(18) Leitz, F. B.; Shorr, J.; Spencer, S.; Denno, N. Research and Development Progress Report, Office of Saline Water, U.S. Department of the Interior, 1974, No. 989.
(19) Kamachi, M.; Kurihara, M.; Stille, J. K. *Macromolecules* **1972**, *5*, 161.
(20) Winnicki, T.; Blazejewska, G.; Mika-Gibala, A. *Desalination* **1980**, *32*, 77.
(21) Funabashi, H.; Miyamoto, Y.; Isono, Y.; Fujimoto, T.; Matsushita, Y.; Nagasawa, M. *Macromolecules* **1983**, *16*, 1.
(22) Isono, Y.; Tanisugi, H.; Endo, K.; Fujimoto, T.; Hasegawa, H.; Hashimoto, T.; Kawai, H. *Macromolecules* **1983**, *16*, 5.
(23) Fujimoto, T.; Ohkoshi, K.; Miyaki, Y.; Nagasawa, M., Submitted to *J. Membr. Sci.*, part 1 of this series.
(24) Miyaki, Y.; Iwata M.; Fujita, Y.; Tanisugi, H.; Isono, Y.; Fujimoto, T., submitted to *Macromolecules*, part 2 of this series.
(25) Meyer, K. H.; Mark, H. *Ber. Dtsch. Chem. Ges.* **1928**, *61*, 1948.
(26) Glazer, J. *J. Polym. Sci.* **1954**, *14*, 225.
(27) Binder, J. L. *J. Polym. Sci., Part A* **1963**, *1*, 37.
(28) Gilbert, E. E. In "Sulfonation and Related Reactions"; Cotton, F. A., Ed.; Wiley: New York, London, Sydney, 1965; p 18.
(29) Leitz, F. B.; McRae, W. A. *Desalination* **1972**, *10*, 293.
(30) Carr, C. W.; Sollner, K. *Biophys. J.* **1964**, *4*, 189.
(31) Weinstein, J. N.; Misra, B. M.; Kalif, D.; Caplan, S. R. *Desalination* **1973**, *12*, 1.

Zwitterion Polymerization of 2-Methyl-2-oxazoline and Acrylic Acid: Characterization of Ether-Soluble Products

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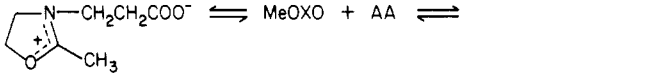
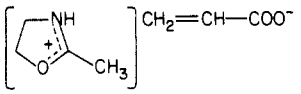
ABSTRACT: 2-Methyl-2-oxazoline (MeOXO) and acrylic acid (AA) were previously found to undergo reaction to form a copolymer, $[CH_2CH_2\text{–}N(COCH_3)CH_2CH_2COO]_n$, which is precipitated from the reaction mixture by adding diethyl ether. A considerable amount (30%) of low molecular weight products remains soluble in the ether solution. The ether-soluble products were fractionated by analytical and preparative HPLC, and the isolated fractions were identified by ^1H and ^{13}C NMR. The formation of the various ether-soluble products is discussed in terms of the overall mechanism of zwitterion polymerization.

Introduction

Zwitterion polymerization of 2-methyl-2-oxazoline (MeOXO) and acrylic acid (AA) was reported by Saegusa and Tomalia and their co-workers.[1,2] Our study of MeOXO–AA provided strong evidence for the copolymer structure, $[CH_2CH_2\text{–}N(COCH_3)CH_2CH_2COO]_n$, and the polymerization mechanism.[3] The initial reactions between MeOXO and AA involve the formation of the genetic zwitterion I and the protonated MeOXO species II. The

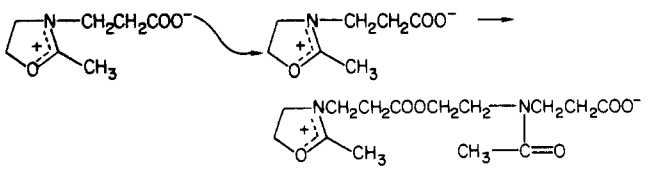


I



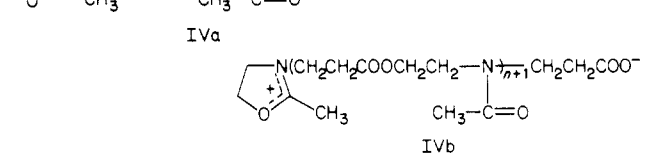
II

former is responsible for initiation and propagation while the latter participates (along with AA) in termination. The genetic zwitterion reacts with itself to form a dimer zwitterion III. Growth continues in a smilar manner by



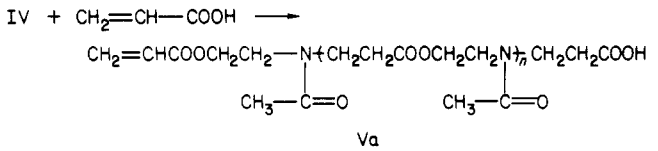
III

the genetic zwitterion reacting with larger-sized zwitterions (macrozwitterions) (IV) and by the reaction of macrozwitterions with each other. Termination occurs by reaction of macrozwitterions with acrylic acid and with II to produce polymer structures Va and Vb containing olefinic, acetamido, and carboxylic end groups.

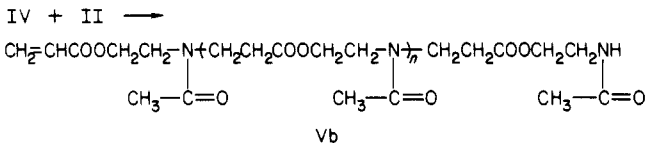


IVa

IVb



Va



Vb

Our previous work was limited to the characterization of the polymer obtained by precipitation of the reaction mixture in diethyl ether. A considerable amount (30%) of products is found in the ether solution. The ether-soluble products have not previously been studied. The characterization of these products is important to fully establish and understand the reactions which lead to low molecular weight products during zwitterion polymerization. In this paper we report on the fractionation and characterization of various products found in the ether solution.

Experimental Section

Materials. Acetonitrile, 2-methyl-2-oxazoline (MeOXO), and acrylic acid (AA, Aldrich) were dried and purified as previously reported.[3] Methanol (HPLC, Fisher) and anhydrous diethyl ether (Fisher) were used as received.

Polymerization and Isolation of Ether-Soluble Products. MeOXO (150 mmol), AA (150 mmol), *p*-methoxyphenol (0.8 mmol), and acetonitrile (15 mL) were mixed inside a drybox, placed in a sample tube, cooled with liquid nitrogen, sealed under vacuum, and heated at 70 °C for 48 h. The reaction mixture was dissolved in 25 mL of methanol and precipitated into 800 mL of anhydrous diethyl ether. The ether solution was decanted from the precipitated product and evaporated under vacuum to give a gummy product, which was then dried in a vacuum oven at 35

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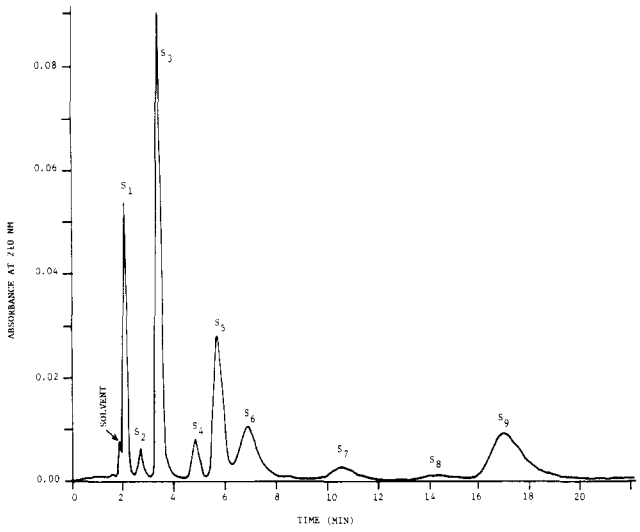


Figure 1. HPLC of ether-soluble products on a μ-Bondapak C_{18} column. Mobile phase: methanol–water–TFA (50:950:0.25).

°C overnight; yield 30%. The present paper is devoted exclusively to the characterization of this ether-soluble product.

High-Performance Liquid Chromatography (HPLC). Analytical HPLC and preparative HPLC were used for various analyses and separations. Analytical HPLC was carried out at room temperature with a Waters system consisting of a Model M-600 solvent delivery unit, a 46K universal liquid chromatography injector, and a Model 450 variable-wavelength UV monitor with an 8-μL flow-through cell fitted with a μ-Bondapak C_{18} column. The mobile phase was CH_3OH–H_2O–CF_3CO_2H (100:900:0.3) at a flow rate of 2 mL/min maintained by a pressure of 2000–2500 psi. Distilled water, methanol (Fisher HPLC grade), and trifluoroacetic acid (Fisher) (TFA) were filtered prior to use. The recorder chart speed was 1/2 in./min. Sample size was in the range 1–10 μg of polymer injected in volumes of 1–25 μL. The UV detector was set at 210 nm at 0.1 AUFS (absorbance units for full scale).

The product mixture isolated from the ether solution was fractionated by preparative HPLC with a Waters Prep LC/System 500 using a μ-Bondapak C_{18} column with methanol–water–TFA (50:950:0.3) as the mobile phase. A solution of the product mixture, 2 g in 10 mL of mobile phase system, was injected into the column and eluted at a flow rate of 100 mL/min. Fifty-milliliter fractions of the eluent were collected and examined by analytical HPLC for purity. After fraction S_6 (see Figure 1) eluted from the column the mobile phase was changed to methanol–water–TFA (100:900:0.3). Pure fractions (i.e., fractions containing one component as determined by HPLC) of the same component were combined. To each 500 mL of the eluent, 5 mg of *p*-methoxyphenol was added (to prevent radical polymerization) and concentrated with a Rotovapor evaporator under reduced pressure (temperature of the distilling pot was maintained at 30–35 °C) to a volume of 10 mL, freeze-dried, and dried in a vacuum desiccator overnight.

Spectroscopic Analysis. ^1H NMR spectra (80 and 200 MHz) were recorded on IBM NR 80 and WP 200 FTNMR spectrometers, respectively. Natural-abundance ^{13}C NMR spectra were recorded on the IBM NR 80 spectrometer operating at 20.1 MHz.

Results and Discussion

In the zwitterion polymerization of MeOXO–AA, the polymerized monomer mixture is precipitated into an excess of diethyl ether to obtain the copolymer. We have previously reported the characterization of the precipitated copolymer.[3] In a typical solution polymerization experiment about 30% of the products go into ether solution when the reaction mixture is precipitated. The product obtained after evaporation of ether is a light yellow, gummy material soluble in methanol, water, DMF, and Me_2SO.

Figure 1 shows the analytical HPLC of the ether-soluble product mixture. By comparison with the HPLC of authentic compounds, S_1 and S_4 were identified as acrylic acid and *p*-methoxyphenol. (*p*-Methoxyphenol had been added to the polymerization system as an inhibitor to prevent radical polymerization of AA.) Assuming all the fractions to have the same extinction coefficient, the percentage of each fraction was calculated based on the peak areas in Figure 1, and the results are shown in Table I. Interestingly, there was no unreacted MeOXO found among the products in the ether solution. In order to ascertain whether or not unreacted monomers are present after the polymerization is complete, a small quantity of the polymerized reaction mixture was analyzed by HPLC. Results showed the absence of any unreacted MeOXO and the presence of only a small amount of AA.

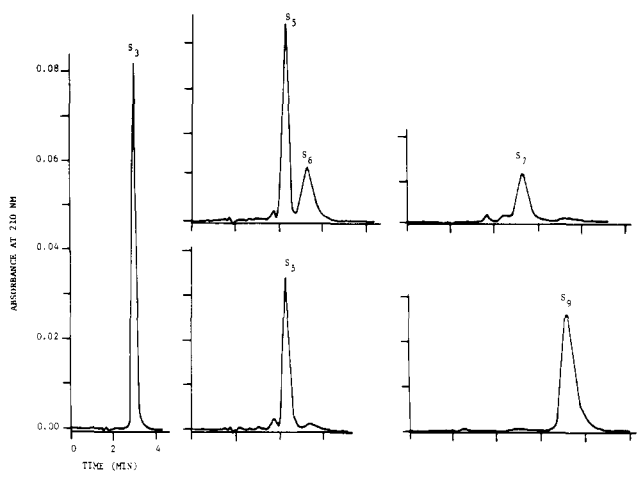


Figure 2. HPLC of purified fractions on a μ-Bondapak C_{18} column. Mobile phase: methanol–water–TFA (100:900:0.25).

Table I
Composition of Products in the Ether Solution

fraction	S_1	S_2	S_3	S_4	S_5	S_6	S_7	S_8	S_9
mol %	11.3	2	32	3	16	11.3	3.3	2	19.1

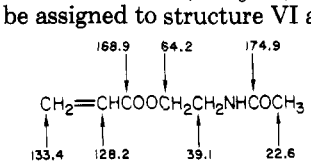
The ether-soluble product mixture was fractionated by preparative HPLC, and the analytical HPLC of the isolated fractions is shown in Figure 2. Fractions S_3 and S_9, the major fractions in the ether solution, were obtained in high-purity form. S_5 and S_7 were obtained with 84% and 71% purities, respectively. S_5 contained about 12% S_6 and small amounts of S_3 and S_4 as impurities. S_7 contained S_9 (12%), S_6 (12%), and S_5 (5%) as impurities. S_6 was isolated as a mixture of 40% S_6 and 60% S_5. S_2 and S_8 could not be isolated mainly due to their presence in very small amounts. S_5, S_6, and S_7 were obtained in quantities sufficient only for ^1H NMR.

Characterization of Isolated Fractions. Fraction S_3. Structure VI is proposed for S_3 based on ^1H and ^{13}C

$$CH_2{=}CHCOOCH_2CH_2NHCOCH_3$$

VI

NMR spectral data. The ^1H NMR spectrum in D_2O (Figure 3) showed signals for olefinic protons (3 H, multiplet, 6.15 ppm), acetamido methyl (3 H, singlet, 1.98 ppm), OCH_2 (2 H, triplet, 4.27 ppm), and NCH_2 (2 H, triplet, 3.49 ppm). When the proton NMR was recorded in Me_2SO, the NH proton signal was observed as a broad singlet at 7.97 ppm. The observed ^{13}C chemical shift values (solvent, D_2O; internal standard, CH_3CN, 1.70 ppm relative to Me_4Si) can be assigned to structure VI as shown below.



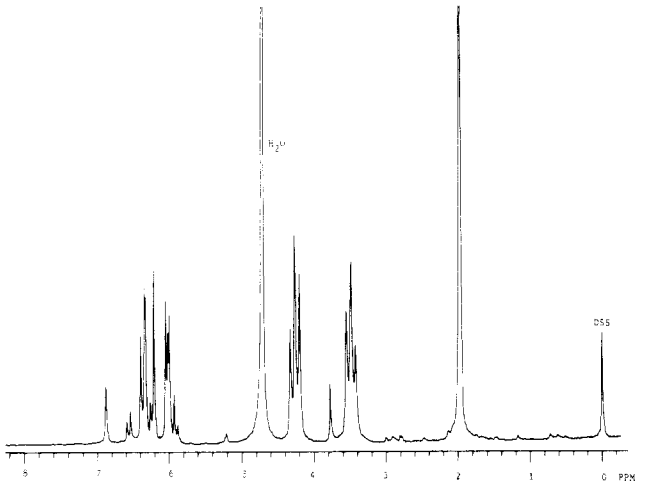


Figure 3. 80-MHz ^1H NMR spectrum of S_3. Conditions: 3% (w/v) in D_2O; 30° pulse angle; 25 °C; 7.9-s delay between pulses; 300 acquisitions; DSS internal standard.

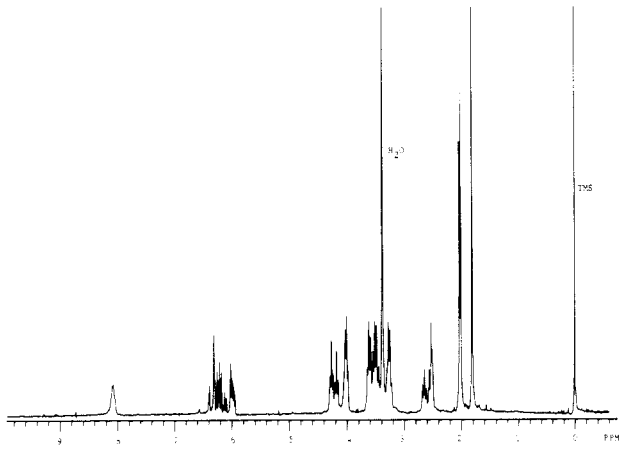
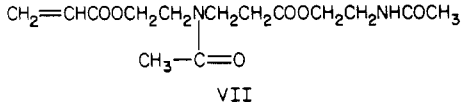


Figure 4. 200-MHz ^1H NMR spectrum of S_9 Conditions: 2.5% (w/v) in Me_2SO-d_6; 30° pulse angle, 25 °C; 12.7-s delay between pulses; 100 acquisitions; Me_4Si internal standard.

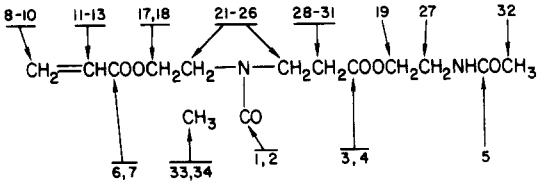
The assignments of the various signals were based on the chemical shift values in relationship to those for analogously substituted carbons.[4] Both ^{13}C and ^1H NMR data are in good agreement with structure VI.

Fraction S_9. Figure 4 shows the 200-MHz ^1H NMR spectrum of S_9. The ^1H NMR data strongly support structure VII for S_9. The singlet at 1.81 ppm and the



VII

doublet at 2.01 ppm have been assigned to the methyl groups of $NHCOCH_3$ and $NCOCH_3$, respectively. The methylene group of CH_2CO appears as two triplets (2.64 and 2.52 ppm) due to restricted rotation around the C–N bond. The effect of C–N restricted rotation is seen for all the methylene, olefinic, and methyl ($NCOCH_3$) ^1H NMR signals. The OCH_2 near the olefinic end group appears as two triplets (4.27 and 4.18 ppm) and the OCH_2 near the acetamido group as two closely spaced triplets (4.01 ppm). The methylene attached to the nitrogen in the acetamido group appears as a multiplet (3.27 ppm) and the other two NCH_2 groups appear as two multiplets (3.62 and 3.48 ppm). The olefinic protons appear as a complex multiplet at 6.15 ppm. The 200-MHz ^1H NMR spectrum, recorded at 125 °C to overcome the effect of C–N restricted rotation, shows the olefinic protons as three sets of quartets (12 lines) as expected for the three different protons in the olefinic group (CH_2=CHCOO). Similarly, the methylene and methyl proton signals were observed as expected for structure VII. Figure 5 shows the ^{13}C NMR spectrum of S_9. The results are consistent with structure VII with the various signals assigned as follows:



Signals 15, 16, and 20 are due to the radical inhibitor, *p*-methoxyphenol. Assignments were based on the chemical shift values in relationship to those for analogously substituted carbons[4] as well as the ^{13}C data of S_3. Similar to the ^1H NMR spectrum, the effect of C–N restricted rotation is seen for ^{13}C signals as we observe more than one signal for many of the carbons in structure VII. Since we have discussed this effect in greater detail in our previous publication,[3] further discussion seems unnecessary here. Both ^{13}C and ^1H NMR data are in excellent agreement with the proposed structure VII for S_9.

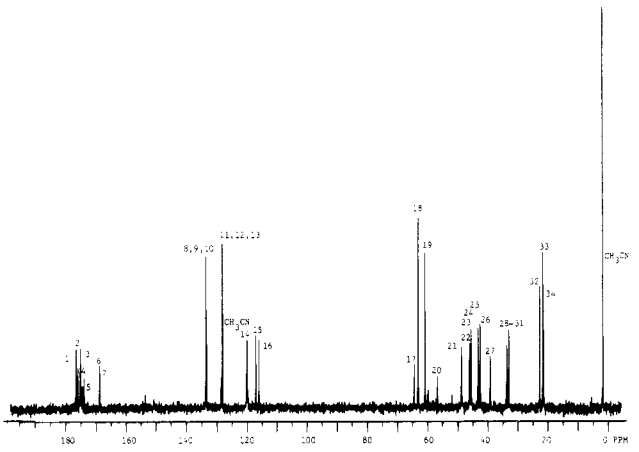
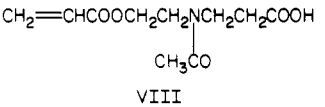


Figure 5. 20.1-MHz ^{13}C NMR spectrum of S_9. Conditions: 15% (w/v) in D_2O; 30° pulse angle; 32 °C; 1.6-s delay between pulses; 44 726 acquisitions; CH_3CN internal standard, CH_3CN, 1.70 ppm relative to Me_4Si.

Fractions S_5, $S_{5,6}$, and S_7. All three fractions showed the presence of a multiplet at 6.15 ppm in the ^1H NMR spectra due to olefinic protons. Further, the olefinic region of the spectrum was similar to those of S_9 and S_3. Figure 6 shows the 200-MHz ^1H NMR spectrum of S_5 recorded at room temperature. When the spectrum was recorded at 125 °C (to overcome the effect due to C–N restricted rotation), the multiplet at 6.15 ppm appeared as 12 lines as expected for the CH_2=CHCOO group. Similar results were observed for $S_{5,6}$ and S_7. On the basis of ^1H NMR data, we conclude that all fractions isolated from the ether solution contained the olefinic group, CH_2=CHCOO, as part of their structures. We should also note here that all the fractions isolated from the precipitated polymer[3] contained the same olefinic end group.

On the basis of the ^1H NMR results the most probable structure that can be proposed for S_5 is VIII. Fraction



VIII

S_5 contained about 12% S_6 as an impurity and the NMR signals at 1.8 and 7.95 ppm in Figure 6 are due to NHC-

Table II
Calculated and Observed ^{1}H NMR Ratios[a,b]

	ratio of CH_2=CHCOO protons to other protons									
	OCH_2		NCH_2		CH_2CO		$NCOCH_3$		$NHCOCH_3$	
fraction	obsd	calcd	obsd	calcd	obsd	calcd	obsd	calcd	obsd	calcd
S_5 (VIII)	0.81	0.67	1.56	1.33	0.81	0.67	1.06	1.00		
$S_{5,6}$ (VIII, IX)	0.67	0.67	1.60	1.60	0.46	0.40	1.06	1.00	0.37	0.40
S_7 (Xa, b)	1.22	1.33	3.77	4.00	0.94	1.30	2.67	3.00		

[a] Calculated based on structures VIII, IX, and Xa,b. [b] 80-MHz ^{1}H NMR was recorded in D_2O (2–2.5% (w/v)) at 25 °C with a 30° pulse angle and DSS internal standard. The delay between pulses was 13 s for S_5 and $S_{5,6}$ and 7 s for S_7, with the number of acquisitions ranging from 100 to 200.

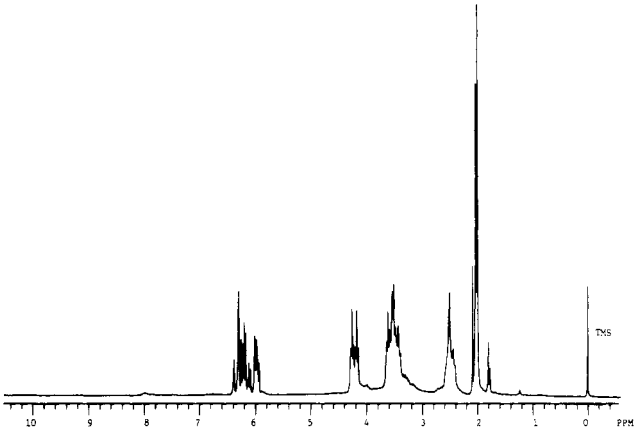
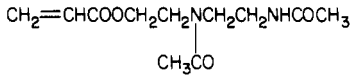


Figure 6. 200-MHz ^{1}H NMR spectrum of S_5. Conditions: 2.5% (w/v) in Me_2SO-d_6 (100%); 30° pulse angle; 25 °C; 12.7-s delay between pulses; 128 acquisitions; Me_4Si internal standard.

OCH_3 of S_6. Various proton ratios calculated from NMR data are shown in Table II and the results agree with structure VIII. When the 200-MHz ^{1}H NMR spectrum of S_5 was recorded at 125 °C, a triplet for OCH_2 (4.2 ppm), a multiplet for the two NCH_2 groups (3.5 ppm), a singlet for $NCOCH_3$ (2.0 ppm), and a multiplet (12 lines) for CH_2=CHCOO (6.1 ppm) were observed, supporting the proposed structure for S_5. The expected carboxylic proton was not observed in the spectrum. This may be due to the presence of traces of water in the NMR sample. However, when a sample of $S_{5,6}$ (60/40 mixture of S_5 and S_6) was thoroughly dried and the 200-MHz ^{1}H NMR spectrum recorded in Me_2SO-d_6 (100% deuterated), a carboxylic proton signal was observed at 12.31 ppm. Further, the unfractionated ether-soluble product mixture also showed a NMR signal for a carboxylic proton at 12.31 ppm.

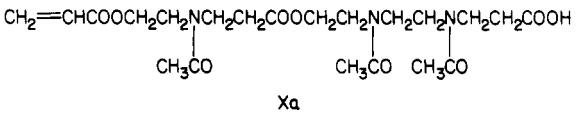
Although S_6 was not isolated in pure form, the structure IX was deduced for S_6 by considering the difference in ^{1}H



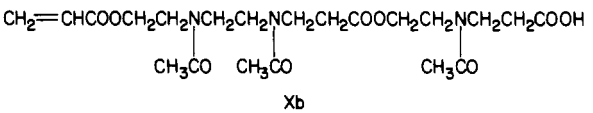
IX

NMR spectra of S_5 and $S_{5,6}$. Table II shows various observed (based on ^{1}H NMR results) and calculated proton ratios for structures VIII and IX for $S_{5,6}$ which contained a 60/40 mixture of S_5 and S_6 (calculated from HPLC). The ratio of S_5 and S_6 was also calculated from the COO*H* and N*H* NMR signal areas and found to be 58/42, in good agreement with the HPLC results. The high-temperature (125 °C) ^{1}H NMR of $S_{5,6}$ showed a triplet at 4.2 ppm (OCH_2), a multiplet (12 lines) for CH_2=CHCOO, a singlet at 2.00 ppm ($NCOCH_3$ of VIII and IX), a singlet at 1.8 ppm ($NHCOCH_3$ of IX), a triplet at 2.45 ppm (CH_2CO of VIII), two triplets at 3.20 and 3.35 ppm (for NCH_2 of IX), and a multiplet at 3.5 ppm (NCH_2 of VIII). The ^{1}H NMR results are in good agreement with the proposed structures VIII and IX.

The isolated fraction S_7 contained a total of 29% S_9, S_6, and S_5 as impurities. The 200-MHz ^{1}H NMR spectrum showed a broad signal for COOH (12.2 ppm), a doublet for $NCOCH_3$ (2.00 ppm), and multiplets for OCH_2 (4.2 ppm), NCH_2 (3.4 ppm), CH_2CO(2.5 ppm), and CH_2=CHCOO (6.15 ppm). Signals due to N*H* and NHCOC*H*$_3$ of S_6 and S_9 were also observed at 7.9 and 1.8 ppm, respectively. The structures which best fit the NMR results for the main component of S_7 are Xa and Xb. A distinction between



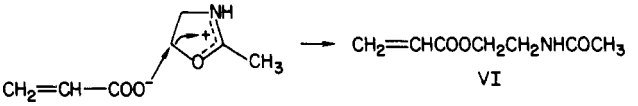
Xa



Xb

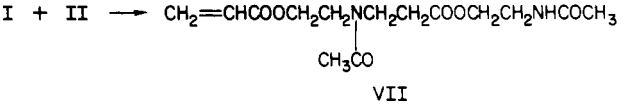
Xa and/or Xb cannot be made since ^{1}H NMR is compatible with both structures. The calculated and observed proton ratios for Xa and Xb are shown in Table II.

Reactions Leading to Various Products in Ether Solution. The formation of the various ether-soluble products can be understood by considering the mechanism proposed for zwitterion polymerization of the MeOXO–AA monomer system. As indicated earlier MeOXO and AA initially form the genetic zwitterion I (which is responsible for initiation and propagation to yield alternating copolymer) and the protonated MeOXO species II (which is responsible for termination of growing zwitterions giving olefinic and acetamido end groups). The major product among those found in the ether solution, S_3, is formed from II by the nucleophilic attack of the acrylate anion to open the oxazolinium ring.



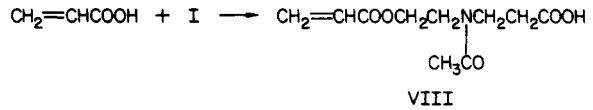
VI

The reaction of genetic zwitterion I with the protonated MeOXO species II results in the formation of S_9, which we have isolated and characterized as VII.



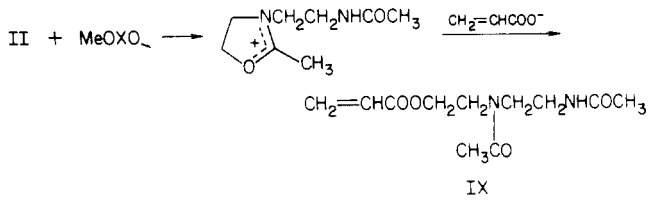
VII

S_5 is formed by the reaction of the genetic zwitterion with acrylic acid



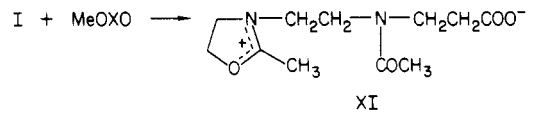
VIII

S_6 is formed by the reaction of MeOXO with II and a subsequent ring-opening nucleophilic attack of the acrylate anion on the oxazolinium ring.



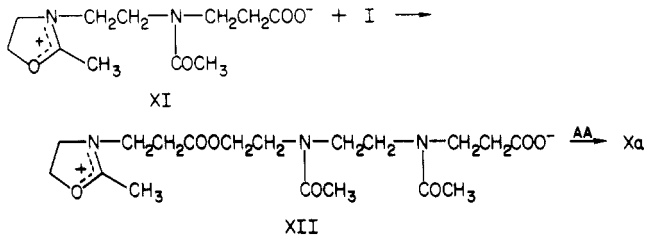
IX

S_7 is formed by a sequence starting with the reaction of the genetic zwitterion with MeOXO to form XI followed



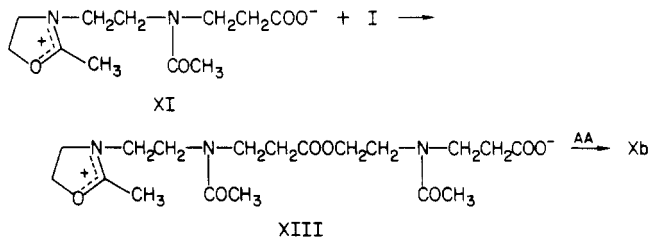
XI

by reaction with another genetic zwitterion and finally with AA. If the carboxylate anionic end of the genetic zwitterion reacts to open the oxazolinium ring of XI to form XII, the final result is Xa after reaction of XII with AA.



XII

If the carboxylate anionic end of XI reacts with the oxazolinium ring of the genetic zwitterion to form XIII, the final result is Xb after reaction of XIII with AA.



XIII

Since we have not found any cyclic products in the ether solution or in the precipitated copolymer,[3] cyclization is not responsible for termination in the zwitterion polymerization of the MeOXO–AA monomer system. There is no evidence of any homopolymerization of AA during zwitterion polymerization.

Some comment is needed on the presence of unreacted AA but not MeOXO in the reaction mixture after the completion of polymerization. All the products isolated from the ether solution contained a 1:1 ratio of AA:MeOXO with the exception of S_5 and S_6, which contained 2:1 and 1:2 ratios, respectively. We have also observed the presence of homosequences of MeOXO in S_6 and S_7. It is therefore possible to expect a few homosequences of MeOXO in the fractions isolated from the ether-insoluble product. The various higher molecular weight products in the ether-insoluble fraction were found to contain equimolar amounts of MeOXO and AA but the analytical limitation of NMR did not allow us to preclude minor amounts of MeOXO homosequences in these products. However, we have observed the presence of an additional hydrolysis product from the ether-insoluble fraction[3] which may have derived from homosequences of MeOXO in the ether-insoluble products. The presence of a small amount of unreacted AA when the polymerization was complete may then be due to reaction of MeOXO to give homosequences.

The overall zwitterion polymerization of the MeOXO–AA monomer system can be described from the results of this study as well as our earlier study[3] on the characterization of ether-insoluble products. The initially formed genetic zwitterion I reacts with itself or with larger-sized zwitterions to give macrozwitterions. Macrozwitterions terminate by reacting with either AA or protonated MeOXO species II to yield products containing one olefinic end group and either a carboxylic or acetamido end group. The genetic zwitterion and the protonated MeOXO species II react with each other or with one or the other monomer to give dimer (S_9) and various other products that were found in the ether-soluble fraction. The ether-insoluble products contained the hexamer up to 16-mer. The trimer, tetramer, and pentamer are believed to be the fractions S_8, P_1, and P_2 that we have not been able to isolate (P_1 and P_2 are in the ether-insoluble portion). Fractionation and characterization of the ether-soluble and ether-insoluble products strongly support the mechanism that is proposed for the zwitterion polymerization of the MeOXO–AA system.

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References and Notes

(1) Saegusa, T.; Kimura, Y.; Kobayashi, S. *Macromolecules* **1977**, *10*, 236.
(2) Tomalia, D. A.; Thill, B. P.; Regulski, T. W. U.S. Patent 4 016 192, Apr 5, 1977.
(3) (a) Odian, G.; Gunatillake, P. A. *Macromolecules* **1984**, *17*, 1297. (b) Odian, G.; Gunatillake, P. A. *Polym. Prepr., Am. Chem. Soc., Div. Polym. Chem.* **1983**, *24* (1), 135.
(4) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. "Spectroscopic Identification of Organic Compounds", 4th ed., Wiley: New York, 1981.