of new SO groups and formation of sulfone groups. These groups increase continuously, but the sulfoxide content slightly decreases.

In summary, from the reported experimental data it may be concluded that oxidation of PHS crystals takes place in two different stages. The first corresponds to a preferential and selective formation of sulfoxide groups at the amorphous interface of the single crystals. At a given sulfoxide content, about 30 wt % for $\bar{M}_n = 9000$, the structure corresponds to the original lamella with a sulfoxidized interface and, consequently, with a higher interfacial free energy. However, the PHS crystalline structure is not affected and the heat of fusion is practically constant. This result is not surprising because it corresponds with the behavior of halogenated[29] or oxidized[23–28] polyethylene single crystals. Moreover, if oxidation takes place at a higher concentration of oxidizing agent, the second stage, formation of sulfone groups, takes place and this attack occurs not only in the interface but also in the crystal lamellae, with partial destruction of the polysulfide crystalline array. When the oxidized PHS crystals are melted and further recrystallized, the melting temperatures show a bigger depression, which corresponds to the behavior of a random copolymer.

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Registry No. Poly(hexamethylene sulfide), 57514-74-6; hexamethylenedithiol-biallyl copolymer, 77932-15-1.

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Structural Analysis of Ethylene–Maleic Anhydride Copolymer, Ammoniated Ethylene–Maleic Anhydride Copolymer, and Carboxyimamidate by ^{13}C and ^{1}H NMR

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ABSTRACT: ^{1}H and ^{13}C NMR have been used to probe the details of the micromolecular structure of carboxyimamidate and its intermediates: low molecular weight ethylene–maleic anhydride copolymer (EMA) and ammoniated ethylene–maleic anhydride copolymer (AEMA). With the aid of shift calculations and numerous model compounds, the complete structure of each polymer has been defined, including end groups, sequencing, and tacticity.

In 1977, a derivative of low molecular weight ethylene–maleic anhydride copolymer (EMA), carboxyimamidate,[1] was reported to be active in reducing metastasis of malignant methylchloanthrene-induced bladder carcinoma in F344 strain rats.[2] Since then, numerous polymeric analogues of carboxyimamidate have been synthesized and submitted for screening, but only a few have shown as much promise as the original lead. Therefore, to define the active site of the copolymer and obtain a better understanding of the nature of the activity, it became important to systematically prepare specific portions of the drug. Very little was known about its specific structure, however, even though considerable data had been collected that defined its physical properties. To avoid synthesizing all possible combinations of the functionalities known to be present in carboxyimamidate, it became imperative to define, as narrowly as possible, the complete structure of the copolymer. Hence ^{13}C NMR was investigated and was found, as indicated in this paper, to be a very sensitive analytical tool. In fact, it was found to be so efficient and reliable in characterizing and differentiating various polymers that it represents a significant advancement in

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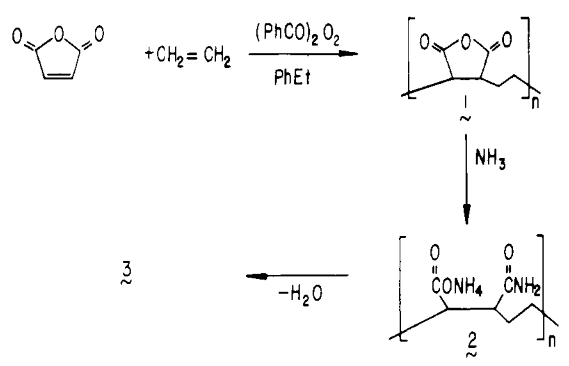
Scheme I



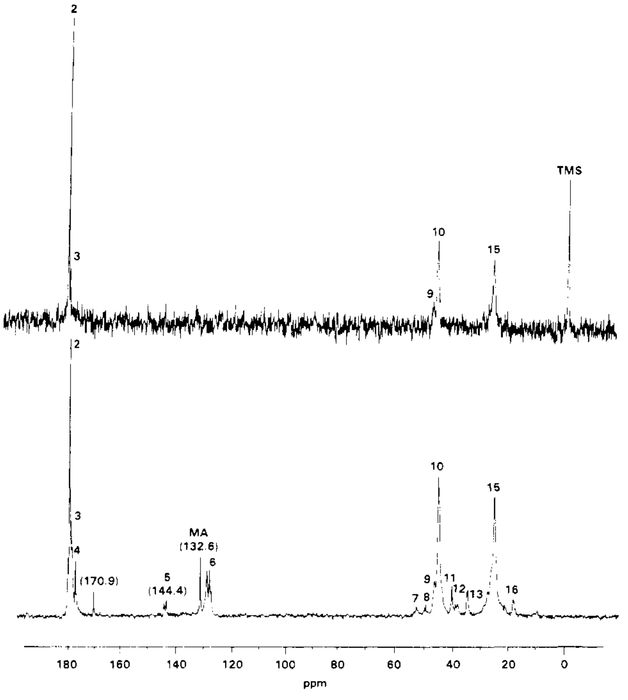


Figure 1. ^{13}C NMR spectra of hydrolyzed high molecular weight EMA (EMA-31) (top) and hydrolyzed low molecular weight EMA (bottom).

our analytical capability. Those results are the basis of this paper.

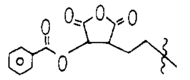
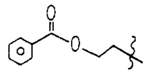
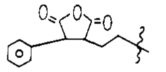
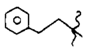
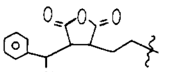
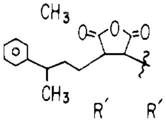
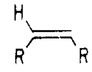
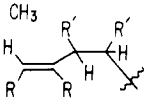
Results and Discussion

Ethylene–Maleic Anhydride Copolymer (EMA). Internal Structure. Initially, numerous ^{13}C spectra were obtained for carboxyimamidate, but because of its complex nature, very little reliable structural information could be obtained from the spectrum. It became necessary, therefore, to examine the precursors to the drug to be able to identify the basic backbone structure before additional functionalization was added.

The first intermediate of carboxyimamidate is the *low molecular weight* EMA (1, Scheme I). Because of its polymeric nature, an NMR solvent could not be found that would provide high concentrations of the copolymer and not interfere with the resulting ^{13}C spectra. Hence the EMA copolymer was hydrolyzed to the free acid (HEMA) in neutral water.[3] This allowed the use of 30–50% concentrations, which reduced acquisition times immensely and provided the opportunity to examine the entire ^{13}C spectra without interference.

Numerous batches of EMA were hydrolyzed and examined by ^{13}C NMR under identical conditions to determine the reproducibility of the copolymerization. The resulting spectra were identical in peak number and peak location, and the relative integrations were within 10% of one another except for two resonances located at 132.6 and 170.9 ppm (Figure 1). These peaks oscillated in height and varied from not observable to 40% of the largest resonance. Based on the shifts of these two peaks and their constant ratio to one another, maleic acid monomer was thought to be present. This was confirmed by spiking the NMR sample with authentic monomer and obtaining an increase in height of the 132.6- and 170.9-ppm resonances. By integrating the spectra of various HEMA samples both before and after the addition of known quantities of maleic acid, the amount of maleic acid impurity was shown to be 2–6%.

Table I
Potential Routes for Polymer Initiation

route	radical	olefin	copolymer
a	benzoyloxy	maleic anhydride	
b	benzoyloxy	ethylene	
c	phenyl	maleic anhydride	
d	phenyl	ethylene	
e	α-phenethyl	maleic anhydride	
f	α-phenethyl	ethylene	
g		either olefin	

To identify which resonances in the spectrum of low molecular weight EMA corresponded to the internal structure, a high molecular weight (~31 000) EMA copolymer, EMA-31, was examined. Because structural features such as end groups, minor imperfections, and impurities comprise only a small mole percent of the entire mixture, the copolymer's resonances could only be attributable to the main internal structure (Figure 1). The main resonances of low molecular weight HEMA (peaks 2, 10, and 15) are identical with those of the hydrolyzed high molecular weight EMA-31. Therefore, these three resonances must represent the symmetrical structure of an alternating ethyl–succinyl unit. The specific assignments of the saturated carbons in the internal ethyl–succinyl unit (Figure 1) are based on calculations using the additivity constants of Clerc, Pretsch, and Sternhell[4] (peak/calculated shift/observed shift): 10/42.9/47.1; 15/24.2/26.7. The remaining resonance at 179.2 ppm (peak 2) must correlate to the carboxyl carbon, which is in accordance with expected shifts.[5] Furthermore, when both the high molecular weight EMA-31 and low molecular weight EMA were examined in their hydrolyzed forms with the identical NMR instrument setting, the ratio of the three main resonances were within 10% of one another. Hence the general internal structure remained the same in spite of the solvent differences in making the two molecular weight copolymers.[6]

Mode of Initiation. When maleic anhydride and ethylene are copolymerized by benzoyl peroxide in ethylbenzene, a variety of initial structures can result (Table I). Pathway g, vinyl radical initiator adding to

Table II
^{13}C NMR Shifts for the Substituted Carbon of Monosubstituted Alkylbenzenes

	alkyl group	pathway modeled	shift, ppm	solvent
1.	$C(CO_2H)HCH_2CO_2H$	c	136.4	H_2O
2.	$C(CO_2H)HC(CO_2H)HCH_2CH_3$	c	137.7	Me_2SO
3.	$CH_2CH_2CH_3$	d	142.6[16]	$CDCl_3$
4.	$CH_2CH_2CH_2CH_3$	d	142.8	$CDCl_3$
5.	$C(CH_3)HC(CO_2H)HC(CO_2H)HCH_2CH_3$	e	144.4	Me_2SO
6.	$C(CH_3)HC(CO_2H)HC(CO_2H)HCH_2CH_2C(CO_2H)HC(CO_2H)H_2$	e	144.7	H_2O
7.	$C(CH_3)HCH_2CH_3$	f	148.4[17]	$(CD_3)_2CO$

available monomer, clearly is not operative because there are no vinyl resonances in the ^{1}H NMR. Except for the aromatic carbons[7] at 128 and 144 ppm and the maleic acid impurity at 132.6 ppm, there are also no resonances in the vinyl region of the ^{13}C NMR spectrum (Figure 1). A similar observation eliminates benzoyloxy radical initiation, pathways a and b, as there are no carbonyl resonances in the 164–175-ppm region[8] except for the monomer maleic acid impurity.

The remaining four pathways for initiation all result in a monosubstituted alkylbenzene. The substituted carbon of such an aromatic ring is an ideal tool for differentiating these pathways because it is very sensitive to the type of substitution and the steric environment to which it is exposed. To distinguish among these four pathways, a model that simulated the environment of the aromatic group for each case was either synthesized or found in the literature. When the ^{13}C spectra of these materials were compared, not only was a wide variation of chemical shifts obtained for the substituted aromatic carbon (Table II), but a diastereomeric "doubling" of that carbon was observed for the models representing pathways c and e. This interpretation for the doubling was confirmed by separating the diastereomers by crystallization and showing that the sum of the two independent ^{13}C spectra was identical with the original spectra. A direct comparison of the shifts of these models to that of hydrolyzed low molecular weight EMA (Figure 1) as well as a comparison of the "doubling" effect clearly shows that initiation of the copolymer chain occurs by pathway e and only pathway e. Furthermore, the model for the pathway (6, Table II) has three other diastereomeric "doublets", at 39.1, 46.7, and 53.3 ppm, that are associated with the phenethyl end of the model, two of which virtually superimpose with resonances observed for low molecular weight HEMA (Figure 1).

Polymer Termination. Ethylene–maleic anhydride copolymers can be terminated by one of several mechanisms:

$$R\cdot + R^1\dot{C}H{-}CHR^2R^3 \rightarrow RH + R^1HC{=}CR^2R^3 \quad (1a)$$

$$R\cdot + \text{ethylbenzene} \rightarrow RH + Ph\dot{C}HCH_3 \quad (1b)$$

$$R\cdot + R^1\cdot \rightarrow R{-}R^1 \quad (1c)$$

For disproportionation (eq 1a) to be a viable pathway, either the polymer must contain unsaturation or some of the phenethyl radical must have been converted to styrene. Not only does the ^{1}H NMR and ^{13}C NMR indicate that the only olefin present in the copolymer is maleic acid, but neither spectrum shows any indication of polystyrene. Disproportionation, therefore, does not occur to any extent.

If chain transfer (eq 1b) were operational, then the growing copolymer would terminate with either a RCH_2CH_3 or a $R'CHCO_2HCH_2CO_2H$ group. In the former case, regardless of the nature of R, the methyl carbon would resonate between 11–15 ppm—an area for which HEMA is devoid of peaks.[9] To determine if the EMA copolymer terminates with a $R'CHCO_2HCH_2CO_2H$ group,

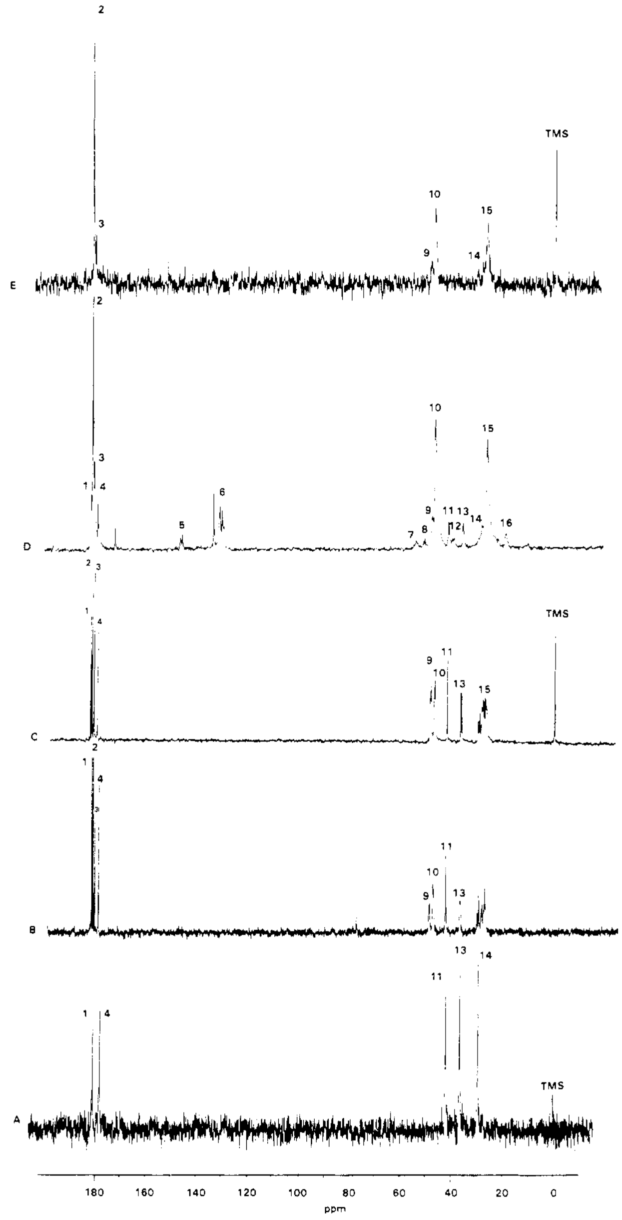
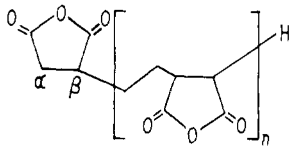


Figure 2. ^{13}C spectra of hydrolyzed models **4a–c**, hydrolyzed low molecular weight EMA, and hydrolyzed high molecular weight EMA: (A) **4a**, 2 succinyl units; (B) **4b**, 4 succinyl units; (C) **4c**, 6 succinyl units; (D) HEMA, ~10 succinyl units; (E) hydrolyzed EMA-31, ~240 succinyl units.

a series of compounds consisting of alternating ethyl-succinyl units was synthesized (**4a–c**), each of which had a succinyl group on each end, and were examined by ^{13}C NMR (Figure 2A–C). The simplest compound of the series, the dimer **4a**, has no internal succinyl groups and therefore should exactly mimic a terminal succinyl group on a copolymer. And as can be seen in Figure 2, HEMA resonances 1, 4, 11, 13, and 14 are perfectly aligned with



4a, n = 1
4b, n = 3
4c, n = 5

the dimer model. Hence termination does occur by chain transfer with the end group being a $RCHCO_2HCH_2CO_2H$ unit.

The third possible mechanism for termination, combination (eq 1c), was examined by comparing the amount of phenethyl initiator to that of the terminating succinyl unit. If the integration of the terminal succinyl unit (per carbon) is appreciably smaller than that of the phenethyl initiator (per carbon), then combination occurs to a considerable extent; if the integrations are similar, then combination is not a significant mode for termination. When EMA was examined under quantifying conditions (see Experimental Section), the resonances representing the phenethyl initiator (Figure 2D, peak 5) and the succinyl end group (Figure 2D, peak 11 or 13) integrated 1:1 within experimental error. Therefore combination does not occur to any appreciable extent.

Tacticity. When the spectrum of the dimer **4a**, which has no internal succinyl units, was compared to that of the tetramer **4b** and the hexamer **4c** models, the resonances corresponding to the internal succinyl units were easily identifiable and superimposed with HEMA resonances 2, 3, 9, 10, and 15 (Figure 2). Five resonances, however, instead of the expected three were obtained for the internal ethyl–succinyl units. These additional resonances apparently represented the alternate diastereomer of the internal succinyl unit. This was confirmed by crystallizing the diasteromeric tetramer to obtain the pure *dl* isomer. The ^{13}C NMR spectrum of this material indicated that peaks 2 and 10 correlated to the *dl* form while peaks 3 and 9 represented the meso from (Figure 2D,E). Hence both high and low molecular weight EMA copolymers are not isotactic. When the copolymers were examined under quantifying conditions (see Experimental Section), the *dl*/meso ratio for each was found to be 86/14.

Ammoniated Ethylene–Maleic Anhydride Copolymer (AEMA). The second step in the synthesis of carboxyimamidate is the ammoniation of low molecular weight EMA (2, Scheme I). To assign the resonances in the ^{13}C spectrum of the AEMA copolymer, the models used to assign the EMA resonances were ammoniated under conditions identical with those of the copolymer (Figure 3).

By comparing the spectrum of hydrolyzed dimer (Figure 2A) to that of ammoniated dimer (Figure 3A), it can be seen that the α- and β-carbon resonances at 36.6 and 42.2 ppm, respectively, and the two carbonyl carbon resonances at 177.3 and 180.2 ppm have each doubled for the ammoniated dimer. This results from ammonia attacking both carbonyls of both anhydride units to give both an amide and an acid functionality at each saturated succinyl carbon. Fortunately, the shifts of one succinyl unit are not affected by the order of the functionalities at its nearest neighbor and a relatively simple spectrum was obtained.

When the ammoniated dimer (Figure 3A) is compared to ammoniated tetramer (Figure 3B), the internal succinyl carbons and the additional bridging CH_2 carbons are easily identified: the internal succinyl carbonyls are represented by resonances 2 and 4, the internal methines are resonances 7–10, and the bridging CH_2 carbons are resonances 15–18. As with the hydrolyzed tetramer, a mixture of diastereomers existed, as was shown by separating the isomers by crystallization and obtaining pure *dl* material[10] (Figure 3C).

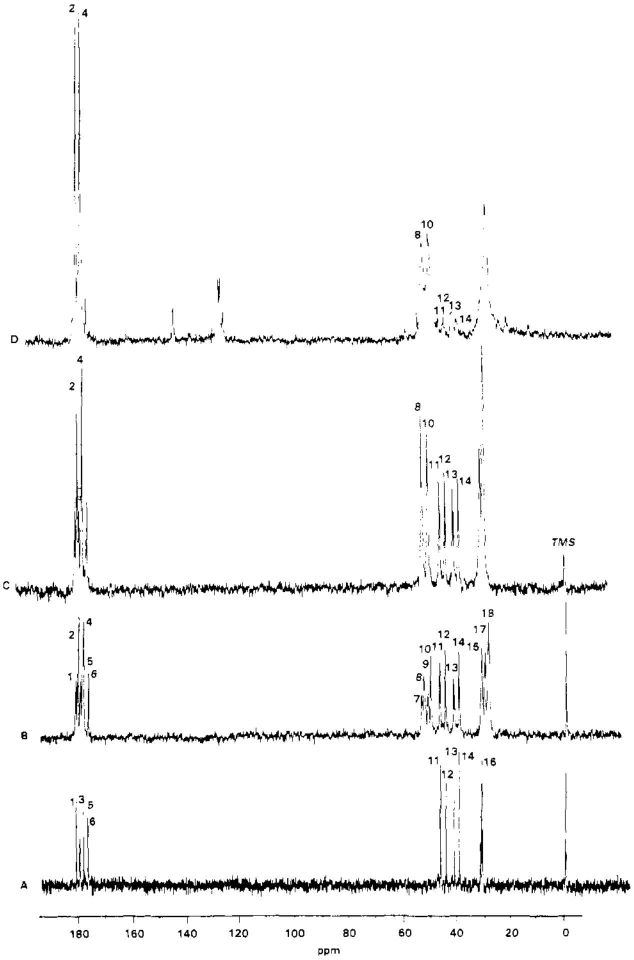


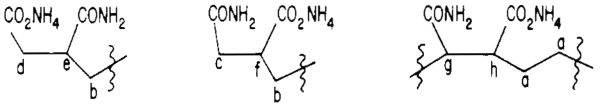
Figure 3. ^{13}C spectra of ammoniated models **4a–c** and low molecular weight AEMA: (A) **4a**, *dl*/meso; (B) **4b**, *dl*/meso; (C) **4c**, *dl*; (D) low molecular weight AEMA.

The peaks for the ammoniated tetramer were further assigned by calculation, which is very reliable because the effects of substituents on ^{13}C chemical shifts are largely additive. By using the additivity values of Clerc, Pretsch, and Sternhell[4] and the information obtained by comparing the spectra of ammoniated dimer and trimer, the assignments shown in Table III were made. These calculated shifts also confirm that the assignments of the various pairs of resonances are accurate.

By comparing the carbonyl regions for the ammoniated dimer and trimer (Figure 3), it easily can be seen that the internal carbonyl carbons are represented by peaks 2 and 4, with the carboxyl carbon being the downfield peak. A similar assignment could also be made for peaks 1, 3, 5, and 6 but we were unable to prove which peaks represented the α- or β-carbonyls.

By examining the ^{13}C spectrum of low molecular weight AEMA (Figure 3D) and comparing it to low molecular weight EMA (Figure 2D), it appears that a doubling of most major succinyl resonances has occurred. As shown by the above model studies, this duplication of peaks represents ammonia adding in a random fashion. The ammonia must add randomly to both carbonyls of the terminal anhydride unit because when HEMA is examined under quantifying conditions (see Experimental Section), peaks 11 and 12 (Figure 3D) are nearly equal in size. This

Table III
Calculated ^{13}C NMR Shifts for the Saturated Carbon Atoms of Ammoniated Tetramer 4b



carbon	calcd shift[4]	assignment[a] exptl shifts/peak no.
a	24.9[b]	28.5/18
b	27.1[b]	30.5[c]/15-17
c	37.0	39.6/14
d	38.6	41.1/13
e	44.9	44.6/12
f	46.5	46.6/11
g	46.3	49.9 (*dl*)/10; 50.9 (meso)/9
h	47.9	52.7 (*dl*)/8; 53.4 (meso)/7

[a] Refers to Figure 3b. [b] These are averaged calculations considering the various combinations of neighboring groups. [c] Average of peaks 15-17.

randomness probably occurs throughout the entire copolymer chain since all the internal anhydrides will have less steric differentiation between the carbonyls than the terminal anhydrides.

Carboxyimamidate. The final step in the synthesis of carboxyimamidate involves the partial dehydration of low molecular weight AEMA to form succinimide functionalities along the copolymer chain. Because of the conditions employed, the backbone structure of AEMA remains the same as in the EMA copolymer and the amount of imide present can be determined by the weight of water removed (approximately 20%) but the location of the imide remains uncertain.

If imide formed at the succinyl unit next to the phenethyl initiating group, the restricted rotation should affect the chemical shift of the C^1 aryl resonance. When AEMA copolymer was *fully* dehydrated, which ensures that an imide is adjacent to the phenethyl group, the shift of the C^1 aryl carbon was 143 ppm, shifted upfield from 144.5 ppm for the AEMA copolymer. In accordance with this, the spectrum of carboxyimamidate (Figure 4C) has two distinct C^1 aryl resonances at 144.5 and 143.0 ppm, which illustrates that some imide is formed adjacent to the phenethyl group.

To determine if imide formation occurs at the terminal succinyl unit and/or at internal succinyl units, tetramer was ammoniated (Figure 4A) and partially dehydrated (Figure 4B). This process produced four new resonances: 1, 8, 11, and 14. If imide is formed at the terminal succinyl unit, then two new resonances should appear slightly upfield of the parent terminal succinyl unit (peaks 9, 10, 12, and 13); if imide is formed internally, then a single new resonance should occur slightly upfield of the internal parent succinyl unit (peaks 6 and 7). Indeed, peaks 11 and 14 and peak 8, respectively, represent these conditions. This interpretation is further supported by calculations. These same three resonances are present in the carboxyimamidate spectrum (Figure 4C), which indicates that the imide functionality forms not only at the initiation site but also internally and at the termination site.

Quantitative Integration of ^{13}C NMR Spectra. For FT NMR to be quantifiable, the pulse delay (P_d) between pulses must be 5 times longer than the relation time (T_1) to ensure that greater than 99% of all the nuclei have had the time to decay back to their ground states. Furthermore, the NOE enhancement must be eliminated by only proton decoupling the material during the data acquisition period (inverse gated decoupling).[5]

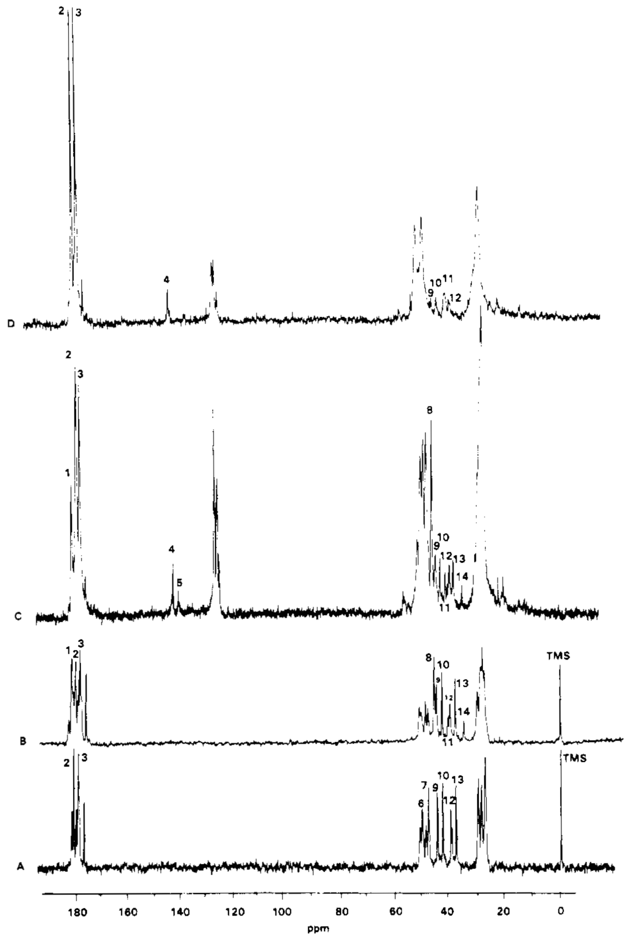


Figure 4. ^{13}C spectra of (A) ammoniated tetramer **4b**, (B) partially dehydrated ammoniated tetramer **4b**, (C) carboxyimamidate, and (D) low molecular weight AEMA.

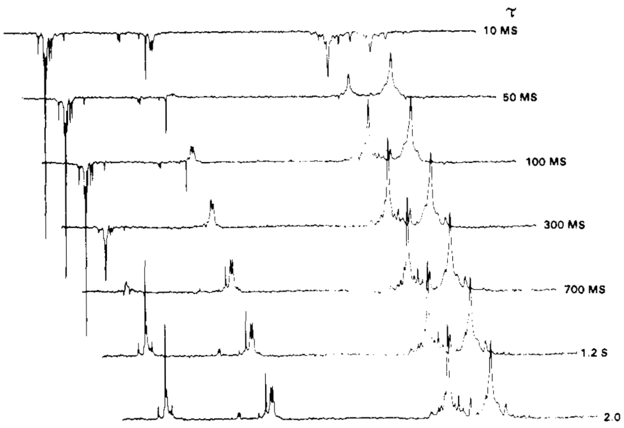


Figure 5. Inversion-recovery T_1 analysis of low molecular weight EMA.

To ensure that a proper pulse delay is chosen, the relaxation time must be known for each carbon nucleus of interest. This was accomplished by a two-pulse sequence (180–τ–90), known as the inversion–recovery method. The spectra in Figure 5 show the result of varying the delay time (τ) from 10 ms to 2 s for low molecular weight EMA. The alkyl backbone carbons invert at the shortest delay time followed in succession by the aryl carbons (ortho, meta, and para), C^1 aryl carbon, vinyl carbons of maleic acid monomer, and the carboxylic acids. Specific relaxation times were calculated from this series of spectra, and according to these relaxation values, all the nuclei of EMA would be fully relaxed within 7.5 s (5 × 1.52). Hence a 7.7-s pulse delay was used for the quantification of EMA as well as carboxyimamidate. New relaxation data were not obtained for carboxyimamidate because it has far too complex a spectrum to obtain accurate relaxation data and because the carbons in carboxyimamidate should have similar relaxation times to those of EMA.

By comparing the values of the integrals obtained for EMA and carboxyimamidate when a 7.7-s delay and inverse gated decoupling were used, the following conclusions about the carboxyimamidate series of copolymers were made:[11] (1) the ratio of the phenethyl end group to the succinyl end group, as shown by the ratio of the integration of the C^1 aryl carbon (Figure 1, peak 5) to the terminal CH_2 (Figure 1, peak 13), is 1:1—this eliminates termination by combination; (2) the peak heights of peaks 11 and 12 and peaks 13 and 14 (Figure 3D) are nearly equal, which proves that ammonia adds randomly to the succinic anhydride units; (3) by measuring the heights of peaks 2 and 3 and peaks 10 and 9, respectively, in Figure 1, the *dl*/meso diastereomeric ratio was found to be 86/14 for both high and low molecular weight EMA copolymers; (4) the phenethyl end group forms a 50/50 mixture of diastereomers with its adjacent methine as shown by the doubling in peaks 5 and 12 in Figure 1; and (5) even though the majority of total imide is located internally (Figure 4C, peak 8), some imide is located on both ends as shown by peaks 5 and 14 in Figure 4—the integration basically implies a statistical distribution.

Molecular Weight Determination. Low molecular weight EMA, AEMA, and carboxyimamidate copolymers have been shown by ^{13}C NMR analysis to have a single phenethyl functionality per polymer chain. This information coupled with the fact that the phenyl resonance is clearly distinguishable from the rest of the copolymer in the ^1H NMR spectrum allows an accurate determination of molecular weight. This is accomplished by making a solution containing both a known amount of copolymer and internal standard, 2,3-pyrazinedicarboxylic acid,[12] and obtaining an accurate integration of the standard and the phenyl group of the copolymer.[13] To minimize measurement errors and increase accuracy, each copolymer was examined by this procedure numerous times over a 50–250-mg weight range (Figure 6). Furthermore, each sample of copolymer examined by this method was previously heated under high vacuum to remove any maleic acid monomer of spurious water. The results of this approach showed that EMA and carboxyimamidate have molecular weights of 1382 ± 19.7 or 1.37% and 1589 ± 42 or 2.5%, respectively. These molecular weights correspond to 9.3 succinyl–CH_2CH_2 repeat units for EMA and 8.8 repeat units for carboxyimamidate plus a phenethyl unit at the initiation end and a succinyl unit at the termination site for each. A good correlation was found among the entire copolymer sequence.

When the internal standard was not used and the aryl group integral was compared directly with the alkyl integral, 9.0 ethyl–succinyl repeat units were obtained. The fact that this value is almost identical with those obtained when the internal standard was used further demonstrates the accuracy of the overall structure assigned to the copolymers because the total structure analysis must be used to determine the number of protons in the alkyl region when the method not using the internal standard is employed.

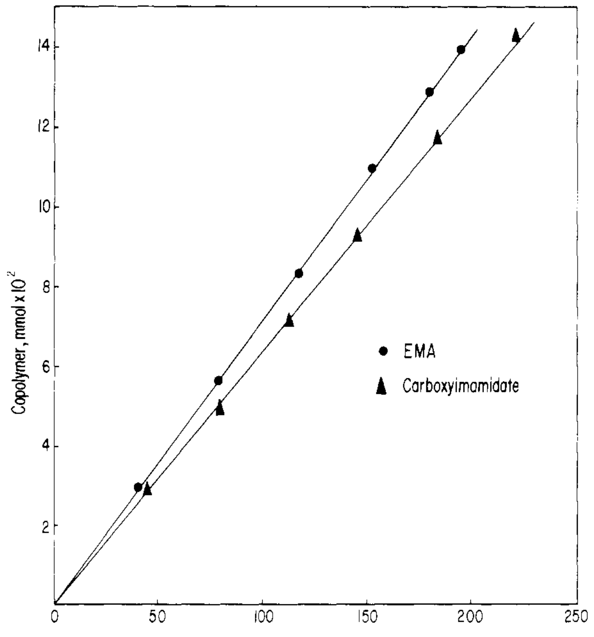
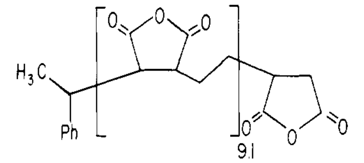


Figure 6. Amount of copolymer by weight vs. molar amount by ^1H NMR integration.

Conclusions

The culmination of these experimental data clearly defines the micromolecular structure of low molecular weight EMA copolymers. The simplest copolymer of this series, low molecular weight EMA, has the following general structure:



The repeating succinyl units, however, are not isotactic but are a 86/14 mixture of *dl*/meso diastereomers. The phenethyl–succinyl unit is also diastereomeric but is a 50/50 mixture.

Both the low molecular weight AEMA and carboxyimamidate copolymers have the same general structure as the low molecular weight EMA. AEMA, however, has had the anhydride units of EMA opened with anhydrous ammonia to form acid/amide functionalities. Carboxyimamidate is structurally identical with AEMA except 20% of the acid/amide groupings in AEMA have been converted to imide functionalities. In both cases the new functionalities have been formed in a completely random fashion.

Experimental Section

Materials. Details for the synthesis of carboxyimamidate were reported previously.[14] High molecular weight ethylene–maleic anhydride copolymer (EMA-31) was obtained from the Specialty Chemical Division of Monsanto Industrial Chemicals Co. A full paper describing the synthesis of the model compounds is forthcoming.

Methods. All ^{13}C spectra were obtained on a JEOL FX-90Q NMR spectrometer, using either a 5- or 10-mm NMR tube. The reference was set with neat $(CH_3)_4Si$ within a coaxial tube. Unless an internal lock was required for resolution purposes, the sample solutions were made as concentrated as possible (20–40%) in H_2O. Virtually all the standard spectra were obtained using the following set of conditions: pulse width, 7.7 μs;[15] pulse delay, 1.18 s; delay, 150 μs; frequency, 5000 Hz (sweep width); accumulation time, 0.8190 s; exponential window: 15 for polymers, 7 for monomers; observation frequency, 22.5 MHz; obset frequency = 32.9 kHz; irradiation set, 54.2 kHz; IRMOD = 1 (complete broad-band decoupling).

When polymer spectra were needed for quantification purposes, the following changes were made: pulse width, 25.2 μs; pulse delay, 7.4 s.

The relaxation times were calculated using the standard "inversion–recovery" method while autostacking the data. These data were analyzed by using the commercial data tabulation program supplied by JEOL.

Acknowledgment. I thank the Monsanto Industrial Chemicals Applied Science Research and Development Group for making available the use of their JEOL FX-90Q heteronuclear NMR spectrometer, specifically B. Katlafsky and E. M. Emory. Furthermore, I thank M. D. Sefcik, J. F. Schaefer, and E. O. Stejskal for helpful discussions concerning ^{13}C quantification.

Registry No. Maleic anhydride, 108-31-6; ethylene, 74-85-1.

References and Notes

(1) Carboxyimamidate has also been referred to as N-137 or CARBETHIMER™.

(2) (a) Falk, R. E., et al. *J. Surg. Res.* **1980**, *28*, 485–491. (b) Falk, R. E., et al. *Br. J. Surg.* **1979**, *66*, 861–863. (c) Falk, R. E., et al. *Surgery* **1970**, *84*, 483–489. (d) Fields, J. E.; Asculai, S. S.; Johnson, J. H.; Johnson, R. R. *J. Med. Chem.* **1982**, *25*, 1060–1064.

(3) The structure for hydrolyzed EMA is identical with that of EMA except that the anhydrides have been converted to dicarboxylic acids.

(4) Clerc, J. T.; Pretsch, E.; Sternhell, S. "^{13}C Kernresonzspektroskoper"; Akademische Verlagogesellschaft: Frankfurt am Main, 1973.

(5) (a) Breitmaier, E.; Voelter, W. "^{13}C NMR Spectroscopy"; Verlag Chemie: New York, 1978. (b) Levy, G. C.; Lichter, R. L.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance Spectroscopy"; Wiley: New York, 1980.

(6) The low molecular weight EMA was formed in ethylbenzene whereas the EMA-31 was formed in ethylene dichloride.

(7) The ^1H NMR has a significant absorption, a broad singlet, at approximately 7.8 ppm, which is indicative of an aromatic functionality. The ^{13}C resonances at 144.4 and 128 ppm are consistent with a monoalkylbenzene[6] and under fully relaxed conditions integrate 1:5; the two resonances for maleic acid monomer integrate 1:1 under these same conditions. This eliminates the possibility of hidden vinyl resonances.

(8) The carbonyl resonances (ppm) of benzoic acid and its derivatives are as follows:[5b] acid, 173.5; methyl ester, 167.0; ethyl ester, 164.9.

(9) Of the 10–15 batches of EMA that were examined by ^{13}C NMR, one batch had a very small resonance at 10.2 ppm, which may indicate a small amount of RCH_2CH_3 termination for that particular batch.

(10) The hydrolyzed tetramer was shown to be approximately a 60/40 ratio of *dl*/meso isomers. Ammoniating the tetramer should give the same isomer ratio; therefore resonances 8 and 10 should represent the *dl* form.

(11) The figures referred to are only to illustrate which peaks were being examined and are not necessarily the quantified spectra from which the conclusions were drawn.

(12) 2,3-Pyrazinedicarboxylic acid was an ideal internal standard because it was an easily handled solid whose spectrum did not interfere with those of the copolymers.

(13) The molecular weight of each polymer (p) using this standard (st) can be obtained by using the following equation: $(MW)^p = 2.5(wt)^p \times (integration)^{st}/(moles)^{st}(integration)^p$.

(14) Fields, J. E.; Asculai, S. S.; Johnson, J. H. U.S. Patent 4 255 537, Mar 10, 1981.

(15) The pulse width required for a 90° flip for EMA in water was experimentally found to be 25.2 μs. Therefore 7.7 μs corresponds to a 30° flip.

(16) Formacek, V.; Desnoyer, L.; Kellerhals, H. P.; Clerc, J. T. "^{13}C Data Bank"; Bruker-Physik: Karlsruhe, 1976; Vol. 1.

(17) Breitmaier, E.; Bauer, G. "^{13}C-NMR-Spektroskopie, eine Arbeitsanleitung mit Ubungen"; Georg Theime Verlag: Stuttgart, 1977.

Quasi-Elastic Light Scattering of Poly(hexyl isocyanate) in Hexane[†]

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ABSTRACT: The field correlation function of light scattered from poly(hexyl isocyanate) (PHIC) in *n*-hexane at 25 °C was analyzed according to the dynamic structure factor of a semiflexible filament as proposed by Fujime, based on the Harris–Hearst model for wormlike chains. In the molecular weight range $M_w > 10^5$, we found the PHIC molecules to be fairly flexible, with $\gamma L = 3.36$ and 6.84 for PHIC with molecular weights of 2.0×10^5 and 4.1×10^5, respectively. In our preliminary analysis, we found excellent agreement between our light scattering results for a non-free-draining polymer (PHIC) in hexane and the free-draining Fujime theory as well as the sedimentation coefficient results of Murakami, Norisuye, and Fujita. Our demonstration suggests that we may have a method that will permit us to determine the flexibility parameter for wormlike polymer chains using Rayleigh line width measurements as a function of the magnitude of the momentum transfer vector, especially when the theory can be modified to include hydrodynamic interactions.

Introduction

Dilute solutions of poly(hexyl isocyanate) (PHIC) were first investigated by Schneider et al.,[1] who showed an unmistakable stiffness of this polymer. Subsequently, Berger and Tidswell[2] and Rubingh and Yu[3] showed that the PHIC chain in tetrahydrofuran and in hexane can be represented by the wormlike chain model. A detailed study has recently been presented by Murakami et al.,[4] who used 19 well-fractionated samples of PHIC ranging in molecular weight from 7×10^4 to 7×10^6 with hexane at 25 °C as a solvent. By means of light scattering, viscosity, and sedimentation velocity measurements, they determined the *z*-average mean square radius of gyration $\langle r_g^2 \rangle_z$, the intrinsic viscosity $[\eta]$, and the sedimentation coefficient s_0 as a function of molecular weight M. A persistence length A (=42 ± 1 nm) and a molar mass per unit contour length M_L (=715 ± 15 nm^{-1}) were computed using the molecular weight dependence of $\langle r_g^2 \rangle_z$ according to the Benoit–Doty theory[5] for the Kratky–Porod wormlike chain. With A and M_L fixed to 42 nm and 715 nm^{-1}, respectively, the data for the intrinsic viscosity $[\eta]$ and the sedimentation coefficient s_0 were then used to compute an

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