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Zwitterion Polymerization of 2-Methyl-2-oxazoline and Acrylic Acid

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ABSTRACT: The zwitterion polymerization of 2-methyl-2-oxazoline (MeOXO) and acrylic acid (AA) has been investigated in bulk and solution (DMF and acetonitrile) at 60–70 °C. Vapor pressure osmometry showed the number-average molecular weight to be in the range 590–2760, depending on reaction conditions. The copolymer composition was established as 1:1 (MeOXO:AA) by proton NMR. Proton and ^{13}C NMR spectroscopy identified the repeating unit as $-CH_2CH_2N(COCH_3)CH_2CH_2COO-$ and the end groups as olefinic, carboxyl, and acetamido. Infrared spectroscopy supports the NMR results. Hydrolysis experiments corroborated both the copolymer composition and identity of end groups. High-performance liquid chromatography showed that the copolymer product consists of different-sized molecules and not all molecules have the same two end groups. A mechanism is proposed to describe the MeOXO–AA polymerization. MeOXO and AA form a genetic zwitterion which is responsible for initiation. Polymer growth involves various-sized zwitterions reacting with each other and with the genetic zwitterion by a ring-opening attack of carboxylate anion on the quaternary MeOXO ring. Termination occurs by reaction of growing zwitterions both with acrylic acid and with a quaternized MeOXO–acrylate salt (formed by proton transfer between MeOXO and AA). Direct proton NMR analysis of the polymerizing MeOXO–AA system gave evidence for the genetic zwitterion.

Introduction

Zwitterion polymerization occurs spontaneously between a pair of nucleophilic (N) and electrophilic (E) monomers. Polymerization is considered to proceed via a zwitterion intermediate $^+NE^-$ to form an alternating copolymer. Saegusa and co-workers have published extensively in this field.[1] Among the nucleophilic monomers studied are cyclic imino ethers and cyclic phosphites and phosphonites; the electrophilic monomers include α,β-unsaturated acids, lactones, and sultones. Other workers in the field include Balakrishnan and Periyasamy,[2] Butler and co-workers,[3] Rivas and co-workers,[4] Schmidt,[5] Tomalia and co-workers,[6] Wilson and Beaman,[7] and Yokota and Kondo.[8]

Although a considerable number of monomer pairs have been reported to undergo zwitterion polymerization, the copolymers are low in molecular weight ($\bar{M}_n$ is typically in the range 1000–3000) and their chemical structures are not well characterized. The one exception to this generalization is the cyclic sulfonium arene oxides, which have been polymerized to high molecular weight by Schmidt.[5,9] We have initiated work in this field with the objectives of establishing the copolymer structure and polymerization mechanism. We are especially interested in the termination reactions that drastically limit the molecular weight. A better understanding of the reaction may allow one to design reaction conditions more favorable for achieving higher molecular weight products in zwitterion polymerization.

Table I
Comparison of Methods A, B, and C for MeOXO–AA Polymerization[a]

polymn method	temp, °C	yield,[d] %	$\bar{M}_n$
A (soln[b])	70	45	1450
A (soln[c])	60	51	920
A (bulk)	70	55	1850
B (soln[b])	70	60	2000
B (bulk)	70	69	1960
B (bulk)	100	21	590
C (bulk)	70	41	2760

[a] *p*-Methoxyphenol present in all experiments. [b] Solution polymerization in CH_3CN. [c] Solution polymerization in DMF. [d] Yield for recrystallized polymer.

The 2-methyl-2-oxazoline (MeOXO)–acrylic acid (AA) system has been studied by Saegusa and co-workers.[10] They proposed a polymerization mechanism involving the initial formation of genetic zwitterion I. The genetic zwitterion reacts with itself in a ring-opening nucleophilic attack of carboxylate anion on the methylene carbon adjacent to the oxygen of the quaternary MeOXO ring to form a dimer zwitterion II. Growth continues in a similar manner by condensation of different-sized zwitterions (referred to as macrozwitterions) with the genetic zwit-

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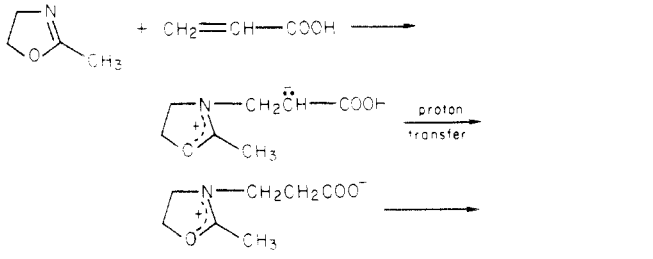
terion and each other to form the alternating copolymer III.



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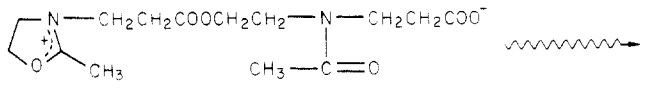
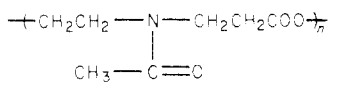


II



III

The reported experimental evidence for the alternating copolymer structure III is quantitatively inconclusive and the copolymer molecular weight is low ($\bar{M}_n$ = 1600). No mention has been made about possible termination reactions responsible for the low molecular weights. Tomalia and co-workers[6b] reported the formation of even lower copolymer molecular weights. This paper describes our work on the MeOXO–AA system. Our approach has been to establish the termination mechanism(s) through characterization of the copolymer with emphasis on identifying the end groups. Some effort has also been made to study different approaches to achieving high molecular weight products.

Experimental Section

Materials. MeOXO and AA (Aldrich) were each dried successively over sodium sulfate and magnesium sulfate for 1 day each and then further dried by two successive treatments with activated molecular sieves (3 Å) for 1 week each. The molecular sieves were activated prior to use by heating at 320 °C for 4 h and then cooling to room temperature in a desiccator.[11] Dried MeOXO and AA were fractionally distilled under reduced nitrogen pressure through a Vigreux column. A small amount of calcium hydride was present in the distillation flask for the MeOXO distillation. MeOXO and AA distilled at 30 and 38 °C, respectively, at 5-torr pressure. The middle fractions were used in our polymerization experiments. Acetonitrile and DMF were dried by using the same procedure as for MeOXO. DMF was fractionally distilled under a nitrogen atmosphere [bp 57 °C (5 torr)]. Acetonitrile was distilled under nitrogen at atmospheric pressure (bp 80–81 °C).

Polymerization. Three methods were used to polymerize the MeOXO–AA system:

Method A. MeOXO (150 mmol), AA (150 mmol), and *p*-methoxyphenol (0.8 mmol), along with solvent (15 mL) when necessary, 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. *p*-Methoxyphenol was present to prevent the radical polymerization of acrylic acid. The polymer was isolated by pouring the reaction mixture into a large excess of anhydrous diethyl ether. The precipitated polymer was dissolved in methanol, reprecipitated with ether, and dried overnight in a vacuum oven at 40 °C.

Method B. Equimolar amounts of MeOXO and AA were placed in separate addition funnels, along with solvents when necessary, under a nitrogen atmosphere. The AA solution contained *p*-methoxyphenol. A four-necked flask was fitted with two addition funnels, a mechanical stirrer, a condenser, and a nitrogen inlet. The monomers were added slowly to the reaction flask, which was held at 70 °C, over a period of 4 h and then allowed to react for an additional 44 h. The polymer was isolated as in method A.

Method C. MeOXO and AA, after purification as described above, were further purified in a high-vacuum (10^{-6} torr) manifold system. MeOXO and AA were each degassed and distilled twice, MeOXO from calcium hydride and AA from 3-Å molecular sieves. Equimolar amounts of each monomer were transferred under vacuum to calibrated break-seal tubes, which were then sealed onto a polymerization tube containing *p*-methoxyphenol. After the polymerization tube was evacuated and sealed, the two monomers were transferred into it by breaking the break seals. The polymerization tube was heated at 70 °C for 48 h and the copolymer isolated as in method A.

Molecular Weight. The number-average molecular weights ($\bar{M}_n$) of the recrystallized copolymers were determined with a Hewlett-Packard vapor pressure osmometer Model 302B at 55 °C with water as the solvent. The instrument was calibrated with dextrose (MW = 180.16) as the standard.

Spectroscopic Analysis. Infrared spectra were recorded with a Beckman 4260 IR spectrometer. Nicolet/Oxford NT-300, IBM WP270SY, and JEOL JNM-MH-100 NMR spectrometers, were used to record the 300-, 270-, and 100-MHz proton NMR spectra, respectively. Natural-abundance ^{13}C NMR spectra were recorded on an IBM NR-80 spectrometer operating at 20.1 MHz. All NMR spectrometers except the JEOL JNM-MH-100 are FTNMR instruments.

Direct NMR Analysis of the Reaction System. The monomers and solvent were purified as previously described. MeOXO (11.8 mmol), AA (11.8 mmol), *p*-methoxyphenol (0.06 mmol), and CD_3CN (15 mL) were mixed under a nitrogen atmosphere, and 0.5 mL of the reaction mixture was placed in a NMR sample tube along with a small amount of Me_4Si as the internal standard. The tube was sealed under vacuum, and the 100-MHz proton spectrum was recorded after the tube was allowed to stand at room temperature for 3 h. The reaction tube was subsequently heated at 60 °C, with the NMR spectrum recorded at room temperature at various time intervals.

High-Performance Liquid Chromatography (HPLC). Analytical and preparative HPLC were used for various separations and analyses. Analytical HPLC was carried out at room temperature with a Waters system consisting of a μ-Bondapak C_{18} column, a Model M-6000 solvent delivery unit, a U6K universal liquid chromatography injector, and a Model 450 variable-wavelength UV monitor with an 8-μL flow-through cell. The mobile phase was either CH_3OH–H_2O–CF_3CO_2H (in a ratio of 350:650:0.8 or 400:600:0.8) or H_2O–CF_3CO_2H (500:0.3) 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 (TFA) (Fisher) were used. All solvents were filtered (Millipore) prior to use. The recorder chart paper speed was 0.5 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) for detection of the amide group; 250 nm was used for detection of the benzene ring.

The MeOXO–AA copolymer was fractionated by preparative HPLC with a Waters Prep LC/System 500 using a μ-Bondapak C_{18} column with methanol–water–TFA (350:650:0.8) as the mobile phase. A solution of copolymer, 2 g in 20 mL of the 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. Fractions that contained more than one component were discarded. Pure fractions (i.e., fractions containing one component as determined by HPLC) of the same component were combined, concentrated with a Rotovapor evaporator under reduced pressure to a volume of 10 mL, freeze-dried, and dried in a vacuum oven at 40 °C with a final overnight drying in a vacuum desiccator, and the 300-MHz proton NMR spectra were recorded in Me_2SO-d_6.

The copolymer was stable under the conditions of the HPLC procedure; i.e., the HPLC solvent system did not hydrolyze the copolymer. This was ascertained by observing the HPLC results to be independent of whether or not the solution of copolymer in the HPLC solvent system was allowed to stand for several hours prior to injection into the HPLC column.

Model Compounds. *N*-(2-Hydroxyethyl)-β-alanine was prepared by adding ethanolamine (45 mmol) in acetonitrile (5 mL)

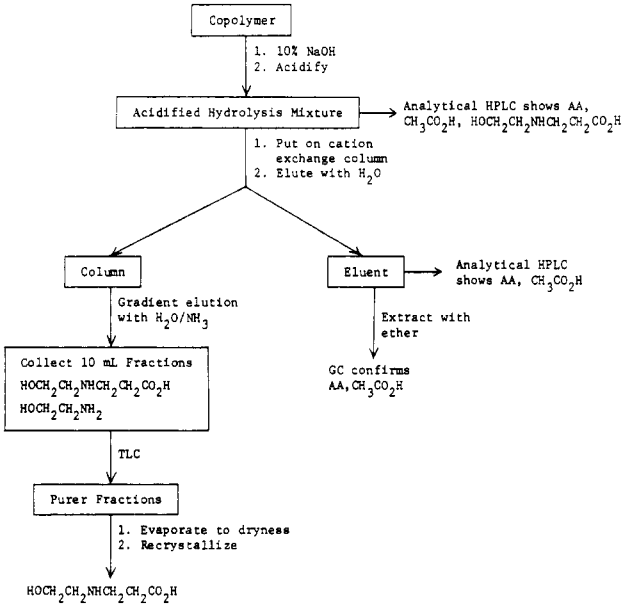


Figure 1. Alkaline hydrolysis of MeOXO–AA copolymer.

dropwise into a stirred solution of β-propiolactone (50 mmol) in acetonitrile (15 mL) over a period of 2 h while maintaining the reaction temperature at 0 °C.[12] The solid formed was filtered, dried, and recrystallized from methanol [mp 146–147 °C (lit. mp 145–147 °C)].

The dibenzoate derivative of ethanolamine was prepared by adding benzoyl chloride (0.03 mol) dropwise into a stirred and cooled solution of ethanolamine (0.01 mol) in 10% sodium hydroxide (10 mL). The reaction mixture was acidified with 3 M HCl to pH 8, and the resulting white precipitate was filtered, washed with water, and recrystallized from ethanol–water (mp 81–83 °C).

N-Methyl-2-methyl-2-oxazolinium iodide was prepared by adding MeOXO (60 mmol) dropwise into a stirred solution of methyl iodide (240 mmol) in ether (40 mL) at 0 °C.[13] The resulting white precipitate was filtered, washed with diethyl ether, and recrystallized from diethyl ether–acetonitrile [mp 145 °C (lit. mp 145–146 °C)].

Bromination of Copolymer. The MeOXO–AA copolymer was brominated by adding a solution of bromine in methanol dropwise into a stirred and cooled (0 °C) solution of the copolymer (0.1 g) in methanol until a yellow color resulted. The solution was stirred at room temperature for 1 h, the solvent was evaporated under suction to yield a light yellow solid product, which was dried overnight in a vacuum desiccator, and the 100-MHz proton NMR spectrum was recorded in Me_2SO-d_6.

Hydrolysis of MeOXO–AA Copolymer. The copolymer was hydrolyzed to aid in its identification. Figure 1 shows the procedure used to isolate and identify the various hydrolysis products. The copolymer (1.0 g) was refluxed in 10% aqueous NaOH at 100 °C for 3 h, the hydrolysate was acidified to pH 3, and a portion was subjected to analytical HPLC. The remainder of the acidified hydrolysate was introduced onto a cation-exchange resin column (Dowex 50X 8-400), and the column was eluted with water. The eluent was analyzed by HPLC and then extracted with ether. The ether extract was concentrated and analyzed by GC. The column was further eluted with water–ammonia by a gradient elution procedure (between pH 10 and 11). Thin-layer chromatography of the various eluent fractions with ninhydrin showed there were two components present, with one component present in much greater amount than the other. Most fractions contained only the major component, *N*-(2-hydroxyethyl)-β-alanine. These fractions were collected, evaporated to dryness, recrystallized from methanol–acetonitrile, and analyzed by NMR. The minor component, ethanolamine, was isolated in a separate hydrolysis experiment: The hydrolyzed copolymer was reacted with excess benzoyl chloride at 0 °C under alkaline conditions. (Under these conditions, *N*-(2-hydroxyethyl)-β-alanine should undergo benzoylation but the product would be soluble as the carboxylate salt.) The reaction mixture was extracted with methylene chloride, the extract evaporated to dryness, and the product subjected to both analytical HPLC and NMR.

Gas Chromatography. GC analysis was performed with a Hewlett-Packard (F&M Scientific) 5750 instrument containing a 5 ft × $^1/_4$ in. 10% ethylene glycol succinate column with column and injection port temperatures of 130 and 185 °C, respectively. Calibration with known samples showed that acetic and acrylic acids had retention times of 165 and 345 s, respectively.

Results and Discussion

Molecular Weight of Copolymer. Copolymerization of MeOXO and AA was carried out under a variety of experimental conditions with the objective of increasing the copolymer molecular weight. Included in this study were variations in the method and order of mixing the monomers, temperature, method of monomer purification, and presence of an added nucleophile. Three polymerization methods were used. Methods A and B employed the usual methods of purification of materials by vacuum distillation and carrying out the polymerization; method C employed a high-vacuum system. Polymerization by method C would involve lower concentrations of adventitious impurities such as H_2O, CO_2, and NH_3. Method A involved the rapid initial mixing of MeOXO and AA followed by their reaction. Method B involved variations of method A in which the monomers were slowly added together, one monomer was slowly added to the other, the reaction was carried out in stages, or nucleophile was added.

Table I shows a comparison of the results from methods A, B, and C. Although Saegusa and co-workers[10] reported only the solution polymerization of MeOXO–AA, we observed that polymerization also occurs in bulk. The bulk polymerization yielded the higher molecular weight product for method A although there was no difference for method B. The lower molecular weight copolymer products were white semisolids with solubility in water, methanol, DMF, and Me_2SO. The higher molecular weight products were white solids with the same solubility characteristics. The highest molecular weight (2760) obtained was for a copolymer made by method C, indicating that adventitious impurities participate in termination, but the effect was not large. Method B generally gave slightly higher molecular weights than method A. When polymerization was carried out in bulk, a small fraction (5–10%) of the product was insoluble whereas the product is completely soluble under other polymerization conditions. The work reported in this paper on polymer characterization relates only to the soluble product. Characterization of the insoluble fraction by solid-state ^{13}C NMR is planned in the future.

Increasing the polymerization temperature to 100 °C significantly decreased the polymer molecular weight as well as the yield. The use of DMF as solvent instead of acetonitrile resulted in lower molecular weight. Similar results were observed by Saegusa and co-workers,[10] who reported $\bar{M}_n$ values of 1600 and 1400, respectively, for MeOXO–AA polymerizations in acetonitrile and DMF. Overall, the molecular weight data in Table I clearly show that even when reaction conditions (method C) are chosen to avoid adventitious terminating agents from the atmosphere as well as those present as impurities in the monomer, there is no large improvement in the copolymer molecular weight.

Method B was used to study the effect of variations in the reaction conditions on molecular weight (Table II). The standard conditions (experiment 1) involved the simultaneous additions of MeOXO and AA to the reaction flask over a 4-h period followed by heating for an additional 44 h. This compares with method A in which the

Table II
Variations of Method B for MeOXO–AA Copolymerization

expt	polymn conditions[a,b]	yield,[c] %	$\bar{M}_n$
1	standard[d]	69	1960
2	MeOXO present initially, AA added slowly[d]	60	1430
3	AA present initially, MeOXO added slowly[d]	50	1170
4	standard[e]	64	1910
5	monomers added in three stages[f]	41	1940
6	2.6 mol % of CH_3ONa added at start of reaction[d]	61	1200
7	1 mol % of CH_3ONa added after 50% of monomers	73	1660
8	monomers added over a period of 2 days	20	1110
9	monomers added over a period of 1 week	8	900

[a] Bulk polymerization at 70 °C with both monomers being simultaneously added unless otherwise noted. [b] All experiments involved equimolar amounts of MeOXO and AA with *p*-methoxyphenol added to AA. [c] Yield for recrystallized polymer. [d] Monomer(s) added over 4 h and then reacted for an additional 44 h. [e] Monomers added quickly and then reacted for 12 h. [f] One-third of MeOXO and AA quickly added in each stage followed by reaction for 12 h.

two monomers were rapidly mixed together and then heated for 48 h. The purpose of the slow addition was to keep the concentration of propagating centers low so as to increase the copolymer molecular weight. Experiment 1 showed some increase in yield and molecular weight relative to method A. However, when the monomer addition period was increased to 2 days (experiment 8) and 1 week (experiment 9), both the yield and molecular weight decreased significantly. If the propagating centers remain active for a long period of time, these experiments should have led to increased molecular weight. The lowered molecular weights indicate the growing macrozwitterions undergo termination during these long addition times. Experiment 4 involved the quick addition of monomers followed by a 12-h reaction time. The copolymer yield and molecular weight were comparable to those obtained at the standard reaction time of 44 h. Experiment 5 involved a three-stage polymerization in which one-third of the MeOXO and one-third of the AA were quickly mixed and reacted for 12 h, followed by two fresh batches of monomer quickly added in sequential fashion with a 12-h reaction time following each addition. No improvement in copolymer molecular weight was observed and the yield actually decreased. Even if the polymer chains have only one of the two active ends still active, this experiment should have yielded higher molecular weights since a fresh batch of the monomers can produce genetic zwitterions that could add to the active end of the polymer chain. Thus, we conclude that the MeOXO–AA system does not behave as one with living characteristics.

Experiments 2 and 3 were carried out with a view to ascertaining whether one or the other of the two monomers was solely responsible for termination reactions that limit molecular weight. One monomer was placed in the reaction flask and the other then added over a 4-h period followed by reaction for an additional 44 h. The decrease in copolymer molecular weight in both experiments indicates the involvement of both AA and MeOXO simultaneously in terminating the propagating macrozwitterions. Control experiments were also carried out to ascertain whether either MeOXO and AA undergoes homopolymerization under our experimental conditions. A small amount (1 mol %) of one monomer was added to the other, and the reaction mixture was heated for 48 h and worked up in the usual manner. No polymer was formed under these conditions. In other experiments (experiments 6 and 7), it was observed that the use of a nucleophile such as $NaOCH_3$ did not result in higher molecular weights as reported in some zwitterion polymerizations.[5]

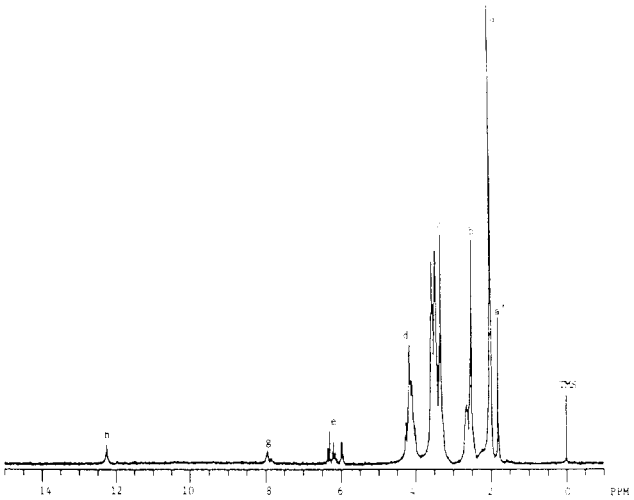


Figure 2. 300-MHz proton NMR spectrum of MeOXO–AA copolymer. Conditions: 1.8% (w/v) in Me_2SO-d_6 (100%); 70° pulse angle; 25 °C; 5-s delay between pulses; 258 acquisitions; Me_4Si internal standard.

We have investigated a large number of different approaches to increase the copolymer molecular weight. The lack of any significant improvement in molecular weight indicates that the both monomers are simultaneously involved in limiting the copolymer molecular weight.

Spectroscopic Characterization of Copolymer. Proton NMR Spectra. A MeOXO–AA copolymer ($\bar{M}_n$ = 1452) prepared by method A using acetonitrile as the solvent was used for characterization experiments. Figure 2 shows the 300-MHz FT proton NMR of the copolymer recorded in Me_2SO-d_6 (100% deuterated). Similar results were obtained at 270 MHz. The NMR signals at 12.25 and 7.95 ppm have been assigned to the COOH and NHCO type protons, respectively, based on the chemical shift values and their behavior in the presence of D_2O. Both signals disappear in D_2O due to exchange between hydrogen and deuterium. The multiplet centered at 6.15 ppm is assigned to olefinic protons of the group $OOC-CH{=}CH_2$. This assignment is confirmed by the proton NMR of the brominated copolymer. The brominated copolymer shows no signals in the region between 4.5 and 7.95 ppm as the $OOCCHBrCH_2Br$ protons absorb upfield of 4.5 ppm. The repeating unit (structure III) of the copolymer shows signals at 1.80 ppm (singlet, $NHCOCH_3$), 2.00 ppm (doublet, $NCOCH_3$), 2.50 ppm (multiplet, CH_2COO), 3.45 ppm (multiplet, CH_2NCH_2), and 4.13 ppm (multiplet, $COOCH_2$).

Although Saegusa and co-workers[10] reported proton NMR data on the MeOXO–AA copolymer, no mention was made of the presence of signals for carboxylic, olefinic, and amido protons. Saegusa and co-workers reported NMR data showing only CH_3CON, CH_2COO, CH_2NCH_2, and $COOCH_2$ protons; no actual spectrum was presented in that paper. They proposed the 1:1 alternating structure III on the basis of the NMR data and elemental analysis. Tomalia and co-workers detected the presence of olefinic end groups by titration with bromine.[6b] Balakrishnan and Periyasamy[2] reported the proton NMR of a 2-methyl-2-oxazoline–methacrylic acid (MeOXO–MAA) copolymer in D_2O. Except for the indicated presence of two weak doublets at 5.2 ppm for olefinic protons, no mention was

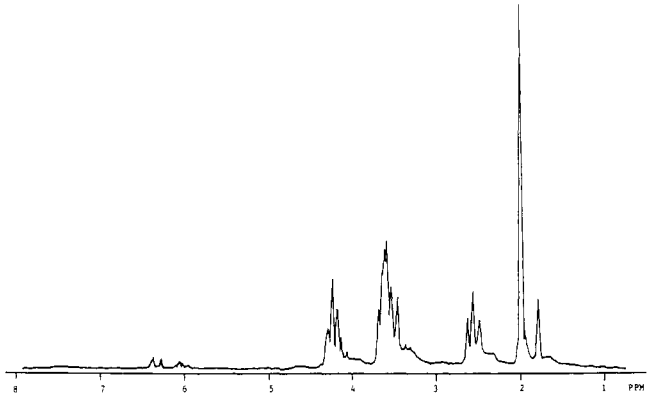


Figure 3. 100-MHz proton NMR of MeOXO–AA copolymer. Conditions: 8% (w/v) in Me_2SO-d_6 (100%); 150 °C.

Table III
Degree of Polymerization of MeOXO-AA Copolymer

	DP calcd from comparison of e protons with protons					
NMR conditions	a	b	c	d	a + b + c + d	a′ + a + b + c + d
300 MHz (70°/6.7 s[a])	17.6	17.6	21.0	16.4	18.2	19.6
270 MHz (30°/11.6 s[a])	21.4	15.6	22.0	17.0	19.2	20.8
270 MHz (30°/6.6 s[a])	18.0	14.0	19.2	15.0	17.2	18.0
av	19.0	15.7	20.7	16.1	18.2	19.5

[a] Pulse angle/delay between pulses.

made of NH and COOH signals. Recording the NMR in D_2O precluded detection of NH and COOH protons. Further, their assignment of a 1:1 alternating structure for the copolymer is not consistent with the reported NMR spectrum. The published spectrum shows the signal areas for the two methyls, at 1.95 ppm (α-methyl of MAA) and 2.0 ppm ($NCOCH_3$), to be about 1:2 instead of 1:1 as it would be for the alternating copolymer.

Since we observe considerably more detail than previously reported for the proton NMR of the MeOXO–AA copolymer, a detailed discussion of the results is worthwhile. The NMR signals for the methylene groups of the repeat unit and the side-chain methyl group become complicated as a result of the restricted rotation around the C–N bond of the amide group. The methyl group protons appear as a pair of closely spaced singlets at 2.0 ppm instead of one singlet. If there were free rotation around the C–N bond, the methylene groups should appear as four triplets. Restricted rotation could theoretically result in four pairs of triplets for the methylene groups. However, this detail is not sufficiently clear in the observed spectrum. The low molecular weight of the copolymer, presence of different end groups, and molecular weight polydispersity further complicate the NMR spectrum at a high field such as 300 MHz. For example, the repeat unit adjacent to an end group can experience a slightly different NMR environment compared to the other repeat units.

The difference in environment resulting from restricted rotation around the C–N bond can be overcome by recording the NMR at a higher temperature. Figure 3 shows the 100-MHz spectrum of the copolymer recorded at 150 °C. The methyl group signal has changed to a sharp singlet. The CH_2COO signal is now a triplet as expected. The two methylenes attached to nitrogen, CH_2NCH_2, appear as a pair of overlapping triplets with some additional signals, which probably arise from end groups, e.g., $OCH_2CH_2NHCOCH_3$. Similarly, the $COOCH_2$ protons

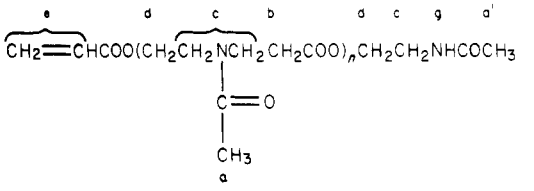
Table IV
Copolymer Composition of MeOXO-AA Copolymer

	MeOXO/AA molar ratio calcd from protons				
NMR conditions	a, b	b, d	b, c	a, c	a–d
300 MHz (70°/6.7 s[a])	0.99	0.92	1.20	0.83	0.94
270 MHz (30°/11.6 s[a])	1.39	1.09	1.43	0.97	1.09
270 MHz (30°/6.6 s[a])	1.29	1.07	1.39	0.93	1.09
av	1.22	1.03	1.34	0.91	1.04

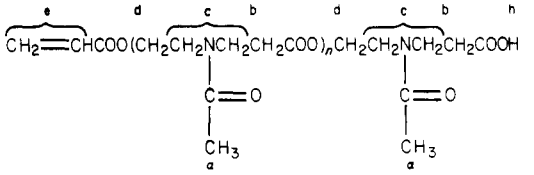
[a] Pulse angle/delay between pulses.

appear as a triplet with additional signals arising from the end groups.

Overall, our NMR spectra show strong qualitative evidence for the 1:1 repeat unit (structure III) and carboxylic (COOH), olefinic (CH_2=$CHCOO$), and acetamido (CH_3CONH) end groups. The following two structures are proposed for the MeOXO–AA copolymer:



IVa



IVb

The 270- and 300-MHz proton NMR results were used to calculate the degree of polymerization (Table III) and copolymer composition (Table IV). NMR analyses were carried out at a 70° pulse angle with 6.7-s delay between pulses and at a 30° pulse angle with 6.6- and 11.6-s delays between pulses to make certain that relaxation times for different protons do not affect the quantitative results. The variations in DP and copolymer composition under the different conditions appear random, indicating that the NMR results were devoid of relaxation problems under the conditions of pulse angle and relaxation delay.

The calculation of DP assumed one olefinic end group per copolymer molecule; i.e., the copolymer consists of molecules with structures IVa and IVb. The a, b, c, and d protons individually as well as the total and total plus a′ protons in comparison with the e protons were used to calculate DP (Table III). Each DP value in Table III has been corrected to include the olefinic end group; i.e., 1 has been added to the value calculated from the NMR data. The various DP calculations differ in the extent to which both carboxyl and acetamido end groups are counted. The last two calculations are probably the most reliable since both carboxyl and acetamido end groups are counted. They are also less prone to an error in the NMR integral value for any one of the different types of protons since they are based on the sum of all the protons. The last two calculations differ in the extent to which the acetamido end groups are counted. The calculation based on (a + b + c + d) protons undercounts the acetamido end groups since the a′ protons are excluded. The last calculation, which uses the a′ protons to count acetamido groups, overcompensates since it ignores the fact that the acetamido group is partially counted through the d and c protons. The average of the two calculations, DP = 18.9, is probably

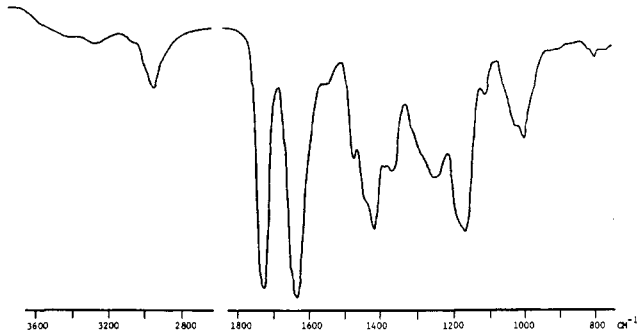


Figure 4. Infrared spectrum of MeOXO–AA copolymer (thin mull on NaCl plate).

a better value than either one of the two. The DP calculated from the NMR data is in excellent agreement with the value of 19.4 obtained from the measurement of $\bar{M}_n$ by vapor pressure.

We should also note the quantitative results for the acetamido NH and carboxyl end group protons. The signal area ratio of olefinic protons to the sum of NH and COOH protons should be 3:1 since structures IVa,b have one olefinic end group for all molecules, with the second end group being either NH or COOH. However, this ratio was found to be about half of the expected value, 1.5:1. The most probable explanation for this result is the presence of traces of moisture in the Me_2SO-d_6. Water associates with NH and COOH, resulting in increases in the signal areas for these protons.

Table IV shows the copolymer compositions calculated from various comparisons of the a, b, c, and d protons. The most appropriate copolymer composition to be calculated is the composition of the repeating unit excluding the end groups in order that one can ascertain the extent to which the zwitterion mechanism is responsible for propagation. Thus, the a′ and e protons have not been used in the calculations. However, some of the calculations in Table IV are still somewhat in error since the signal areas for d and c protons include contributions from the corresponding end groups. This error is less than 5% since it introduces an error only for the molecules containing acetamido end groups. The carboxyl end group contains one each of the AA and MeOXO units while the acetamido end group contains only an MeOXO-derived unit. This error is less than the experimental error inherent in the NMR analytical method and is not considered further. The copolymer composition in the last column, for reasons described above, is probably the most reliable value. The MeOXO–AA ratio is unity within experimental error (at least ±10%). The deviation from participation of equimolar amounts of MeOXO and AA in the propagation process is no more than one MeOXO molecule per ten each of MeOXO and AA.

Infrared Spectrum. The infrared spectrum of the copolymer (Figure 4) supports structures IVa,b. Two strong absorption bands are observed at 1735 and 1642 cm^{-1} for the ester and amide carbonyl groups, respectively, of the repeating unit of the copolymer. Three broad bands observed in the 3000–3600-cm^{-1} region of the infrared spectrum arise from the end groups of structures IVa,b. The band centered near 3050 cm^{-1}, which appears as a shoulder to the sp^3 C–H stretching vibration near 2955 cm^{-1}, is assigned to the carboxyl O–H stretching vibration (dimeric carboxyl) of structure IVb and/or the olefinic C–H stretching vibration.[14] The absorption band centered at 3290 cm^{-1} is assigned to the N–H stretching vibration of the acetamido end group of structure IVa. The absorption band centered at 3400 cm^{-1} is assigned to the N–H

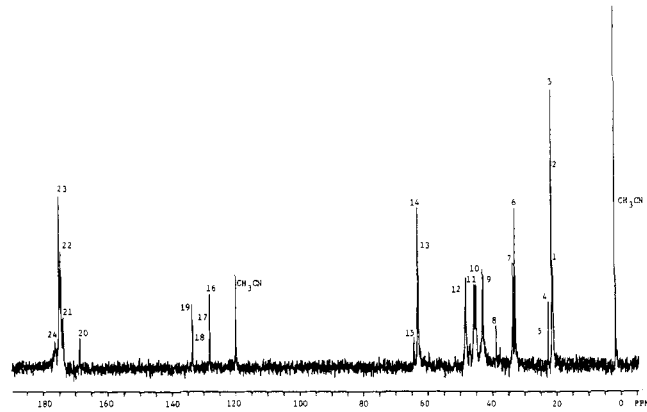
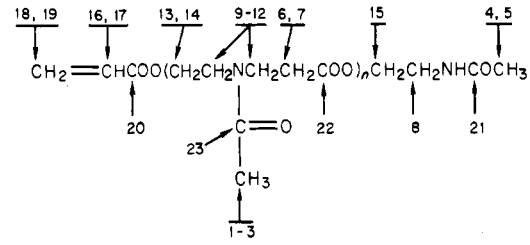


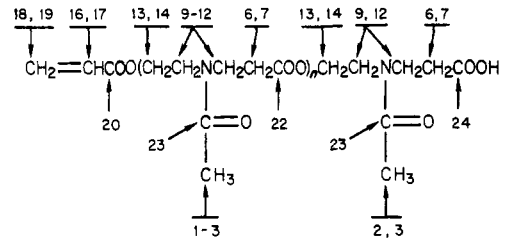
Figure 5. 20.1-MHz ^{13}C NMR spectrum of MeOXO–AA copolymer. Conditions: 20% (w/v) in D_2O; 30° pulse angle; 33 °C; 1.6-s delay between pulses; 80 000 acquisitions; CH_3CN internal standard (1.70 ppm relative to Me_4Si).

stretching vibration and/or the carboxyl O–H stretching vibration (nondimeric carboxyl) of structure IVb. The other infrared absorption bands are assigned as follows: 1422 cm^{-1} (C–N stretch), 1172 cm^{-1} (C–O stretch), 1375 cm^{-1} (C–H bend), 810 cm^{-1} (CH_2 wagging of olefinic group). Absorption bands arising from C=C stretching vibration and N–H bending vibration (amide II band) would be expected near the amide carbonyl band at 1642 cm^{-1}. As seen in Figure 3, the shape of the 1642-cm^{-1} band suggests the possible overlapping of all three absorption bands.

^{13}C NMR Spectrum. Figure 5 shows the ^{13}C NMR spectrum of the MeOXO–AA copolymer. The results are consistent with the proposed structures IVa,b with the various signals assigned as follows:



IVa



IVb

The chemical shift values of the different signals are listed in Table V. The assignments of the various signals were based on the chemical shift values in relationship to those for analogously substituted carbons.[14] Signals 1–5 were assigned to methyl carbons, signals 6–15 to methylene carbons, signals 16–19 to olefinic carbons, and signals 20–24 to carbonyl carbons. These assignments were also facilitated by the results of single-frequency off-resonance (SFOR) experiments in which we observed the expected splitting of each carbon signal by protons directly attached to the carbon. Within each of the groups of carbon signals, a number of further assignments were relatively easy to make based on chemical shift values. For example, methylene carbons attached to oxygens (signals 13–15) have higher chemical shifts than those attached to amide

Table V
^{13}C Chemical Shifts of MeOXO–AA Copolymer

C no. in IVa,b	shift,[a] ppm	C no. in IVa,b	shift,[a] ppm
1	21.16	13	63.06
2	21.44	14	63.27
3	21.61	15	64.36
4	22.75	16	128.09
5	22.88	17	128.24
6	33.09	18	133.42
7	33.75	19	133.65
8	39.02	20	168.65
9	43.16	21	173.78
10	45.32	22	174.39
11	45.82	23	174.99
12	48.45	24	176.18

[a] Chemical shifts are relative to CH_3CN (methyl carbon 1.70 ppm relative to Me_4Si).

nitrogens (signals 8–12), which, in turn, have higher chemical shifts than those attached to ester or acid carbonyls (signals 6 and 7). Within some of the groups, specific assignments were made based on a comparison of signal areas and these should be considered as tentative assignments since we have no information on relaxation times for different carbons. Thus, signals 2 and 3 were assigned to the methyl of the repeating unit while signals 1, 4 and 5 were assigned to the methyls on the acetamido end group and the repeating unit nearest the olefinic end group since the signal areas for the former were much greater than for the latter. Similarly, signals 13 and 14 were assigned to the repeat unit OCH_2 carbon while signal 15 was assigned to the OCH_2 of the acetamido end groups; signals 22 and 23 were assigned to the carbonyls of the repeating unit while signals 20, 21, and 24 were assigned to the carbonyls of various end groups. Two assignments, signals 22 and 23, are relatively arbitrary. The expected difference in chemical shifts for these ester and amide carbonyls is too small to allow one to differentiate between them with any certainty.

The ^{13}C NMR spectrum shows considerable complexity—many of the carbons show two signals and some of the signals have significant shoulders. Some of this is evident in Figure 5. It was confirmed when we viewed the spectrum on an expanded scale. Many of the carbons show two signals due to restricted rotation about the C–N amide bond. This is the case for the methyl carbons of the repeating unit (signals 2 and 3) and the acetamido end group (signals 4 and 5), each of the four methylene carbons of the repeating unit (signals 6, 7, and 9–14), each of the carbons of the olefinic end group (signals 16–19), and most of the carbonyl carbons (signals 20–24). The presence of greater complexity than two signals per carbon is evident since one observes shoulders on signals 7–12 and 15, the presence of the small signal between signals 11 and 12, and the presence of more than one shoulder on each of signals 21–23. This complexity in the ^{13}C NMR spectrum is ascribed to the low molecular weight of the MeOXO–AA copolymer. Each of the repeating units in a molecule of the copolymer is not exactly equivalent. The same type of carbon atom (e.g., the CH_2N carbon) has slightly different chemical shifts depending on its placement relative to the end groups.

High-Performance Liquid Chromatography. Analytical HPLC of the MeOXO–AA copolymer showed the presence of at least 13 different fractions (Figure 6). Separate HPLC experiments using a known solution of MeOXO and AA indicated the absence of unreacted monomers in the copolymer. This confirms that the olefinic and carboxyl proton and ^{13}C signals in the NMR of the

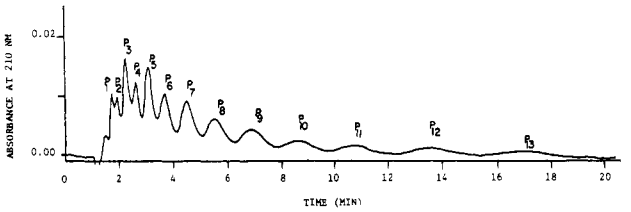


Figure 6. HPLC of MeOXO–AA copolymer on a μ-Bondapak C_{18} column. Mobile phase: methanol–water–TFA (350:650:0.8).

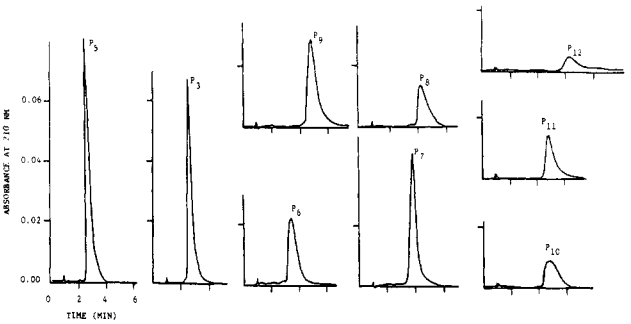


Figure 7. HPLC of purified fractions on a μ-Bondapak C_{18} column. Mobile phase: methanol–water–TFA (350:650:0.8) for fractions P_3 through P_9 and methanol–water–TFA (400:600:0.8) for fractions P_{10} through P_{12}. The scale is the same on all plots.

Table VI
Degree of Polymerization of MeOXO–AA Copolymer Fractions

fraction	DP	MeOXO/AA
P_3	12.4	0.91
P_5	13.2	0.82
P_6	14.2	0.96
P_7	17.8	0.89
P_8	18.0	0.84
P_9	20.0	0.87
P_{10}	26.6	1.03
P_{11}	33.2	0.88
P_{12}	27.0	0.90
P_{13}	26.2	0.89

copolymer are due to olefinic and carboxyl end groups and not unreacted acrylic acid. The copolymer was fractionated by using preparative HPLC, with 10 of the 13 fractions being isolated. Fractions P_1, P_2, and P_4 could not be isolated since they eluted from the column as mixtures (as detected by analytical HPLC). Analytical HPLC of 9 of the 10 isolated fractions are shown in Figure 7. Each of the 10 isolated fractions was analyzed by 300-MHz proton NMR. All fractions showed similar signals for the repeating unit of the copolymer and for olefinic end groups. However, there were considerable differences in whether or not signals for acetamido and carboxyl end groups were present. Fractions P_6, P_8, P_9, and P_{10} showed signals for acetamido end groups but not for carboxyl. Fractions P_3, P_5, P_7, P_{11}, P_{12}, and P_{13} showed strong signals for carboxyl end groups and much weaker signals for acetamido end groups. The first group of fractions (P_6, P_8, P_9, and P_{10}) have structure IVa in which the end groups are olefinic and acetamido. The other fractions have mainly structure IVb in which the end groups are olefinic and carboxyl with the presence of minor amounts of structure IVa species.

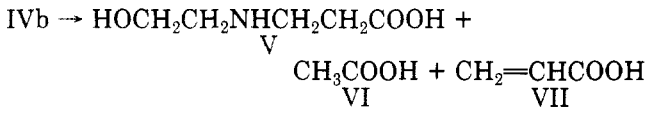
The copolymer compositions of the repeating units for the various fractions were calculated from the signal areas for a, b, c, and d protons and are shown in Table VI. The MeOXO:AA ratio is close to unity as found for the unfractionated copolymer sample. DP values for the fractions were calculated from a comparison of the signals areas for a′, a, b, c, and d protons to the signal area for e protons.

The results (Table VI) indicate that the HPLC separation is based on a combination of factors, including molecular weight and end group. For example, the fractions containing acetamido end groups elute from the column in increasing order of molecular weight. For the lower DP fractions compare P_7 and P_8), those with acetamido end groups elute after those with carboxyl end groups when the DP is the same for the two types of fractions. However, the reverse is true for the higher DP fractions (compare P_{10} and P_{12}). Another anomaly is the reverse dependence of elution time on molecular weight for fractions P_{11}, P_{12}, and P_{13}. These results indicate that some factor other than molecular weight and end group affects the order of elution. Perhaps there are conformational differences[15] between the various fractions that override the other two factors.

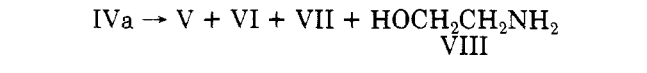
Fractions with low and some intermediate DP values are absent from the results shown in Table VI. The missing low-DP fractions probably comprise the unisolated fractions P_1, P_2, and P_4 as well as the ether solution that results when the MeOXO–AA copolymer is precipitated from the reaction mixture. (Work is in progress to characterize the components of the ether solution.) The absence of some intermediate-DP fractions may indicate that some of the isolated fractions contain mixtures. For example, P_{10} may contain molecules with DP less than 26.6 as well as greater than 26.6.

None of the isolated fractions are cyclic since all fractions showed the presence of two different end groups. This does not, however, preclude the presence of cyclic products in the unisolated fractions or in the ether solution.

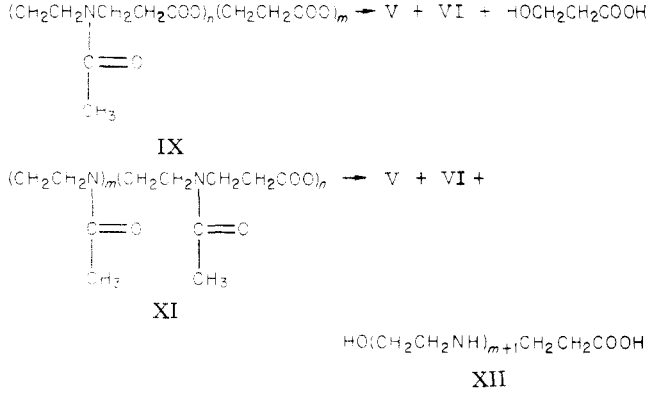
Hydrolysis of Copolymer. Further proof for the proposed structures IVa,b was obtained by analysis of the products from alkaline hydrolysis of the unfractionated copolymer. Hydrolysis of IVb would yield *N*-(2-hydroxyethyl)-β-alanine and acetic acid from the repeating unit as well as from the carboxyl end group and acrylic acid from the olefinic end group.



Hydrolysis of IVa would yield the same three products along with ethanolamine from the acetamido end group.



The presence of homosequences of either MeOXO or AA would result in the additional hydrolysis product X or XII, respectively.



Although Saegusa and co-workers[10] reported evidence from hydrolysis experiments to support the alternating

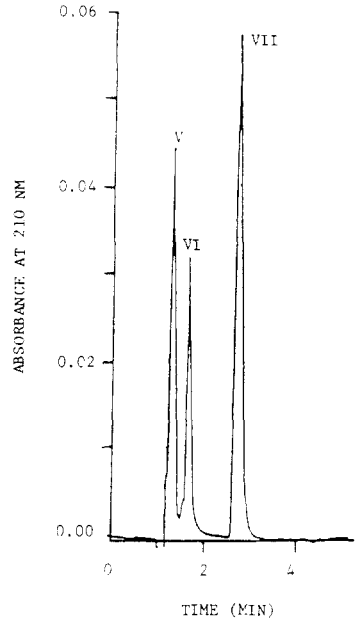


Figure 8. HPLC of MeOXO–AA copolymer hydrolysate on a μ-Bondapak C_{18} column using water–TFA (500:0.3) as the mobile phase.

structure III, the results were less than conclusive since no attempt was made to isolate any of the possible hydrolysis products nor to identify those originating from the end groups. We worked up the reaction mixture from alkaline hydrolysis of the copolymer according to the scheme in Figure 1. Figure 8 shows the analytical HPLC of the hydrolysate after acidification with hydrochloric acid. The three peaks are attributed to *N*-(2-hydroxyethyl)-β-alanine, acetic acid, and acrylic acid, respectively, in order of increasing retention time by injecting authentic samples of each compound. (The observed large peak area for acrylic acid compared to the other components is due to its much higher extinction coefficient at 210 nm.) The acidified hydrolysate was placed on a cation-exchange column and then eluted with water. Analytical HPLC of the eluent and GC of its ether extract both confirmed the presence of acetic and acrylic acids. Gradient elution of the column with aqueous ammonia resulted in the isolation of *N*-(2-hydroxyethyl)-β-alanine, which was identified by proton NMR analysis by comparison with an authentic sample (Figure 9).

The presence of ethanolamine was confirmed by isolation of the dibenzoyl derivative and comparison of the NMR and analytical HPLC with those of an authentic sample (Figures 10 and 11). In the benzoylation procedure, a second (minor) product was obtained along with the dibenzoate of ethanolamine. This is the component with a retention time slightly below 7 min in the HPLC shown in Figure 10. (The component with a 2-min retention time is the solvent.) The minor product was separated by HPLC and its proton NMR observed. The proton NMR showed complex absorptions in the aromatic region 7.1–7.9 ppm and broad aliphatic absorptions at 3.6, 3.8, and 4.4 ppm with an overall aromatic:aliphatic proton ratio of about 2.1:1. The most likely possibility for this product is the tribenzoate derivative of *N*-(2-hydroxyethyl)-β-alanine, which would have an aromatic:aliphatic proton ratio of 1.9:1 and complex or broad patterns for both the aromatic and aliphatic regions. Benzoate derivatives of X and XII are not likely possibilities. The dibenzoate derivative of X would have a simple absorption pattern in the aliphatic region and an aromatic: aliphatic proton ratio of 2.5:1. The tetrabenzoate of XII (with *m*

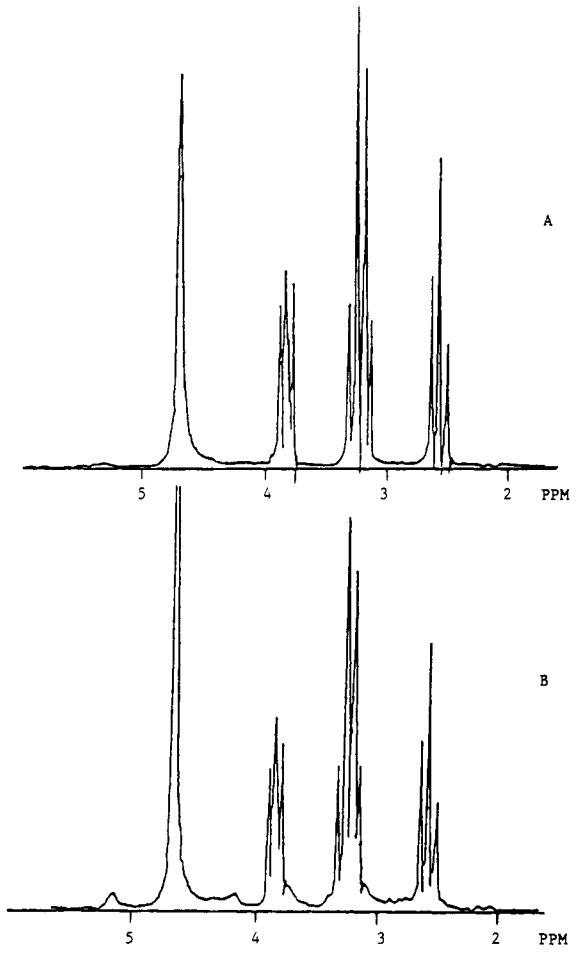


Figure 9. 100-MHz proton NMR spectra of (A) *N*-(2-hydroxyethyl)-β-alanine (authentic sample) in D_2O (8% (w/v)) at room temperature and (B) sample isolated from hydrolyzed MeOXO–AA copolymer in D_2O (6% (w/v)) at room temperature. Internal standard: DSS.

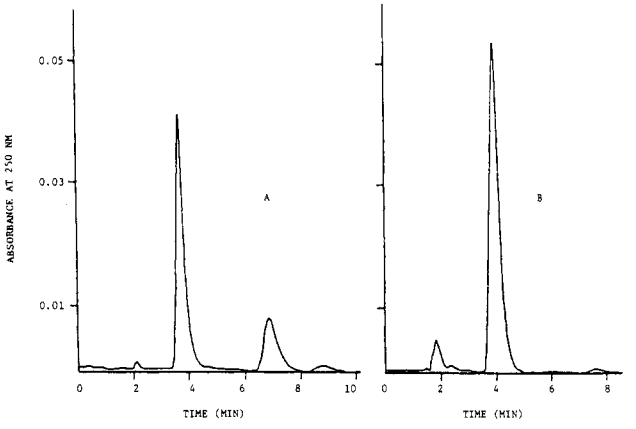


Figure 10. HPLC of crude benzoylated product (A) and product after purification (B). Stationary phase: μ-Bondapak C_{18} column. Mobile phase: methanol–water–TFA (550:450:0.6).

= 1) would have the required complex aliphatic and aromatic absorptions but an aromatic:aliphatic proton ratio of only 1.67:1.

In summary, the hydrolysis experiments have shown the presence of the expected hydrolysis products from structures IVa,b. No experimental evidence has been found for significant amounts of homosequences of either MeOXO or AA.

Direct Proton NMR Analysis of Reaction Mixture. Attempts to isolate the genetic zwitterion under low-temperature (0 °C) conditions were unsuccessful. Direct NMR analysis of the MeOXO–AA reaction mixture was carried out to obtain direct evidence for the formation of genetic (and macro) zwitterions. NMR should detect the presence of such species since the protons of the methyl group attached to the oxazolinium ring will be shifted downfield relative to the corresponding protons of the monomer or polymer. For example, MeOXO shows proton signals at 1.98 ppm (CCH_3), 3.66 ppm (NCH_2), and 4.04 ppm (OCH_2) while *N*-methyl-2-methyl-2-oxazolinium iodide shows signals at 2.32 ppm (CCH_3), 3.32 ppm (NCH_3), 4.16 ppm (NCH_2), and 4.91 ppm (OCH_2) (spectra taken at 100 MHz in CD_3CN with Me_4Si as internal standard).

Figure 12A shows the 1.5–3-ppm region of the 100-MHz proton NMR of an equimolar MeOXO–AA reaction mixture in CD_3CN 3 h after mixing of the reactants. The signal at 1.98 ppm is due to the CCH_3 of MeOXO and the new signal at 2.32 ppm is assigned to the CCH_3 of the genetic zwitterion intermediate. As the reaction subsequently proceeds at 60 °C, one observes (Figure 12B,C) various signals for the copolymer: 1.90 ppm (CH_3 of acetamido end group), 2.06 ppm (CH_3 of repeating unit), and 2.50 ppm (CH_2CO of repeating unit). The intensity of the signal at 2.32 ppm decreased while those at 1.90, 2.06, and 2.50 ppm increased with the progress of the reaction. The NMR spectrum at 40 h is shown in Figure 12D; further reaction at 60 °C did not change the spectrum. This is essentially the same spectrum as that for the isolated copolymer (Figure 2) except that there are some differences in chemical shift values attributable to the different solvents used (CD_3CN and Me_2SO-d_6, respectively). The largest differences are those for the NH (7.12 ppm in CD_3CN and 7.95 ppm in Me_2SO-d_6) and COOH (10.55 ppm in CD_3CN and 12.55 ppm in Me_2SO-d_6).

The assignment of the 2.32-ppm signal in Figure 12A to the genetic zwitterion appears definitive since the model compound *N*-methyl-2-methyl-2-oxazolinium iodide as a corresponding signal at 2.32 ppm. Other possibilities for this downfield-shifted CCH_3 signal are the CCH_3 of protonated MeOXO and the CCH_3 of the macrozwitterion. The former is excluded since no NH type of signal was observed in the spectrum of the reaction mixture 3 h after mixing. The latter is excluded since no signals characteristic of the repeating unit are present in Figure 12A.

Two experiments were performed in an attempt to obtain high concentrations of the genetic zwitterion which might then result in significantly higher copolymer molecular weights. Equimolar amounts of MeOXO and AA were mixed and stored for 10 h with liquid nitrogen cooling and then the proton NMR spectrum was recorded at room temperature. No NMR signals other than those for the two monomers were observed. The same result was found when the experiment was carried out with ice-water cooling. Genetic zwitterion formation at reasonable rates appears to occur only at ambient or high temperatures.

Proposed Reaction Mechanism. A summary of the experimental results is useful before the proposed reaction mechanism is presented. The copolymer composition has been established as equimolar by proton NMR. Proton and ^{13}C NMR have identified the end groups as olefin, carboxyl, and acetamido. Infrared spectroscopy supports this conclusion. Hydrolysis experiments corroborate both the copolymer composition and identity of end groups. Direct proton NMR analysis of the reaction mixture gave evidence for the genetic zwitterion. HPLC showed that the copolymer product consists of different-sized molecules and not all molecules have the same two end groups.

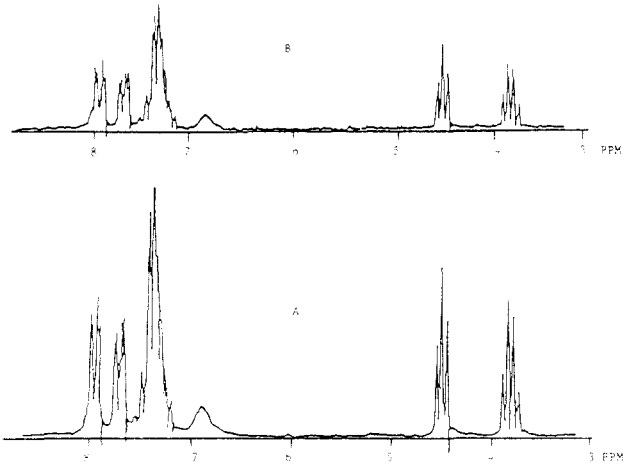
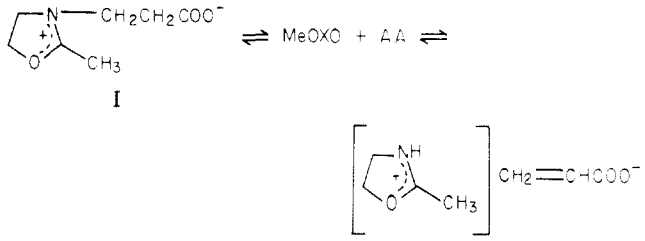


Figure 11. 100-MHz proton NMR spectra of (A) $PhCOOCH_2CH_2NHCOPh$ (authentic sample) in $CDCl_3$ (8% (w/v)) at room temperature and (B) compound isolated after benzoylation of hydrolyzed MeOXO–AA copolymer in $CDCl_3$ (4% (w/v)) at room temperature. Internal standard: Me_4Si.

The following reaction mechanism is proposed to describe the MeOXO–AA polymerization. MeOXO and AA react to form the initiating species I (the genetic zwitterion) and the protonated MeOXO–acrylate salt XIII (formed by proton transfer between MeOXO and AA).

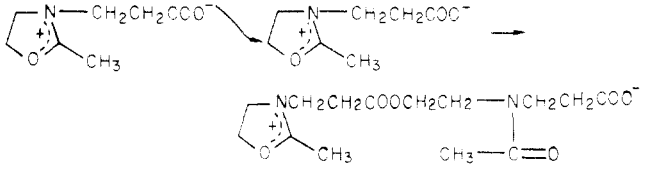


I

XIII

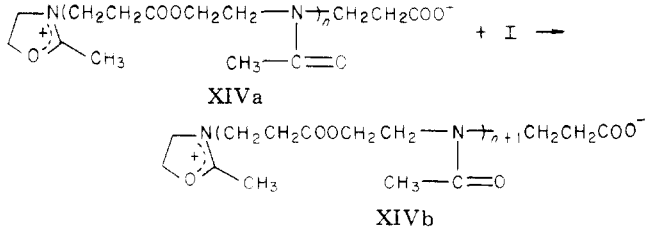
Our results on the direct NMR of the MeOXO–AA reaction mixture indicate that either the equilibrium concentration of XIII is too low to be observed by NMR or its rate of formation is lower than that of I at room temperature.

Propagation is initiated by reaction of the genetic zwitterion with itself to form II



II

Growth continues in a similar manner by the genetic zwitterion reacting with larger sized zwitterions (macrozwitterions)



XIVa

XIVb

and by the reaction of macrozwitterions with each other.

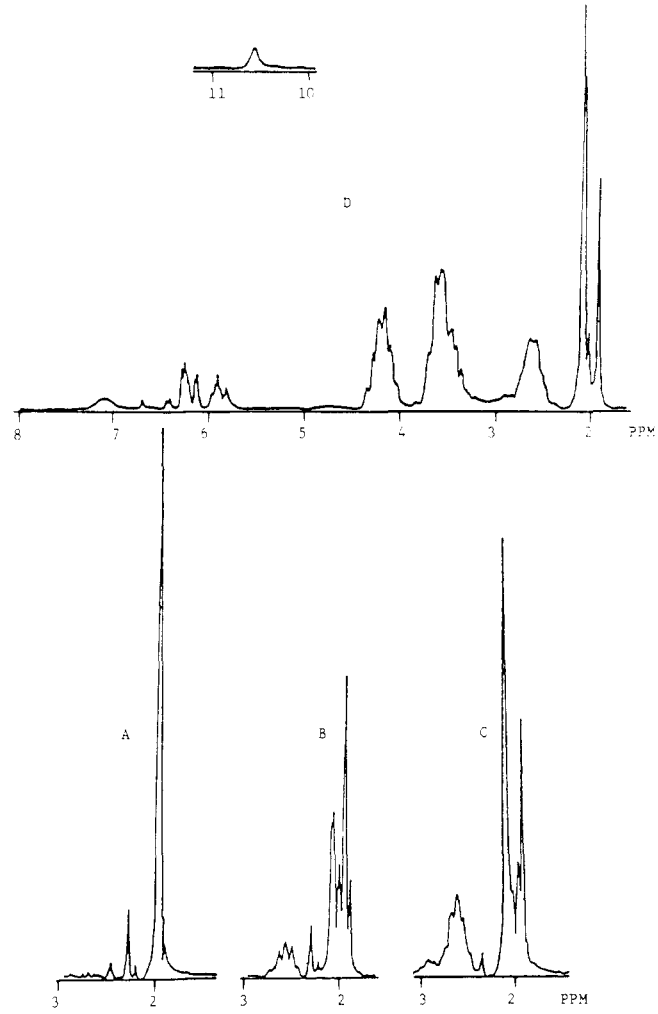
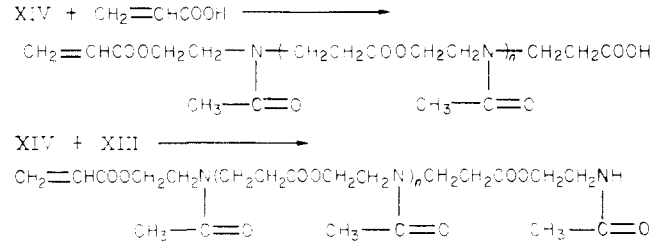


Figure 12. 100-MHz proton NMR spectra of an equimolar mixture of AA and MeOXO in CD_3CN: (A) 3 h after mixing; (B) 2 h at 60 °C; (C) 15 h at 60 °C; (D) complete spectrum after 40 h at 60 °C.

Termination occurs by reaction of macrozwitterions with acrylic acid and with XIII.



The proposed polymerization mechanism is consistent with all of the experimental results. The inability to achieve high molecular weights in the MeOXO–AA system is explained by early termination of macrozwitterion propagating centers by reaction with acrylic acid and the protonated MeOXO–acrylate salt. The observation of acetamido NH and methyl protons in the reaction mixture after only 2 h at 60 °C confirms the early termination reaction with XIII.

The early termination also explains why the MeOXO–AA system does not have living characteristics. In this respect, the MeOXO–AA system differs from the 2-oxazoline–β-propiolactone system, which is reported by Saegusa and co-workers[16] to behave as a living polymerization. The apparent lack of termination in the latter system may reside in the absence of strong proton donors corresponding to acrylic acid and XIII.

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Registry No. MeOXO, 1120-64-5; AA, 79-10-7.

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Chemical Synthesis of a New Polysaccharide. Ring-Opening Polymerization of 1,6-Anhydro-2,3,4-tri-*O*-benzyl-β-D-allopyranose and Preparation of Stereoregular (1→6)-α-D-Allopyranan

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ABSTRACT: The cationic ring-opening polymerization of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-allopyranose (TBALL) was investigated with phosphorus pentafluoride as catalyst at low temperature to synthesize a new (1→6)-α-linked polysaccharide. Polymerization at a catalyst concentration of more than 4 mol % and at the optimum monomer concentration gave a stereoregular polymer with high molecular weight in high conversion. The calculation of the initiation efficiency of PF_5 and the examination of the ^{31}P NMR spectrum of the polymerization system indicated that complexation of PF_5 with TBALL monomer occurred and that propagating species were produced even several tens of hours after initiation. Polymerizations of TBALL with other Lewis acids as catalysts were also investigated. The polymer structure was determined by optical rotation and ^1H and ^{13}C NMR spectroscopy. In addition, the copolymerization of TBALL (M_1) and a 1,6-anhydroglucose derivative (M_2) was studied and the monomer reactivity ratios calculated by the Kelen–Tüdös method were found to be $r_1 = 0.44$ and $r_2 = 2.69$. Debenzylation of the polymer gave a free polysaccharide that was only soluble in DMF–N_2O_4 mixture. The ^{13}C NMR spectrum and the periodate oxidation of the debenzylated polymer indicated that the polymer was stereoregular (1→6)-α-D-allopyranan.

Three 1,6-anhydro-β-D-hexopyranose derivatives obtained from D-glucose,[1-3] D-mannose,[4] and D-galactose[5] have provided synthetic (1→6)-α-D-hexopyranans with high molecular weights through cationic ring-opening polymerizations. 1,6-Anhydro-2,3,4-tri-*O*-benzyl-β-D-altropyranose in which the configurations at the C-2 and C-3 carbons are different from those of the glucose derivative showed almost no homopolymerizability, though it was found that a copolymer of the 1,6-anhydroaltrose derivative can be obtained when a 1,6-anhydroglucose derivative is chosen as a comonomer.[6]

Schuerch and co-workers reported that the ring-opening polymerizability of tri-*O*-benzylated 1,6-anhydro sugars decreases in the order 1,6-anhydro-β-D-manno- > -D-gluco- > D-galactopyranose.[7,8] The reason for the difference in the polymerizability has been ascribed to steric and energetic factors inherent in the individual monomers.

Of the remaining four D-aldohexoses, D-allose gives 1,6-anhydro-β-D-allopyranose in which two hydroxyls are in axial position and a hydroxyl is in equatorial position according to the X-ray structural analysis of its crystal.[9] Thus, the 1,6-anhydro-β-D-allopyranose derivative is expected to have polymerizability. Recently, it was found that D-allose is a component of a natural polysaccharide.[10]

In this study, to synthesize the fourth (1→6)-α-D-glycan, preparation and cationic ring-opening polymerization of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-allopyranose (TBALL) are investigated. Since 2,3,4-tri-*O*-benzyl-(1→6)-α-D-allopyranan with high molecular weight is obtained under appropriate conditions, debenzylation of the polymer into a free polysaccharide is carried out. Structural analysis and solubility data for the free polysaccharide (1→6)-α-D-allopyranan, which is not naturally occurring, are reported. In addition, the relative polymerizability of TBALL is reported from the copolymerization studies of TBALL with 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose.

Results and Discussion

Polymerization Behavior with PF_5 Catalyst. Cationic ring-opening polymerization of 1,6-anhydro-2,3,4-

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