Rational Selection of Initiating/Catalytic Systems for the Copper-Mediated Atom Transfer Radical Polymerization of Basic Monomers in Protic Media: ATRP of 4-Vinylpyridine

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ABSTRACT: The successful ATRP of a coordinating monomer, 4-vinylpyridine (4VP), in aqueous media at 30 °C is reported. In the presence of basic and nucleophilic monomers such as 4VP, the use of the chloride-containing ATRP initiating/catalytic system is essential to achieve good polymerization control and narrow molecular weight distribution. This is due to the significantly slower reaction of the monomer or polymer with secondary alkyl chloride-type dormant chain ends compared to their alkyl bromide counterparts. When a bromide-based ATRP initiating/catalytic system was used, the obtained polymers had polymodal molecular weight distributions reflecting the formation of branched chains, whereas the polymers obtained with chloride-based initiating/catalytic system had narrow, monomodal, and symmetrical molecular weight distributions. The polymerization of 4VP mediated by the Cu^{I} complex of 2,2′-bipyridine was slow due to the low value of the ATRP equilibrium constant, in agreement with the low reducing power of the complex. Very good control over the polymerization was accomplished with the $Cu^{I}Cl$ complexes of *N*,*N*,*N*′,*N*′′,*N*′′′,*N*′′′-hexamethyltriethylenetetramine or tris(2-pyridylmethyl)amine (TPMA) as the ATRP catalysts. The TPMA complex is more reducing and therefore catalytically more active. In protic solvents, a significant part of the deactivating Cu^{II} halide complex dissociates and the radical deactivation becomes inefficient, leading to polymers with relatively high polydispersity. The use of a catalyst containing sufficient initial concentration of $Cu^{II}Cl_2$ complex (30% of the total Cu) improved the polymerization control.

Introduction

Significant attention has been paid to the synthesis of well-defined polymers with predefined molecular weight, narrow molecular weight distribution, and high degree of chain end functionalization. To achieve this goal, living polymerizations[1,2] in which termination reactions are virtually absent are used. Living anionic[3] and cationic[4] polymerization techniques have been very successful in the preparation of a multitude of polymeric materials. However, these methods suffer from several drawbacks, including the limited choice of monomers and solvents and the high sensitivity to moisture and carbon dioxide. Controlled/living radical polymerizations (CRP), developed in the past decade, combine the tolerance of conventional radical polymerization toward a variety of functional groups with the ability to control molecular weights and chain end functionalization, characteristic of ionic living polymerization processes. In all CRP methods, this control is achieved by establishing an equilibrium between dormant and active (i.e., able to propagate) species, the former being predominant. The most widely applied CRP techniques are stable free radical (mostly nitroxide)-mediated polymerization,[5,6] atom transfer radical polymerization (ATRP),[7−10] reversible addition−fragmentation chain transfer (RAFT) polymerization,[11−13] and iodide degenerative transfer polymerization.[14]

ATRP is a metal complex-mediated reaction that relies on the reversible reaction between an alkyl halide initiator RX (X = Cl or Br) and a low oxidation state metal complex $Mt^{z}L_{m}$ (L = ligand), yielding a radical that propagates in the presence of a monomer M and a high oxidation state complex with a coordinated halide ligand $XMt^{z+1}L_{n}$. The complexes of various metals[9] have been applied to mediate ATRP, but to date, copper has found the broadest application. A very important recent development in ATRP is the discovery that in the presence of reducing agents, such as ascorbic acid, Sn^{II} compounds, or hydrazines, the polymerization can be carried out in the presence of limited amounts of air[15] and using a very low, in the ppm range, catalyst concentration.[16−18] The reducing agent regenerates the low oxidation state complex (activator) which would normally be converted relatively quickly (especially when used at low concentration) to the higher oxidation state complex (deactivator) due to the persistent radical effect. Rules for the rational selection of an ATRP catalyst that possesses sufficient activity and yields polymers of low polydispersity index (PDI = M_w/M_n) were recently outlined.[19] In brief, for copper-mediated reactions, the ligand L should form very stable complexes with both the Cu^{I} and Cu^{II} oxidation states (i.e., the stability constants β_m^{I} and β_m^{II} should be large) in order to avoid competitive complexation by the monomer, polymer, or solvent. For ligands forming 1:1 complexes with Cu ions, to ensure high catalytic activity, the ratio β_1^{II}/β_1^{I} (the index "1" is omitted later in this text for simplicity) as well as the halogenophilicity (i.e., the affinity of the Cu^{II} complex for halide ions, K_X) should be as high as possible. If the reactions are performed in aqueous or protic media, disproportionation of the Cu^{I} complex should be avoided, and this is possible only with ligands for which $\beta^{II}/(\beta^{I})^2[L] \leq 1/K_{disp}$ (K_{disp} is the disproportionation equilibrium constant of noncomplexed Cu^{I} ions in the same solvent). All ligands chosen in this study meet the last requirement. Finally, because of the more efficient radical deactivation[20] by bromide-containing compared to chloride-containing Cu^{II} complexes, in

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most cases bromide-based catalysts are preferred.[21,22] This is only valid when the ATRP reactions are carried out in the absence of basic/nucleophilic compounds (monomers, solvents, or other additives) that can react with alkyl halides and therefore cause a loss of chain end functionality of the polymeric dormant species.

ATRP has been successfully employed in the synthesis of a large variety of well-defined polymeric materials derived from styrenes, (meth)acrylates, acrylonitrile, and acrylamides, including end-functionalized polymers,[23] segmented and gradient copolymers,[24] and hybrid composites[25] as well as polyelectrolytes.[26] The last class of materials, the polyelectrolytes,[27,28] have gained importance due to their unique solution properties; some applications include ion-exchange resins, superabsorbents, and materials for water purification and selective membranes. Many polyelectrolytes are stimuli-responsive, and they and their bioconjugates have found significant applications in cosmetics and controlled (drug) delivery.[29] Segmented copolymers with hydrophilic units form micelles in solution[30] and are used as surfactants and in crystal engineering.[31,32]

4-Vinylpyridine (4VP) is an example of a basic/nucleophilic and coordinating monomer. The corresponding pH-responsive polymer, poly4VP,[33] is a weak polybase that dissolves in water only when sufficiently protonated.[34] Many metal ions bind strongly to this polymeric polydentate ligand. An important application of poly4VP is in ion-exchange resins,[35,36] for instance in water purification. The mild basicity of poly4VP is useful in the synthesis of alkyl triflate esters.[37] The polymer can serve as a precursor of *N*-alkyl quaternized polyelectrolytes,[34,38] polybetaines (both with carboxylate[39,40] and sulfonate[40,41] groups), and *N*-oxide.[42] The similar quaternization reactions of the isomer, poly2VP, are significantly less efficient and slower due to steric hindrance.[43,44] Besides living anionic polymerization,[45] various CRP methods have been applied to prepare well-defined polymers derived from 4VP: nitroxide-mediated polymerization,[40,46−49] ATRP,[50−52] and RAFT.[53] The first technique generally requires high temperatures (>120 °C with TEMPO or its 4-substituted derivatives[40,46,47,49] or 110 °C with a β-phopshonylated nitroxide[48]). RAFT yields well-defined polymers derived from 4VP in bulk or in DMF, but the reactions are generally relatively slow. Moreover, although RAFT polymerizations are suitable for aqueous media, the chain-transfer agents are unstable at elevated pH,[54] and it is somewhat challenging to preserve the chain end functionality during the polymerization of basic monomers.

The preparation of well-defined polymers with 4VP units by copper-mediated ATRP has proven successful, provided a ligand that binds strongly to the copper center, such as the hexamethylated tris(2-aminoethyl)amine (Me_6TREN), is used. It was demonstrated that the use of the copper chloride-based rather than bromide-based initiating/catalytic system is necessary to obtain polymers with narrow molecular weight distribution.[50] However, detailed studies on the influence of the ligand and halide on the polymerization rate and control as well as a quantitative description of the side reactions that take place during the ATRP of 4VP are lacking in the literature. Moreover, the development of environmentally benign ATRP[55] reactions employing water-based solvents[21,56−59] is highly desirable. This work addresses all mentioned issues.

Experimental Section

Materials. The monomer, 4VP, was passed through a column filled with basic alumina prior to use in order to remove the polymerization inhibitor. The macroinitiator, poly(ethylene oxide) methyl ether 2-bromosiobutyrate (MePEOBiB; molecular weight 699 g/mol),[60] and tris(2-pyridylmethyl)amine (TPMA)[61] were prepared by literature procedures. To remove oxygen from the macroinitiator and *N*,*N*,*N*′,*N*″,*N*‴,*N*‴-hexamethyldiethylenetriamine (HMTETA), 1-phenylethyl bromide (1-PhEtBr), 1-phenylethyl chloride (1-PhEtCl), and acetonitrile (MeCN) used in the determination of K_{ATRP}, the reagents were purged with nitrogen for at least 3−4 h prior to use. All other reagents were used as received.

ATRP of 4VP in Protic Solvents. A mixture of CD_3OD (1 mL) and D_2O (1 mL) was degassed by six freeze−pump−thaw cycles, the mixture was frozen in liquid nitrogen, the flask was filled with nitrogen, and Cu^IBr (0.0266 g, 0.185 mmol) was added quickly. The flask was closed with a glass stopper and was then evacuated and backfilled with nitrogen several times. Deoxygenated HMTETA (50.4 μL, 0.185 mmol) was injected, and the reaction flask was placed in a water bath thermostated at 30 °C. The nitrogen-purged monomer, 4VP (2 mL, 18.56 mmol), was added upon stirring followed by the MeOPEOBiB macroinitiator (0.108 mL). Samples were periodically withdrawn with a nitrogen-purged syringe and were diluted with either CD_3OD (NMR analysis) or 50 mM solution of LiBr in DMF (SEC analysis). Similar experiments were performed using bpy (0.370 mmol) as the ligand and also mixtures of Cu^IBr (0.0186 g, 0.130 mmol) and $Cu^{II}Br_2$ (0.0124 g, 0.055 mmol, 30% of the total Cu) with HMTETA (0.185 mmol). The complexes of Cu^ICl and its mixtures with $Cu^{II}Cl_2$ (30% of the total Cu) with HMTETA (0.185 mmol) or TPMA (0.185 mmol) were also employed as catalysts in this study.

Analyses. Monomer conversions were determined by ^{1}H NMR spectroscopy. The spectra were recorded on a Bruker instrument operating at 300 MHz in CD_3OD using TMS as the reference. To determine molecular weights, polymer samples were dissolved in 50 mM solution of LiBr in DMF, containing a small amount of toluene or diphenyl ether as elution volume marker, and analyzed by size exclusion chromatography (SEC). The solutions were not filtered through columns filled with alumina, which is the usual practice for the catalyst removal, because it was observed that the SEC traces of the polymers before and after such filtration differed (the latter showed narrower molecular weight distributions). SEC measurements were conducted using 50 mM solution of LiBr in DMF as the eluent (flow rate 1 mL/min, 50 °C), with a series of three Styragel columns (10^5, 10^3, 100 Å; Polymer Standard Services) and a Waters 2410 differential refractometer. Calibration based on polystyrene standards was used. Cyclic voltammetry (CV) measurements were carried out at room temperature using a Perkin-Elmer potentiostat/galvanostat 263A at a scan rate of 0.20 V s^{-1}. Both the counter electrode (0.5 mm) and the working electrodes were made of platinum, and the reference electrode was Ag/AgCl (saturated KCl). The complexes of $Cu^{II}Br_2$ with various ligands (bpy, HMTETA, or TPMA) were prepared in methanol containing 0.1 M tetrabutylammonium hexafluorophosphate (Bu_4NPF_6) as the background electrolyte. The solutions (1.0 mM with respect to copper) were purged with nitrogen prior to the measurements. The ATRP equilibrium constants were determined by reacting 1-PhEtX (X = Br or Cl, 5−100 mM) with a Cu^I complex (5 mM) in MeCN at 22 ± 2 °C as described in the literature.[62]

Results and Discussion

Prior to the polymerization experiments, it was important to quantify the side reactions that could take place in the ATRP of 4VP in protic media. Such studies are necessary for the rational selection of the catalytic/initiating system of this monomer. The major side reactions that were examined included hydrolysis, methanolysis, and reaction with pyridine of alkyl halides structurally resembling the dormant species of poly4VP. These could be minimized when chloride-based as opposed to bromide-based catalytic/initiating systems were employed in the polymerization. Furthermore, the appropriate ligands for the ATRP of the coordinating 4VP were identified.

1. Selection of the Alkyl Halide Initiator. The polydispersity index of polymers prepared by ATRP, reflecting the polymer-

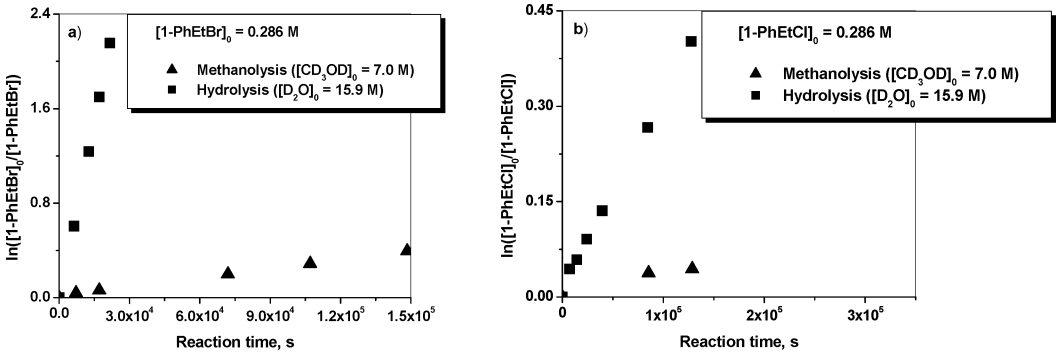


Figure 1. Solvolysis of 1-PhEtBr (a) and 1-PhEtCl (b) at 25 °C in acetone-d_6 under pseudo-first-order reaction conditions.

Table 1. Pseudo-First-Order Rate Constants of Solvolysis of Alkyl Halides in Acetone at 25 °C

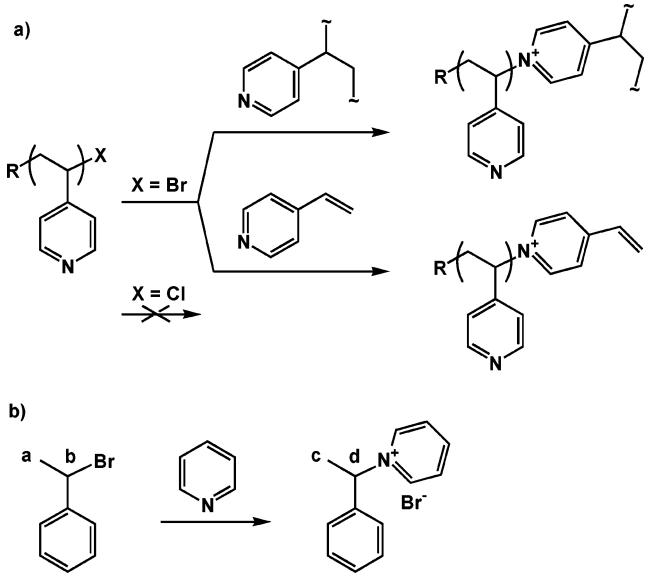
initiator	cosolvent (nucleophile)	k_{solv}, M^{-1} s^{-1}	k_{solv}, M^{-1} s^{-1} (lit.)
1-PhEtBr	D_2O	6.3×10^{-6}	4.2×10^{-6} (16.6 M H_2O in dioxane, 25 °C)[65]
	CD_3OD	3.7×10^{-7}	
1-PhEtCl	D_2O	1.9×10^{-7}	1.7×10^{-7} (16.6 M H_2O in dioxane, 25 °C)[66]
	CD_3OD	5.1×10^{-8}	

ization control, depends on the efficiency of deactivation according to eq 1.[63,64]

$$\mathrm{PDI} = \frac{M_w}{M_n} = 1 + \left(\frac{k_p[RX]_0}{k_{deact}[XCu^{II}L_n]}\right)\left(\frac{2}{conv} - 1\right) \qquad (1)$$

In eq 1, k_p is the propagation rate constant of the monomer, k_{deact} is the rate constant of deactivation of radicals by the complex $XCu^{II}L_m$, and the abbreviation "conv" refers to the monomer conversion. In general, the values of k_{deact} are higher for X = Br than for X = Cl, and therefore, better polymerization control can be expected in systems in which alkyl bromide initiators and copper bromide-based catalysts are used.[20] Indeed, this has been observed in the ATRP of methacrylates in protic media.[21,22] However, when styrene-type monomers (including 4VP) forming a secondary alkyl halide dormant species are polymerized under ATRP conditions, the chain ends are susceptible to nucleophilic substitution or elimination reactions, which are particularly pronounced in reactions carried out in nucleophilic/basic solvents. These reactions effectively "kill" the polymer chain ends, and the obtained polymers have relatively broad molecular weight distributions and low degree of halide end-functionalization. The rates of nucleophilic substitution are determined by the nature of the halogen at the polymer chain end. The rate constants of solvolysis of 1-PhEtX (X = Br or Cl) which resemble structurally the polymeric chain ends of polystyrene or poly4VP prepared by ATRP were determined. The reactions of these alkyl halides with nucleophilic solvents (deuterated water or methanol) were monitored by ^{1}H NMR spectroscopy at 25 °C in acetone-d_6 at pseudo-first-order conditions (Figure 1). The measured pseudo-first-order solvolysis rate constants are listed in Table 1 and agree well with literature values determined under similar conditions. The solvolysis of the bromides was faster by about an order of magnitude than that of the chlorides. In addition, for both alkyl halides, the hydrolysis reaction was faster than the methanolysis. As a conclusion of these studies, when polymerizing 4VP or water-soluble styrene derivatives in aqueous media, the use of alkyl chloride rather than alkyl bromide initiators should be advantageous because the chloride end groups are better preserved during the process. These results are important for aqueous ATRP in general and should also be taken into consideration when preparing and purifying styrene-type macroinitiators. Aqueous mixtures should be avoided in reprecipitation procedures in order to preserve the chain end functionality.

Scheme 1. Reaction of (a) Poly4VP-Derived Alkyl Bromide Chain End with Pyridine Units of 4VP and/or Poly4VP Leading to Formation of Branched Structures and (b) 1-PhEtBr (Model Compound) with Pyridine



In the ATRP of a basic monomer such as 4VP, pyridine groups from both the free monomer and polymer can react with the polymer chain ends. The nucleophilic substitution would lead to formation of pyridinium salts and therefore to branching (Scheme 1). Elimination reactions are in principle also feasible. To understand better these processes, model reactions of 1-PhEtX (X = Br, Cl) with pyridine-d_5 in acetone-d_6 at 27 °C were studied by means of ^{1}H NMR spectroscopy (Figure 2). The pyridinolysis of 1-PhEtBr (pseudo-first-order rate constant $k_{Py} = 6.7 \times 10^{-6}$ M^{-1} s^{-1}) was much faster than that of 1-PhEtCl (which was too slow to be measured). Formation of pyridinium salt rather than elimination of HBr was the main reaction. This is in agreement with earlier studies of the reaction of 1-PhEtBr derivatives with pyridine in acetonitrile ($k_2 = 5.54 \times 10^{-5}$ M^{-1} s^{-1}).[67] In the ATRP of 4VP, formation of pyridinium salts should occur if a bromide-based catalytic/initiating system is employed, leading to polymers with poorly controlled architecture, due to branching (Scheme 1). This problem should be avoided if chloride-based systems are used.

At first, it was surprising that although hydrolysis and methanolysis of 1-PhEtBr were faster by about an order of magnitude than these of 1-PhEtCl, the rates of pyridinolysis of the two compounds differed more. It is well-documented that

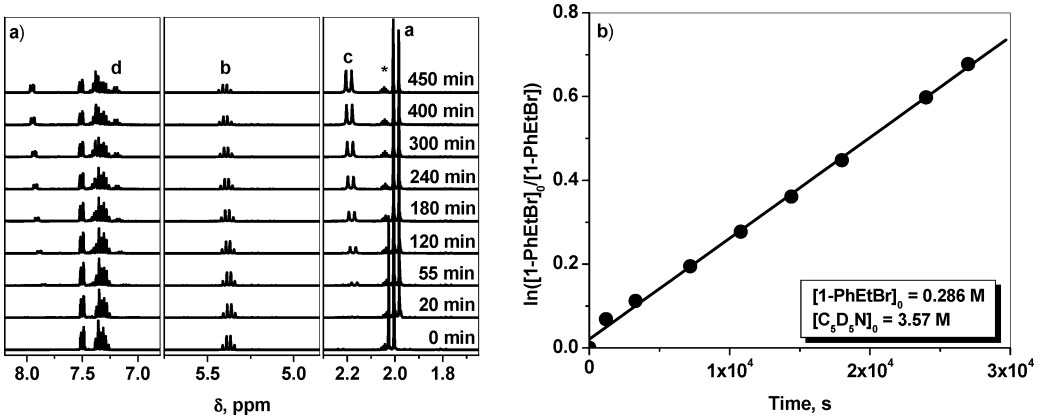


Figure 2. Pyridinolysis of 1-PhEtBr in acetone at 27 °C: (a) evolution of ^{1}H NMR spectra of the reaction mixture with time (the designated signals belong to protons from the starting halide and the formed pyridinium salt, as indicated in Scheme 1; the asterisk shows the acetone peak); (b) kinetic plot of 1-PhEtBr consumption. Pseudo-first-order pyridinolysis rate constant $k_{Py} = 6.7 \times 10^{-6}$ M^{-1} s^{-1}.

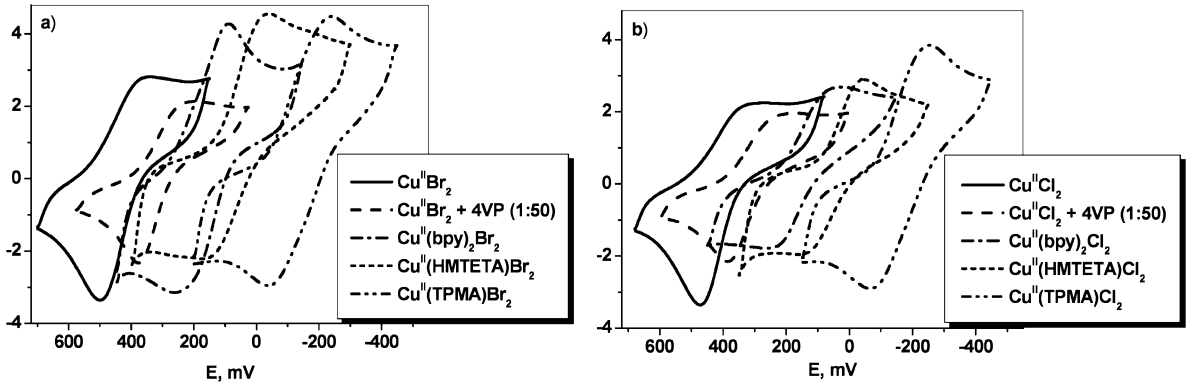


Figure 3. CV traces of Cu^{II} bromide (a) and chloride (b) complexes with various ligands in methanol.

the rate constants of nucleophilic substitution reactions depend greatly upon the solvent polarity and ability to form hydrogen bonds[68] as well as upon the nature of the leaving groups, termed nucleofugacity, which is also solvent-dependent.[69] It has been shown earlier that the rate constants of aminolysis of alkyl bromides and chlorides in polar aprotic solvents differ more than the rate constants of hydrolysis or methanolysis. For example, the ratio of the second-order rate constants in the reaction of *n*-butyl halides with pyridine in DMF is k_2(RBr)/k_2(RCl) = 100, whereas the ratio of the solvolysis rate constants in methanol−water mixtures (92:8 by volume) is 25 (at 75 °C).[70] Also, the ratio of second-order rate constants in the reaction of 2-phenylethyl bromide and chloride with 1,4-diazabicyclo[2.2.2]-octane are k_2(RBr)/k_2(RCl) = 169 in acetone (dielectric constant 21) and 50 in ethanol (with similar dielectric constant of 25).[71] It is therefore not surprising that the reactivities of 1-PhEtBr and 1-PhEtCl toward pyridine in an acetone−pyridine mixture (nonprotic and of relatively low polarity) are markedly more different than those toward water and methanol (in protic and more polar media).

The solvolysis and pyridinolysis studies clearly show that, to preserve the living polymer chains throughout the ATRP of styrene-type monomers in the presence of nucleophilic compounds, alkyl chloride initiators should be used. If these are not readily available, alkyl bromide initiators can also be utilized but only in conjunction with Cu^{I}Cl-based catalysts. Halogen exchange[72,73] occurs converting the initiator and the polymeric chain ends to the desired alkyl chloride groups that are comparatively stable with respect to nucleophilic substitution. The halogen exchange is particularly fast for active alkyl bromide initiators (characterized by high ATRP equilibrium constants), i.e., for structures that generate stabilized tertiary or secondary radicals, such as 2-bromoisobutyrates or 2-bromopropionates. The use of active ATRP catalysts is also beneficial for a fast halogen exchange.[74] In this work, 2-bromoisobutyrate macroinitiator derived from poly(ethylene oxide) monomethyl ether was used.

Table 2. Redox Potentials of Copper Complexes Measured in Methanol[a]

complex	$E_{p,a}$, V	$E_{p,c}$, V	ΔE_p, mV	$E_{1/2}$, V
Cu^{II}Br$_2$	0.500	0.340	140	0.420
Cu^{II}Cl$_2$	0.472	0.270	202	0.371
Cu^{II}Br$_2$ + 50 equiv 4VP	0.377	0.199	178	0.288
Cu^{II}Cl$_2$ + 50 equiv 4VP	0.386	0.173	213	0.280
Cu^{II}(bpy)$_2$Br$_2$	0.262	0.090	172	0.176
Cu^{II}(bpy)$_2$Cl$_2$	0.264	0.029	235	0.147
Cu^{II}(HMTETA)Br$_2$	0.175	−0.040	215	0.068
Cu^{II}(HMTETA)Cl$_2$	0.162	−0.048	210	0.057
Cu^{II}(TPMA)Br$_2$	−0.039	−0.241	202	−0.140
Cu^{II}(TPMA)Cl$_2$	−0.067	−0.255	188	−0.161

[a] 0.1 M NBu_4PF_6, 1.0 mM Cu^{II} complex, scan rate 0.20 V s^{-1}; potentials reported vs Ag/AgCl (+0.199 V vs NHE). $E_{p,a}$ and $E_{p,c}$ are the peak potentials of the oxidation and reduction waves, respectively. $E_{1/2} = (E_{p,a} + E_{p,c})/2$.

2. Selection of the Ligand. The activity of Cu-based ATRP catalysts is related to their redox potentials, with more reducing complexes being catalytically more active. In the present work, several ligands were employed as components of the catalysts, namely bpy, HMTETA, and TPMA. All three ligands are appropriate for ATRP in aqueous media.[19,26,55] The electrochemical properties of the Cu^{I} complexes were studied by CV in methanol (Figure 3 and Table 2). In the absence of added ligand, both Cu^{II} halides have relatively high redox potentials (420 mV for Cu^{II}Br$_2$ and 370 mV for Cu^{II}Cl$_2$), and consequently they cannot be used as ATRP catalysts. The addition of 4VP to

Table 3. Values of K_{ATRP} for the Reaction of 1-PhEtX (X = Cl or Br) with Cu^IX Complexes of bpy, HMTETA, and TPMA in MeCN at Room Temperature[a]

	K_{ATRP} (1-PhEtX)	
catalyst	X = Br	X = Cl
$Cu^I(bpy)_2X$	8.5×10^{-10} (2)	
Cu^I(HMTETA)X	2.9×10^{-9} (3)	7.9×10^{-10} (2)
Cu^I(TPMA)X	4.58×10^{-6}; ref 62	8.60×10^{-7}; ref 62

[a] The number in parentheses is the number of independent measurements used to calculate the average value of K_{ATRP}.

the solutions of the halides (50 equiv relative to $Cu^{II}X_2$) led to a marked decrease in the redox potentials (by ca. 100 mV), reflecting the coordination of the monomer to the metal center. However, the formed complexes were still too weakly reducing to be used as mediators of the ATRP of 4VP in the absence of any additional ligand. The redox potentials of the studied complexes decreased in the order 4VP > bpy > HMTETA > TPMA, and it is expected that the catalytic activity should increase in this order.

The CV of Cu complexes of these and other N-based ligands with a coordinated bromide and chloride anion were previously studied in MeCN.[75] It was shown that the chloride complexes were more reducing by 80−145 mV than their bromide analogues, when the voltammograms were characterized by relatively low ΔE_p values. This reflects the higher chlorophilicity vs bromophilicity of the Cu^{II} complexes in MeCN. In a protic solvent (methanol), however, the difference in the redox potentials of the bromide and chloride complexes is somewhat lower (8−30 mV), the chloride complex again being more reducing. This is related to the relatively close values of association constants of the two halide anions to Cu^{II} in protic solvents.[21]

The ATRP equilibrium constants were determined for the reaction of some of the reported bromide and chloride complexes with the model compound 1-PhEtX (X = Br and Cl) structurally resembling the dormant species in the ATRP of 4VP (Table 3). Unfortunately, because of the fast methanolysis and hydrolysis of 1-PhEtX (vide supra), the K_{ATRP} values could not be determined in methanol or its mixtures with water, and the reactions were carried out in MeCN.

The catalytic activity of the studied Cu^I complexes is ligand-dependent and, as expected from the electrochemical studies, decreases in the order TPMA > HMTETA > bpy. The lower K_{ATRP} values of 1-PhEtCl compared to 1-PhEtBr reflect the larger bond dissociation energy of the C−Cl relative to C−Br bond. The data in Table 3 indicate that the rates of polymerization in the ATRP of 4VP mediated by Cu^I(HMTETA)Cl and by $Cu^I(bpy)_2Br$ should be close. However, on the basis of solvolysis studies presented earlier, the polymerization control in protic media should be better in the presence of the former catalyst due to the markedly slower solvolytic loss of alkyl chloride compared to alkyl bromide end groups.

3. ATRP of 4VP in Aqueous Media. The ATRP of 4VP in aqueous medium using $Cu^I(bpy)_2Br$ as the catalyst was relatively slow (Figure 4a), in accordance with the low value of K_{ATRP} for the reaction of the model compound 1-PhEtBr with the bpy-based catalyst. Complexation of the monomer to the copper center of the catalyst, via displacement of the relatively weakly bound bpy ($\log K_1^{II} = \log \beta^{II} = 8.15$, $\log K_2^{II} = 5.50$[76]) by the large excess of 4VP, may also occur leading to the formation of a complex that is very inefficient as a catalyst (see the data in Table 2). Judging from the data in Table 2, HMTETA should be a more suitable ligand because the Cu^I complex is more active and is yet stable toward disproportionation.[19,26,55] In addition, 4VP is much less likely to displace the strongly coordinating HMTETA ($\log \beta^{II} = 12.60$[77]) than a bpy ligand from the catalyst. Indeed, the ATRP of 4VP using Cu^I(HMTETA)Br was significantly faster than with

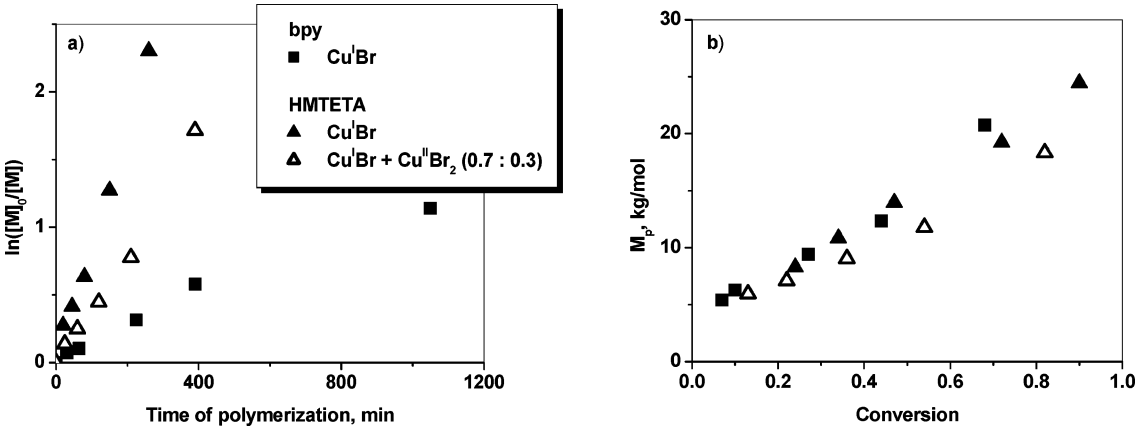


Figure 4. ATRP of 4VP in CD_3OD-D_2O (1:1) at 30 °C using Cu^I(HMTETA)Br (with or without added deactivator) and $Cu^I(bpy)_2Br$ as the catalysts: (a) kinetics and (b) evolution of molecular weights (major peak of MWD) with conversion.

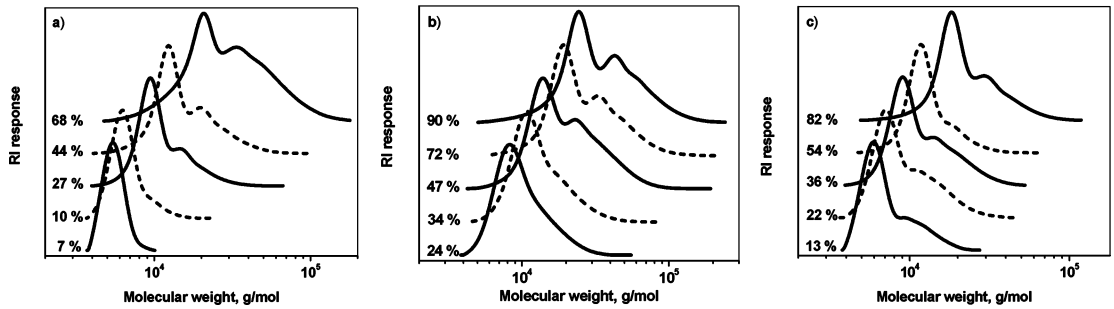


Figure 5. Evolution of MWD (SEC traces) of poly4VP prepared by ATRP using (a) $Cu^I(bpy)_2Br$, (b) Cu^I(HMTETA)Br, and (c) Cu^I(HMTETA)Br + Cu^{II}(HMTETA)Br_2 (0.7:0.3). Monomer conversion is shown at each curve.

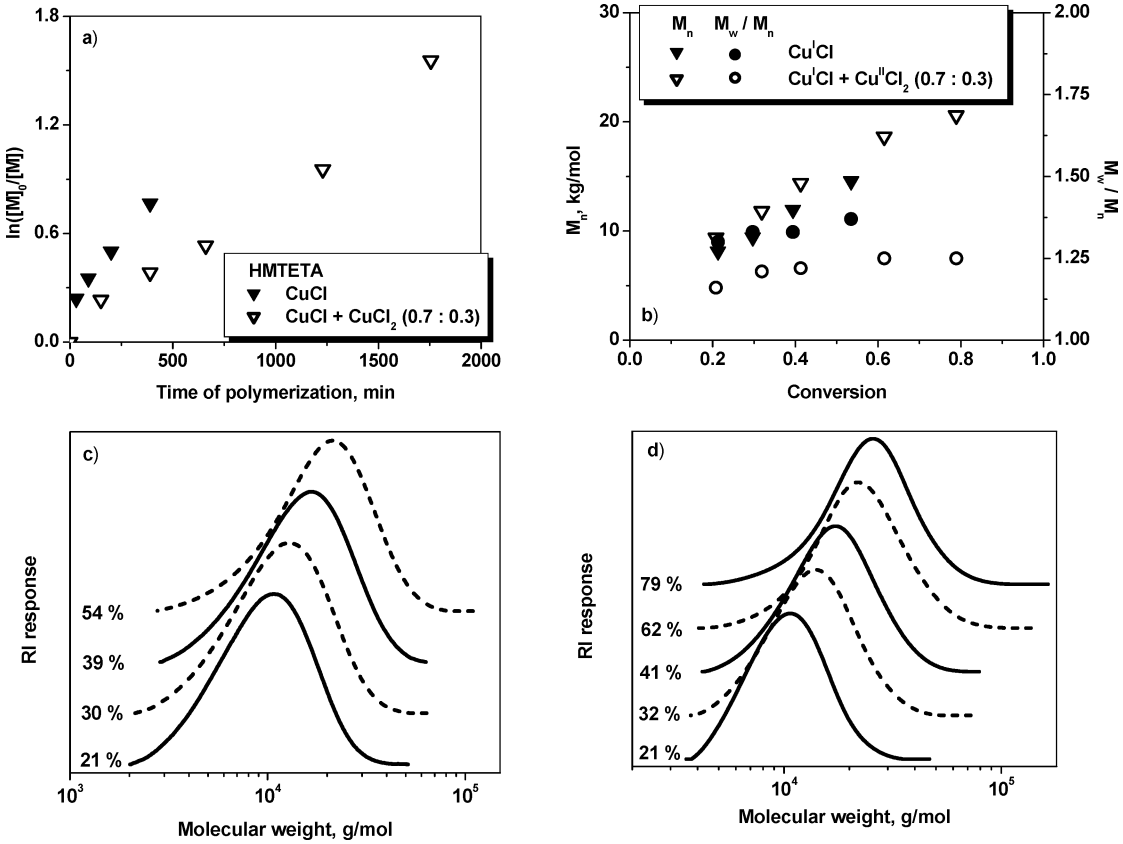


Figure 6. Kinetics (a) and evolution of molecular weights and M_w/M_n (b) or SEC traces (c and d) with conversion in the ATRP of 4VP using Cu^I(HMTETA)Cl (filled symbols and c) or Cu^I(HMTETA)Cl + Cu^{II}(HMTETA)Cl_2 (0.7:0.3) (open symbols and d). Monomer conversion is shown at each curve.

$Cu^I(bpy)_2Br$ (Figure 4a), and molecular weights increased linearly with conversion (Figure 4b). However, in all cases, the molecular weight distributions (MWD) of the obtained polymers were polymodal (Figure 5), which was attributed to reaction of monomer or polymer with bromide chain ends. Such reactions would cause the formation of branched structures, as shown in Scheme 1a. The addition of $Cu^{II}Br_2$ complex did not affect the shape of the molecular weight distribution (Figure 5c), proving that the polymodality was not due to coupling reactions resulting from inefficient deactivation. On the basis of the hydrolysis and methanolysis studies presented above, it could be expected that Cu^I(HMTETA)Cl would be a better catalyst for 4VP in aqueous media.

When Cu^I(HMTETA)Cl was employed as the catalyst, the polymerization was slower than with Cu^I(HMTETA)Br (Figure 6a) due to differences in the corresponding K_{ATRP} values (Table 3). The reaction was also somewhat faster than that mediated by $Cu^I(bpy)_2Br$ although similar rates can be predicted on the basis of the data in Table 3. The differences in the rates are most likely a result of the constant loss of alkyl bromide initiating groups throughout the reaction employing the bromide-based catalyst. Displacement of a bpy ligand by 4VP may also be responsible for the formation of catalyst of lower activity and may also account for the observed slower polymerization rate. Importantly, the SEC traces of the poly4VP obtained with Cu^I(HMTETA)Cl catalyst were all monomodal (Figure 6c), confirming that indeed the ATRP of 4VP in protic media was optimized.

The stability of the $Cu^{II}-X$ bond in protic/aqueous media is significantly lower than in nonprotic solvents; it also decreases as the amount of water in mixed water−alcohol solvents is increased. For instance, the formation constant (halogenophilicity, K_X) of $[Cu^{II}(bpy)_2X]^+$ from the complex $[Cu^{II}(bpy)_2]^{2+}$ and a halide anion is lower by about 2 orders of magnitude in a water−methanol mixture (1:1 by volume) than in pure methanol ($K_{Br} = 29$ and 4.7×10^3 and $K_{Cl} = 52$ and 4.5×10^3 in the two solvents, respectively).[21] As a consequence, when ATRP reactions are carried out in water or other protic solvents, part of the deactivating complex containing $Cu^{II}-X$ bonds dissociates, leading to inefficient deactivation, fast polymerization rates, and, most importantly, poor polymerization control, as predicted from eq 1. Halide ligand loss from the deactivator is further compounded by coordination of 4VP to the Cu^{II} center. There are two ways to enhance the deactivation of radicals in ATRP in protic solvents: the use of catalysts containing initially relatively large amount of Cu^{II} halide complexes (up to 80% of the total Cu) and/or the addition of halide salts to the reaction mixture. The actual concentration of deactivator $XCu^{II}L_m$ present in the reaction medium depends on its stability, K_X, and the total concentrations of Cu^{II} complexes and halide ions:[19,21]

$$[XCu^{II}L_m] = \frac{F - \sqrt{F^2 - 4K_X{}^2[Cu^{II}L_m]_{tot}[X]_{tot}}}{2K_X} \quad (F = 1 + K_X[Cu^{II}L_m]_{tot} + K_X[X]_{tot}) \quad (2)$$

As seen from Figure 6b, the polydispersity of poly4VP produced in the ATRP of 4VP using a catalyst containing only Cu^I(HMTETA)Cl was relatively high (1.35−1.45). However, when the catalyst contained 30% (with respect to the total Cu) of the deactivating complex Cu^{II}(HMTETA)Cl_2, the polymerization control was improved (polydispersity in the range 1.15−1.25) due to the increased deactivation efficiency. This was accompanied by a slower polymerization. The molecular weight

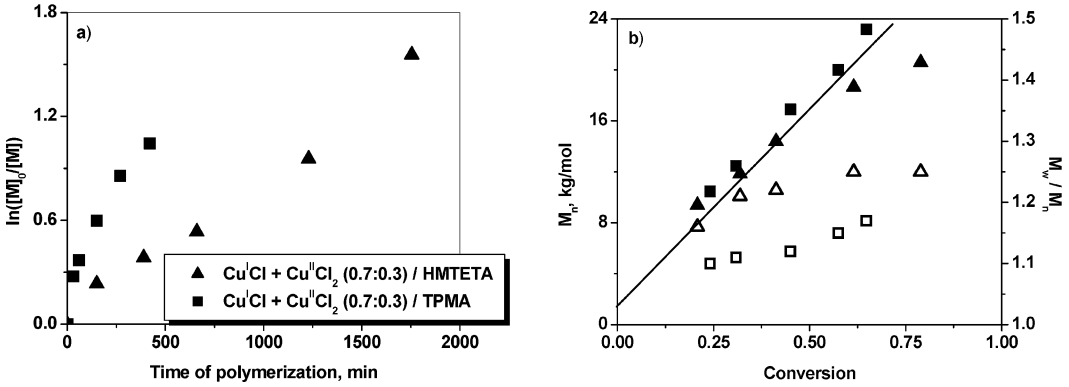


Figure 7. Kinetics (a) and evolution of molecular weights (filled symbols) and M_w/M_n (open symbols) with conversion (b) in the ATRP of 4VP in water−methanol (1:1 by volume) at 30 °C using a mixture of Cu^ICl and $Cu^{II}Cl_2$ (0.7:0.3) with HMTETA (triangles) or TPMA (squares).

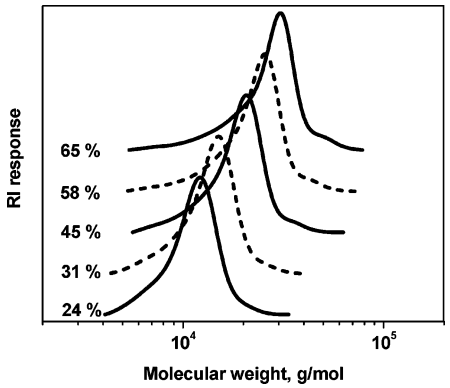


Figure 8. Evolution of molecular weight distribution (SEC traces) of poly4VP prepared by ATRP using $Cu^I(TPMA)Cl + Cu^{II}(TPMA)Cl_2$ (0.7:0.3) as the catalyst. Monomer conversion is shown at each curve.

distributions in both cases were symmetrical and monomodal (Figure 6c,d).

Although the use of HMTETA-based Cu^ICl complex containing sufficient amount of the $Cu^{II}Cl_2$ complex lead to very good polymerization control, it was still desirable to shorten the reaction time. For this purpose, a mixture of the Cu^ICl and $Cu^{II}Cl_2$ complexes (0.7:0.3) of TPMA was used to mediate the ATRP of 4VP. On the basis of the electrochemical data (Figure 3 and Table 2) and the ATRP equilibrium constants (Table 3), it was expected that ATRP reactions catalyzed by TPMA complexes should be faster than those catalyzed by the HMTETA complexes. In addition to the large β^{II}/β^I ratio (4.9×10^4)[78] of the TPMA complexes, which determines high catalytic activity, the ratio $\beta^{II}/(\beta^I)^2[L]$ is low (6.2×10^{-5} at [TPMA] = 10^{-4} M),[78] meaning that disproportionation in aqueous media is negligible.[19,26,55] Figure 7a shows the kinetics of polymerization of 4VP, and Figure 7b shows the linear increase of the molecular weight with monomer conversion for catalysts derived from the two ligands. Not only was the polymerization rate increased but also the control was improved with catalysts derived from TPMA, compared to HMTETA.

Figure 8 shows the SEC traces of poly4VP obtained in an ATRP reaction using TPMA-based complex. The molecular weight distributions shift symmetrically to higher molecular weight with monomer conversion, and only at relatively high conversion (>60%) is a small amount of coupling observed.

Conclusions

Typically, copper bromide-based ATRP catalysts provide better polymerization control than their chloride analogues due to more efficient radical deactivation. However, this paper demonstrates that, in special cases of ATRP of monomers forming dormant species that are prone to participate in nucleophilic substitution reactions with the solvent, monomer, or polymer, the use of chloride-based ATRP catalyst is essential to achieve good control and narrow molecular weight distribution of the polymers. When a copper bromide-based catalyst was used in the aqueous ATRP of 4VP, the obtained polymers had polymodal molecular weight distributions reflecting the formation of branched chains. The polymerization mediated by the Cu^I complex of 2,2′-bipyridine was slow due to the low value of the ATRP equilibrium constant, in agreement with the low reducing power of the complex. The successful ATRP of 4VP was carried out in protic media at 30 °C using the Cu^ICl complexes of HMTETA or TPMA as the ATRP catalysts. The latter ligand forms more reducing and therefore catalytically more active Cu^I complex. Importantly, the Cu^I complexes of neither HMTETA nor TPMA disproportionate in water due to the low $\beta^{II}/(\beta^I)^2[L]$ values. In protic media, a significant part of the Cu^{II} halide complex generated in the ATRP process dissociates, and radical deactivation becomes inefficient. The use of catalyst initially containing $Cu^{II}Cl_2$ complex (30% of the total Cu) resulted in excellent polymerization control.

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