Deactivation Efficiency and Degree of Control over Polymerization in ATRP in Protic Solvents

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ABSTRACT: Copper-mediated ATRP in protic solvents is characterized by inefficient deactivation due to reversible dissociation of a halide ligand from the ATRP deactivator $Cu^{II}L_nX$ (L = bipyridine or another amine or imine, X = Br, Cl), which may be followed by competitive coordination of solvent to the Cu^{II} center. This process is strongly solvent-dependent and leads to fast and often poorly controlled polymerizations. The loss of a halide ligand from the deactivator in ATRP reactions in the presence of water or other coordinating compounds can be suppressed by the addition of halide salts allowing the regeneration of the dissociated Cu^{II}−X species and, therefore, increasing the deactivation rate. The deactivation step in ATRP, which is of primary importance for control over the polymerization, can also be accelerated by employing a catalyst system initially containing a sufficiently large amount of Cu^{II}−halide complex. These approaches are illustrated by conducting the controlled radical polymerization of 2-hydroxyethyl methacrylate, 2-(*N*,*N*-dimethylamino)ethyl methacrylate, 2-(trimethylammonio)ethyl methacrylate trifluoromethanesulfonate, and 2-(dimethylethylammonio)ethyl methacrylate bromide.

Introduction

Hydrophilic polymeric materials, including neutral polymers, polyelectrolytes, and ionomers, are widely used in the fabrication of ion-exchange resins, superabsorbents, water-purification materials, selective membranes, etc.[1,2] Other areas of application include controlled delivery, crystal and tissue engineering, and "smart" or responsive materials. These polymers are of interest for large volume markets such as coatings, surfactants, adhesives, and cosmetics, to mention a few. They are mainly produced by radical polymerization due to its tolerance to protic solvents, including water, polar functional groups, and a variety of impurities often encountered in industrial processes. However, a major drawback of conventional radical polymerization is the lack of control over molecular weight distribution and the impossibility to prepare well-defined complex structures such as end-functionalized polymers or block copolymers due to rapid transfer and termination reactions.

These intrinsic problems for the conventional radical polymerization can be overcome using one of the controlled radical polymerization techniques developed in the past decade.[3−6] Atom transfer radical polymerization (ATRP)[7,8] is one of the most broadly applied methods of controlled radical polymerization because of its easy experimental setup, the use of readily accessible and inexpensive catalysts (usually copper complexes of aliphatic amines or imines or pyridines), and simple initiators (alkyl halides). ATRP relies on the reversible reaction of a low-oxidation-state metal complex with an alkyl halide generating radicals and the corresponding high-oxidation-state metal complex with a coordinated halide ligand.[9,10] The "livingness" of this polymerization process can be ascertained from a linear first-order kinetic plot, accompanied by a linear increase in polymer molecular weights with conversion, and the value of the number-average degree of polymerization being determined by the monomer-to-initiator ratio. The polymers produced by ATRP are halogen-terminated and can be further used as macroinitiators in chain-extension reactions[11] or as precursors of end-functionalized polymers.[12]

During the past few years, there has been a tendency to replace the volatile, flammable, and toxic organic solvents used in synthetic reactions with "greener" ones. Examples of employing water,[13−20] supercritical carbon dioxide,[21] and ionic liquids[22−24] as solvents for ATRP have been reported. Both heterogeneous and homogeneous aqueous ATRP systems have been studied,[25,26] but because of the occurrence of several side reactions, the number of water-soluble monomers polymerized in controlled fashion is still limited. Moreover, most of the water-soluble polymers successfully prepared by aqueous ATRP were of relatively low molecular weight with targeted degrees of polymerization (DP) at complete conversion in the range of 10−75. It has been observed that ATRP in aqueous homogeneous media is fast and yields polymers of relatively high polydispersity index (PDI = M_w/M_n), indicating loss of control.[27] The polymerization reactions are accelerated as the amount of water in the medium increases,[28] which has been attributed to coordination of water to the copper-based ATRP catalyst. The ATRP of poly(ethylene oxide) monomethyl ether methacrylate,[15,17] another oxygen-containing compound potentially able to coordinate to copper ions, was also fast, which supported the idea of water coordination. The mode of coordination was not clarified but was assumed to involve displacement of the nitrogen ligand from the catalyst by water. The process seemed to be promoted by the polymerization itself, since no such displacement was observed by NMR of aqueous solutions of CuBr/pyridylmethaneimine complexes at room temperature over a 48 h period.[27] Polarity effects were also credited as being a possible cause for the fast ATRP reactions in the presence of water.[15,17,27] Although some of the mentioned reactions might indeed occur to a certain extent and could plausibly be held responsible

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for the observed kinetic results and evolution of molecular weight distributions, we provide experimental evidence for another important hydrolytic reaction of the ATRP catalyst, namely the solvolytic loss of a halide ligand from the deactivating higher oxidation state metal complex.

Preliminary studies carried out in our labs have already identified several side reactions in ATRP systems in the presence of water: hydrolytic displacement of the halogen atom from the initiator or the dormant polymeric species, especially at elevated temperatures, disproportionation of the Cu^{I}-based ATRP catalyst,[20] and hydrolysis of the ATRP deactivator.[19] The last reaction involves reversible dissociation of halide ligand from the higher oxidation state complex, presumably followed by coordination of water. The deactivator concentration is thus lowered, which reduces the rate of deactivation, eventually leading to fast polymerizations and loss of control. A recent EXAFS study of typical ATRP deactivators with aliphatic amine ligands demonstrated the marked heterolytic dissociation of the $Cu^{II}-Br$ bonds in aqueous media.[29] The understanding of such reactions is crucial for improving the synthesis of well-defined polymers by ATRP in aqueous solvents. Herein, we provide a theoretical description of the complex equilibria in ATRP in protic media. This quantitative treatment can be applied to any similar system involving dissociation (and/or displacement by solvent, monomer, or other coordinating species present in the system) of halide ligands from the ATRP deactivator. In the present paper, we report on the ATRP of four water-soluble monomers: 2-hydroxyethyl methacrylate (HEMA) and 2-(*N*,*N*-dimethylamino)ethyl methacrylate (DMAEMA), 2-(trimethylammonio)ethyl methacrylate trifluoromethanesulfonate (TMATf), and 2-(dimethylethylammonio)ethyl methacrylate bromide (DMEABr). The controlled copper-mediated radical polymerization of these monomers in both nonaqueous[30,31] and aqueous media[20,28,32] has already been reported, but we reinvestigated these systems and used them as an illustration and experimental evidence for the provided theory.

Experimental Section

Materials. HEMA and DMAEMA (99%, Aldrich) were purified by passing the neat liquids through a column filled with basic alumina to remove the inhibitor. CuBr and CuCl (Acros) were purified using a slightly altered literature procedure,[33] namely washing with glacial acetic acid followed by 2-propanol. All other reagents and solvents were used as received without further purification.

Synthesis of ATRP Macroinitiator. The 2-bromoisobutyrate ester of poly(ethylene oxide) monomethyl ether (MePEOBiB) was employed as the macroinitiator, since it can be used for determination of molecular weights of the prepared polymers by NMR spectroscopy. It was synthesized using previously reported procedure.[34,35] In 30 mL of CH_2Cl_2, 3.348 g (20.05 mmol) of 2-bromoisobutyric acid was dissolved in an ice−water bath. A solution of 11.07 g (20.13 mmol) of MePEO(OH) of $M_n = 550$ g/mol was added upon stirring followed by 4.134 g (20.04 mmol) of dicyclohexylcarbodiimide and 0.113 g of 4-(*N*,*N*-dimethylamino)pyridine.[36,37] The mixture was then stirred at room temperature for 5 h, and the precipitated dicyclohexylurea was filtered off and washed on the filter with ca. 130 mL of CH_2Cl_2. The solvent was removed from the combined filtered solution and washings in a rotary evaporator. A slightly yellowish turbid oil was obtained. It was then purified by repetitive freezing and warming to room temperature until no impurities crystallized out any longer. After final filtration, the yield of the clear oil was 12.84 g (92%). The ester was characterized by IR (strong absorbance in the carbonyl region at 1720 cm^{-1}, insignificant absorbance for OH group at 3600−3200 cm^{-1}) and ^1H NMR (δ 1.93 ppm, 6H, $(CH_3)_2CBr$; 3.38 ppm, 3H, CH_3O; 3.65 ppm, 50H, $(CH_2CH_2O)_n$—this signal was used as a reference for molecular weight determination; and 4.32 ppm, 2H, $COOCH_2$) spectroscopy. (For comparison, the ^1H NMR spectrum of the starting alcohol MePEO(OH) consists of two signals at 3.39 and 3.65 ppm, with relative intensities 3:52.)

Synthesis of Quaternized Monomers TMATf and DMEABr. DMAEMA (3.5 mL, 0.021 mol) containing polymerization inhibitor was dissolved in 30 mL of benzene. The solution was cooled in an ice−water bath, and upon stirring, methyl trifluoromethanesulfonate (2.5 mL, 0.022 mol) was added dropwise. The ammonium salt precipitated as a white solid. The mixture was stirred for an additional 2 h at room temperature. The salt was filtered, washed with 50 mL of benzene on the filter, and dried in vacuum. Yield: 5.90 g (86%). ^1H NMR (δ, ppm, in methanol-d_4): 6.17 (dq, 1H, $=CH$) 5.71 (dq, 1H, $=CH$), 4.64 (m, 2H, CH_2O), 3.82 (m, 2H, CH_2N^+), 3.27 (s, 9H, $(CH_3)_3N^+$), and 1.98 (dd, 3H, $=CCH_3$). The other monomer, DMEABr, was synthesized in a similar manner, but bromoethane was used as the alkylating agent and the reaction was carried out for 30 h. ^1H NMR (δ, ppm, in methanol-d_4): 6.18 (dq, 1H, $=CH$) 5.74 (dq, 1H, $=CH$), 4.66 (m, 2H, CH_2O), 3.82 (m, 2H, $CH_2\mathit{CH_2}N^+$), 3.61 (q, 2H, $CH_3\mathit{CH_2}N^+$), 3.24 (s, 6H, $(CH_3)_2N^+$), 1.99 (dd, 3H, $=CCH_3$), and 1.44 (t, 3H, $\mathit{CH_3}CH_2N^+$).

ATRP of Neutral Monomers in Aqueous Homogeneous Media. 2 mL (16.5 mmol) of HEMA and 2 mL of solvent (methanol or methanol−water mixtures) were mixed and degassed by five freeze−pump−thaw cycles. The reaction flask was filled with nitrogen and the catalyst (a mixture of cuprous and cupric halides (0.165 mmol of total copper), and 0.0515 g (0.33 mmol) of bpy was added to the still frozen mixture. The flask was then closed and evacuated and backfilled with nitrogen three times. A homogeneous brown solution was obtained after melting the mixture. Polymerizations were conducted in a water bath thermostated at 25, 30, or 35 °C. The pre-deoxygenated macroinitiator (90 μL) was added last. Conversion was determined by gravimetry after precipitation in ether and drying to give a constant weight in a vacuum oven at 40−50 °C. The amount of nonpolymeric solids in the product was taken into account in the calculations. Gas chromatography (GC) was also used in some cases to determine conversions; 0.15 mL of toluene was added to the reaction mixture in these cases as an internal standard. When it was necessary to study the suppression of catalyst hydrolysis, tetrabutylammonium halide salts were initially dissolved in the mixture of monomer and solvent. In some cases, different molar ratios of catalyst to initiator were used. The polymerization of DMAEMA was carried out under similar conditions. Conversion of DMAEMA was determined by GC using DMF as the internal standard.

ATRP of the Ionic Monomers in Aqueous Homogeneous Media. The monomer (5 mmol) was dissolved in 3 mL of solvent (D_2O or mixtures of D_2O and pyridine-d_5 (Py)), and the solution was degassed by five freeze−pump−thaw cycles. The reaction flask was filled with nitrogen and the catalyst (mixture of CuBr and $CuBr_2$; 0.05 mmol of total copper), and 0.0156 g (0.1 mmol) of bpy was added to the still frozen solution. The flask was closed, evacuated, and backfilled with nitrogen three times. A homogeneous brown solution was obtained after the flask was immersed in a water bath thermostated at 25 °C. The macroinitiator (0.05 mmol) was added last. Conversion was determined by NMR (the copper-containing catalyst was not removed from the samples).

Determination of Halogenophilicity Constants.[38] Solutions containing the complex cation $[Cu^{II}(bpy)_2]^{2+}$ with a weakly coordinating counterion, namely trifluoromethanesulfonate, TfO^-, were titrated with either tetrabutylammonium bromide or benzyltriethylammonium chloride in a given solvent (several methanol−water mixtures as well as pure methanol were examined). Spectra of the original solution containing no halide ions and of solutions containing *n* equivalents of halide vs Cu^{II} were collected. Portions of the halide salt were added until no further change in the spectrum was observed (i.e., the entire amount of $[Cu^{II}(bpy)_2]^{2+}$ was converted to $[Cu^{II}(bpy)_2X]^+$). The equilibrium constant of halide association to $[Cu^{II}(bpy)_2]^{2+}$, termed herein halogenophilicity K_X (X = Br or Cl), was determined using the following equation:

$$K_X = \frac{\Delta A/\Delta\epsilon}{([Cu^{II}]_{tot} - \Delta A/\Delta\epsilon)(n[Cu^{II}]_{tot} - \Delta A/\Delta\epsilon)} \qquad (1)$$

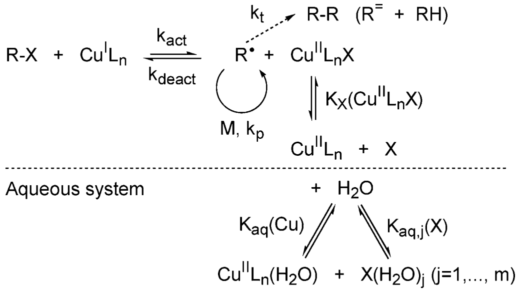
ΔA is the difference between the absorbance (measured at a given wavelength) of a solution containing halide salt (n equivalents vs Cu^{II}) and of the starting solution before addition of the halide. The total copper concentration is $[Cu^{II}]_{tot}$. The apparent extinction coefficient $\Delta\epsilon$ is defined as the difference between the extinction coefficients of the complex $[Cu^{II}(bpy)_2X]^+$ (calculated from the spectrum of solution of "saturated" with halide−copper complex) and the starting tetracoordinated $[Cu^{II}(bpy)_2]^{2+}$. Equation 1 is valid only if two species absorbing light are present in the solution. Halide salts are "transparent" in the studied spectral region (400−1400 nm), and if water does not coordinate to the complex $[Cu^{II}(bpy)_2]^{2+}$, the requirement is fulfilled. However, if increasing amounts of water are added to the complex $[Cu^{II}(bpy)_2]^{2+}$ dissolved in anhydrous methanol, an isosbestic point was observed at 896 nm, implying water coordination. Therefore, in aqueous solutions of $[Cu^{II}(bpy)_2](TfO)_2$ in the presence of halide salt, three absorbing species exist, namely $[Cu^{II}(bpy)_2]^{2+}$, $[Cu^{II}(bpy)_2X]^+$, and $[Cu^{II}(bpy)_2(H_2O)]^{2+}$. To apply eq 1, one has to perform all calculations using wavelength corresponding to the isosbestic point, i.e., at 896 nm, which was done in the present work. From the separate solutions containing different concentrations of halide salt, values of K_X were determined, and then the average value was calculated (for more details, see the Supporting Information).

Analyses. ^1H NMR spectra were recorded on a Bruker instrument operating at 300 MHz using TMS as the reference compound. Conversions were determined by NMR, by gravimetry, or on a Shimadzu GC-14A gas chromatograph equipped with a flame ionization detector and using a capillary column (CEC-Wax, 30 m × 0.53 mm × 1.0 μm, Chrom Expert Co.). The initial temperature was 80 °C (1 min hold), and the final temperature of 180 °C (4 min hold) was reached at a heating rate of 20 °C/min. To determine molecular weights, dried polymer samples were dissolved in 50 mM solution of LiBr in DMF, containing a small amount of toluene as internal standard, 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 Styrogel columns (10^5, 10^3, and 100 Å; Polymer Standard Services) and a Waters 2410 differential refractometer. Calibration based on poly(methyl methacrylate) standards was used. Number-average molecular weights could also be conveniently determined using NMR by comparison of the areas of peaks corresponding to the PEO moiety from the macroinitiator and to the methacrylate polymer. Electronic spectra were collected on a Perkin-Elmer UV/vis/NIR Lambda 900 spectrophotometer. A baseline correction was performed for each solvent mixture studied.

Results and Discussion

Factors Affecting the Rate and Control over Polymerization in Protic Media. ATRP reactions in aqueous solvents are usually fast even at ambient temperature, and the polymerizations are accelerated as the amount of water in the solvent is increased (see Figure 3). So far, no quantitative explanation of the marked effect of solvent composition on the rate of ATRP has been provided. It is the purpose of the following text to demonstrate the impact of deactivator dissociation on the deactivation rate and therefore the overall polymerization rate. These rates are important since they affect the control over polymerization. Copper-mediated ATRP is based on the reversible reaction between an alkyl halide RX (X = Br or Cl) and a cuprous complex Cu^IL_n (L is typically a nitrogen-containing ligand) producing, in a process named activation (with rate constant k_{act} and rate R_{act}), radicals and a higher oxidation state complex with coordinated halide ligand $Cu^{II}L_nX$. (Throughout the text, all charges of ionic species are omitted for simplicity.) The radicals generated in the activation step give rise to polymer chains through an addition (with rate constant k_p) across the double bond of the monomer M. The $Cu^{II}L_nX$ complex can deactivate (with rate constant k_{deact} and rate R_{deact}) the radicals via a homolytic cleavage of the Cu^{II}−X bond, thus being reduced to the complex Cu^IL_n. The process is presented at the top part of Scheme 1. At the bottom part of this scheme, the processes causing insufficient deactivation in the presence of coordinating/solvating compounds are shown. Solvents such as water are able to coordinate to the metal center in the coordinatively unsaturated $Cu^{II}L_n$ complex or to solvate the halide ions via hydrogen bond formation. Therefore, the dissociation equilibrium of the deactivator $Cu^{II}L_nX$ is shifted to complexes that do not contain halide ligand and are unable to deactivate the propagating radicals. This results in loss of the living character of polymerization. The quantitative description of the complex equilibria involved is given in the next section.

Scheme 1. Basic Equilibria in Aqueous ATRP Systems



The rate of ATRP, assuming steady-state kinetics, is given by[9,39]

$$R_p = k_p K_{ATRP} \frac{[RX][Cu^IL_n]}{[Cu^{II}L_nX]}[M] \qquad (2)$$

The reaction solvent can, in principle, influence k_p, K_{ATRP}, and the deactivator concentration $[Cu^{II}L_nX]$. The extent to which water or other protic solvents can affect the activity (i.e., the propagation rate constant k_p) of a polar monomer is usually related to the strength of formed hydrogen bonds. This specific solvation is known to activate several monomers with polar groups, but the effect is usually small.[40−42] The increase in polymerization rate in aqueous solvents compared to that in organic aprotic solvents can thus be attributed to either an increase of K_{ATRP} or a decrease of the deactivator concentration (in other words, increase of R_{act} or decrease of R_{deact}, or both simultaneously) in the presence of water.

The overall ATRP equilibrium can be represented[43] as a combination of four simpler reversible reactions:

oxidation of the Cu^IL_n complex (characterized by the equilibrium constant of electron transfer K_{ET}), reduction of a halogen atom to a halide ion (electron affinity K_{EA} of X), C−X bond homolysis (K_{BH}), and association of halide ion to $Cu^{II}L_n$ (termed halogenophilicity K_X).

$$K_{ATRP} \equiv \frac{k_{act}}{k_{deact}} = K_{ET}K_{EA}K_{BH}K_X \tag{3}$$

The equilibrium constants K_{EA} and K_X depend strongly upon solvent composition. The halide ions (especially the smaller ones) formed in the reduction of halogen atoms are solvated and are thus stabilized in proton donor solvents.[44] Consequently, the values of K_{EA} are expected to be large in such media. The values of K_X vary by several orders of magnitude as the solvent polarity and solvation ability are changed. Therefore, it is expected that the values of $K_{ATRP} = k_{act}/k_{deact}$ will be strongly influenced by the solvent composition. Indeed, it was recently shown that the activation rate constant k_{act} for ethyl 2-bromoisobutyrate reacting with CuBr/bpy complex increased by a factor of 4 when the reaction solvent was changed from pure acetonitrile to a mixture of acetonitrile with 56 wt % water.[45] Herein, it is demonstrated that not only K_{ATRP} (eq 3) but also $[Cu^{II}L_nX]$ (which affects R_{deact}) depend on K_X.

The reversible deactivation step of the ATRP equilibrium is of primary importance for achieving a well-controlled polymerization, and its rate is given by

$$R_{deact} = k_{deact}[R^\bullet][Cu^{II}L_nX] \tag{4}$$

If the deactivator concentration in the reaction system is depleted due to halide ligand dissociation and/or competitive complexation with solvent, as presented at the bottom of Scheme 1, the deactivation will be slower. This side reaction is especially pronounced in water-rich solvents. Equation 4 shows that R_{deact} depends on the actual amount of cupric complex with a coordinated halide ligand $Cu^{II}L_nX$ in the reaction mixture. The lower deactivator concentration leads to increased polydispersity of the polymers produced, according to a relationship, first derived for the case of living ionic polymerization,[46,47] which was later[48] modified to describe the somewhat simpler case of living radical polymerization, and finally generalized for all polymerizations involving exchange reactions:[49]

$$\mathrm{PDI} = \frac{M_w}{M_n} = 1 + \left(\frac{k_p[RX]_0}{k_{deact}[Cu^{II}L_nX]}\right)\left(\frac{2}{\rho} - 1\right) \tag{5}$$

In the above equation ρ is the monomer conversion.

In summary, the rate constants k_{act} and k_{deact} (and therefore the equilibrium constant K_{ATRP}) as well as the deactivator concentration $[Cu^{II}L_nX]$, which determine the ATRP rate and the degree of control over polymerization, depend on the reaction medium composition. This is, at least in part, due to the influence of the solvent composition on the value of K_X. The following sections are dedicated to the quantitative description of the formation of the ATRP deactivator and to K_X determination in various protic solvents. In all studied systems the ligand L was 2,2′-bipyridine (bpy).

Quantitative Description of the Complex Equilibria Taking Place in ATRP Systems. The Importance of the Halogenophilicity of the Higher Oxidation State Metal Complex. The formation of a complex containing j coordinated ligands L is described by the stepwise $K_{j,L}$ or the overall $\beta_{j,L}$ stability constants (with $\beta_{n,L} = K_{1,L} \times K_{2,L} \times ... \times K_{n,L}$).[50,51] To simplify the mathematical expressions, the index j is herein omitted when it is unity. Since the Cu^{II} monohalide complex containing two bpy ligands $Cu^{II}(bpy)_2X$ is the actual ATRP deactivator, its reversible formation characterized by the equilibrium constant K_X (eq 6) is of particular interest.

$$Cu^{II}(bpy)_2 + X \rightleftarrows Cu^{II}(bpy)_2X$$

$$K_X = \frac{[Cu^{II}(bpy)_2X]}{[Cu^{II}(bpy)_2][X]} \tag{6}$$

Note that the charges are omitted and X in eq 6 is a halide ion. As a result of earlier studies on the complex equilibria in the ternary Cu^{II}−bromide−bpy system,[52] the presence of Cu^{II} complexes with zero, one, or three coordinated bpy molecules can be neglected within the concentration ranges of ligand used (0.04−0.08 M bpy). On the basis of the same work, stability constants such as $K_{2,X}(Cu^{II}(bpy)_2X_2)$, etc., describing the formation of polyhalide cupric complexes, are not considered here. In other words, it is assumed that all Cu^{II}-containing species present in the reaction mixture contain two bpy ligands and can coordinate a maximum of one halide or other monodentate ligand. In any reaction medium, some part of the $Cu^{II}(bpy)_2X$ complex formed in the ATRP equilibrium during the polymerization reaction or added initially to the reaction mixture dissociates forming $Cu^{II}(bpy)_2$, which cannot deactivate radicals. The percent of dissociated or "lost" deactivator can be correlated with K_X and with the total concentration of Cu^{II}-containing species in the system. For this purpose, it is assumed that initially all Cu^{II} is in the form of $Cu^{II}(bpy)_2X$, and therefore the total concentration of Cu^{II} is $[Cu^{II}]_{tot} = [Cu^{II}(bpy)_2X]_0$. The equilibrium (6) is quickly established and $[Cu^{II}]_{tot} = [Cu^{II}(bpy)_2X] + [Cu^{II}(bpy)_2]$, with $[Cu^{II}(bpy)_2]$ being the concentration of dissociated deactivator. From (6)

$$K_X = \frac{[Cu^{II}]_{tot} - [Cu^{II}(bpy)_2]}{[Cu^{II}(bpy)_2][X]} = \frac{[Cu^{II}]_{tot} - [Cu^{II}(bpy)_2]}{[Cu^{II}(bpy)_2]^2} \tag{7}$$

The percent of "lost" deactivator, i.e., dissociated Cu^{II}−X bonds, is obtained by solving the quadratic equation (7) with respect to $[Cu^{II}(bpy)_2]$:

$$\frac{[Cu^{II}(bpy)_2]}{[Cu^{II}]_{tot}} \times 100 = \frac{-1 + \sqrt{1 + 4K_X[Cu^{II}]_{tot}}}{2K_X[Cu^{II}]_{tot}} \times 100 \tag{8}$$

The remaining deactivator is therefore given by

$$\frac{[Cu^{II}(bpy)_2X]}{[Cu^{II}]_{tot}} \times 100 = \frac{2K_X[Cu^{II}]_{tot} + 1 - \sqrt{1 + 4K_X[Cu^{II}]_{tot}}}{2K_X[Cu^{II}]_{tot}} \times 100 \tag{9}$$

The impact of K_X on the concentration distribution is evident from eqs 8 and 9: at $[Cu^{II}(bpy)_2X]_0 = 0.01$ M (typical concentration in ATRP systems), only about 3%

of the deactivator is “lost” due to dissociation in a solvent in which $K_X = 10^5$, 27% when $K_X = 10^3$, and as much as 92% for the case when $K_X = 10$. The K_X values in aprotic solvents (hydrocarbons, ethers, ketones, DMF, etc.) are of the order of 10^4-10^5,[52] meaning that deactivator loss via dissociation is insignificant in ATRP reactions in such solvents. However, in polar protic solvents, such as alcohols or water, where the values of K_X are of the order of $10-10^3$ (vide infra), the dissociation of the $Cu^{II}L_nX$ complex becomes pronounced. The relationship (9) is plotted in Figure 2 for the values of K_X determined experimentally in various methanol−water mixtures.

For the general case when the concentrations of $[Cu^{II}(bpy)_2]$ and X are not equal, the concentration of the remaining, nondissociated, deactivator, which participates in the deactivation process (see Scheme 1 and eq 4), can also be determined from eq 6:

$$K_X = \frac{[Cu^{II}(bpy)_2X]}{([Cu^{II}]_{tot} - [Cu^{II}(bpy)_2X])[X]} \tag{10}$$

$$[Cu^{II}(bpy)_2X] = \frac{K_X[Cu^{II}]_{tot}[X]}{1 + K_X[X]} \tag{11}$$

Inserting eq 11 into eq 4, one obtains an expression for the rate of deactivation in an ATRP system in which the deactivator dissociation is taken into consideration:

$$R_{deact} = k_{deact}[R^{\bullet}]\frac{K_X[Cu^{II}]_{tot}[X]}{1 + K_X[X]} \tag{12}$$

Equations 11 and 12 are not convenient to use because the concentration of free, noncoordinated, halide ions is generally unknown. It is more useful to determine the dependence of $[Cu^{II}(bpy)_2X]$ and R_{deact} on the total concentrations $[Cu^{II}]_{tot}$ and $[X]_{tot}$, which can be done by solving a quadratic equation. Assume a $Cu^{II}(bpy)_2$ compound (not necessarily with a coordinated halide ligand, with a total concentration of $[Cu^{II}]_{tot}$) and a halide (total concentration $[X]_{tot}$) are mixed. After formation of the complex $Cu^{II}(bpy)_2X$, the concentration of $Cu^{II}(bpy)_2$ that cannot deactivate radicals will be $[Cu^{II}(bpy)_2] = [Cu^{II}]_{tot} - [Cu^{II}(bpy)_2X]$. The concentration of free halide will be $[X] = [X]_{tot} - [Cu^{II}(bpy)_2X]$. If these expressions are inserted into (6), a quadratic equation is obtained which can be solved for $[Cu^{II}(bpy)_2X]$:

$$[Cu^{II}(bpy)_2X] = \frac{F - \sqrt{F^2 - 4{K_X}^2[Cu^{II}]_{tot}[X]_{tot}}}{2K_X} \qquad (F \equiv 1 + K_X[Cu^{II}]_{tot} + K_X[X]_{tot}) \tag{13}$$

The relationship (13) is plotted in Figure 1a for several values of the stability constant K_X, where $[X]_{tot}$ is varied at a fixed $[Cu^{II}]_{tot}$. For stable Cu^{II} monohalide complexes ($K_X > 1000$, which is the case for most ATRP reactions in aprotic solvents), the deactivator concentration is very close to this of the total Cu^{II} species present in solution. However, if the value of K_X is of the order of $10-10^3$ (protic solvents), only the addition of large amounts of halide ensures sufficient concentration of the deactivator $Cu^{II}(bpy)_2X$. In other words, for achieving a well-controlled polymerization in protic media, an excess halide salts is required to “regenerate” the dissociated deactivator. The deactivator dissociation is concentration-dependent, as other similar equilibria.[51] Equation 13 and Figure 1b show that for a given reaction mixture composition (fixed K_X) the more dilute the system with respect to the deactivator, the larger percent of it is in the dissociated, inactive, form. Therefore, larger excess of halide vs $[Cu^{II}]_{tot}$ should be added to form a sufficient amount of deactivator in more dilute with respect to Cu^{II} systems.

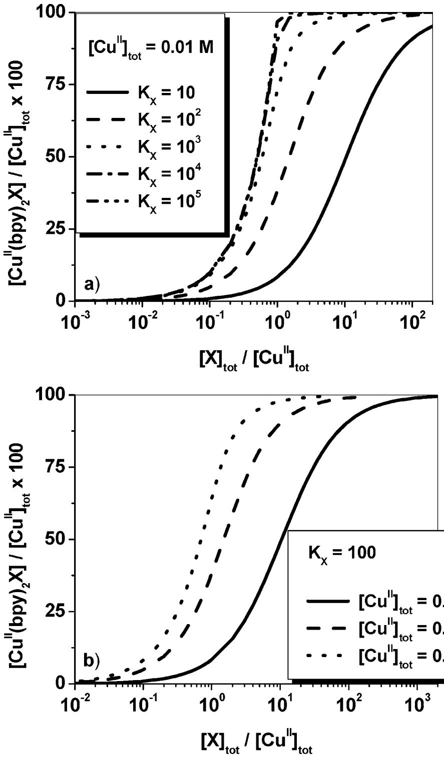


Figure 1. Relationship between concentration of $[Cu^{II}(bpy)_2X]$ and “excess” of X vs Cu^{II} for (a) fixed $[Cu^{II}]_{tot}$ = 0.01 M and variable K_X or (b) fixed stability of the complex $K_X = 100$ and various values of $[Cu^{II}]_{tot}$.

Table 1. Association Constants of $[Cu^{II}(bpy)_2]^{2+}$ with X^- (X = Br or Cl) in Protic Media Determined Spectrophotometrically at 896 nm[a]

H_2O/MeOH (v/v)	$[H_2O]$, M	K_{Br}	K_{Cl}
0/100	0	4710 ± 523 (3)	4478 ± 108 (2)
10/90	5.6	826 ± 11 (3)	884 ± 25 (4)
15/85	8.3	486 ± 41 (4)	532 ± 48 (4)
25/75	13.9	186 ± 30 (7)	234 ± 15 (5)
35/65	19.4	84 ± 7 (7)	144 ± 15 (5)
50/50	27.8	29 ± 6 (8)	52 ± 4 (5)

[a] The number in parentheses after each value of K_X (X = Br or Cl) indicates the number of spectra used for the calculation of the association constant.

Experimental Determination of Halogenophilicity in Protic Solvents. The halogenophilicity values in several different solvent mixtures for both bromide and chloride are listed in Table 1. The halogenophilicity of the bromide-based deactivating complex is decreased by a factor of 44 upon changing the solvent from DMF ($K_{Br} = 2.09 \times 10^5$)[52] to methanol. An additional 162-fold decrease is observed when 50 vol % of water is added to the methanol. Using eq 8, it can be calculated that for initial deactivator concentration $[Cu^{II}(bpy)_2Br]_0$ = 0.01 M, about 2% of the deactivator is dissociated in DMF, 12% in methanol, but as much as 79% in a 1:1 mixture of water and methanol. The percent of remaining deactivator $[Cu^{II}(bpy)_2Br]$ as a function of its initial

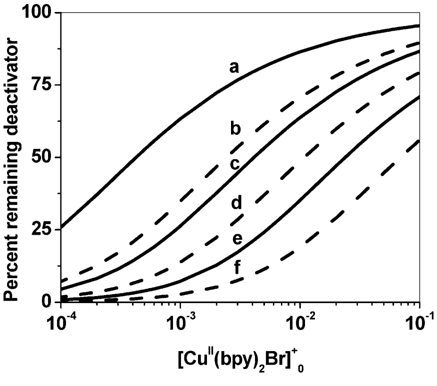


Figure 2. Relationship between the percent of remaining after dissociation deactivator and its initial concentration $[Cu^{II}(bpy)_2Br]_0 = [Cu^{II}]_{tot}$ in (a) methanol ($K_{Br} = 4700$) and mixtures of methanol and water containing varying amounts of water: (b) 10 vol % ($K_{Br} = 826$), (c) 15 vol % ($K_{Br} = 486$), (d) 25 vol % ($K_{Br} = 186$), (e) 35 vol % ($K_{Br} = 84$), and (f) 50 vol % ($K_{Br} = 29$).

concentration is plotted in Figure 2 for six protic solvent compositions (eq 9).

Solvent and ligand exchange reactions at a Cu^{II} center are characterized by large rate constants of the order of 10^4–10^9 s^{-1}.[53–56] Thus, because of the rapid association/dissociation equilibria of Cu^{II} complexes, the calculated concentration distributions of Cu^{II} species are most likely reached within the time scale of the polymerizations.

The stability of the Cu^{II}–halide complex in solvents containing increasing amounts of water decreases due to the strong aquation of both products of dissociation of $[Cu^{II}(bpy)_2X]$, namely $[Cu^{II}(bpy)_2]$ and X (bottom of Scheme 1). On one hand, a water molecule can coordinate to $[Cu^{II}(bpy)_2]$, forming the complex with a pentacoordinated central ion $[Cu^{II}(bpy)_2(H_2O)]$. Indeed, the crystal structures of pentacoordinated Cu^{II} complexes containing one water molecule and two bpy[57,58] or the similar 1,10-phenanthroline[59,60] ligands have been reported. The Cu^{2+} ion forms several aqua complexes, and the formation constant of the first of them, $Cu(H_2O)^{2+}$, has been determined, $K_{aq}(Cu(H_2O)^{2+}) = 4.17$.[61] On the other hand, water has a strong affinity toward halide ions, and the formation of halide hydrates with up to four water molecules has been studied.[44] Using the concept of conditional stability constants K_X^*, introduced by Schwarzenbach[62] and widely employed in coordination chemistry,[50] it can be shown that the dependence of $(K_X - K_X^*)/K_X^*$ on the concentration of the reactive solvent such as water has the polynomial form

$$\frac{K_X - K_X^*}{K_X^*} = K_{Cu,aq}\sum_{i=0}^{m} K_{X,aq,i}[H_2O]^{i+1} + \sum_{j=1}^{m} K_{X,aq,j}[H_2O]^{j} \quad (14)$$

The asterisk denotes the conditional stability constant in a solvent in which side reactions such as coordination or strong solvation are possible, and K_X is the stability constant measured in a "reference" solvent. The meaning of the symbols is apparent from Scheme 1. Equation 14 can be used to predict the value of the halogenophilicity in a solvent of any composition, provided that $K_{Cu,aq}$, which describes the formation of the monoaqua complex $[Cu^{II}L_n(H_2O)]$, is known. The gas-phase values of $K_{aq,j}(X)$ ($j = 1, ..., 4$) have been experimentally determined.[44] Consequently, the rate of deactivation can be directly correlated to the concentration of water in any aqueous water-based mixed solvent. For this purpose, the value of K_X^* should be inserted in eq 13 instead of K_X, which in turn is used to calculate R_{deact} or PDI according to eqs 4 and 5, respectively. Note that even though water might be weakly coordinating compound, it is present at large concentration resulting in a low K_X^*.

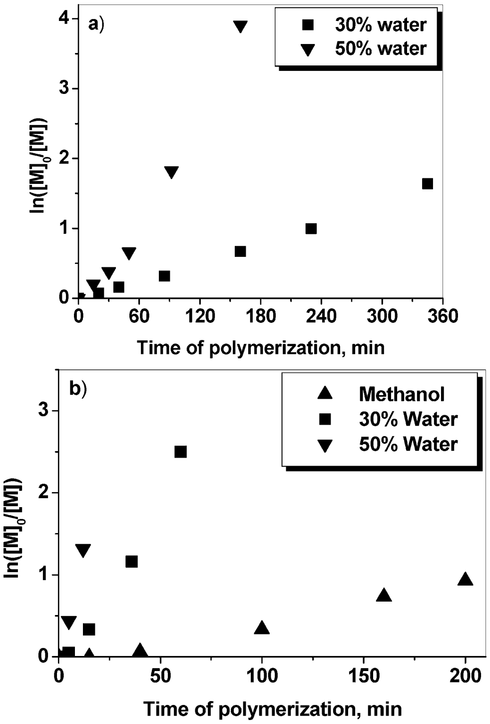


Figure 3. Kinetics (by gravimetry) of the ATRP of HEMA in methanol and water–methanol mixtures containing varying amounts of water (volume percent in the solvent is given in the figures) at (a) 35 °C using chloride-based catalyst (40% CuCl + 60% $CuCl_2$/bpy) and (b) 25 °C using bromide-based catalyst (70% CuBr + 30% $CuBr_2$/bpy). Conditions: $[HEMA]_0$:$[MePEOBiB]_0$:$[Cu]_{tot}$:[bpy] = 100:1:1:2; volume ratio HEMA: solvent = 1:1.

Role of Solvent Composition upon Rates and Degree of Polymerization Control. The validity of the theoretical description provided above was tested for several ATRP systems in protic media. The reversible dissociation of halide ligands from the ATRP deactivator in protic solvents can account to a large extent for the fast polymerizations when water is used as the (co)solvent for copper-mediated ATRP. This is illustrated in Figure 3, which shows the kinetic results for the polymerization of HEMA (the targeted DP at complete monomer conversion was 100) in two different mixtures of water and methanol (1:1 and 1:2.3 by volume), as well as in pure methanol using either copper chloride- or bromide-based ATRP catalysts. The results are in broad agreement with those reported by Armes and co-workers,[28] who studied the ATRP of HEMA targeting lower DP (30–75) in water–methanol (1:1 by volume) and methanol.

The polymers obtained in the ATRP of HEMA using CuBr with 30% of $CuBr_2$/bpy-based catalyst (the systems in Figure 3b) had polydispersities in the range of 1.4–1.5 (at 28–60% conversions) when pure methanol was employed as the solvent and of 1.6–2.1 (at 36–99%

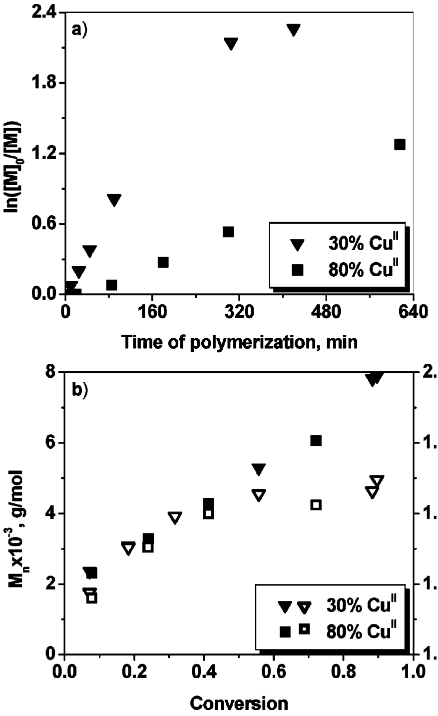


Figure 4. ATRP of DMAEMA in water–methanol (1:2 by volume) at 25 °C at two different concentrations of deactivator: (a) kinetics and (b) evolution of molecular weight (closed symbols) and polydispersity (open symbols) with conversion. $[DMAEMA]_0$:$[MePEOBiB]_0$:$[Cu]_{tot}$:[bpy] = 100:1:1:2; volume ratio DMAEMA:solvent = 1:1. The molecular weight at 0% monomer conversion corresponds to the molecular weight of the PEO-based macroinitiator.

conversions) with methanol–water (1:1 by volume). This is in agreement with eqs 5 and 13.

Influence of the Initial Deactivator Concentration on the Rates and Control over Polymerization in ATRP in Protic Media. To prepare well-defined polymeric materials using copper-mediated ATRP in an aqueous system, R_{deact} should be sufficiently large. This can be accomplished by employing ATRP catalyst containing relatively large initial amount of Cu^{II}, which would ensure the presence of sufficient concentration of deactivator even after its dissociation in the protic solvent (Figure 1b). ATRP in nonaqueous solvents is very slow or even stops in the presence of high concentrations of Cu^{II} complexes.[63] However, it was reported[18] that relatively fast ATRP reactions can be carried out in homogeneous aqueous media even in the presence of large amounts of the deactivating Cu^{II} species. This phenomenon can now be explained in light of the theory presented above: a significant part of the initially added ATRP deactivator is dissociated in the protic solvent. The degree of dissociation or solvolysis can be calculated from eq 8 and using the halogenophilicity values from Table 1.

The influence of variable amounts of initially added deactivator on the kinetics and evolution of the molecular weights in the ATRP of DMAEMA was examined, and the results are presented in Figure 4.

Similar results were obtained for the ATRP of HEMA using bromide-based catalysts (Figure 5).

The semilogarithmic kinetic plots do not deviate significantly from linearity, indicating a constant concentration of active species. This indicates that hydrolysis of the alkyl halide initiator and dormant species was relatively slow as compared to the polymerization at ambient temperature. In addition, molecular weights increased in a linear fashion with conversion, confirming that polymerization was living in nature, although with slow exchange due to the insufficient deactivator concentration. The results clearly indicate that addition of deactivator was necessary to achieve good control over the polymerization. With little or no Cu^{II} complex initially added, the reactions were very fast and the polydispersities were high.

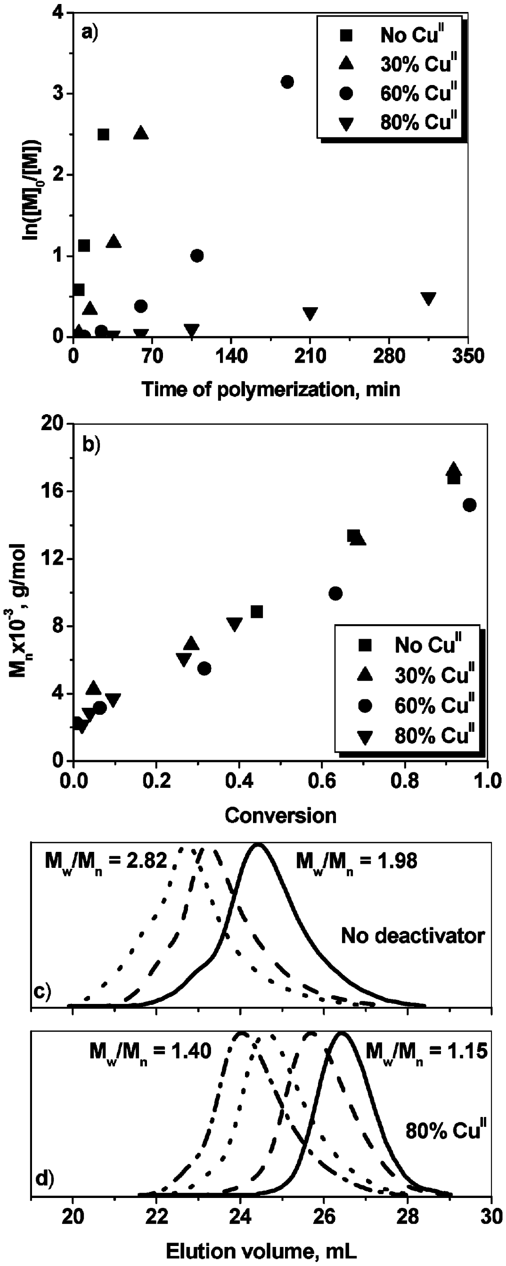


Figure 5. ATRP of HEMA in water–methanol (1:2.3 by volume) at 25 °C at various deactivator concentrations: (a) kinetics, (b) evolution of molecular weights with conversion, (c) evolution of SEC traces for the system containing no added deactivator, and (d) in the presence of 80% of deactivator. The numbers at the SEC traces in (c) and (d) indicate the polydispersities. $[HEMA]_0$:$[MePEOBiB]_0$:$[Cu]_{tot}$:[bpy] = 100:1:1:2; volume ratio HEMA:solvent = 1:1.

Role of Concentration and Nature of the Halide Ion. An alternative way to enhance the deactivation and improve control is to suppress the deactivator dissociation/solvolysis using competitive coordination of halide ligands to the Cu^{II} center by addition of halide salts to

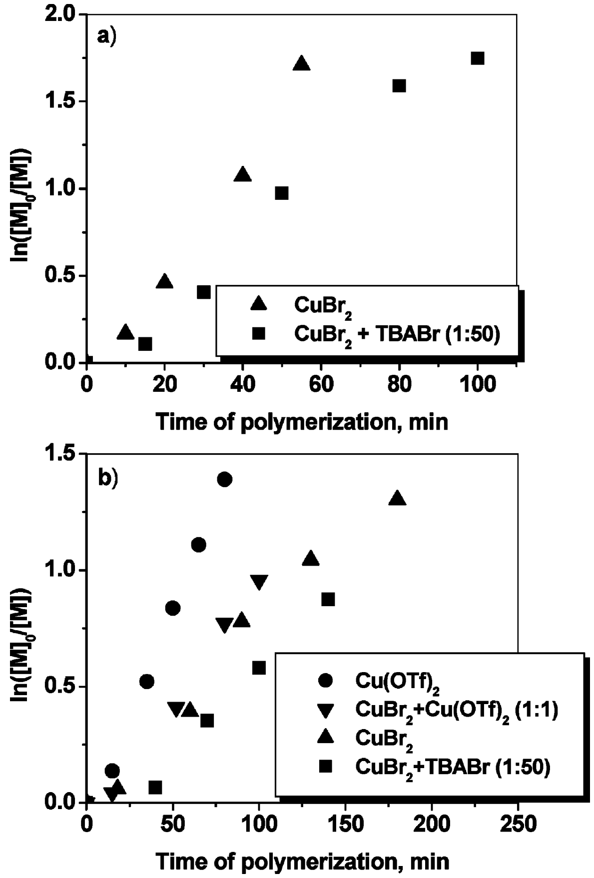


Figure 6. Kinetics (by GC) of ATRP of HEMA in protic media at 30 °C using catalyst containing 60% of deactivator in the presence of variable amounts of bromide ions. $[HEMA]_0$:$[MePEOBiB]_0$:$[Cu]_{tot}$:[bpy] = 100:1:0.5:1; volume ratio HEMA: solvent = 1:1. Amounts of water in the solvent: (a) 25 vol % and (b) 15 vol %.

the polymerizing mixture. Figure 6 shows the semilogarithmic kinetic plots for the ATRP of HEMA in water–methanol (1:2.3) in the presence of copper bromide-based catalyst, containing the same amount of $[Cu^{II}]_{tot}$ but various amounts of bromide ions. The variation of the bromide ion concentration was achieved by using different Cu^{II} salts complexed with bpy: $Cu(CF_3SO_3)_2$ (the only sources of bromide ions were the activator $Cu^I(bpy)_2Br$ and the initiator), a mixture of $Cu(CF_3SO_3)_2$ and $CuBr_2$ (1:1), or only $CuBr_2$. The bromide concentration could be further increased by adding tetrabutylammonium bromide to the catalyst containing $CuBr_2$ as the Cu^{II} source. The polymerization slowed down (i.e., the rate of deactivation increased) in the order of increasing bromide concentration, in agreement with eqs 4 and 13. The polymerization rate could be predicted from the rate of deactivation, which in turn could be evaluated from the concentration of deactivator present. The calculated relative rates of ATRP and the experimental values for the two systems shown in Figure 6 are presented in Table 2. Since the values of K_{ATRP} are solvent-dependent, the relative polymerization rates can be calculated only for a given solvent composition for which K_{ATRP} is constant (neglecting the effect of added salts which in principle can alter its value due to polarity changes). The total concentration of bromide was calculated assuming the activator does not contain any coordinated bromide. Taking into account these approximations, the agreement between theory and experiment is satisfactory.

Table 2. Calculated and Observed Relative Polymerization Rates for the ATRP of HEMA in Two Water–Methanol Mixtures in the Presence of Various Amounts of TBABr[a]

$[H_2O]$, M (vol %)	K_{Br}	$[Br^-]_{tot}$, M	$R_{p,rel}$(exptl)	$R_{p,rel}$(calcd)
8.3 (15)	486	0.6573	1.0	1.0
8.3 (15)	486	0.0373	1.3	1.1
8.3 (15)	486	0.0209	1.6	1.2
8.3 (15)	486	0.0084	2.3	1.9
13.9 (25)	186	0.6573	1.0	1.0
13.9 (25)	186	0.0373	1.4	1.2

[a] $[Cu^{II}]_{tot}$ = 0.0124 M.

Similar conclusions can be drawn from the kinetic results from the ATRP of HEMA in water–methanol (1:1) using a copper chloride-based catalyst, with and without added tetrabutylammonium chloride (Figure 7), the addition of chloride salt suppresses the deactivator hydrolysis, thus decreasing the rate of polymerization and improving the control (Figure 7b).

The influence of halide ion concentration on the rate and control over polymerization has already been demonstrated for the ATRP of quaternized DMAEMA in protic media.[20] In this work we provide more details on the ATRP of TMATf and DMEABr in a 1:1 water–pyridine mixture (Figure 8). The role of pyridine was to suppress the disproportionation of the ATRP catalyst.[20] The polymerization of the bromide counterion-containing monomer was slower and better controlled as compared to this of the monomer with a trifluo-

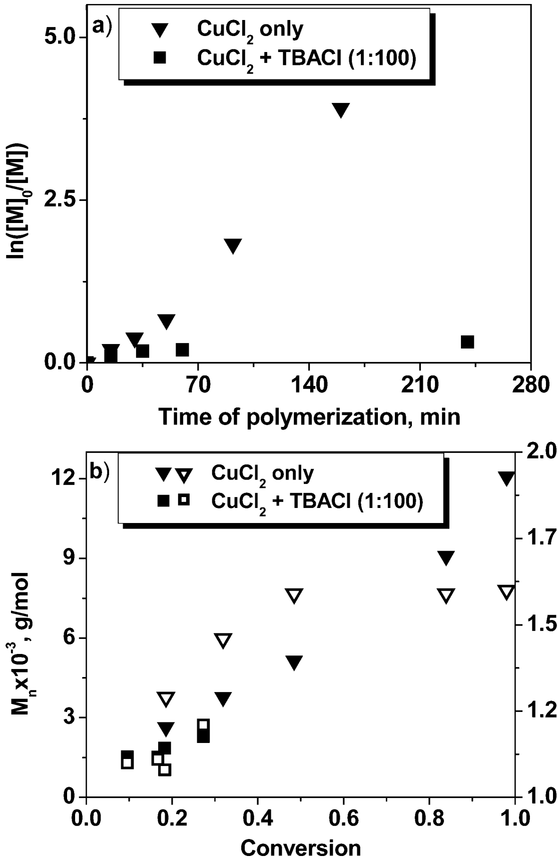


Figure 7. ATRP of HEMA at 35 °C in water–methanol (1:1) using copper chloride complexes of bpy as the ATRP catalyst (40% CuCl + 60% $CuCl_2$/bpy) for two different concentrations of chloride anions: (a) kinetics and (b) evolution of molecular weight (filled symbols) and polydispersity (open symbols) with conversion. $[HEMA]_0$:$[MePEOBiB]_0$:$[Cu]_{tot}$:[bpy] = 100:1:1:2; volume ratio HEMA:solvent = 1:1.

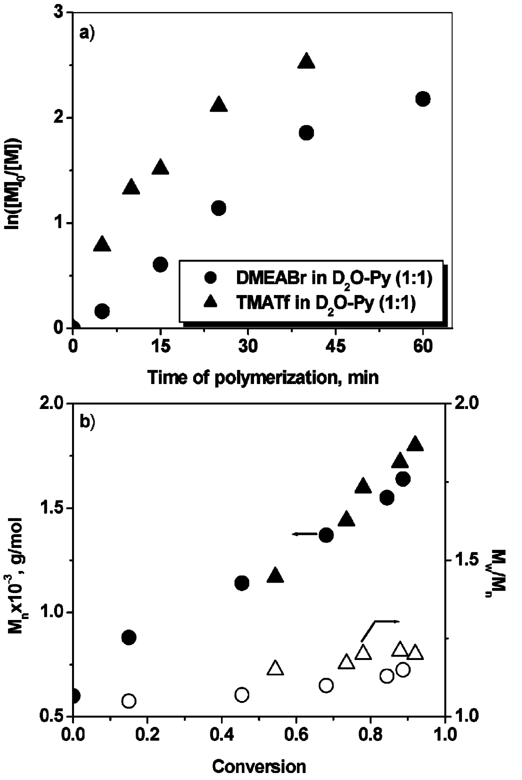


Figure 8. Kinetics (a) and evolution of molecular weights with conversion (b) for the ATRP of DMEABr (circles) and TMATf (triangles) in water–Py (1:1 v/v) at 25 °C using a CuBr + 20% $CuBr_2$/bpy as the catalyst. Targeted (at complete monomer conversion) DP = 100.

romethanesulfonate counterion. The effect of the halide ions was easily observed since they, being counterions of the monomer, were present in a 500-fold excess relative to Cu^{II}. (The targeted degree of polymerization at complete monomer conversion was 100, with a ratio of initiator to total Cu (20% of deactivator) equal to unity.)

Armes et al.[64] have recently shown that the ATRP of DMAEMA quaternized with chloromethane was somewhat slower and better controlled in the presence of sodium chloride (1:1 vs the monomer), although the effect of the addition of extra chloride was not much pronounced. By inspecting Figure 1 and eq 13, this observation can now be clearly understood. The 2-fold increase of the amount of halide (from 30 to 60 equiv vs the total Cu) does not result in a large change of deactivator concentration, although it can still slightly improve the control.

The final issue to be addressed is the importance of the nature of the halide ligand in the ATRP deactivator. Figure 9 shows the evolution of polydispersity with conversion for the aqueous ATRP of HEMA in the presence of four catalytic bpy-containing systems: two of them based on chloride and two on bromide copper complexes (with a fixed amount of deactivator added initially to the polymerizing system—either 0 or 30% of the total copper). In general, the polymerization control in aqueous ATRP was slightly worse with the chloride-based catalyst. Since in a given protic solvent the values of K_X for X = Br or Cl (and therefore those of $[Cu^{II}(bpy)_2X]$, vide supra) are very close, the differences in the observed PDI can be attributed to differences in the values of k_{deact} (see eq 5). Indeed, the deactivation rate constant of 1-phenylethyl radical with $[Cu^{II}(dinonylbpy)_2Br]$ at 75 °C is 2.5×10^7 M^{-1} s^{-1}, which is around 6 times higher than for the chloride-based system ($k_{deact} = 4.3 \times 10^6$ M^{-1} s^{-1}).[65] It is thus expected that the PDI values should be larger in the presence of chloride-based deactivator. It should be noted, however, that the use of chloride catalyst may be advantageous in some cases (basic monomers) since the nucleophilic substitution of chlorine from the polymer chain end is slower than for bromine-based systems and the contribution of this chain-breaking reaction is smaller.

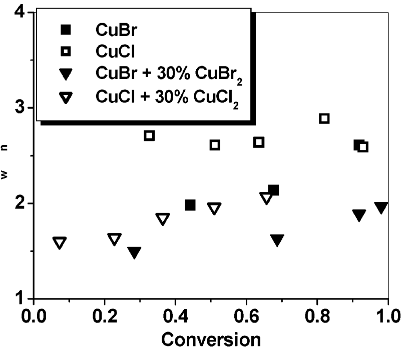


Figure 9. Polydispersity as a function of conversion for polyHEMA prepared by ATRP in water–methanol (1:2.3 by volume) at 25 °C with copper bromide (closed symbols) or copper chloride (open symbols)/bpy-based catalysts. $[HEMA]_0$:$[MePEOBiB]_0$:$[Cu]_{tot}$:[bpy] = 100:1:1:2; volume ratio HEMA: solvent = 1:1.

Using the aforementioned approaches to suppress the deactivator dissociation allows for controlled copper-mediated radical polymerization of water-soluble monomers in aqueous homogeneous media and production of well-defined hydrophilic polymeric materials. To evaluate the chain-end functionality of the synthesized polymers, chain-extension reactions were performed. For instance, a polyHEMA-based macroinitiator (M_n = 3600 g/mol, M_w/M_n = 1.43) was successfully employed for chain extension with DMAEMA at 35 °C in water–methanol (1:2.3) using 70% CuCl + 30% $CuCl_2$/bpy as the catalyst. The conversion reached 43% in 2 h, and the final product had a M_n = 6400 g/mol and M_w/M_n = 1.16. The low polydispersity of the double hydrophilic block copolymer proves the high degree of end-functionalization of the starting macroinitiator and the absence of any significant chain-breaking reactions. It also demonstrates the low polydispersity of the second, polyDMAEMA, block (estimated as 1.11).[66]

Although hydrolytic loss of halide ligand from the deactivator in aqueous ATRP is a major side reaction, as evidenced in the present paper, other interactions of reaction components with water or polar monomers can also contribute to the relatively poor control over the polymerizations. Such reactions include, inter alia, monomer coordination to the copper catalyst, substitution or elimination reactions of the alkyl halide initiators, and dormant chain ends in the presence of water or monomers with nucleophilic or basic groups. It was reported[27] that even relatively stable copper complexes with ligands such as pyridylmethaneimine rapidly decomposed in aqueous solution at higher temperatures (50 °C). Some monomers can participate in side reactions in the course of the polymerization. A recently reported example is the methanolysis of tertiary amine methacrylates producing methyl methacrylate and the corresponding substituted *N,N*-dialkylamino alcohol, which can coordinate to copper ions.[67] In addition, to fully understand the kinetic behavior of the protic-solvent-based ATRP systems, one has to examine the effect of solvent composition on the value of K_{ATRP}. This effect is currently being studied.

Conclusions

A theoretical description and experimental evidence of a significant side reactions taking place in the copper-mediated ATRP in protic media—reversible dissociation and substitution (by a solvent or potentially by a polar monomer molecule) of halide ligand from the deactivating $\mathrm{Cu^{II}}$ complex—are presented. These reactions lead to inefficient deactivation and therefore to faster polymerizations with unsatisfactory control, particularly in the case of aqueous ATRP. The association/dissociation equilibrium between a halide ligand and a $\mathrm{Cu^{II}}$–bpy complex is characterized by the halogenophilicity constant K_{X}. The values of the halogenophilicity for both bromine- and chlorine-based ATRP deactivators were determined spectrophotometrically in methanol and various mixtures of methanol with water. The halogenophilicity in methanol is lower by 1–2 orders of magnitude than in “conventional” aprotic ATRP solvents such as DMF. Additional decrease of K_{X} by about 2 orders of magnitude is observed by changing the solvent from pure methanol to a 1:1 (by volume) mixture of methanol and water. Thus, the degree of deactivator dissociation depends strongly upon the solvent composition (being more pronounced in water-rich solvents). In addition, it is influenced by the total concentrations of $\mathrm{Cu^{II}}$ and halide present in the system. It is shown that the addition of relatively large amounts (up to 80% of the total copper catalyst) of $\mathrm{Cu^{II}}$ halide significantly improves the level of control over polymerization. Furthermore, extra halide salts can be added to the systems in order to suppress the deactivator solvolysis and additionally improve the control over the polymerization. Using these approaches, well-defined hydrophilic homo- and copolymers of 2-hydroxyethyl methacrylate, 2-(*N*,*N*-dimethylamino)ethyl methacrylate, 2-(trimethylammonio)ethyl methacrylate trifluoromethanesulfonate, and 2-(dimethylethylammonio)ethyl methacrylate bromide were prepared by ATRP in aqueous media.

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Supporting Information Available: Electronic spectra of the complex $[\mathrm{Cu^{II}(bpy)_2}](\mathrm{OTf})_2$ in methanol–water mixtures; electronic spectra used for the determination of the halogenophilicity K_{X} (X = Br and Cl) of the complex $[\mathrm{Cu^{II}(bpy)_2}](\mathrm{OTf})_2$ in pure methanol and methanol containing 10, 15, 25, 35, and 50 vol % of water. This material is available free of charge via the Internet at http://pubs.acs.org.

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