Journal of Macromolecular Science, Part A
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597274

SYNTHESIS OF POLYMERS WITH AMINO END GROUPS BY ATOM TRANSFER RADICAL POLYMERIZATION

Veerle Coessens[a]; Krzysztof Matyjaszewski[a]
[a] Department of Chemistry, Carnegie Mellon University, Pittsburgh, PA, U.S.A.

Online publication date: 22 June 1999

To cite this Article Coessens, Veerle and Matyjaszewski, Krzysztof(1999) 'SYNTHESIS OF POLYMERS WITH AMINO END GROUPS BY ATOM TRANSFER RADICAL POLYMERIZATION', Journal of Macromolecular Science, Part A, 36: 5, 811 — 826
To link to this Article: DOI: 10.1081/MA-100101565
URL: http://dx.doi.org/10.1081/MA-100101565

J.M.S.—PURE APPL. CHEM., A36(5&6), pp. 811–826 (1999)

SYNTHESIS OF POLYMERS WITH AMINO END GROUPS BY ATOM TRANSFER RADICAL POLYMERIZATION

VEERLE COESSENS and
KRZYSZTOF MATYJASZEWSKI*

Department of Chemistry
Carnegie Mellon University
4400 Fifth Avenue
Pittsburgh, PA 15213

Key Words: Atom Transfer Radical Polymerization, End Group Functionalization, Amines

ABSTRACT

Atom Transfer Radical Polymerization (ATRP) is a controlled radical polymerization process that produces polymers with predictable molecular weights, narrow polydispersities, and well-defined halogen end groups. The key factor in the control of the polymerization process is the presence of a metal/ligand complex that provides a fast, reversible activation and deactivation of the growing polymer chains. The ligands, used to complex the metal are mostly tertiary amino compounds. However, amines can interact with the halogen end groups of the initiator molecules or of the growing chains. Our investigations concern-ing this issue indicate that under the experimental conditions used during the polymerization process, interactions of end groups with tertiary amines are negligible. Ammonia and primary amines, e.g., n-butylamine, however can react with the halogen end groups. Moreover, after the polymerization reaction they can be used as

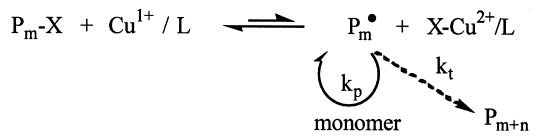
* Author to whom correspondence should be addressed.
Fax: (412) 268-6897, E-mail: km3b+@andrew.cmu.edu.

nucleophilic agents to replace the halogens by other functional end groups. The use of difunctional molecules such as ethanolamine leads to the incorporation of alcohol end groups at the chain ends.

INTRODUCTION

Atom transfer radical polymerization (ATRP) is a controlled radical polymerization process that provides well-defined polymers, DP = Δ[M]/[I]o, with low polydispersities [1-6]. Control over the radical polymerization is obtained by using a transition metal complex which induces an extremely fast, reversible activation and deactivation of the propagating chains (Scheme 1). The end groups of the polymers are determined by the initiator, mostly an alkyl halide. The alkyl group of the initiator is transferred to one chain end, the halogen to the other chain end. The halide end groups can further be used in several ways. The polymer chain can be extended with the formation of block copolymers [7] or the halogen end group can be replaced by hydrogen [8] or by other functional groups such as azides [9-11].

In a previous report, it was shown that the bromine end groups were available for nucleophilic substitution reactions [11]. The reaction of bromine terminated polymer chains with sodium azide occurred fast and chemoselective in quantitative yields [11-12]. The replacement of the halogen end groups with other nucleophiles such as amines was therefore considered. Model reactions of 1-phenylethyl halide, methyl 2-halopropionate and ethyl 2-bromoisobutyrate with n-butylamine were performed to investigate the feasibility of the nucleophilic replacement of the halide end groups by amines. Based on the results obtained for these model compounds, the substititution of polymer end groups was studied. Polystyrene and poly(methyl acrylate) with bromine end groups were prepared by ATRP and the halogen end groups were replaced by amines suitable for nucleophilic displacement. As low molecular weight polymers were utilized, the transformation of the end groups was followed by a combination of



Scheme 1. Mechanism of ATRP.

different analytical techniques such as ^{1}H-NMR and ESIMS (Electrospray Ionization Mass Spectrometry).

In addition, the possibility to react the end groups with ammonia or tertiary amines was studied. Substitution of the halogen end groups by ammonia was considered as a potential route to obtain primary amino end groups at the polymer chain end. The studies with the tertiary amines could give us an insight in the possible interactions between the polymer end groups and the ligands during the ATRP process. In ATRP, the catalyst complex used is CuX (X=Br, Cl) in combination with a tertiary amino compound such as 2,2′-dipyridyl (bpy) [1] or N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA) [13]. Interactions between the ligand and the initiator or the end groups of growing chains, leading to chain termination reactions during the polymerization process, were of concern. Model studies were performed to investigate possible side reactions.

EXPERIMENTAL

Materials

CuBr was purified by stirring in acetic acid, washing with methanol, then drying. All other reagents, purchased from Aldrich or Acros, were used as received.

Analysis

GPC measurements were carried out using a Waters 510 liquid chromatography pump equipped with PSS GPC columns (guard, 10^5Å, 10^3Å, and 10^2Å), with a Waters 410 differential refractometer. Calibration was carried out with linear polystyrene standards. GC measurements were carried out using a Shimadzu GC-14A equipped with a wide-bore capillary column (J&W Scientific, DB-WAX). A 300 MHz Brüker NMR spectrometer was used for ^{1}H-NMR analysis. ESIMS was conducted using a Finnegan LCQ, equipped with an octupole and an ion trap mass analyzer. Polymer solutions (10^{-4} M in methanol, doped with H^+) were injected at 7 μl/min. The spray voltage was 0.02 kV, the capillary voltage 0.07 V.

Model Studies with Primary Amines

To a 1 M solution of the model compounds, 1-phenylethyl bromide, 1-phenylethyl choride, methyl 2-bromopropionate, methyl 2-chloropropionate or

ethyl 2-bromoisobutyrate in DMSO, triethylamine (1.1 eq.) and n-butylamine (1.1 eq.) were added. The reaction was stirred at room temperature and samples for GC were withdrawn regularly.

Example: ^{1}H-NMR (CH_3-CH(COOMe)-NH-$(CH_2)_3$-CH_3): δ = 1.10 ($C\underline{H}_3$-), 3.22 (-C<u>H</u>-), 3.58 (<u>Me</u>), 2.35 (NH-C<u>H</u>$_2$), 1.25 (-C<u>H</u>$_2$-C<u>H</u>$_2$-), 0.85 (-C<u>H</u>$_3$) ppm.

Preparation of Polymers by ATRP

Monomer (styrene or methyl acrylate) and solvent (p-dimethoxybenzene for styrene and ethylene carbonate for acrylates), ratio 1/1, were mixed with CuBr and 2,2′-bipyridyl (ratio 1/3) and after degassing, initiator (initiator/CuBr:1/0.5) was added. The polymerization reactions were run to 90% conversion at 110˚C (styrene) or at 90˚C (acrylate).

Polymer End Group Substitution Reactions, General Procedure

Polymers were dissolved in DMSO (0.05 M solution) and a 10 to 25-fold excess of amines was added. After stirring the reaction mixtures at room temperature for 48 hours, the polymers were or extracted (water/chloroform) in the chloroform phase, which was subsequently dried with $MgSO_4$ and evaporated, or precipitated in methanol (polystyrene) or precipitated in hexanes (poly-acrylate). After drying, the polymers were analyzed with ^{1}H-NMR and ESIMS.

Model Studies with Ethanolamine

Methyl 2-bromopropionate or 1-phenylethyl bromide were reacted with ethanolamine in the presence of triethylamine (1/1/1) in DMSO.

^{1}H-NMR (CH_3-CH(Ph)-NH-CH_2-CH_2-OH): δ = 1.22 ($C\underline{H}_3$-), 3.70 (-C<u>H</u>-), 7.15-7.30 (<u>Ph</u>), hidden under the DMSO-peak at 2.50 (NH-C<u>H</u>$_2$), 3.37 (C<u>H</u>$_2$-OH) ppm.

^{1}H-NMR (CH_3-CH(COOMe)-NH-CH_2-CH_2-OH): δ = 1.12 ($C\underline{H}_3$-), 3.27 (-C<u>H</u>-), 3.60 (<u>Me</u>), under DMSO-peak at 2.50 (NH-C<u>H</u>$_2$), 3.38 (C<u>H</u>$_2$-OH) ppm.

Model Studies with Tertiary Amines

The model compounds (0.5 M in DMSO) were dissolved in DMSO-d_6 and tertiary amine (1 eq.) was added. The reactions were stirred at room temperature and the reaction mixtures were analyzed by ^{1}H-NMR.

RESULTS AND DISCUSSION

Substitution of the Halogen End Group by Primary Amines

n-Butylamine was chosen as a nucleophile representing the primary amines. It was reacted with methyl 2-halopropionate, 1-phenylethyl halide and ethyl 2-bromoisobutyrate, models for respectively poly(methylacrylate), polystyrene and poly(methyl methacrylate). The model compounds were dissolved in DMSO (1 M solution) and triethylamine as proton trap (1.1 eq.) and n-butylamine (1.1 eq.) were added. The disappearance of the model compounds was followed by GC. In Figure 1, the course of the reactions of n-butylamine with methyl 2-halopropionate and ethyl 2-bromoisobutyrate are shown. In Figure 2, reactions with 1-phenylethyl halides are shown.

In Table 1, the rate constants for the different reactions are shown. They were calculated assuming that in the model reactions the initial concentrations of substrate and amine were comparable. The initial slopes of the second-order plots were used to calculate the rate constants as the kinetics showed deviation from second-order behavior at higher conversions (conversion > 40%).

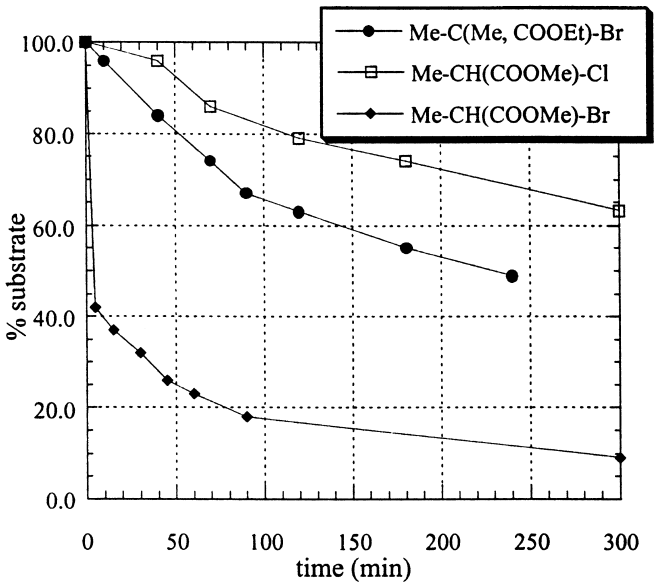


Figure 1. Kinetics of the reaction of methyl 2-halopropionate and ethyl 2-bromoisobutyrate (1 M in DMSO) with n-butylamine (1.1 eq.) in the presence of triethylamine (1.1 eq.) at 25˚C.

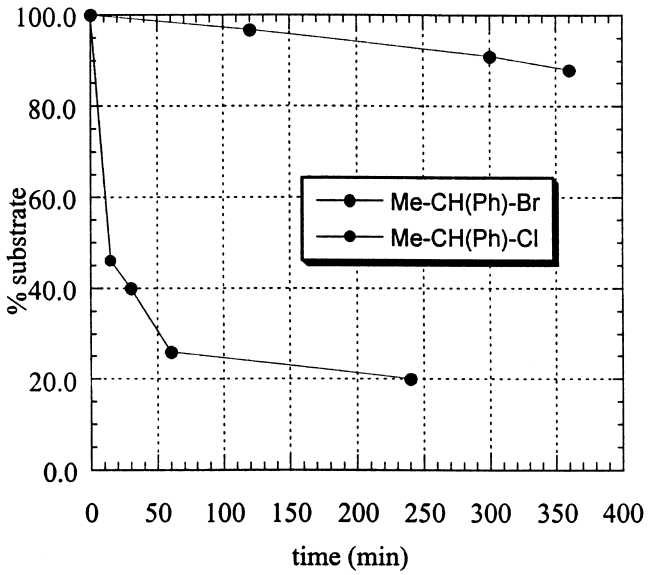


Figure 2. Kinetics of the reaction of 1-phenylethyl halides (1 M in DMSO) with n-butylamine (1.1 eq.) in the presence of triethylamine (1.1 eq.) at 25˚C.

Comparing the rate of the reactions of 1-phenylethyl chloride and methyl 2-chloropropionate with n-butylamine, respectively with sodium azide [11], we can conclude that the reactions with azide occur 10 times faster than with n-butylamine. For the brominated species, the reactions with the primary amines proceeded still fast although they slowed down after 50% conversion was reached. Fast completion of the reactions was obtained by using an excess of n-butylamine. ^{1}H-NMR of the reaction mixtures were performed to ensure that the desired compounds were formed. For the brominated species, the expected prod-

Table 1. Rate Constants for the Reaction of RX (1 M) with n-Butylamine (1.1 eq.) in the Presence of Ttriethylamine (1.1 eq.) at 25˚C

RX	k (M^{-1} s^{-1})
MeBrP	$4.6\ 10^{-3}$
1-PEBr	$7.5\ 10^{-4}$
EBiB	$7.32\ 10^{-5}$
MeClP	$3.28\ 10^{-5}$
1-PECl	$6.17\ 10^{-6}$

ucts were formed (^{1}H-NMR : see Experimental), for the chlorinated species that reacted slower, some side reactions were observed e.g. elimination for 1-phenylethyl chloride and hydrolysis of the methyl ester for methyl 2-chloropropionate. Although a primary amine is a good nucleophile, its basicity increases the probability of side reactions. Based on the results of these model studies, substitution of the bromine terminated polymers with primary amines was expected to occur effectively, chlorine terminated polymers are more likely to undergo side reactions.

Bromine end functionalized poly(methyl acrylate) (M_n = 2080; M_w/M_n = 1.12) was reacted with n-butylamine. The product was characterized by ^{1}H-NMR and electrospray ionization (ESI) MS (Figure 3). The observed mass of the peaks of the major series corresponds in an error range of +/- 1 with the theoretical mass of the product, [87 (CH_3-CH(COOMe)-) + n x 86 (-CH_2-CH(COOMe)-) + 72 (NH-Bu) + 1 (H)]$^+$. The minor series at lower m/z correspond to the double ionized (H^+, Na^+) species.

Using the concept, the replacement of a halogen end group by a primary amine, a hydroxyl group can be introduced at the chain end using ethanolamine as nucleophile. Model reactions of respectively 1-phenylethyl bromide and methyl 2-bromopropionate with ethanolamine were performed. When the model compounds were mixed with ethanolamine and triethylamine in a 1/1/1 ratio, the desired products were formed (^{1}H-NMR: see Experimental). However, when an

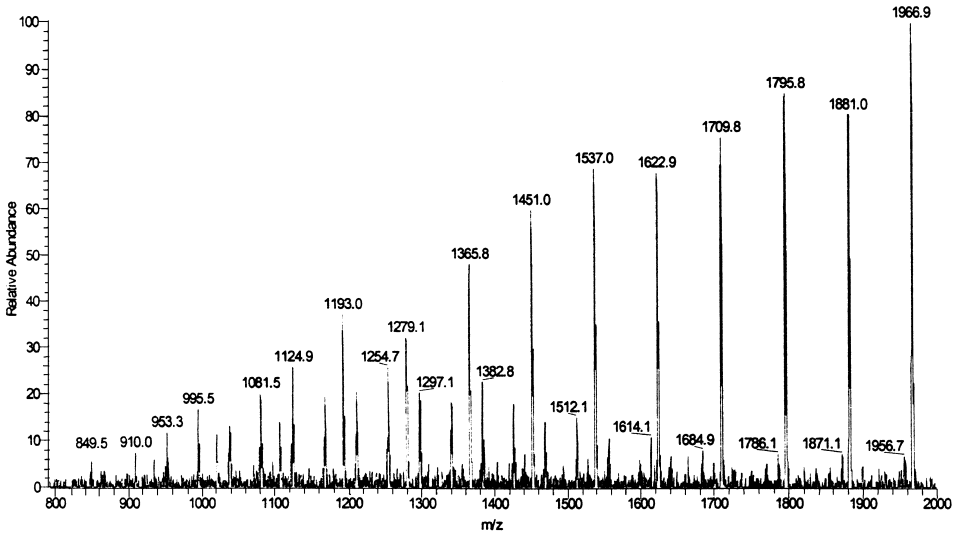


Figure 3. ESIMS spectrum of pMA-NH-Bu.

excess of ethanolamine was added to methyl 2-bromopropionate, a side reaction involving the substitution the methyl ester occurred and the double substituted product (Figure 4, ESIMS: m/z = 177) was formed. The attack of the nucleophile on the methyl ester is presumably due to the prior formation of a 6-membered ring intermediate after the substitution of the bromine.

Polystyrene-Br (M_w=1129, M_w/M_n=1.15) was reacted at room temperature in DMSO with a 10-fold excess of ethanolamine. The halogen end groups were substituted completely after 48 hours without the occurrence of any side reactions, as indicated by ESIMS, m/z = [105 (CH_3-CH(Ph)-) + n x 104 (-CH_2-CH(Ph)-) + 60 (NH-$(CH_2)_2$-OH) + 1 (H)]$^+$, and the ^{1}H-NMR spectrum of pSty-NH$(CH_2)_2$OH (Figure 5).

When bromine end functionalized poly(methyl acrylate) was reacted with ethanolamine, substitution of the bromine end group as well as reaction of ethanolamine with the methyl ester was observed. In order to avoid this multiple substitution, n-butanolamine instead of ethanolamine was used as nucleophile. In the reaction of methyl 2-bromopropionate with an excess of n-butanolamine, attack on the methyl ester did not occur. Reaction of poly(methyl acrylate) with n-butanolamine gave the desired product pMA-NH-$(CH_2)_4$-OH, as indicated by the ESI MS spectrum shown in Figure 6, m/z = [87 (CH_3-CH(COOMe)-) + n x 86 (-CH_2-CH(COOMe)-) + 88 (NH-$(CH_2)_4$-OH) + 1 (H)]$^+$).

Substitution of the Halogen End Groups by Ammonia

Substitution of the halogen end groups by ammonia was considered as a potential route to obtain primary amino end groups at the polymer chain ends. Model studies to investigate the possibility of such a substitution reaction were performed. When 1-phenylethyl bromide (1-PEBr) was reacted with ammonia (3 eq.) at room temperature in DMSO, the double substituted product

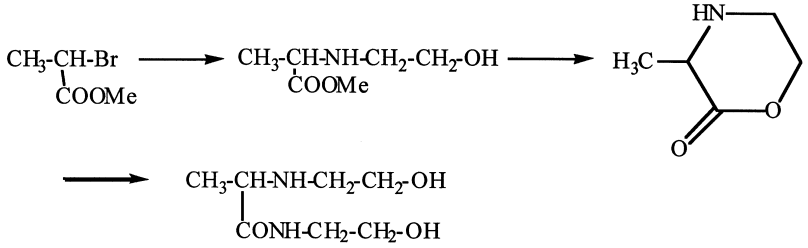


Figure 4. Methyl 2-bromopropionate reacted with an excess of ethanolamine leads to double substituted product.

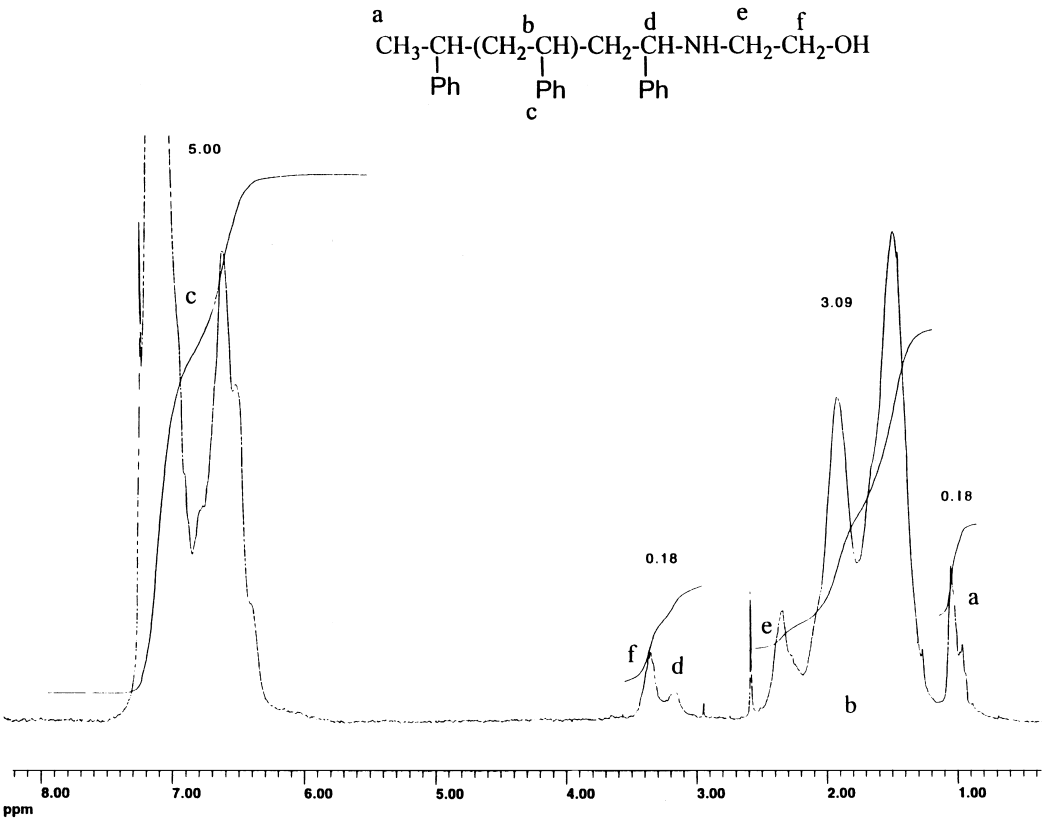


Figure 5. ^{1}H-NMR spectrum of pSty-NH-$(CH_2)_2$-OH.

$[CH_3CH(Ph)]_2NH$ was formed almost exclusively. The primary amine, formed after the substitution of the bromine of 1-PEBr is a better nucleophile than ammonia itself, therefore double substitution is obtained. Even with 10 equivalents of ammonia, 45% double substituted product was obtained. Methyl 2-bromopropionate, reacted with 3 equivalents of ammonia led to 80% of the expected product and 20% double substituted product. With a 10-fold excess of ammonia, double substitution could be avoided. However, when pMA-Br was reacted with a 25-fold excess of ammonia at room temperature, the ESIMS spectrum indicated that incorporation of two amino groups had occurred. The resulting product was presumably formed by substitution of the bromine end group by ammonia, followed by an intramolecular cyclization and subsequent ring opening (Figure 7).

The reaction of the halogen end groups with ammonia is not an efficient way to obtain primary amino end groups. To obtain primary amino end groups

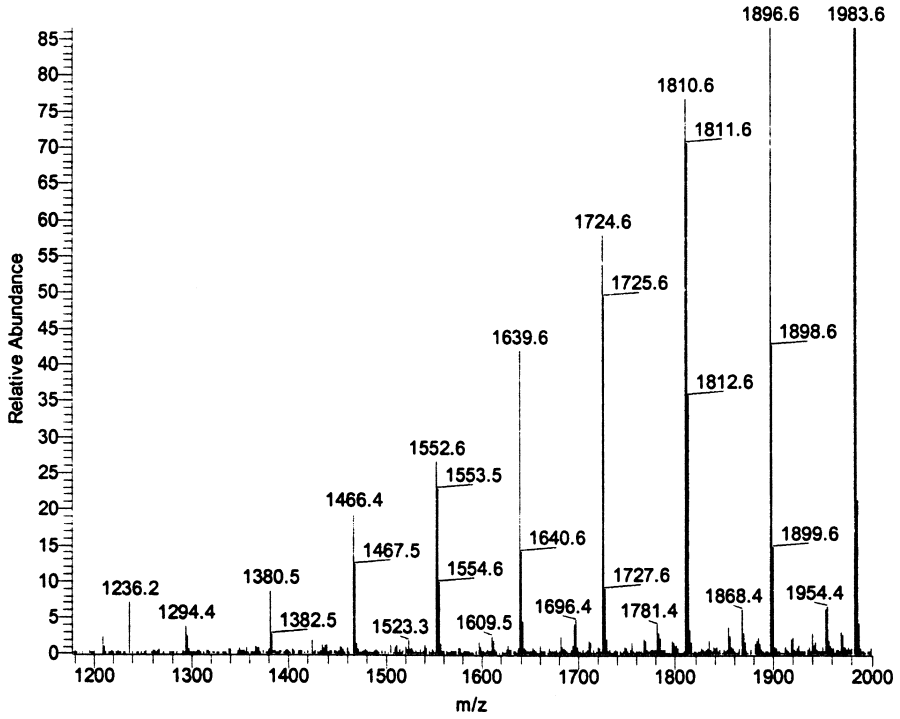


Figure 6. ESI MS spectrum of pMA-NH-$(CH_2)_4$-OH.

more efficiently, the halogen end groups have to be converted to azides, then to phosphoranimine end groups which can be subsequently hydrolyzed resulting in amino end substituted polymer, as described in a previous publication [9].

Substitution of the Halogen End Groups by Tertiary Amines or Interactions Between Ligands and Polymer End Groups

Initiators which mimic the polymer end groups were reacted with tertiary amines. Methyl 2-chloropropionate (MClP) and methyl 2-bromopro-pionate (MBP) (0.5M in DMSO), models for polyacrylates with chlorine or bromine end groups, were reacted with one equivalent of the following amines: pyridine, 2,2′-dipyridyl (bpy), triethylamine (TEA), dimethylethylamine (DMEA) or N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA). Dimethylsulfoxide was chosen as solvent because it is well known that it favors S_N2-substitution reactions. After 8 hours reaction at 25˚C, conversions were measured with ^{1}H-NMR (e.g., Figures 8 and 9).

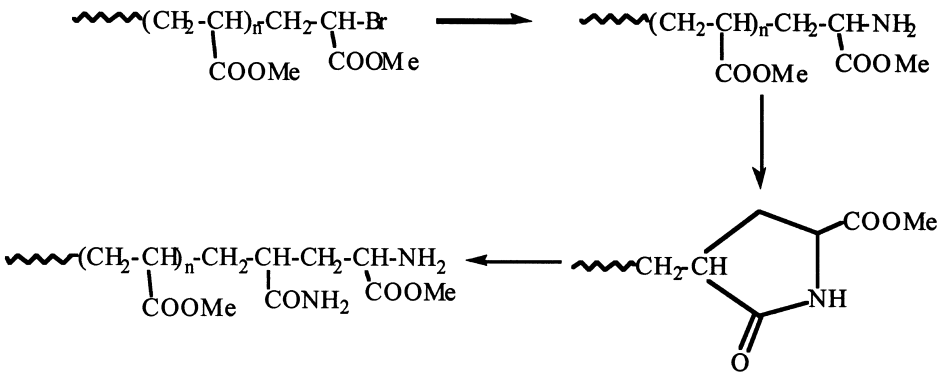


Figure 7. pMA-Br, reacted with an excess of ammonia**.**

Methyl 2-chloropropionate did not react (< 5% conversion) with any of the amines mentioned before, methyl 2-bromoproprionate did not react with bpy or with TEA. However, when methyl 2-bromopropionate was mixed with pyridine, DMEA or PMDETA, formation of quaternary ammonium salts was observed, the conversions being respectively 28, 57, and 74%.

These data indicate that chlorine end groups are not as sensitive towards side reactions as bromine end groups. Neither substitution nor elimination was observed when MClP was mixed with the amines. Side reactions resulting in termination of growing chains are thus not likely to happen during ATRP of polymers with chlorine end groups. Model studies with MBP indicated that reactions of brominated substrates with ligands were more likely to occur. MBP reacted slowly with pyridine but did not react with bpy. When bpy or substituted bipyridines are used as ligands in ATRP of acrylates, side reactions are not likely to occur. However, when the linear amine PMDETA was used as ligand, side reactions were of concern. The tertiary amine TEA did not react with MBP, probably due to steric effects but DMEA and PMDETA reacted with MBP resulting in the formation of quaternary ammonium salts. Similarly, the reaction of 1-phenylethyl bromide with DMEA or PMDETA resulted in substitution products (as example: Figure 10).

However, it has to be taken into account that during the ATRP process, the ligand is to a large extent complexed with the metal. PMDETA is generally used in a 1 to 1 ratio with CuBr, therefore the concentration of free ligand is low. Moreover, the solvent plays an important role in the rate of the substitution reactions. DMSO was used as solvent because of its S_N2-promoting action However, polymerization reactions are performed or in bulk or in less polar sol-

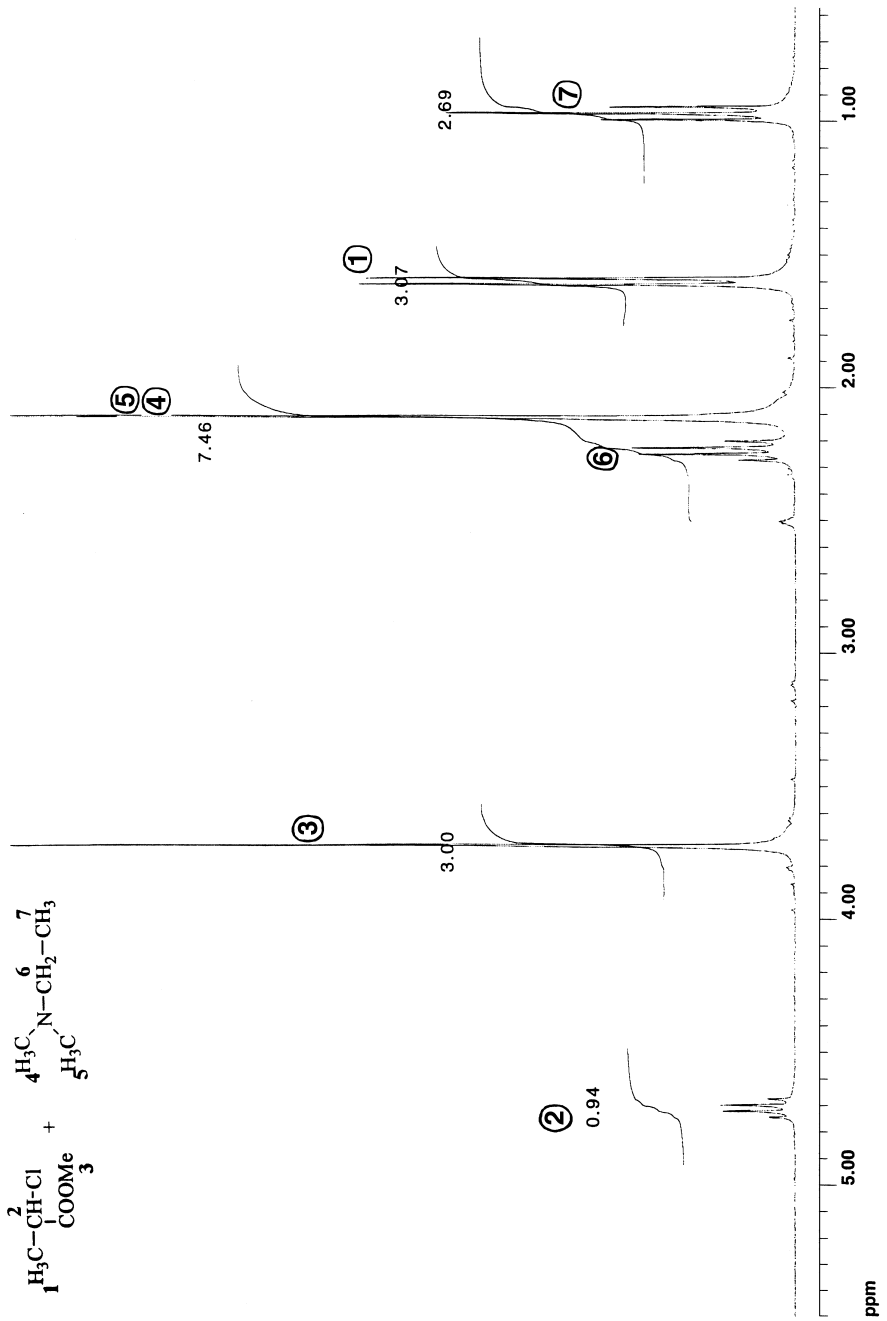


Figure 8. ^{1}H-NMR of the reaction mixture of methyl 2-chloropropionate with dimethylethylamine in DMSO-d6 after 8 hours reaction at 25°C.

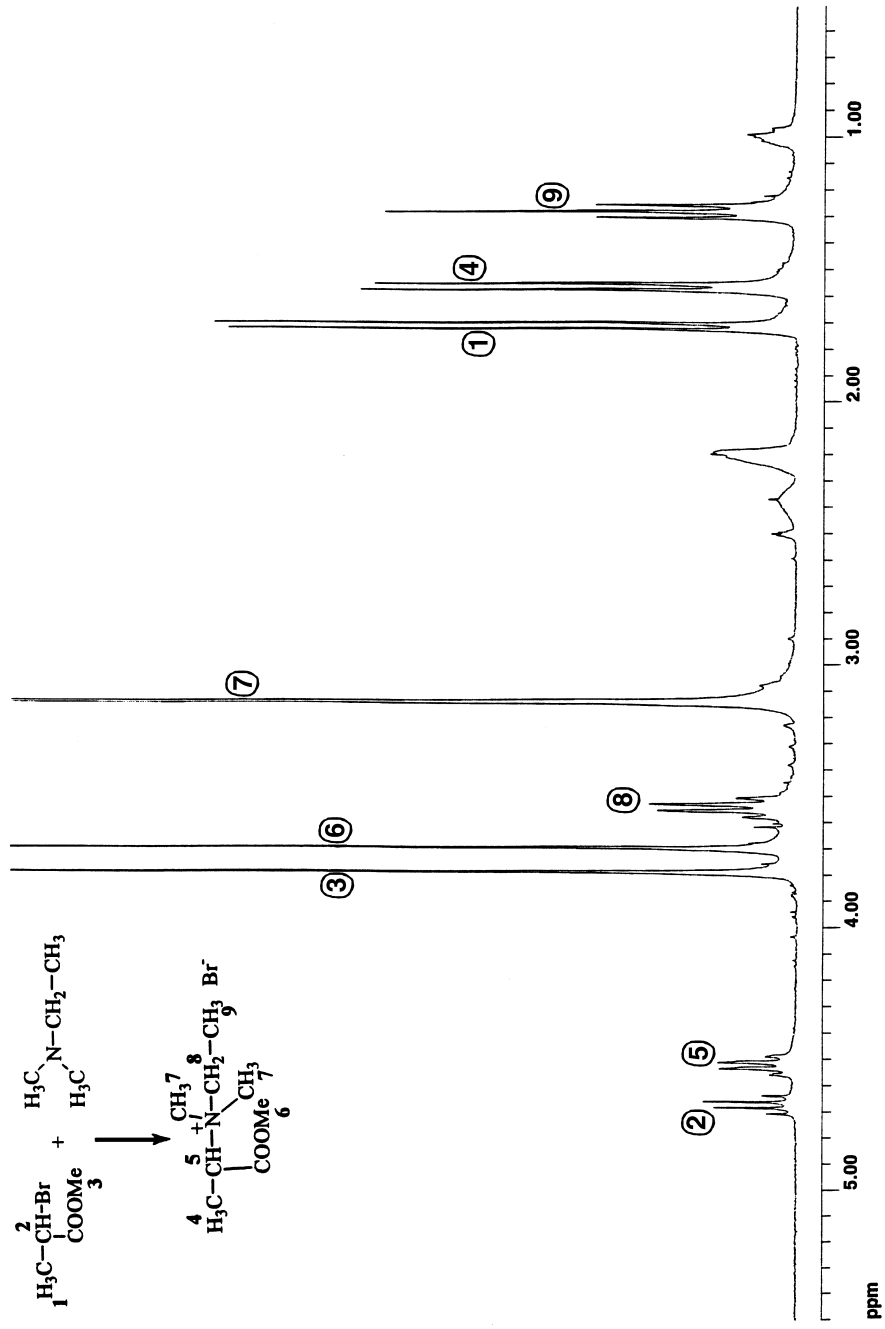


Figure 9. ^{1}H-NMR of the reaction mixture of methyl 2-bromopropionate with dimethylethylamine in DMSO-d6 after 8 hours reaction at 25°C.

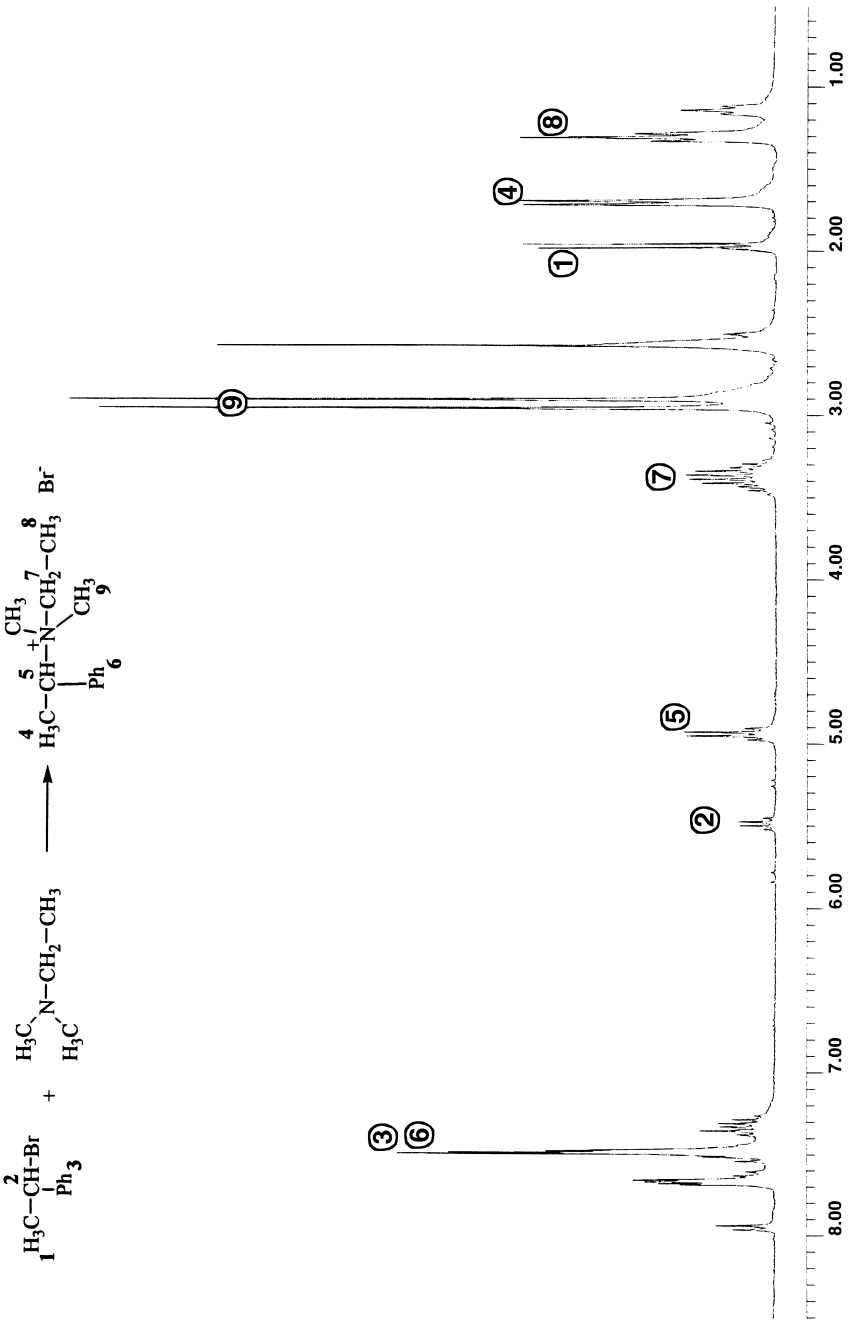


Figure 10. ^{1}H-NMR of the reaction mixture of 1-phenylethyl bromide with dimethylethylamine in DMSO-d6 after 1.5 hours reaction at 25°C.

vents. For comparison, the course of the reaction between methyl 2-bromopropionate and n-butylamine was followed in different solvents such as DMSO, toluene and THF (MBP (1.2 M in solvent)/n-butylamine/Et_3N: 1/1/1). After one hour in DMSO, 78% conversion was reached, in THF, 45% and in toluene, 18% conversion was obtained. This result can be ascribed to the fact that the solvent in nucleophilic substitution reactions strongly influences the magnitude of the rate constants.

To mimic polymerization conditions, methyl 2-bromopropionate was dissolved in ethyl acetate (model for methyl acrylate) in the presence of equivalent amounts of CuBr and PMDETA. After 3 hours reaction at 60˚C, the reaction mixture was filtered through alumina, ethyl acetate was evaporated. The ^{1}H-NMR of the residue showed that neither substitution reactions nor elimination reactions had taken place. Under these reaction conditions, coupling of substrate remained below 5%. Based on these model studies, we conclude that for polyacrylates with bromine end groups, side reactions with the ligand PMDETA are not likely. The complexation of the ligand with the metal, the absence of a S_N2-promoting solvent and the fast polymerization rate prevent side reactions during the polymerization process. ^{1}H-NMR of low molecular weight polyacrylates indicates no loss of bromine end groups.

CONCLUSION

ATRP leads to polymers with well-defined halogen end groups. Bromine end groups are readily substituted by primary amines such as n-butylamine and ethanolamine. The reaction of the end groups with ammonia did not lead to primary amino end functionalized polymers. The interaction of the end groups with tertiary amines, which are used as ligands during the polymerization process, was investigated. Under the reaction conditions used during a polymerization, reaction of the end groups with tertiary amines are not very important.

ACKNOWLEDGEMENT

The authors wish to acknowledge the Industrial Members of the ATRP Consortium at Carnegie Mellon University.

REFERENCES

[1] K. Matyjaszewski, *Controlled Radical Polymerization*, ACS Symposium Series 685, Washington, D.C. (1998).

[2] J. S. Wang and K. Matyjaszewski, *Macromolecules, 28,* 7901 (1995).

[3] J. S. Wang and K. Matyjaszewski, *J. Am. Chem. Soc., 117,* 5614 (1995).

[4] T. E. Patten, T. Abernathy, and K. Matyjaszewski, *Science, 272*, 866 (1996).

[5] K. Matyjaszewski, T. Patten, and J. Xia, *J. Am. Chem. Soc., 119,* 674 (1997).

[6] M. Sawamoto and M. Kamigaito, *Trends in Polymer Science, 4,* 371 (1996).

[7] D. A. Shipp, J.-L. Wang, and K. Matyjaszewski, *Macromolecules, 31*, in press (1998).

[8] V. Coessens and K. Matyjaszewski, *Macromol. Rapid Commun.,* submitted.

[9] V. Coessens, Y. Nakagawa, and K. Matyjaszewski, *Polymer Bulletin, 40,* 135 (1998).

[10] K. Matyjaszewski, V. Coessens, Y. Nakagawa, J. Xia, J. Qiu, S. Gaynor, S. Coca, and C. Jasieczek, *ACS Symposium Series, 704,* 16 (1998).

[11] V. Coessens and K. Matyjaszewski, *J. Macromol. Sci., Pure & Applied Chem*., in press.

[12] K. Matyjaszewski, Y. Nakagawa, and S. G. Gaynor, *Macromol. Rapid Commun., 18,* 1057 (1997).

[13] J. Xia and K. Matyjaszewski, *Macromolecules, 30,* 7697 (1997).

Received December 6, 1998