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Zwitterionic Polymerization of 1-[(4-Carboxyphenyl)methyl]quinuclidinium Hydroxide Inner Salt

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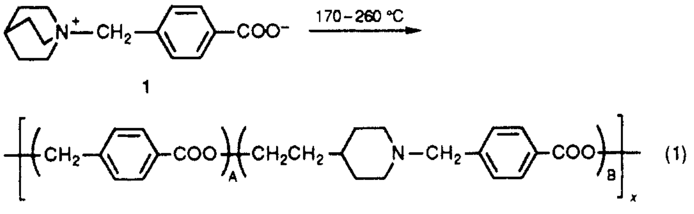
ABSTRACT: 1-[(4-Carboxyphenyl)methyl]quinuclidinium hydroxide inner salt, zwitterion 1, was prepared from quinuclidine and 4-(chloromethyl)benzoic acid as a monohydrate. The monohydrate was stable at room temperature but lost its water of hydration at 90 °C under vacuum to form a stable anhydrous zwitterion. Bulk zwitterionic polymerization of both the monohydrate and the anhydrous zwitterion 1 has been studied at 170–260 °C. Random copolymers with the general structure 2 were produced with number-average molecular weights varying from 4000 to 17 000. Both the composition of the copolymer (A:B ratio) and molecular weight were affected by reaction conditions such as temperature, time, and vacuum. ^1H, ^{13}C, and 2D COSY NMR and FT-IR spectroscopies were used for identification of structures 1 and 2. The molecular weight of polymer 2 was determined by VPO, and thermal properties of the polymer were evaluated by DSC and TGA.



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(1)

Introduction

Various types of zwitterion polymerization systems have been studied. Most of the systems involved the proposal that reaction proceeds by the formation of low concentrations of zwitterion intermediates when a nucleophile and electrophile (e.g., 2-methyl-2-oxazoline and acrylic acid) were reacted.[1] The polymer molecular weights were very low in almost all systems, due most likely to termination reactions with the nucleophile and electrophile reactants.[2] Zwitterion intermediates were also proposed for the polymerization of the single reactant system of a 2-(mercaptoalkyl)-2-oxazoline. High molecular weight products (up to 16 000) were obtained in this system since nucleophilic and electrophilic reactants, which participate in terminations, were absent.[3] The highest polymer molecular weights (up to 50 000) were achieved for polymerizations of zwitterions of sufficient stability to be isolated. The first such system studied was the tetrahydrothiophenium–arene oxide zwitterion.[4-6] The present paper extends our studies to the stable zwitterion system 1 which contains ammonium and carboxylate ionic centers.

Experimental Section

Materials. All the chemicals were from Aldrich and used without further purification.

Synthesis of 1-[(4-Carboxyphenyl)methyl]quinuclidinium Hydroxide Inner Salt. 4-(Chloromethyl)benzoic acid (9.0 g, 0.0528 mol) was dissolved in 25 mL of tetrahydrofuran (THF) and cooled in an ice-water bath. Quinuclidine (6.1 g, 0.0532 mol), dissolved in THF (25 mL), was added dropwise to the 4-(chloromethyl)benzoic acid solution with stirring at 5 °C. The reaction mixture yielded a white precipitate after stirring at 25 °C overnight. The white precipitate was filtered and then washed with two 25-mL portions of THF followed by 25 mL of ethyl ether. After drying under a nitrogen flow for 2 h, 13.4 g of the white precipitate, a mixture of 1 and 3 (the hydrochloride of 1), was obtained.

The white precipitate (5.7 g) was dissolved in 25 mL of methanol in a beaker, and then an activated anion-exchange resin (Dowex 1 × 2-200 ion-exchange resin) was slowly added into the solution until the pH reached 10.5. The solution with the resin was filtered, and the resin was washed with three 20-mL portions of methanol. The filtrate was concentrated to 30 mL and added to 400 mL of ethyl ether dropwise to give a white precipitate. The precipitate was filtered and washed with three 20-mL portions of ethyl ether. After the precipitate was dried under nitrogen flow for 4 h, it was then dried in a vacuum oven at 25 °C overnight to yield white crystals (3.0 g) of the monohydrate, 1. The overall yield for these two steps was 50.8%.

Anhydrous 1 was obtained as a white fine powder by heating monohydrate 1 under a vacuum of 0.1 Torr at 90–100 °C for 40 h.

The degree of hydration was determined by both Karl-Fischer titration[7] and TGA. The amount of sample used for the titration was approximately 250 mg.

Zwitterionic Polymerization of 1-[(4-Carboxyphenyl)methyl]quinuclidinium Inner Hydroxide Salt (1). Polymerization was carried out for both monohydrated and anhydrous zwitterions 1. The monohydrate or anhydrous sample (0.4–0.5 g) was sealed in a polymerization tube in a nitrogen atmosphere or under a vacuum of 0.1 Torr or continuously evacuated at 0.1 Torr of pressure without sealing the tube. The polymerization tube was kept in an oil bath at a specified temperature in the range 170–260 °C for a specified period to complete the polymerization. The polymer produced was a semitransparent, strong, and plasticlike material colored from white to yellow.

Since zwitterion 1 polymerized before it melted, some of the starting material (less than 1%) was left unreacted. The polymer was purified by dissolving in 10 mL of methylene chloride. The zwitterion did not dissolve in methylene chloride and was removed by either centrifugation or filtration. The clear filtrate was added to 100 mL of ethyl ether at 25 °C to precipitate the polymer product.

Analytical Methods. ^1H, 2D COSY, and ^{13}C NMR spectra were obtained with an IBM WP 200SY FT-NMR spectrometer

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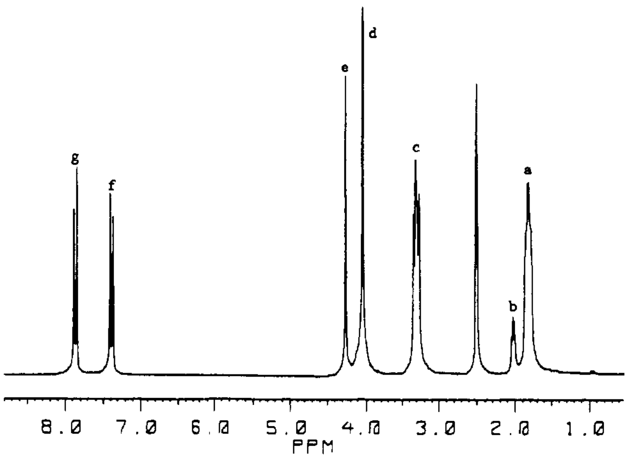


Figure 1. 200.1-MHz ^1H NMR spectrum of monohydrate 1: solvent, DMSO-d_6/D_2O (20:1 by volume); concentration, 6%; temperature, 40 °C.

with a 5-mm $^{13}C/^1H$ dual probe.

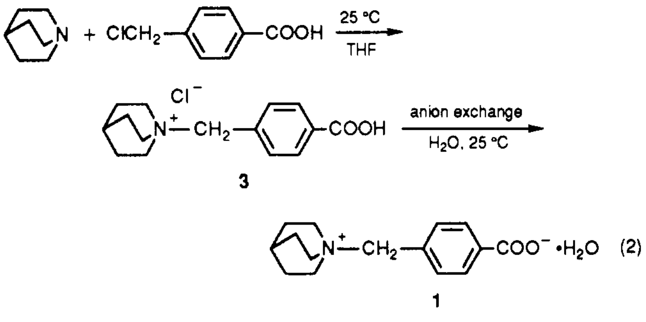
IR spectra were recorded on a Bio-Rad Digilab FTS-40 spectrometer. The IR spectrum of monohydrate 1 was obtained from a KBr pellet and copolymer 2 from a thin film deposited from a chloroform solution on a NaCl plate.

A UIC Model 070 vapor-pressure osmometer was used to measure the number-average molecular weight of the polymer product. The measurement was carried out at 40 °C using 3–10% solutions of polymer in chloroform. The measurement of molecular weight was also attempted by GPC using a Waters 150-C ALC GPC. GPC was not applicable to our system, since there was a rather strong interaction between the polymer and the gel of the GPC column which prevented polymer flow.

A Perkin-Elmer DSC-7 was used for both DSC and TGA. The amount of sample used for TGA was 8 mg, and that for DSC was 10 mg. The heating rate for TGA was 10 °C/min and that for DSC 20 °C/min with a heating range from 40 to 300 °C.

Results and Discussion

Zwitterion Synthesis. Zwitterion 1 was prepared from 4-(chloromethyl)benzoic acid and quinuclidine through a two-step process:



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(2)

1-[(4-Carboxyphenyl)methyl]quinuclidinium hydrochloride inner salt 3 is formed in the first step. This is followed by exchange of Cl^- by OH^- to produce the monohydrate of zwitterion 1. The structure of 1 was determined by NMR and elemental analysis. ^1H and ^{13}C NMR spectra of monohydrate 1 are shown in Figures 1 and 2.

The assignments for the ^1H NMR spectrum (Figure 1) are as follows: δ 1.80 (m, 6 H, methylene protons H_a); 2.00 (m, 1 H, proton H_b); 2.49 (m, DMSO-d_6 solvent peak); 3.39 (t, J = 9.5 Hz, 6 H, methylene protons H_c); 4.02 [s, protons of water, which is contributed by the zwitterion hydrate and solvents (D_2O and DMSO-d_6]; 4.25 (s, 2 H, methylene protons H_e); 7.36 (d, J = 11.3 Hz, 2 H, aromatic protons H_f); 7.86 (d, J = 11.3 Hz, 2 H, aromatic protons H_g).

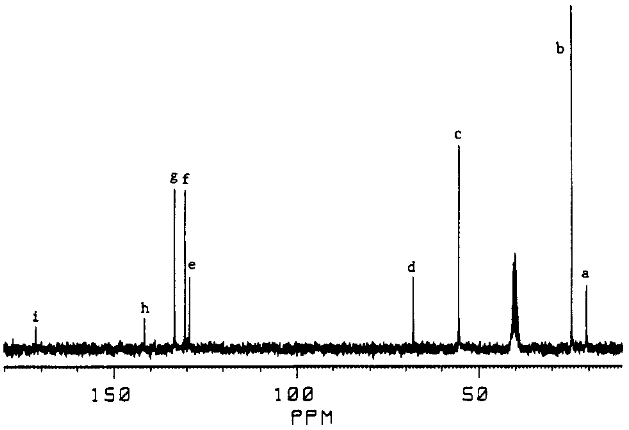
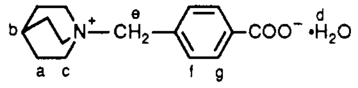


Figure 2. 50.3-MHz ^{13}C NMR spectrum of monohydrate 1: solvent, DMSO-d_6/D_2O (20:1); concentration, 6%; temperature, 40 °C.



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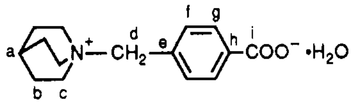
The assignments for the ^{13}C NMR spectrum (Figure 2) are as follows: δ 20.1 (tertiary carbon C_a); 24.1 (methylene carbons C_b); 39.5 (m, DMSO solvent peak); 55.0 (methylene carbon C_c); 67.6 (methylene carbon C_d); 120.0 (aromatic quaternary carbon C_e); 130.2 (aromatic carbon C_f); 133.0 (aromatic carbon C_g); 141.4 (aromatic quaternary carbon C_h); 171.2 (carbonyl carbon C_i).



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IR absorption bands of monohydrate 1 are as follows: 3600–3100 (ν_{O-H} of hydration water); 3070 and 3055 (ν_{O-H} of aromatic ring); 2947, 2904, and 2877 (ν_{C-H} of methylene); 2225 (ν_{C-N} of amine salt); 1994 and 1840 (combination bands of aromatic ring); 1685, 1600, and 1558 (ν_{C-C} of benzene ring); 1605 and 1415 ($\nu_{as(O-C-O)}$ and $\nu_{s(O-C-O)}$ of carboxylate ion); 1390 (δ_{CH_2} of methylene); 1215 and 1170 (ω_{CH_2} of methylene); 1072 and 1018 (ν_{C-N} of amine salt); 806 cm^{-1} ($\delta_{C-H(out\ of\ plane)}$ of benzene ring).

Elem anal. Calcd for monohydrate 1 ($C_{15}H_{21}O_3N$): C, 68.42; H, 8.04; N, 5.32. Found: C, 68.50; H, 7.98; N, 5.41. Calcd for anhydrous 1 ($C_{15}H_{19}O_2N$): C, 73.44; H, 7.81; N, 5.71. Found: C, 73.38; H, 7.87; N, 5.75.

In addition to elemental analysis, the amount of water of hydration of zwitterion 1 was determined by Karl–Fischer titration and TGA. Karl–Fischer titration results showed the hydrate of 1 to contain 6.55 wt % water (calcd for monohydrate: 6.82 wt %). The TGA showed the amount of water to be 6.80 wt %. TGA and Karl–Fischer titration support the elemental analysis. The zwitterion hydrate is a monohydrate within the limits of the three methods.

Polymerization of Zwitterion 1. The bulk polymerization was carried out for both anhydrous and hydrate forms of 1 at 170–260 °C. As the reaction temperature increased, the time needed to complete the polymerization decreased tremendously and the color of the polymer became darker, from pale yellow to brown. Spectroscopic analysis showed that both anhydrous 1 and monohydrate 1 yielded the same copolymer, copolymer 2. Typical ^1H 2D COSY, and ^{13}C NMR spectra of polymer 2 are shown in Figures 3–5.

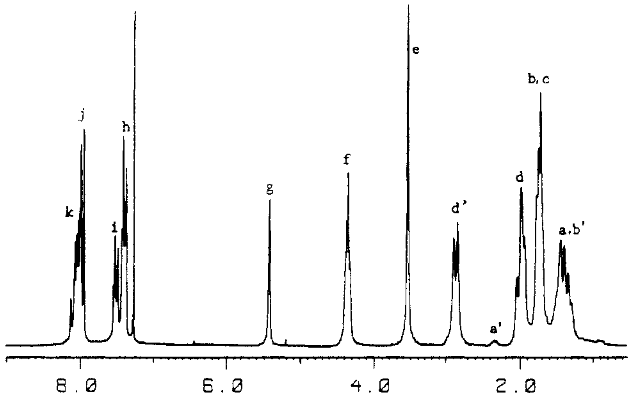


Figure 3. 200.1-MHz ^1H NMR spectrum of polymer **2**: concentration, 3%; solvent, $CDCl_3$; temperature, 25 °C.

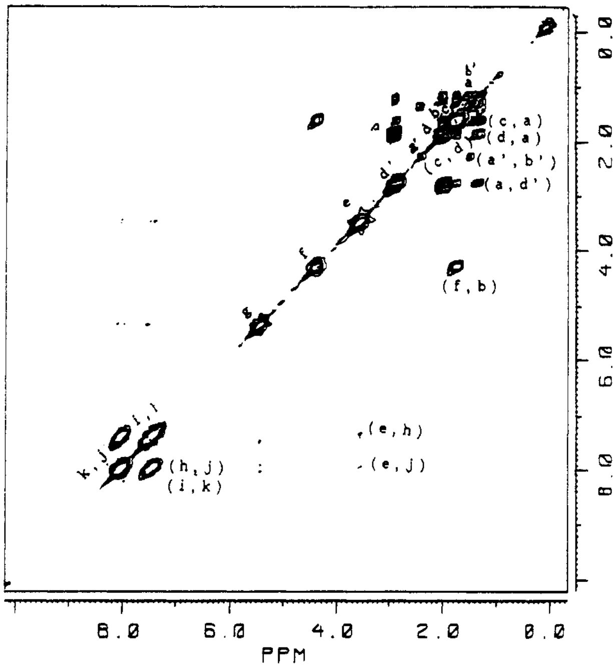


Figure 4. 2D COSY experiment of polymer **2**: solvent, $CDCl_3$; concentration, 7%; temperature, 300 °C.

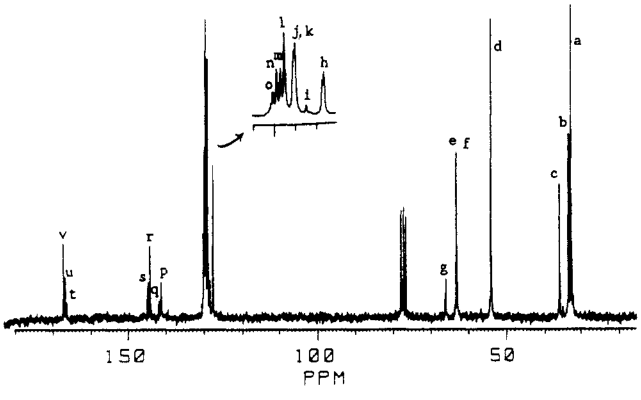
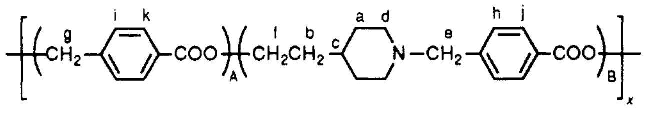


Figure 5. 50.3-MHz ^{13}C NMR spectrum of polymer **2**: concentration, 7%; solvent, $CDCl_3$; temperature, 25 °C.

The assignments for the ^1H NMR spectrum (Figure 3) are as follows: δ 1.22–1.56 (m, H_a); 1.56–1.85 (m, overlapped H_b and H_c protons); 1.85–2.09 (m) and 2.87 (d) (H_d protons at axial and equatorial positions); 3.52 (s, H_e protons); 5.41 (m, H_g protons); 7.27 (s, solvent peak); 7.32–7.58 and 7.89–8.15 (m, aromatic protons, the peaks with higher intensities corresponding to H_h and H_j protons and the peaks with lower intensities corresponding to H_i and H_k protons); 2.33 (m, proton $H_{a'}$, which is contributed by the quinuclidinium end group as shown in eq 7). Since protons H_e and H_g are the same type of methylene protons, belonging to repeating units A and B, respectively, the ratio of the two different repeat units, A:B, can be measured by the signal areas of peaks e and g.

Table I
Elemental Analysis Results of Polymer 2 with Various A:B Ratios

	calcd			found		
A:B ratio by ^1H NMR	C %	H %	N %	C %	H %	N %
17.4:82.6	73.26	7.46	5.12	72.57	7.80	5.62
32.6:67.4	73.07	7.11	4.32	71.85	6.87	4.24
68.8:31.2	72.46	6.00	2.59	71.69	6.33	3.28



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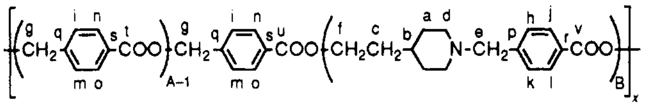
Due to the overlapping of the proton signals, a 2D COSY experiment (Figure 4) was run to confirm the assignments for the ^1H NMR spectrum. The assignments for the cross peaks in figure 4 are as follows: peak (a,c), coupling between H_a and H_c; peak (c,d), coupling between H_c and H_d; peak (a,d), coupling between H_a and H_d; peak (d,d′), coupling between H_d and $H_{d'}$; peak (d′,c), coupling between H_d and H_c; peak (a,d′), coupling between H_a and $H_{d'}$; peak (f,b), coupling between H_f and H_b; peak (g,i), long-range coupling between H_g and H_i; peak (e,h), long-range coupling between H_e and H_h; peak (h,j) or (i,k), coupling between H_h and H_j or H_i and H_k; peak (a′,b′), coupling between $H_{a'}$ and $H_{b'}$ of the quinuclidinium end group as shown in eq 7.

The assignments for the ^{13}C NMR spectrum (Figure 5) are as follows: δ 32.1 (C_a); 32.7 (C_b); 35.1 (C_c); 53.6 (C_d); 62.7 (C_e); 62.9 [C_f (C_e and C_f are partially overlapped)]; 65.6 (C_g); 127.4 (C_h); 128.3 (C_i); 128.7 (C_k); 128.9 (C_j); 129.3 (C_l); 129.5 (C_m); 129.9 (C_n); 129.9 (C_o); 141.1 (C_p); 141.5 (C_q); 144.0 (C_r); 144.5 (C_s); 165.6 (C_t); 166.0 (C_u); 166.4 (C_v).



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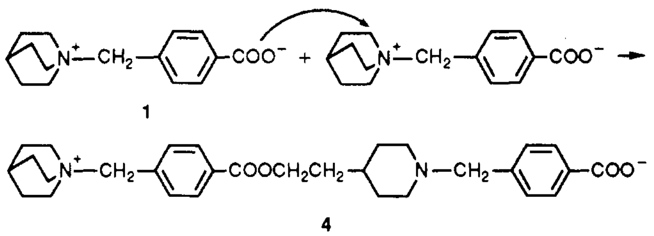
IR absorption bands of polymer **2** are as follows: 3017 (ν_{C-H} of aromatic ring); 2924, 2847, 2797, and 2762 (ν_{C-H} of methylene and methine groups); 1933 and 1813 (combination bands of aromatic ring); 1720 ($\nu_{C=O}$ of carbonyl group); 1623, 1578, and 1506 (ν_{C-C} of benzene ring); 1466, 1447, and 1416 (δ_{C-H} of methylene group); 1265 and 1123 ($\nu_{as(C-O-C)}$ and $\nu_{s(C-O-C)}$ of ester, respectively); 864 cm^{-1} ($\delta_{C-H(out\ of\ plane)}$ of benzene ring).

Elemental analyses of several polymer samples with different A:B values are shown in Table I. The data are generally consistent with the theoretical values, with the differences probably being indicative of the limitations of measurement of A:B ratios by ^1H NMR analysis and of the elemental analysis of polymeric materials.

Reaction Mechanism

It is obvious that **1** did not undergo a conventional zwitterionic polymerization, since the resultant polymer contains both A and B as repeating units instead of having only B units. During the process of polymerization, as soon as the sealed polymerization tube containing **1**, either monohydrate or anhydrous, was heated at the selected temperature, a sublimate was formed on the top of the tube. This sublimate was identified as quinuclidine by ^{1}H NMR spectroscopy. For the hydrate, there was also water condensed at the top of the tube.

A reaction mechanism is proposed based on the experimental observations and the structure of polymer 2. Initiation involves the complex set of reactions shown in eqs 3–6. Zwitterion 1 undergoes self-reaction to yield dimer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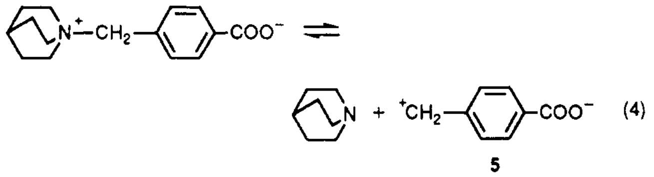
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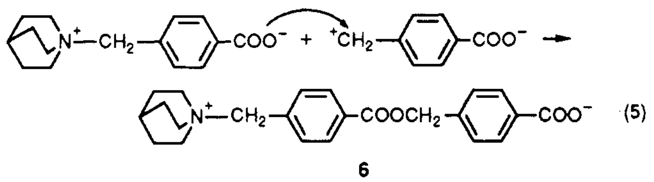
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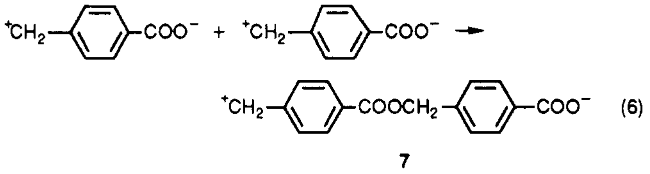

(6)

zwitterion 4 (eq 3). Zwitterion 1 also loses quinuclidine to form zwitterion 5 (eq 4).[8] Zwitterion 5 undergoes self-reaction to form dimer zwitterion 7 (eq 6). Cross-reaction between zwitterions 1 and 5 yields dimer zwitterion 6 (eq 5). It should be noted that, instead of the heterolytic dissociation represented by eq 4, it is also possible that a carboxy attack on the methylene unit attached to the phenyl ring results in the displacement of quinuclidine. However, we believe the reaction represented in eq 4 is more likely than the alternative due to the formation of a stable benzyl cation. Also, the steric hindrance due to the phenyl ring and quinuclidine should help prevent nucleophilic attack by carboxylate anion on the methylene unit attached to the phenyl ring. Propagation follows in a similar manner, with various-sized zwitterions undergoing self- and cross-reaction. Any-sized zwitterion which contains a quinuclidinium end group can undergo loss of quinuclidine prior to propagation. There are two basic types of zwitterions in the reaction systems. Both contain one carboxylate anionic end group. The two types of zwitterions differ in that one contains a quinuclidinium end group (e.g., 1, 4, and 6) while the other contains a benzyl carbocation end group (e.g., 5 and 7). Thus, propagation involves a combination of carboxylate anion attack on benzyl carbocation and quinuclidinium centers.]-

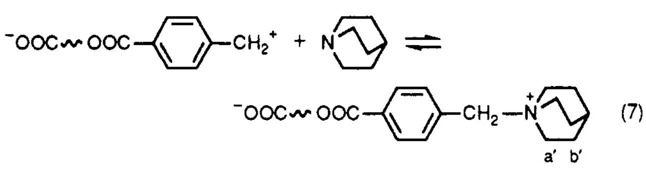
Table II shows the results of polymerizations under different reaction conditions. The number-average molecular weight was determined by VPO and the A:B ratio was measured by the ^{1}H NMR signal areas of peaks e and g (Figure 3). Several conclusions can be drawn. Although the polymerization of the hydrate of zwitterion 1 gives the same type of polymer as the anhydrous zwitterion, the molecular weights and the A:B ratios of the polymers prepared from the monohydrate are somewhat lower than those prepared from the anhydrous zwitterion. The polymers prepared from samples sealed under nitrogen have somewhat lower molecular weights and A:B ratios than the polymers prepared from samples under vacuum. As the temperature increased, the A:B ratio increased for both polymers prepared from anhydrous 1 and monohydrate of 1. The molecular weight of the polymer prepared at 180 °C under a continuous vacuum was the highest. The molecular weight increased as the reaction time increased, while the A:B ratio was slightly increased (see polymerization of monohydrate 1 at 240 °C).

Table II
Compositions of Polymer 2 Prepared under Different Conditions

reaction condition		composition A:B		$\bar{M}_n \times 10^{-3}$	
temp (°C)	time (h)	in vacuum[a]	in nitrogen[b]	in vacuum	in nitrogen
		Anhydrous			
180	27	31.5:68.5	23.9:76.1	9.3	
190	23	32.6:67.4	26.3:73.7	8.8	7.1
205	12	33.1:66.9	28.0:72.0	10.2	
220	9	43.4:56.6	31.5:68.5	8.0	7.0
		Hydrate			
180	72	17.4:82.6		4.3	
202	24	22.7:77.3		6.0	
240	0.317	26.8:73.2			
240	0.633	27.1:72.9		5.3	
240	0.95	28.6:71.4		6.4	
180[c]	48	68.8:31.2		16.6	

[a] Sample sealed in a vacuum of 0.1 Torr. [b] Sample sealed in a nitrogen atmosphere. [c] Sample polymerized with continuous pumping in a vacuum of 0.1 Torr.

The results indicate that the loss of quinuclidine from various zwitterionic species is reversible. That is, the following reaction is important:


(7)

Higher reaction temperatures result in increasing the A:B ratio; i.e., the copolymer becomes richer in the repeat unit A derived from expulsion of quinuclidine. At higher reaction temperature, the quinuclidine concentration in the reaction mixture is decreased. Reaction 7 is less important, with the result that the concentration of quinuclidinium end group is decreased relative to the concentration of benzyl carbocation end groups. The polymer is richer in B repeat unit when synthesized from zwitterion 1 monohydrate than when synthesized from the anhydrous zwitterion. The presence of water in the reaction mixture apparently decreases the extent of quinuclidine expulsion, but the reason is unclear. Perhaps water stabilizes the quinuclidinium end groups. Further support for this mechanism concerning the effect of water comes from the polymerization carried out under a continuous vacuum. The water concentration in the reaction mixture is decreased most rapidly, quinuclidine expulsion is maximum, and the polymer composition shows the highest amount of A repeat units of all the samples.

We have no direct evidence to support any termination mechanism. The polymer molecular weight varied only

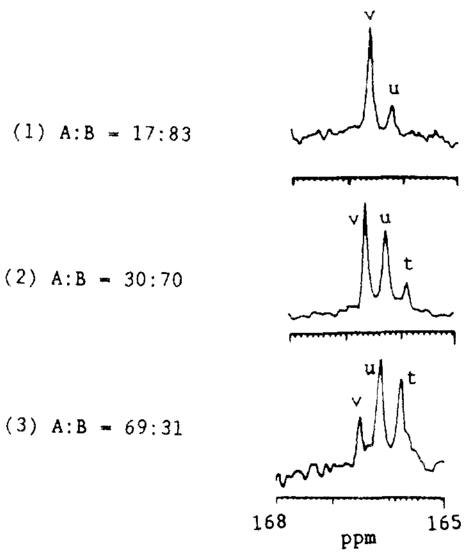


Figure 6. 50.3-MHz ^{13}C NMR spectra of polymer **2** with different A:B ratios: carbonyl carbon region, 165–168 ppm.

within a relatively narrow range. In general, polymer molecular weight appears to be related to the concentration of water present in the reaction mixture. The polymer molecular weights were higher for samples prepared from anhydrous zwitterion compared to zwitterion monohydrate. The highest polymer molecular weight (1.66×10^4) was obtained in the polymerization carried out under a continuous vacuum where the water is rapidly removed from the reaction mixture. The most likely mechanism for the effect of water on molecular weight is termination of quinuclidinium, carboxylate, and benzyl carbocation centers by reaction with water. The expected results for such terminations is the formation of carboxyl and hydroxyl polymer end groups, from both benzyl carbocation and quinuclidinium centers. However, we have no direct experimental evidence for these or other end groups.

The ^{13}C NMR spectra of polymer **2** samples with different A:B ratios support the random polymer chain structure. The expanded 165–168 ppm regions of the ^{13}C NMR spectra show three different carbonyl carbon signals (Figure 6). They are assigned as follows: peak v, carbonyl carbon of the B-block; peak u, carbonyl carbon of the A-block adjacent to the B-block; peak t, carbonyl carbon of the A-block. The relative signal areas of the peaks are in agreement with the A:B ratio. For the polymer with an A:B ratio of 17:83, there is little probability of forming the A-block and peak t of the A-block was not observed. As the A:B ratio increased, the probability of forming an A-block increased as evidenced by an increase in the signal area of peak t.

The thermal properties of polymer **2** were evaluated by DSC and TGA. The DSC scans of polymer **2** showed that there was a T_g at 73 °C, no melt transition, and the polymer started to decompose at 300 °C. TGA data also showed that the polymer was reasonably stable since the weight loss of the polymer was less than 2% at 280 °C. The polymer showed a sharp decline in weight at >310 °C.

Acknowledgment. We gratefully acknowledge financial support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the PSC–CUNY Research Program of City University of New York.

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(8) One of the reviewers suggested a reasonable alternative to eq 4: carboxylate attack on the methylene unit between the quinuclidinium and benzene rings to displace quinuclidine and form A repeating units.

Registry No. 1, 142457-40-7; 1 (homopolymer), 142457-42-9; 1 (SRU), 142457-43-0; $ClCH_2C_6H_4$-*p*-CO_2H, 1642-81-5; quinuclidine, 100-76-5.