polymers determined by GPC were close to the corresponding theoretical ones ($M_{n,th}$), indicating a well-controlled manner.

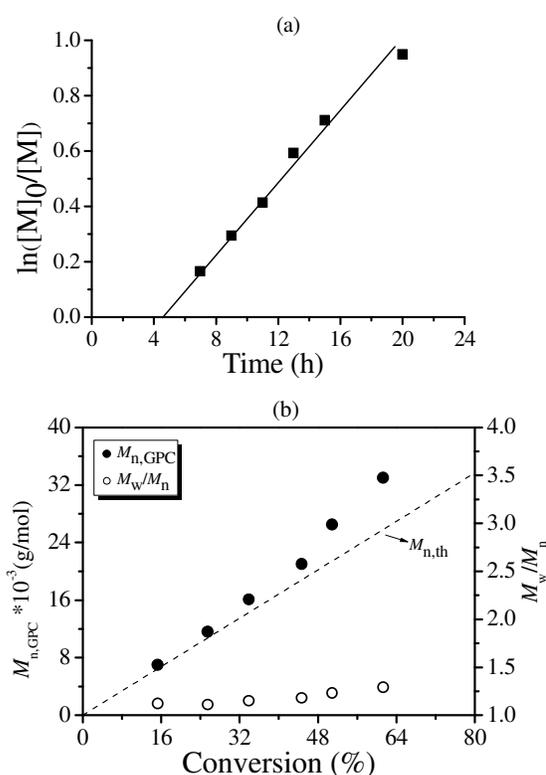


Figure 1. $\ln([M]_0/[M])$ as a function of time (a) and number-average molecular weight ($M_{n,GPC}$) and molecular weight distribution (M_w/M_n) versus conversion (b) for TPSC-based AGET ATRP of styrene in the presence of a limited amount of air at 100 °C. Polymerization conditions: $[St]_0/[EBiB]_0/[CuCl_2 \cdot 2H_2O]_0/[TPMA]_0/[Glucose]_0 = 400/1/1/1.5/2$, $V_{St} = 2.0$ mL, $V_{heptane} = 1.0$ mL, $V_{toluene} = 1.0$ mL, MPEG₇₅₀NIL = 0.5 g, $[O_2]_0 = 7.9 \times 10^{-3}$ mol/L.

The chain-end of the PS prepared by TPSC-based AGET ATRP with EBiB as the initiator in ionic liquid was analyzed by MALDI-TOF MS as shown in Figure 2, in which there was one main series of peaks whose interval was regular, ca. 104.06, the molar mass of St, and the observed experimental isotopic mass distribution values in main peak series of MALDI-TOF spectrum (with the subtraction of m/z value of silver cation (Ag^+ , 106.91)) are in good agreement with the

theoretical values in eq 1:

$$M_{\text{theory}} = 104.06 n + M(\text{C}_6\text{H}_{11}\text{O}_2) + M(\text{Ag}^+) \quad (1)$$

The lower intensity of peak series can be assigned to a reaction product with water due to the moisture in the air and the solvent.²³

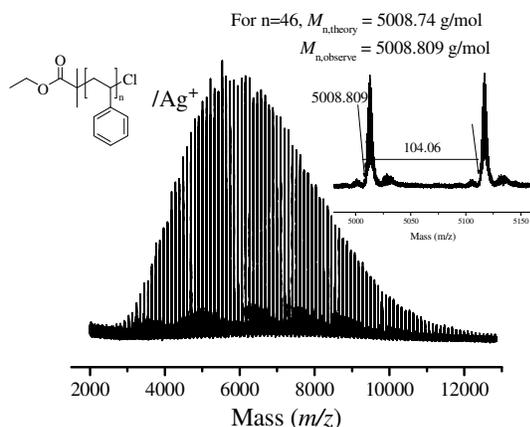


Figure 2. MALDI-TOF MS spectrum of polystyrene ($M_{n,\text{GPC}} = 7000$ g/mol, $M_w/M_n = 1.12$) obtained from TPSC-based AGET ATRP.

In addition, chain extension of the obtained polystyrene was carried out with fresh styrene under AGET ATRP in bulk. Here, the obtained polystyrene ($M_{n,\text{GPC}} = 7000$ g/mol, $M_w/M_n = 1.12$) was used as the macro-initiator in chain-extension experiment. Figure S2 (ESI) shows that the molecular weight of the resultant polymer ($M_{n,\text{GPC}} = 57200$ g/mol, $M_w/M_n = 1.17$) increased obviously in comparison with the macro-initiator, which further confirmed the “living” features of TPSC-based AGET ATRP of styrene in the ionic liquid.

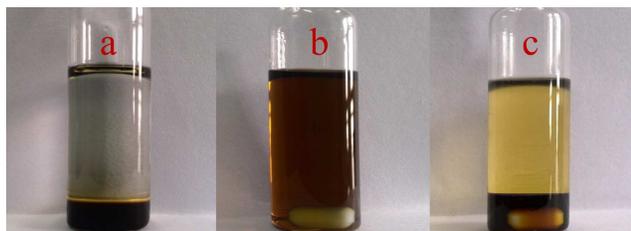


Figure 3. Photographs of TPSC-based AGET ATRP of styrene in ionic liquid: (a) before polymerization at room temperature; (b) during polymerization at 100 °C; and (c) after polymerization and cooled down to room temperature.

The general principle of TPSC-based AGET ATRP of styrene was illustrated in Scheme 1 and the photographs of phase transformation process were shown in Figure 3. Before polymerization, the system formed two phases, the lower phase is the ionic liquid, MPEG₇₅₀NIL, containing the catalyst; the upper phase is the monomer solution. At reaction temperature (100 °C), the system became homogenous and transparent solution. After polymerization, two phases formed gradually when cooled down. The lower phase was the ionic liquid, MPEG₇₅₀NIL, containing the catalyst; the upper phase was the polymer solution. The light yellow of the polymer solution was caused by a small amount of the ionic liquid residue. At the beginning, the catalyst was reused for the

polymerization without adding extra ligand, TPMA. Unfortunately, the polymerization rate decreased obviously, although the molecular weight distribution remained narrow. This may due to somewhat loss of ligand during the recovery of the catalyst. To further confirm the assumption, the partition coefficient of TPMA between ionic liquid and the mixture of toluene and heptane was measured by Ultraviolet and visible spectroscopy (UV-Vis). The results indicated that the concentration of TPMA in the mixture of toluene and heptane decreased slightly after adding CuCl₂·2H₂O. The partition coefficient of TPMA between the mixture solvent of toluene and *n*-heptane and MPEG₇₅₀NIL are 3.82 and 1.74 without and with adding CuCl₂·2H₂O, respectively. Because of good solubility of TPMA in organic phase, extra amount of ligand should be added to make up for the loss of TPMA when employing the recycled catalyst.

To investigate catalyst recycle performance of the TPSC-based AGET ATRP, the recycling experiments were conducted in the presence of a limited amount of air using ionic liquid phase containing catalyst complex directly and the results are shown in Figure 4. It can be seen that the copper concentration decreased in MPEG₇₅₀NIL after several recovery polymerization slightly. For example, even if after sixth recycles, the copper content remained 96.0% of the original catalyst amount. The loss of the copper was mainly caused by the wrap of the polymer solution due to its higher viscosity. At the same time, the conversion changed slightly and all the polymerizations were under control ($M_w/M_n \leq 1.41$), indicating high recycle efficiency of the catalyst. The catalyst could be recovered and used 5 additional times with the polymerization under control. In addition, besides styrene, we also extend this novel TPSC-based AGET ATRP system to the monomers of *n*-butyl acrylate, methyl acrylate and methyl methacrylate. It was found that 99.5% (Figure S3, ESI), 97.5% (Figure S4, ESI) and 99.6% (Figure S5, ESI) of copper catalyst were remained after the first cycle for the cases of *n*-butyl acrylate, methyl acrylate and methyl methacrylate, respectively, indicating good monomer universality of this polymerization system.

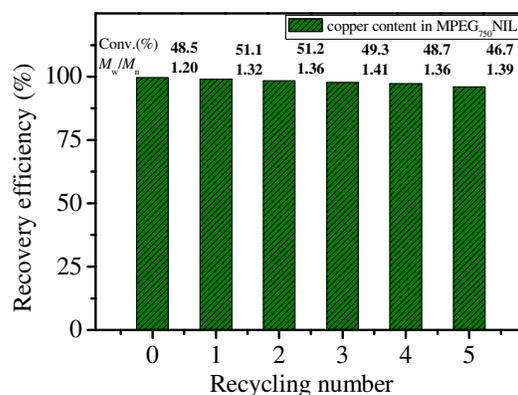


Figure 4. Recycle efficiency of the catalysts of TPSC-based AGET ATRP of styrene in ionic liquid. The copper content in MPEG₇₅₀NIL were 99.6%, 99.0%, 98.4%, 97.7%, 97.3% and 96.0% after the first, the second, the third, the fourth, the fifth and the sixth polymerization respectively, based on the original amount of copper. For the catalyst reused polymerization, some extra amount of TPMA (10.0 mg)

calculated by the partition coefficient of TPMA between the mixture solvent of toluene and *n*-heptane and MPEG₇₅₀NIL which was measured by UV-*vis* was added additionally. Polymerization condition: *t* = 14 h, [O₂]₀ = 7.9 × 10⁻³ mol/L.

In summary, a novel TPSC-based AGET ATRP system was successfully constructed in thermo-regulated ionic liquid in the presence of a limited amount of air, using styrene as the model monomer, CuCl₂, TPMA, EBiB and glucose as the catalyst, ligand, initiator and reducing agent and respectively. This novel catalysis strategy allows not only highly efficient homogeneous polymerization but also easy catalyst recovery and reuse by simply decanting because of the phase separation when the temperature goes down. The catalyst could be reused for 5 times with negligible loss of catalytic activity. The polymerizations proceeded in a well-controlled manner as evidenced by polymerization kinetics and chain-extension experiment. The financial support from the National Natural Science Foundation of China (Nos. 21174096, 21274100 and 21234005), the Specialized Research Fund for the Doctoral Program of Higher Education (No. 20103201110005), the Project of International Cooperation of the Ministry of Science and Technology of China (No.2011DFA50530).

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