Chapter 7

The Optimized Construction of Supramolecular Polymers from Homoditopic Molecules Containing Secondary Ammonium Ion and Crown Ether Moieties

7.1. Introduction

In pursuit of efficient construction of supramolecular linear polymers from the complementary homoditopic molecules, we demonstrated with the dilution studies in the previous chapter that the increased end-to end distance of the linear dimers should favor the linear extension of the supramolecular polymers by minimizing the formation of cyclic dimers.[1]   In this chapter we investigate the efficiencies of the construction of supramolecular polymers **4** from the biscrown ether **1** and a series of diammonium salts **2** as illustrated in Figure 7.1.

Figure 7.1. Cartoon illustration of the construction of the supramolecules **3** and **4** from monoditopic molecules **1** and **2**.

7.2. Results and Discussion

7.2.1. Synthesis

Poly(ethylene glycol) (PEG) of M_n = 2,000 g/mol was used as the precursor for **2d** (Figure 7.2). Chlorination of the PEG with thionyl chloride and pyridine yielded the

corresponding dichloride product, which was then reacted with 4-hydroxybenzaldehyde in the presence of K_2CO_3 to afford the dialdehyde precursor. The reaction of the dialdehyde and benzylamine with simultaneous removal of H_2O *via* azeotropic distillation gave the corresponding diimine, which was subsequently reduced to afford the diamine. Acidification of the diamine, followed by ion exchange reaction gave the diammonium salt **2d**.
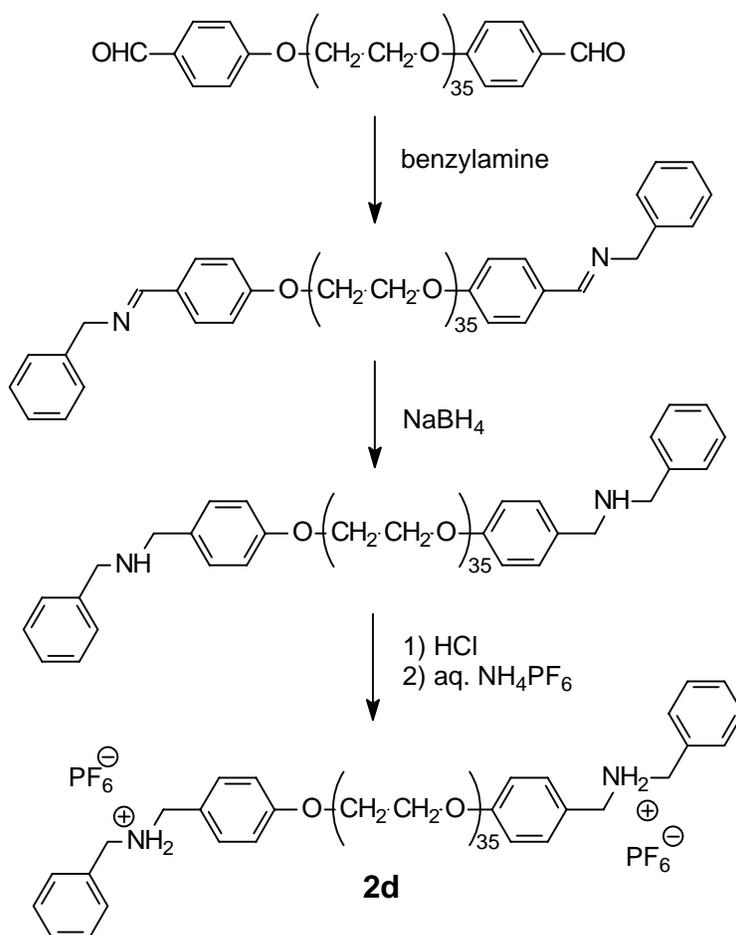

Figure 7.2. Synthesis of **2d**.

7.2.2. Complexation studies in solution

Solutions of **1** mixed with equimolar solutions of the homoditopic molecules **2a-c** were characterized by ^{1}H NMR spectroscopy in acetone-d_6/chloroform-d, 1/1, v/v at 22°C (Figure 7.3). In the case of the construction of supramolecular polymers from **1** and **2a**, the ^{1}H NMR spectra obtained at different concentrations indicated that the efficiencies of

formation of the cyclic dimer **3a**, reflected in the percentage complexed in **3a**, were greater than those of **3b** formation (chapter 5) at any concentration we investigated (Table 7.1). It is noteworthy that equimolar solutions higher than 1.0 M could not be achieved due to the poor solubility of **2a** in noncompetitive solvents. In the equimolar solutions of **1** and **2a** at 0.5 M, the supramolecular polymer **4a** has an average molecular weight (M_n) of 6.1 kDa, which is nearly a two-fold decrease with respect to that of **4b** (Table 7.1).[2,3] These observations are consistent with the dilute solution studies of the previous chapter in which we demonstrated that the shorter the end-to-end distance of the linear dimer complex, the higher the percentage of the cyclic dimer complex formation.
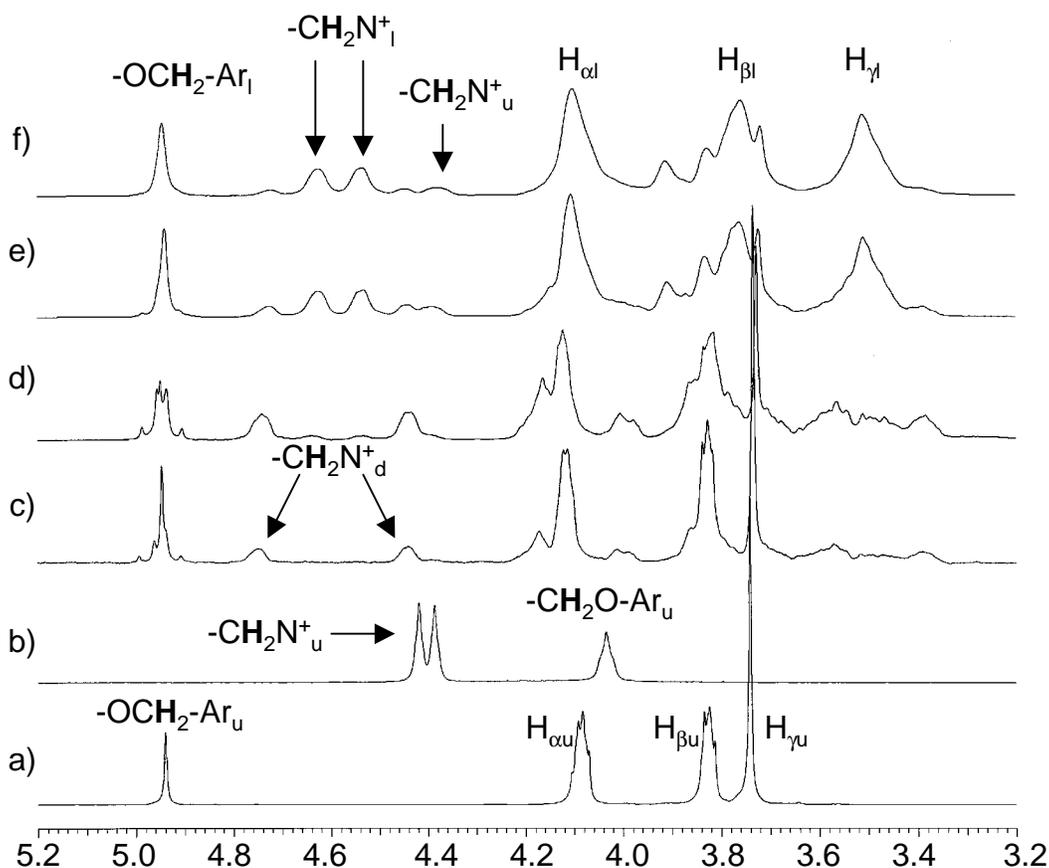
Figure 7.3. The stacked ^{1}H NMR spectra of solutions of **1** and **2a** at a) 1.0×10^{-2} /0, b) $0/1.0 \times 10^{-2}$, c) 1.0×10^{-3}, d) 1.0×10^{-2}, e) 0.1, and f) 0.5 M each (400 MHz, acetone-d_6/chloroform-d (1/1, v/v), 22°C). The three sets of signals are for uncomplexed **2a** (u), **3a** (d), and **4a** (l).

Table 7.1. Analyses of percentages of ammonium ion moieties in cyclic dimer **3a** and supramolecular polymer **4a**, and the average number of repeat units, n, in **4a**.[a]

equimolar conc. (M)	% in **3a** at +22°C	% uncomp. at +22°C	n[b] at +22°C	M_n[c] at +22°C (kDa)
0.50	17	13	3.2	6.1
0.10	25	14	2.7	5.1
1.0×10^{-2}	78	7	1.6	3.0
1.0×10^{-3}	86	9	0.78	1.5

a) Calculated from the ^{1}H NMR spectra of equimolar solutions (acetone-d_6/chloroform-d, 1/1, v/v) of **1** and **2a** at various concentrations and temperatures.
b) n was determined by solving the expression; $n=(100-\%$ of ammonium ion units in **3a**)/2(% uncomplexed ammonium ion units).
c) The number average molecular weight (M_n) of the aggregate was calculated using the following equation; $M_n = n \times 1896$ Da (repeat unit mass).

In contrast, the ^{1}H NMR spectra of equimolar solutions of **1** and **2c** (Figure 7.4) indicated quite convincingly that the formation of the cyclic dimer complex **3c** was reduced compared to the systems of **1** and **2a** (Table 7.2) and **1** and **2b** (Table 5.1). As an example, in the equimolar solutions of **1** and **2c** at 1.0×10^{-3} M, the percentage of ammonium ion moieties in the cyclic dimer **3c** was reduced to 38% from 86 and 72% in the systems of **1** and **2a** and **1** and **2b**, respectively. More importantly, in equimolar solutions of **1** and **2c** at higher than 0.5 M the cyclic dimer **3c** was not formed at all. From the end group analysis of supramolecular polymer **4c**, the average molecular weight of **4c** is estimated to be 24 kDa in the equimolar solutions at 0.5 and 1.0 M. It should be noted that the equimolar solution at 2.0 M could not be made due to the poor solubility of **2c**. The average number of repeat units, n, in **4** and the percentages of ammonium ion in cyclic dimer **3** were plotted as a function of solution concentration (Figures 7.5 and 7.6, respectively).
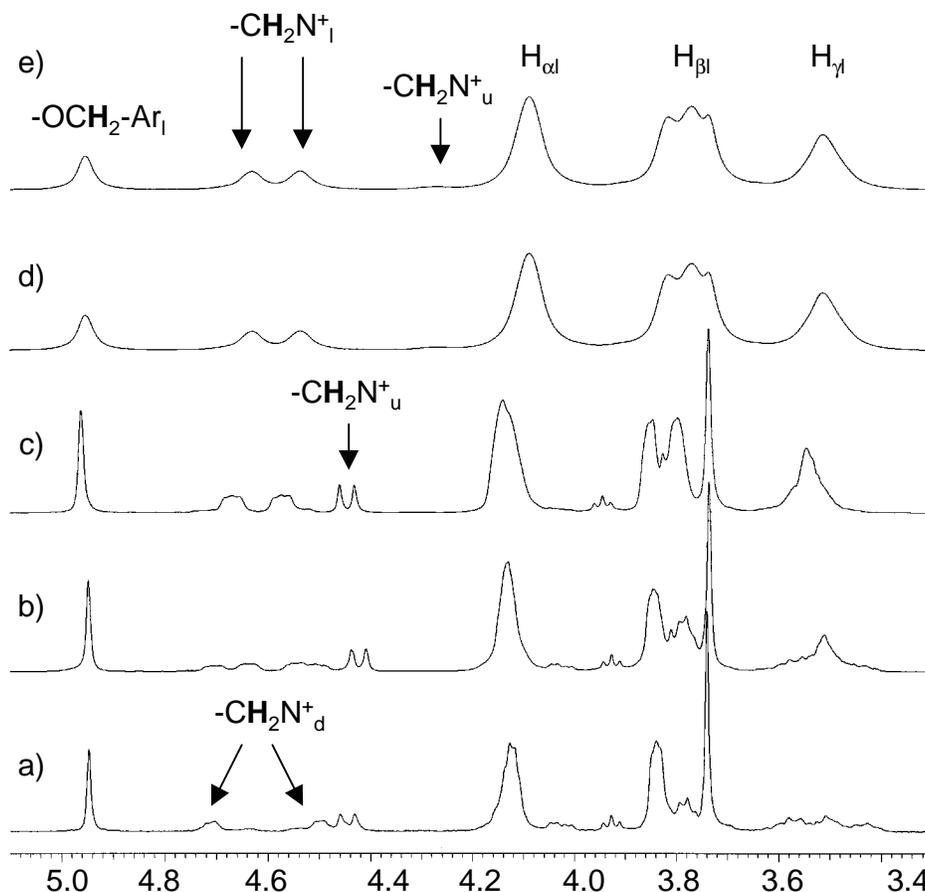
Figure 7.4. The stacked ^{1}H NMR spectra of solutions of **1** and **2c** at a) 1.0×10^{-3}, b) 1.0×10^{-2}, c) 0.1, d) 0.5, and e) 1.0 M each (400 MHz, acetone-d_6/chloroform-d (1/1, v/v), 22°C). The three sets of signals are for uncomplexed **2c** (u), **3c** (d), and **4c** (l).
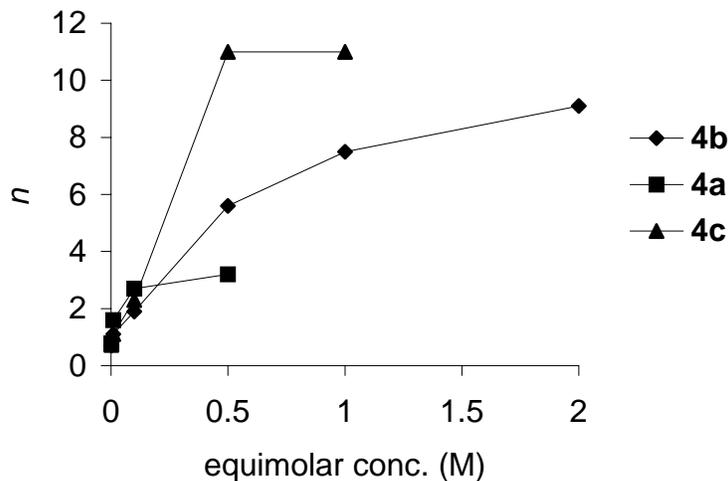
Table 7.2. Analyses of percentages of ammonium ion moieties in cyclic dimer **3c** and supramolecular polymer **4c**, and the average number of repeat units, n, in **4c**.[a]

| equimolar conc. (M)	% in **3c** at +22°C	% uncomp. at +22°C	n[b] at +22°C	M_n[c] at +22°C (kDa)
1.0	0	4.4	11	24
0.50	0	4.7	11	24
0.10	8.3	20	2.3	4.9
1.0×10^{-2}	28	34	1.1	2.4
1.0×10^{-3}	38	43	0.72	1.5

a) Calculated from the ^{1}H NMR spectra of equimolar solutions (acetone-d_6/chloroform-d, 1/1, v/v) of **1** and **2c** at various concentrations and temperatures.
b) n was determined by solving the expression; n=(100-% of ammonium ion units in **3c**)/2(% uncomplexed ammonium ion units).
c) The number average molecular weight (M_n) of the aggregate was calculated using the following equation; $M_n = n \times 2148$ Da (repeat unit mass).

Figure 7.5. The average number of repeat units, *n*, in **4** as a function of concentration of **1** and **2**.
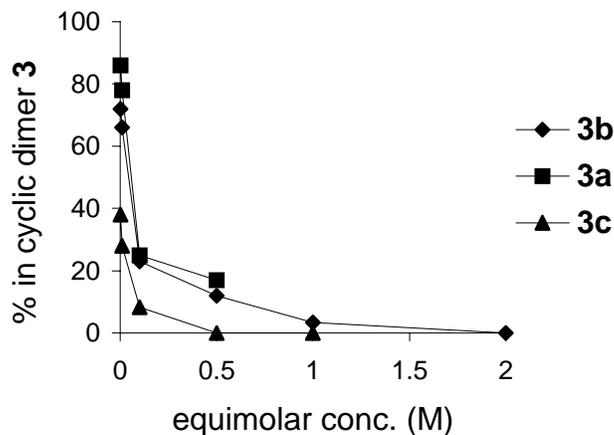
Figure 7.6. The percentages of ammonium salt moieties in cyclic dimer **3** as a function of concentration of **1** and **2**.

To extend the efforts toward the construction of supramolecular polymers from complementary homoditopic molecules, we prepared **2d** containing an oligomeric PEO unit of M_n=2000 g/mol as the linker segment. The PEO unit of low molecular weight seemed to be an appropriate linker due to the ease of functionaliztion and purification. We anticipated that **2d** when mixed with an equimolar amount of **1** would exhibit a

significant improvement in the efficiency of linear polymer formation over other previously investigated systems because of the large end-to-end distance generated in the linear dimer complex. The ^{1}H NMR spectrum of chloroform-d solutions of **2d** and DB24C8 (1.0 x 10^{-2}/2.0 x 10^{-2} M at 22°C) were recorded in an attempt to study the binding affinity of **2d** toward DB24C8. The spectrum exhibited four sets of signals corresponding to free ammonium salt moiety, complexed ammonium salt moiety, free DB24C8, and complexed DB24C8 as a result of slow exchange on the ^{1}H NMR time scale. The association constant (K_a) was determined to be 19 M^{-1} (chloroform-d at 22°C) with an assumption that the ammonium salt moieties in **2d** act independently to complex with DB24C8. The significantly low K_a value obtained relative to the model system of dibenzylammonium hexafluorophosphate and DB24C8 (2.7 x 10^5 M^{-1} at 25°C) is presumably a consequence of intra- and inter-molecular hydrogen bonding between the oxygen atoms of the PEO linker segment and ammonium salt moieties of **2d**. As a result the ammonium salt moieties are considerably less accessible to complex with DB24C8. The same effect was noted for solutions of **2d** and DB24C8 when acetone-d_6 was used as the solvent (K_a=18 M^{-1} at 22°C). These findings discouraged us from pursuing the construction of supramolecular polymers from **1** and **2d**.

7.3. Conclusion

As predicted by the dilution studies in the previous chapter, the efficiencies of the formation of the supramolecular polymers from complementary homoditopic molecules were influenced by the end-to-end distance of the linear dimer complexes.

7.4. Experimental

Chemicals were used as obtained from Aldrich without further purification unless otherwise noted. Solvents were dried and distilled according to literature procedures prior to use. Melting points (mp) were taken in capillary tubes on a Melt-Temp II melting point apparatus and are corrected. The ^{1}H NMR spectra were recorded on a Varian Unity 400 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Elemental analyses were provided by Atlantic Microlab Inc. The LRFAB and

HRFAB mass spectra were obtained from the Washington University Mass Spectrometry Resource.

α,ω-bis[*p*-(*N*-benzyl)amminomethylphenoxy]oligo(ethylene glycol) (2d). To a 100 mL round bottom flask equipped with a condenser, magnetic stirrer, and N_2 inlet were added poly(ethylene glycol) of M_n = 2,000 g/mol (11.18 g, 5.59 mmol), thionyl chloride (4.00 g, 33.6 mmol), pyridine (2.66 g, 33.6 mmol), and toluene (50 mL) and the reaction mixture was stirred at reflux for 48 h. After a small amount of H_2O was added to quench the reaction, the salts were filtered and the filtrate was concentrated to give a brown liquid, which was passed through a short column of silica gel using EtOAc to afford poly(ethylene glycol)dichloride as an off-white solid (9.22 g, 80% yield), T_m=49°C. ^{1}H NMR (400 MHz, chloroform-*d*, 22°C): δ=3.61-3.63 (-(OCH_2CH_2)$_n$-, br s)]. To a 100 mL round bottom flask equipped with a condenser, magnetic stirrer, and N_2 inlet were added the dichloride polymer, 4-hydroxybenzaldehyde (2.76 g, 22.6 mmol), K_2CO_3 (31.24 g, 226 mmol), and DMF (50 mL) and the reaction mixture was stirred at 110°C for 5 days. The salts were filtered with Celite® and the filtrate was concentrated to give a brown liquid, which was subjected to a short column of silica gel first using EtOAc and then MeOH to afforded the α,ω-poly(ethylene glycol)dialdehyde as a brown liquid (3.13 g, 83% yield). ^{1}H NMR (400 MHz, chloroform-*d*, 22°C): δ= 3.63-3.69 (-(OCH_2CH_2)$_n$-, br s), 3.89 (-OCH_2CH$_2$Ar, t, J = 4.8 Hz), 4.21 (-OCH$_2$CH_2Ar, t, J = 4.8 Hz), 7.02 (Ar, d, J = 8.4 Hz), 7.83 (Ar, d, J = 8.4 Hz), and 9.88 (CHO, s). To a 250 mL round bottom flask equipped with a Dean-Stark trap, a condenser, and a N_2 inlet were added poly(ethylene glycol)dialdehyde (0.75 g. 0.375 mmol) and toluene (100mL). To this solution was added benzylamine (0.48 g, 4.48 mmol) and the mixture was refluxed for 12h. The solvent was removed to give a yellow viscous liquid, which was precipitated into anhydrous hexanes to afford an off-white solid (0.68 g, 91% yield). ^{1}H NMR (400 MHz, chloroform-*d*, 22°C): δ=3.64-3.67 (-(OCH_2CH_2)$_n$-, br s), 3.87 (-OCH_2CH$_2$Ar, t, J = 4.4 Hz), 4.17 (-OCH$_2$CH_2Ar, t, J = 4.4 Hz), 4.81 (=N-CH_2Ar, s), 6.95 (-N=CHAr, d, J = 8.4 Hz), 7.26-7.35 (=N-CH$_2$*Ar*, m), 7.78 (-N=CH*Ar*, d, J = 8.4 Hz), and 8.28 (-N=CHAr, s). To a 100 mL round bottom flask equipped with a magnetic stirrer, condenser, and N_2 inlet were added the poly(ethylene glycol)diimine (0.60 g, 0.30 mmol) and MeOH (50

mL). To this solution were added small portions of NaBH$_4$ (23 mg, 0.60 mmol) and the mixture was brought to gentle reflux and stirred for 12h. The solvent was removed to afford a white solid, which was suspended in H$_2$O and neutralized with 2M HCl. The product was extracted with CHCl$_3$, the organic layers were combined, dried over MgSO$_4$, and concentrated to give a brown liquid, (0.57 g, 95% yield). ^{1}H NMR (400 MHz, chloroform-*d*, 22°C): δ=3.63-3.72 (-(OC*H$_2$*C*H$_2$*)$_n$-, br s), 3.81 (-OC*H$_2$*CH$_2$Ar, t, *J* = 4.4 Hz), 3.84 (-OCH$_2$C*H$_2$*Ar, t, *J* = 4.4 Hz), 4.02 (-NC*H$_2$*Ar, m), 6.88 (-OCH$_2$CH$_2$*Ar*, d, *J* = 8.4 Hz), 7.32-7.45 (-NCH$_2$*Ar*, m), and 7.52 (-OCH$_2$CH$_2$*Ar*, d, *J* = 8.4 Hz). To a 100 mL round bottom flask equipped with a magnetic stirrer were added poly(ethylene glycol)diamine (0.55 g, 0.28 mmol) and MeOH (50 mL). To this solution was added 2M HCl (10 mL) and the mixture was stirred for 1 h. The solvent was removed to give an off-white solid, which was then suspended in acetone and aq. NH$_4$PF$_6$ was added until complete dissolution occurred. The solvent was evaporated and the resulting solid was washed thoroughly with H$_2$O to afford a brown liquid **2d** (0.54 g, 98% yield). ^{1}H NMR (400 MHz, chlorofrom-*d*, 22°C): δ=3.55-3.62 (-(OC*H$_2$*C*H$_2$*)$_n$-, br s), 3.85 (-OC*H$_2$*CH$_2$Ar, t, *J* = 4.4 Hz), 4.14 (-OCH$_2$C*H$_2$*Ar, t, *J* = 4.4 Hz), 4.30 (-NC*H$_2$*Ar, m), 6.94 (-OCH$_2$CH$_2$*Ar*, d, *J* = 8.4 Hz), 7.38-7.42 (-NCH$_2$*Ar*, m), 7.47 (-OCH$_2$CH$_2$*Ar*, d, *J* = 8.4 Hz), and 7.74 (-N*H$_2$*$^+$-, s).

7.5. References

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2) Yamaguchi, N.; Gibson, H. W. *Angew. Chem. Int. Ed.* **1999**, *38*, 143-147.

3) Yamaguchi, N.; Gibson, H. W. *Am. Chem. Soc. Div. Polym. Mater. Sci. Eng.* **1999**, *80*, 217-218.