Effect of Water on Copper Mediated Living Radical Polymerization

*Sébastien Perrier, David M. Haddleton**

Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK
D.M.Haddleton@warwick.ac.uk

Summary: The use of water as a solvent for copper mediated living radical polymerization has been further investigated. Optimal conditions for effective living radical polymerization using catalyst complexes based on CuBr and N-(n-alkyl)-2-pyridylmethanimine ligands were found, leading to well defined polymer structures. The effect of water on the rate of polymerization was studied, and it was found that competitive complexation of ligand and water occurs at copper in addition to an enhanced polymerization rate on increasing the polarity of the medium.

Introduction

Since its inception in 1995 transition metal mediated living radical polymerization has been used extensively for the synthesis of polymers with well-defined molecular weight and architecture.[1,2] The exact nature of the active catalyst is not very well understood and might well vary between different metals and indeed even between similar and related ligands with the same metal based catalysts.[3] The nature of the solvent in transition metal mediated living radical polymerization obviously plays an important role. For example, THF is an excellent co-ordinating solvent whereas 2-propanol,[4] DMF,[5] ethylene or propylene carbonate,[6] diethyl ether[6] and 1,2-diethoxy ethane[7] enhance the rate of polymerization.

Water was first introduced in a transition metal living radical polymerization system by Sawamoto and co-workers who found that upon addition of a small amount of water (10 equiv. to the initiator) at about 45% conversion of the polymerization, no effect was observed and the polymerization continued with an apparent living character.[8] The very first aqueous copper mediated living radical polymerization was realized by Matyjaszewski *et al.*, with the polymerization of 2-hydroxyethyl acrylate in presence of Cu(I)Br / 2-2'-bipyridine (bpy) carried out in water at 90°C. [9] High conversion (87%) was achieved after 12 h at 90°C in an aqueous medium (50 vol. %),

 CCC 1022-1360/00/$ 17.50+.50/0

with a final product of M_n = 14,700 and PDI = 1.34. Armes *et al.* investigated different hydrophilic monomers for copper mediated living radical polymerization based on a Cu(I)X / bpy catalyst complex (X = Br for styrene-like monomers or X = Cl for methacrylates). Polymerization of Poly(ethylene glycol) methacrylate,[11] sodium 4-vinylbenzoate,[12] carboxybetaine[13] and 2-(N-morpholino) ethyl methacrylate[14] monomers using various initiators at room temperature showed characteristics of effective living polymerization. Furthermore, in the case of Poly(ethylene glycol) methacrylate and sodium 4-vinylbenzoate, a conversion of 99% was reached in less than 1 h, whilst when using 2-(N-morpholino) ethyl methacrylate and Cu(I)Br, 99% conversion was obtained after 20 minutes with PDI = 1.20.[14]

However, more difficulties were encountered when such system was applied to sodium methacrylate,[10] leading to final products with polydispersity indices of 1.20-1.30 with a slower polymerization rate (70-80% conversion in 10 h). Acrylamide has also been investigated by Rademacher *et al.* who reported a mixture H_2O / DMF in a ratio 9/1 (v/v) as solvent for the polymerization of N, N-dimethylacrylamide in presence of Cu(I)Br and various ligands (hexamethyltriethylenetetraamine (HMTETA), Tris[2-(dimethylamino)ethyl]-amine (Me_6-TREN) and 1,4,8,11-Tetramethyl-1,4,8,11-tetraazacyclotetradecane (Me_4Cyclam)). Polymerization occurred in less than one minute, but no control over the polymer structure was achieved. More recently, a mixture of water / methanol was successfully used by Armes's group to carry out the polymerization of 2-hydroxyethyl methacrylate, more success was achieved with Cu(I)Br / bpy in comparison to Cu(I)Cl / bpy.[15] A conversion of 99% was obtained in 1 h at ambient temperature with the final product showing polydispersities of approximately 1.20-1.30.

Our group has been investigating the effect of polar solvents on the copper mediated polymerization of methacrylate catalysed by a Cu(I)Br/N-(n-alkyl)-2-pyridylmethanimine ligand complex.[7] Polar solvents have been found to increase the polymerization rate, possibly due to the combined effect of a decrease in the necessary energy for the breaking of the C-Br bond and competitive coordination of solvent and ligand on the copper species. These observations were confirmed by the study of Chambard *et al.* who reported the positive effect of solvent polarity on the

k_{act} during the copper mediated living radical polymerization of butyl acrylate.[16a, 16b] Water is a highly polar coordinating solvent, which invariably enhances the rate of copper, mediated polymerization. Polarity effects are also evoked by these observations for various aspects of the mechanism and transition-states.

In this present study, we have investigated the effect of water on the copper mediated living radical polymerization of methacrylates. In order to compare these findings with previous results obtained in other solvents, α-Methoxy poly(ethylene oxide)methacrylate was chosen as the model monomer with Cu(I)Br and N-(n-propyl)-2-pyridylmethanimine ligand as catalyst.

Experimental Part

General procedures

Experiments were carried out using standard Schlenk techniques under an inert atmosphere of nitrogen. NMR spectra were recorded on a Bruker AC400 spectrometer. Online ^{1}H NMR measurements to monitor the polymerizations were carried out under a nitrogen atmosphere using Young's tap modified NMR tubes with D_2O as a locking agent. Long relaxation delays (5 s) and low spin angles (<15°) were applied to give quantitative results. Molar mass distributions were measured using size exclusion chromatography (SEC) at ambient temperature, on a system equipped with a guard column and one 3 μm mixed E column (Polymer Laboratories) with differential refractive index detection using tetrahydrofuran as eluent, at a flow rate of 1 mL min^{-1}. Poly(MMA) standards in the range (200 to 6 × 104 g mol^{-1}) were used for specific calibration.

Reagents

N-(*n*-Alkyl)-2-pyridylmethanimine, (**3**)[3] and 1,2-dihydroxypropane-3-oxy-(2-bromo-2-methylpropionyl) (**1**)[17] were synthesized as previously reported and stored under anhydrous conditions prior to use. Copper(I) bromide (Aldrich, 98%) was purified according to the method of Keller and Wycoff.[18] α-Methoxy poly(ethylene oxide)methacrylate (poly(ethylene glycol) methyl ether methacrylate, MeO(PEG)MA) with an M_n = ca. 475 was obtained from Aldrich inhibited with 100 ppm monomethyl ether hydroquinone (MeHQ) and 300 ppm butylated hydroxytoluene (BHT) and used without further purification. D_2O (99.9% at.%D, GOSS Scientific Instrument Ltd.), copper(II) bromide (99%, Aldrich) were used as

received. All other reagents and solvents were obtained from Aldrich at the highest purity available and used without further purification.

Stability of the catalyst complex in aqueous solution

Cu(I)Br and where appropriate Cu(II)Br were placed in a Schlenk tube under a nitrogen atmosphere. *N*-(n-Propyl)-2-pyridylmethanimine ligand, **3**, was added (2 mol equiv. to Cu(I)Br). Deoxygenated D_2O was added under nitrogen and the solution was stirred for 5 min. Once the medium was homogeneous, 1 ml of the solution was transferred to a Young's tap modified NMR tube at ambient temperature, time t = 0 was taken once the tube was at the reaction temperature in the NMR spectrometer.

Typical polymerization procedure for poly[poly(ethylene glycol) methyl ether methacrylate] with a targeted degree of polymerization (DP_{Theo} = 10) and a ratio M / I / Cu / Ligand = 10 / 1 / 1 / 3

CuBr (0.0589 g, 0.412 mmol) was placed in a Schlenk tube under a nitrogen atmosphere. Deoxygenated *N*-(n-propyl)-2-pyridylmethanimine ligand (3 mol equiv. to CuBr, 1.24 mmol, 0.190 mL) was added, followed by deoxygenated water (2 g). The solution was heated for 5 min at 40°C, to ensure the dissolution of the complex in water. MeO(PEG)MA (2.00 g, 4.12 mmol), and 1,2-dihydroxypropane-3-oxy-(2-bromo-2-methylpropionyl) initiator (0.412 mmol, 0.0993 g) were mixed separately and deoxygenated by three freeze-pump-thaw cycles. Finally a solution of macromonomer and initiator was injected into the catalyst solution and the Schlenk tube immersed in a thermostated water bath (time = 0). Samples for analysis of the MMD and monomer conversion were taken at different intervals throughout the reaction.

When using a mixture of (Cu(I) / Cu(II) = 90/10, 50/50, 10/90 mole%) the quantity of Cu(I) and Cu(II) were modified keeping the overall quantity of copper(X) bromide = 0.412 mmol. When a lower concentration of copper was used, a stock solution in water was prepared prior to use.

Typical polymerization followed by ^1H NMR

For the reactions monitored by on-line ^1H NMR, the procedure was essentially the same as above but replacing H_2O by D_2O. An aliquot of 1 ml of the solution was transferred to a Young's tap modified NMR tube, time t = 0 was taken once the tube was at the reaction temperature in the NMR spectrometer.

Results and Discussion

Stability of the catalyst complex in water

As the synthesis of *N*-(n-alkyl)-2-pyridylmethanimine ligands involves a condensation reaction with evolution of water,[3] one might expect their hydrolysis when used in polymerizations in the presence of water. Therefore, before undertaking any polymerizations, the stability of the ligand and the catalyst complex in presence of water needed to be investigated. When varying the alkyl chain length of the ligand, *N*-(n-alkyl)-2-pyridylmethanimine with alkyl chains of more than three carbons were found to give a non water-miscible catalyst complex. When the number of carbon on the alkyl chain was reduced to 3 or 2, the solution appeared homogeneous, showing a characteristic dark brown color of the Cu(I)Br / *N*-(n-alkyl)-2-pyridylmethanimine complex. As the previous polymerizations of MeO(PEG)-MA were undertaken using either octyl or propyl ligand,[7] the latter was chosen for further investigation.

In order to investigate the catalyst stability under polymerization conditions, the copper complex was formed in a ratio Cu(I)Br / **3** = 1/2 in D_2O under an inert atmosphere in a Young's tap modified NMR tube. Spectra were recorded every 15 minutes over 48 h, at different temperatures. At 25°C, no change was observed in the NMR spectra of the complex (Figure 1). This is good evidence that the ligands stay complexed to the copper catalyst. In order to test the influence of the concentration, the amount of complex was reduced even further and Cu(II)Br was introduced in an attempt to reduce the rate of polymerization. Even in the extreme case of a complex formed with Cu(I)Br / Cu(II)Br = 1/9 and a concentration of copper (Cu(I) + Cu(II)) reduced by 100 with respect to the *normal* polymerization concentration, no free ligand evolution was observed by ^{1}H NMR.

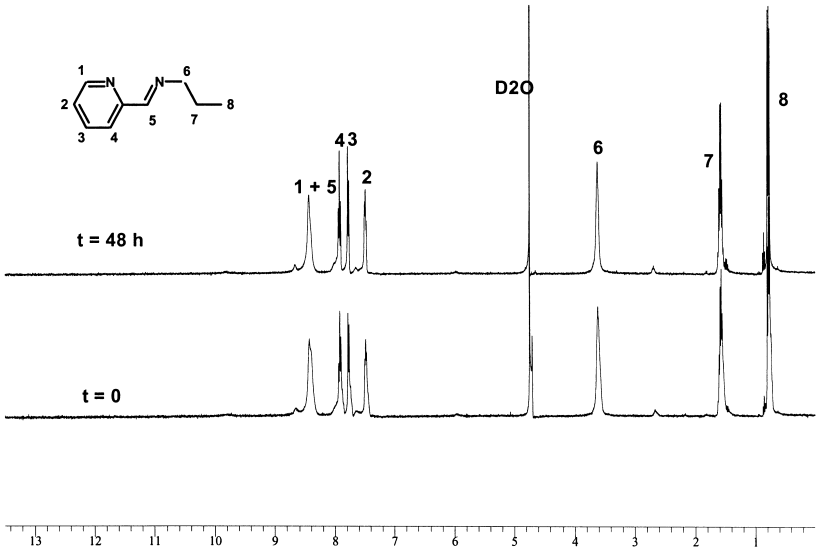

Figure 1. Selection of the ^{1}H NMR (400 MHz) spectra of bis(*N*-(*n*-propyl)-2-pyridylmethanimine)copper(I) complex in D_2O as prepared and after 48 hours at 25°C under nitrogen.

An increase in the temperature to 50°C results in complex decomposition after approximately 1 h, releasing free ligand after 100 min. Free ligand was not hydrolyzed with an absence of a signal from an aldehyde proton at lower field (Figure 2).

After 100 min, when there is no signal from complexed ligand, a red-orange precipitate was observed and the solution turned slightly blue. As Cu(I) is not stable in aqueous solution undergoing disproportionation into Cu(0) (precipitate) and Cu(II), which forms the ion $Cu(H_2O)_6^{2+}$ (blue).[19] This disproportionation is thought to occur following the ligand displacement by water, giving the thermodynamic product. At 25°C, the kinetic driving force is insufficient to displace bidentate imine ligands by water molecules. Thus it is important to carry out all the polymerization reactions below the decomposition temperature and 25°C was arbitrarily chosen as the reaction temperature for the remainder of the study.

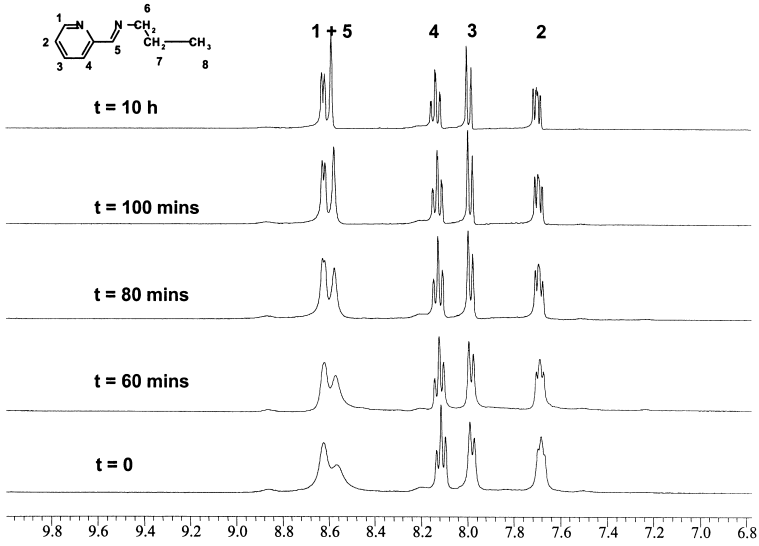

Figure 2. Selection of the ^{1}H NMR (400 MHz) spectra of bis(*N*-(*n*-propyl)-2-pyridylmethanimine)copper(I) complex in D_2O as a function of time on leaving at 50°C under nitrogen in a Young's tap NMR tube. Expansion of the aromatic region.

Polymerization of MeO(PEG)-MA in aqueous solution

Polymerization of MeO(PEG)-MA was first carried out using our typical polymerization conditions,[3] using Cu(I)Br / *N*-(n-propyl)-2-pyridylmethanimine ligand in a ratio 1/3 as catalyst and 1,2-dihydroxypropane-3-oxy-(2-bromo-2-methylpropionyl) as water-soluble initiator (Figure 3).

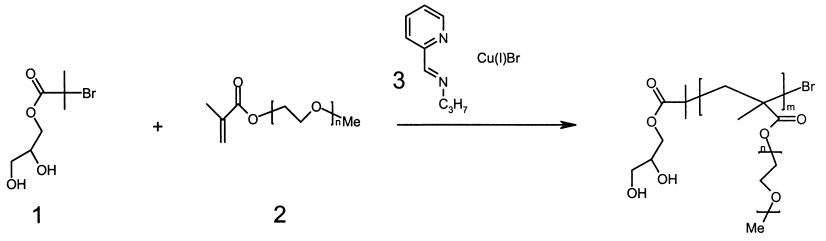

Figure 3. Polymerization of α-methoxy ω–methacryloyl poly(ethyleneoxy) (MeOPEG-MA) using 1,2-dihydroxypropane-3-oxy-(2-bromo-2-methylpropionyl) as a water-soluble initiator mediated by CuBr / *N*-(*n*-propyl)-2-pyridylmethanimine.

Polymerization was followed by ^{1}H NMR, as previously reported,[7] using D_2O as solvent. Samples were taken from the normal reactor in parallel to the NMR experiment in order to follow the evolution of the apparent molecular weight by PMMA calibrated SEC. When using a ratio M / (**1**) / Cu(I)Br / (**3**) = 10 / 1 / 1/ 3, in 50% w/w D_2O, 100% conversion were achieved in less than 5 min. As expected from such a rapid polymerization, no control was gained over the final product properties, and SEC analysis indicated a relatively broad mass distribution, with a tail to high mass (PDI = 1.40, see figure 4).

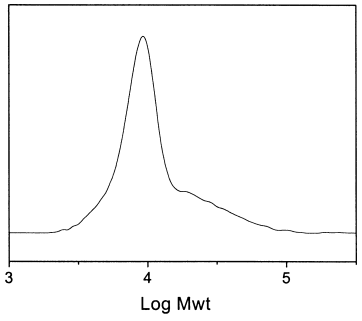

Figure 4. Mass distribution of the product of the polymerization of MeOPEG-MA in D_2O at [M] / [**1**] / [CuBr] / [**3**] = 10 / 1 / 1 / 3, 50% w/w -% monomer with respect to D_2O (100% conversion in less than 5 minutes).

This SEC trace can be explained by the rapid formation of active species in solution, which undergo uncontrolled polymerization (see the tail towards high molecular weight). After a few minutes, when the equilibrium between Cu(I) and Cu(II) is stabilized, controlled polymerization is achieved, as shown by the narrow peak observed for lower molecular weights species. Therefore the introduction of some Cu(II) species at the very beginning of the reaction acts as a deactivator, slowing the overall polymerization and avoiding uncontrolled reactions. Different ratios of Cu(I)Br / Cu(II)Br were investigated and Cu(I) / Cu(II) = 50 mol. % was found to give the optimum results with 100% conversion achieved in approximately 1 h, leading to a product with a molecular weight close to the theoretical with a polydispersity index = 1.10. When using a ratio Cu(I) / Cu(II) = 10/90, effective polymerization was still obtained, reaching 100% conversion in 20 h, with a final PDI

= 1.15, and M_n close to that expected. In order to test the influence of the catalyst, the overall concentration of copper was reduced, keeping the same ratio Cu(I) / Cu(II). On reduction of the copper concentration to 1/20th of the previous one, apparent controlled polymerization was still achieved, with 97% conversion reached in 17 h. The polydispersity of the final product stayed low at approximately 1.15. Reducing the concentration of copper by two orders of magnitude (M / (**1**) / Cu(I)Br / Cu(II)Br / (**3**) = 10 / 1 / 0.001 / 0.009 / 0.03 (the concentration of Cu(I)Br was then equal to the 1/1000th of that normal employed) led to an effective polymerization, with 50% conversion reached in 4 h, and the polydispersity of the final product was found to be = 1.15. When polymerization was stopped the solution showed a red-orange precipitate dispersed in a slightly blue solution.

As the catalyst remained stable under the same conditions, with no polymerization involved, it seems that the polymerization process itself influences the potential coordination of H_2O molecules in competition with the ligand. It has already been demonstrated that in the case of the polymerization of acrylates[16] or methacrylates,[7] polar solvents can act as competitive ligand on copper. As water is a bad ligand for copper(I) but a good ligand for copper(II), this would displaces the equilibrium towards the right increasing the concentration of the active species (Figure 5). This increase in [R*] would result in an increase of the overall rate of polymerization, explaining the faster kinetics observed in aqueous copper mediated radical polymerization.

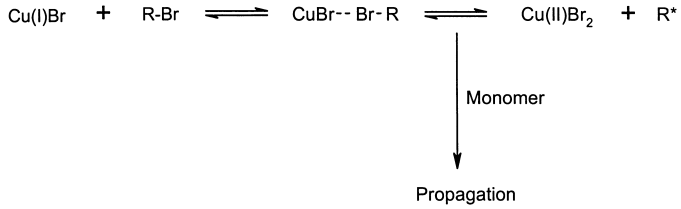

Figure 5. Scheme for the mechanism of copper mediated radical polymerization.

In the extreme case, when the concentration in catalyst is very low, this displacement is irreversible, leading to the loss of the catalyst from the system and the polymerization halts.

Polarity effect

An alternative explanation for the enhancement of the rate of reaction is the increase of the polarity of the medium. The presence of water in the polymerization medium increases the polarity of the solution, which could have a direct effect on the polymerization itself.

An increase in the polarity of the reaction medium might have a marked influence on the stability of the reactants/intermediates and transition states involved in the typical events of the transition-metal mediated living radical polymerization process, (the activation/deactivation process) resulting in the stabilization of the charge separation in the transition-state. In the present case higher rate coefficients for activation and lower rate coefficients for deactivation would explain the observed increase in the overall rate of polymerization. Enhanced rate coefficients of activation upon increase of solvent polarity have been found by Chambard *et al.*[16] for poly(butylacrylate) macroinitiators using 4,4'-di-*n*-heptyl-2,2'-bipyridine, which can be explained by a change in catalyst structure and/or the above elucidated change in energy levels. Contradictory results, however, were found for poly(styrene) macroinitiators[16]. In order to quantify the effect of the polarity of the solution over the rate of polymerization, a classification of different polymerization reactions according to their polarity was undertaken, using a solvatochromic dye, the Nile Red. This relies on empirical scales of solvent polarity, using solvatochromic dyes for which the absorption or emission band maxima shift according to the polarity of the medium in which they are dissolved.[20-25] From the results summarized in table 1, an increase in polarity enhances the polymerization rate.

Table 1. λ_{max} and E_{NR} for Nile Red in different media.

	λ / nm	E_{NR} [a]
Water	593.2	201.8
MeO(PEG)MA/water (50/50)	572.8	209.0
MeO(PEG)MA/toluene (50/50)	533.6	224.3
MMA/1,2-Diethoxy ethane (50/50)	530.5	225.6
MMA/toluene (50/50)	526.4	227.4
PMMA/toluene (50/50)	526.4	227.4
1,2-Diethoxy ethane	522.3	229.2
Toluene	521.5	229.5
n-Hexane	484.4	247.1

[a] $E_{NR} = (h*c*Na / \lambda)*10^6$ kJ mol^{-1}

Conclusion

It has been shown that aqueous copper mediated living radical polymerization can be undertaken using CuBr / *N*-(*n*-alkyl)-2-pyridylmethanimine complex, leading to well defined structure products in aqueous media. Water has the effect of a dramatic enhancement of the polymerization rate. This can find explanation in the potential competitive coordination to the copper of the molecule of H_2O and ligand, as well as the direct influence of the polarity of the medium on the stability of the polymerization intermediates.

References

1)Wang, J. S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614.

2)Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 1721.

3)Haddleton, D. M.; Crossman, M. C.; Dana, B. H.; Duncalf, D. J.; Heming, A. M.; Kukulj, D.; Shooter, A. J. *Macromolecules* **1999**, *32*, 2110.

4)Xia, J.; Zhang, X.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 3531.

5)Pascual, S.; Coutin, B.; Tardi, M.; Polton, A.; Vairon, J.-P. *Macromolecules* **1998**, *32*, 1432.

6)Matyjaszewski, K.; Nakagawa, Y.; Jasieczek, C. B. *Macromolecules* **1998**, *31*, 1535.

7)Haddleton, D. M.; Perrier, S.; Bon, S. A. F. *Macromolecules* **2000**, *33*, 8246.

8)Nishikawa, T.; Ando, T.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1997**, *30*, 2244.

9)Coca, S.; Jasieczek, C. B.; Beers, K. L.; Matyjaszewski, K. *J. Polym. Sci. , Polym. Chem.* **1998**, *36*, 1417.

10)Ashford, E. J.; Naldi, V.; O'Dell, R.; Billingham, N. C.; Armes, S. P. *Chem. Comm.* **1999**, 1285.

11)Wang, X. S.; Armes, S. P. *Macromolecules* **2000**, *33*, 6640.

12)Wang, X. S.; Jackson, R. A.; Armes, S. P. *Macromolecules* **2000**, *33*, 255.

13)Ma, Y.; Armes, S. P.; Billingham, N. *Abs. of Papers of the Amer. Chem. Soc.* **2001**, *84*, 143.

14)Malet, F. L. G.; Billingham, N. C.; Armes, S. P. *Abs. of Papers of the Amer.*

Chem. Soc. **2000**, *220*, 460-POLY.

15)Robinson, K. L.; Khan, M. A.; de Paz Banez, M. V.; Wang, X. S.; Armes, S. P. *Macromolecules* **2001**, *34*, 3155.

16) (a) Chambard, G.; Klumperman, B.; German, A. L. *Macromolecules* **2000**, *33*, 4417 (b) Chambard, G.; de Man, P.; Klumperman, B., *Macromol. Symp.* **2000**, *150*, 45.

17)Perrier, S.; Armes, S. P.; Wang, X. S.; Malet, F.; Haddleton, D. M. *J. Polym. Sci. , Polym. Chem.* **2001**, *39*, 1696.

18)Bailar, J. C.; Emeleus, H. J.; Nyholm, R.; Trotman-Dickenson, A. F. *Comprehensive Inorganic Chemistry*; Pergamon Press:, 1973; Vol. 3.

19)Cotton, F. A.; Wilkinson, G.; Gaus, P. L. *Basic Inorganic Chemistry*; Wiley:, 1987.

20)Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319.

21)Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; 2nd ed.; VCH: Weinham, 1988.

22)Reichardt, C. *Chem. Soc. Rev.* **1992**, *21*, 147.

23)Buncel, E.; Rajagopal, S. *Acc. Chem. Res.* **1990**, *23*, 226.

24)Kosower, E. M. *J. Am. Chem. Soc.* **1958**, *80*, 3253.

25)Marcus, Y. *Chem. Soc. Rev.* **1993**, *22*, 409.