Nuclear Magnetic Resonance Microstructure Analysis of Tetrafluoroethylene–Propylene Copolymers

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ABSTRACT: Five tetrafluoroethylene–propylene copolymers containing 38 to 65 mol % tetrafluoroethylene were prepared by emulsion polymerization. The high resolution 220 MHz ^1H and 94.1 MHz ^{19}F NMR spectra of the copolymers contain resolvable patterns associated with different triad (3-monomer) sequences. Computer simulations of the spectra were attempted, but both the ^1H and ^{19}F NMR spectra were too complex to be amenable to rigorous analysis. However, the different characteristic methyl proton resonances were used to determine the amount of alternating and nonalternating propylene sequences in the copolymers. Similarly, the intensity ratios of the different regions of the ^{19}F NMR spectra provided information on the amount of alternating and nonalternating tetrafluoroethylene sequence in the copolymers. The various triad sequences determined from both ^1H and ^{19}F NMR spectra were consistent, thereby also verifying tentative assignments of the observed resonances.

Nuclear magnetic resonance is widely used for microstructure analysis of polymers.[2] Although proton resonance is usually preferred, ^{19}F and ^{13}C NMR can have even greater utility for microstructure analysis because of their larger chemical shift range. Studies of two or more resonance regions, e.g., ^1H and ^{19}F, are frequently useful in providing a more complete analysis of microstructure.

Various fluorine-containing copolymers have been investigated by NMR. They include the copolymers of vinylidene fluoride ($C_2H_2F_2$) and hexafluoropropylene[3] (C_3F_6), chlorotrifluoroethylene (C_2ClF_3) and isobutylene,[4] and tetrafluoroethylene (C_2F_4) and isobutylene.[5]

Ishigure et al.[6] used ^{19}F NMR to study copolymers of tetrafluoroethylene (TFE) with propylene and with propylene-d_6. We report here studies covering a larger composition range and employing both 220 MHz ^1H and 94.1 MHz ^{19}F NMR spectra. The ^{19}F NMR spectra were simplified by broad-band proton decoupling to eliminate the effects of ^{19}F–^1H couplings.

Experimental Section

The TFE/propylene copolymers were prepared by continuous emulsion polymerization.[7] Each copolymer was analyzed for fluorine content using the method of Wickbold.[8] The compositions of the TFE/propylene copolymers prepared for this microstructure study are listed in Table I.

The 220 MHz ^1H NMR spectra were obtained with a Varian HR-220 NMR spectrometer. The 94.1 MHz ^{19}F NMR spectra were obtained with a modified Varian HA-100 or a Varian XL-100-15 NMR spectrometer. The solvent used for the NMR analyses was an equal volume mixture of tetrahydrofuran-d_8 and "Freon" 113 ($C_2Cl_3F_3$). The sample temperatures were 23° for the proton spectra and 35° for the fluorine spectra.

By vapor pressure osmometry all samples, except sample 1, were found to be above 5000 molecular weight. There was no indication of end group interferences in either ^{19}F or ^1H NMR spectra from any of the samples.

Results and Discussion

^1H Spectra. Figure 1 shows the ^1H NMR spectra of samples 1 and 4 which are propylene rich and TFE rich, respectively. (In both spectra the two lines at δ 1.75 and 3.60 are attributed to the protons in the deuterated tetrahydrofuran. They do not interfere with the lines of interest.) The methyl region (δ 0.8 to 1.3) is the region of prime interest. In Figure 1A there are four lines in this region, but in Figure 1B only three are observed and two are relatively weak. The four methyl lines and their triad comonomer sequence structure assignments are listed in Table II. These assignments were based on the known chemical shift (δ 0.88) of the methyl group in the heteroatactic triad configuration of polypropylene[9] corrected for the essentially additive shift effect of adjacent CF_2 groups.[10] The effects of α-, β-, and γ-carbon substituents are detectable at 220 MHz. Thus, the CF_2 groups in the TFE affect the methyl group resonance of propylene by producing three additional unique sequences having (1) one γ CF_2, (2) one β CF_2 and one γ CF_2, and (3) one β CF_2 and two γ CH_2's. The effect of γ and β CF_2 groups is to shift the methyl resonance downfield by 0.14 and 0.10 ppm, respectively. One β and two γ CF_2 groups would give a calculated downfield shift of 0.38 ppm; the observed shift is 0.40 ppm (δ 1.28–0.88). The assignments made here follow the model compound work of Elleman et al.[10] and are consistent with the assignments made in ^1H NMR by Ishigure[5] for the methyl group in copolymers of TFE and isobutylene.

Note that in Figure 1B the strong line at δ 1.28 can only be assigned to the alternating sequence structure indicated, because this copolymer sample was TFE rich.

Of the four methyl lines in the ^1H NMR spectra of these TFE/P copolymers, three are attributable to nonalternating structures, and only one (δ 1.28) is attributable to an alternating structure. By comparing the relative integrated intensity of this line with that of the other three methyl lines a calculation of the alternating and nonalternating propylene content of each sample can be made. The results of such analyses are plotted in Figure 2 as nonalternating structure content vs. the molar concentration of propylene in the copolymer. The precision of the propylene data is about 5% relative. The plot shows that there is a small but significant amount of nonalternating propylene sequences even at low concentrations of propylene. As the propylene content increases, there is the expected increase in the nonalternating propylene content which follows the curve drawn through the experimental points that were obtained from the analysis of the five samples.

Copolymers containing nonalternating propylene-centered triads must also have nonalternating TFE-centered triads at compositions near 50 mol %. Then, above 50 mol % propylene the concentration of these nonalternating TFE-centered triads must be low. The ^{19}F NMR spectra confirmed the presence of these nonalternating sequences at low concentrations of propylene as well as those slightly above 50 mol % propylene.

^{19}F–(^1H) Spectra. The proton-decoupled ^{19}F NMR spectra of samples 3 and 5 (51.2 and 65.4 mol % TFE, respectively) are shown in Figure 3. They consist of the resonance pattern of the alternating copolymer (the δ −110 to

Table I

Sample No.	Wt % F	Wt % TFE	Mol % TFE	Mol % P
1	45.1	59.4	38.0	62.0
2	50.1	65.9	44.8	55.2
3	54.3	71.4	51.2	48.8
4	57.6	75.8	56.8	43.2
5	62.2	81.9	65.4	34.6

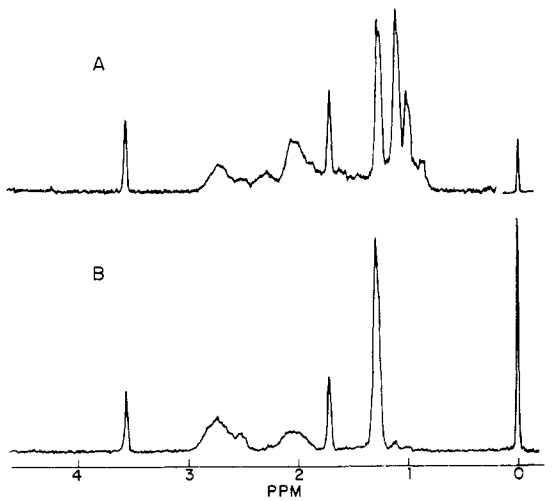


Figure 1. ^1H NMR spectra (220 MHz) of C_2F_4–C_3H_6 copolymers (solvent, 50% THF (d_8) and 50% F-113): (A) 62.0 mol % propylene; (B) 43.2 mol % propylene.

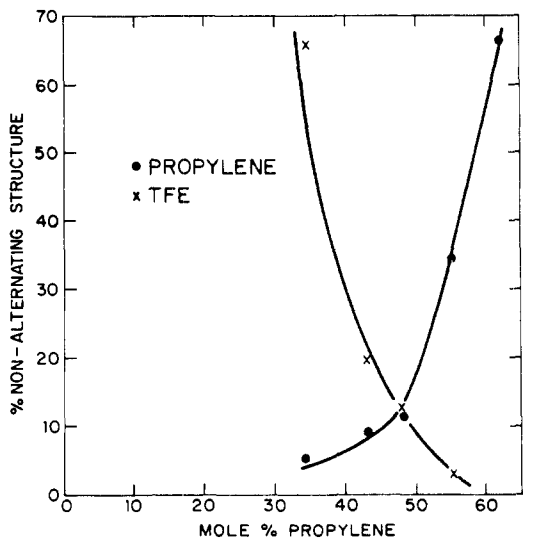


Figure 2. Plot of nonalternating structure content with concentration (mol %) of propylene: (●) experimental data (±5%) for propylene; (×) experimental data (±10%) for TFE.

−120 region) plus additional resonances which are attributable to other sequences. The ^1H decoupled ^{19}F NMR spectrum of Figure 3A closely resembles the spectrum of the alternating copolymer of TFE with deuterated propylene of ref 6 (Figure 1B), except for the additional resonances in the δ −120 to −125 region. At higher TFE content, e.g., Figure 3B, the intensity of these resonances increases, but there are also some surprising changes in the δ −110 to −120 (alternating copolymer) region.

Computer analyses of the ^{19}F spectra were undertaken to confirm tentative pattern assignments and to make quantitative estimates of alternating vs. nonalternating sequences.

Table II
Propylene Sequence Assignments

Chemical shift (δ) of methyl resonance	Triad sequence assignments[a]
1.28	$-CF_2CF_2-CH_2C(CH_3)H-CF_2CF_2-$
1.12	$-CH_2C(CH_3)H-CH_2C(CH_3)H-CF_2CF_2-$
1.02	$-CF_2CF_2-CH_2C(CH_3)H-CH_2C(CH_3)H-$
0.88	$-CH_2C(CH_3)H-CH_2C(CH_3)H-CH_2C(CH_3)H-$

[a] Tactic placement effects were not resolved and therefore are not assigned.

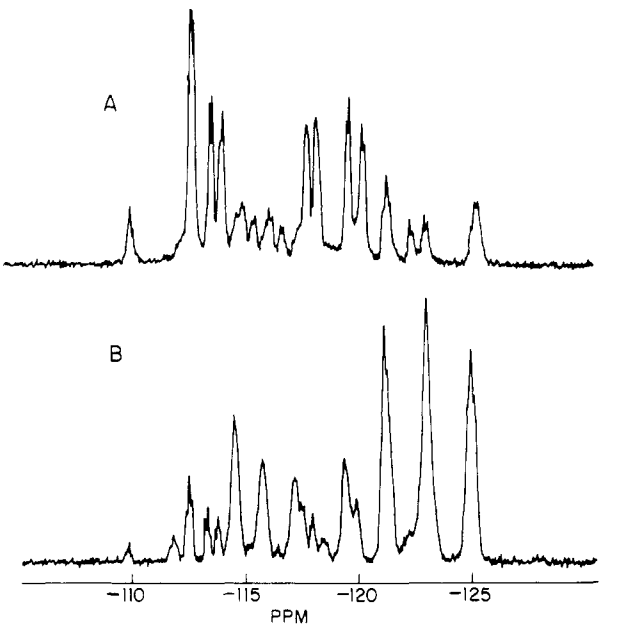
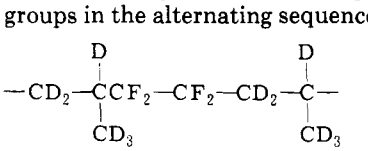


Figure 3. ^{19}F NMR heteronuclear "noise decoupled" spectra (94.1 MHz) of C_2F_4–C_3H_6 copolymers (solvent, 50% THF (d_8) and 50% F-113): (A) 51.2 mol % C_2F_4; (B) 65.4 mol % C_2F_4.

Analysis of the fluorine spectra of Ishigure et al.[6] appeared to be the best starting point. Their copolymers appeared to be strictly alternating, and the spectra were therefore somewhat simpler than ours. The spectrum of their alternating copolymer had ten complex multiplets, but the spectrum of the alternating copolymer with propylene-d_6 simplified to two ABCD patterns of eight multiplets each. Two of the multiplets overlapped. The two patterns were correctly attributed to meso and racemic arrangements of the asymmetric centers of the two adjacent propylene units flanking the TFE.

Analysis of the resonance patterns (ref 6, Figures 1B and 2) of the TFE groups in the alternating sequence



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were undertaken, using computer program LACX.[11] Spin simulation and iterative analyses were based on the ABCD approximation, neglecting deuterium–fluorine couplings. The meso and racemic triad patterns were assumed to be independent, and therefore, each was analyzable in the

four-spin approximation. The assignment of the meso vs. racemic triad patterns is ambiguous. We assume that the pattern with the largest chemical shift differences is due to the meso triad.

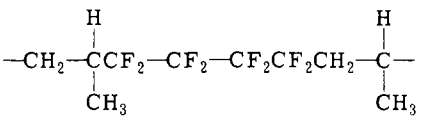
About 80 spin simulation and 20 iterative trials were run in attempts to match the spectrum of the meso triad.

The parameters of Ishigure et al.[6] clearly failed to match the observed spectra. All four permutations of the chemical shifts were run to check for possible mislabeling. The best, but not satisfactory, approximation was obtained with their parameters. Several other parameter combinations gave as good or better matches, however. Ishigure et al. analyzed the spectra as an ABXY system by a perturbation method. This approximation is clearly unsatisfactory, since the observed spectrum is that of a strongly coupled ABCD system.

None of our trials gave a satisfactory fit to the observed spectra. The iterative trials were highly sensitive to interchange of line assignments within a multiplet, and the interchanges frequently resulted in a drastically altered spectrum. Thus, progressive convergence to an improved solution was not possible. The chief difficulty arose from the inadequate resolution of the observed spectra. The calculated spectra consist of 8 multiplets of 4 lines each whereas the published spectra did not resolve the smallest splittings, probably because the deuterium spins were not decoupled. One would expect line broadening for the deuterium couplings of the order of 5 Hz, as observed. The proton-decoupled ^{19}F NMR spectra of this work were incompletely resolved, and were not amenable to exact parameter analysis.

Although the exact parameters for the alternating copolymer spectrum could not be determined, the relative intensities of the multiplets could be estimated reliably, and provided the basis for empirical transition lists for NMRMRG[12] trials. A list of input frequencies was derived from the spectrum of Figure 3A, and the relative intensity for each multiplet was derived from the ABCD approximations. (The relative intensities are not highly sensitive to the exact values of the smaller coupling constants.)

A second set of transitions due to one of the nonalternating (NA) TFE sequences, **2**, was prepared.



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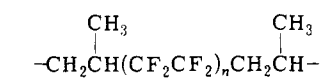
For the NMRMRG[12] trials, only the two nonalternating (NA) multiplets at δ −122 and −130 were used, assuming that these are attributed to the two central CF_2 groups of sequence **2**. The other two CF_2 resonances of nonalternating sequence **2** appear to produce a complex pattern in the δ −114 to −116 region, but this pattern could not be deduced in detail because of overlap with the alternating copolymer pattern. It was omitted in the trials.

A close approximation to Figure 3A was obtained with the trial spectrum shown as Figure 4. The assumed fraction of TFE in nonalternating TFE-centered triads was 0.2.

An alternate, more direct, and reliable method of analysis was developed as follows. Ishigure et al. made tentative detailed assignments of nonalternating CF_2 resonances from spectra of copolymers rich in TFE. The spectra of TFE-rich copolymers are more complex and the tentative



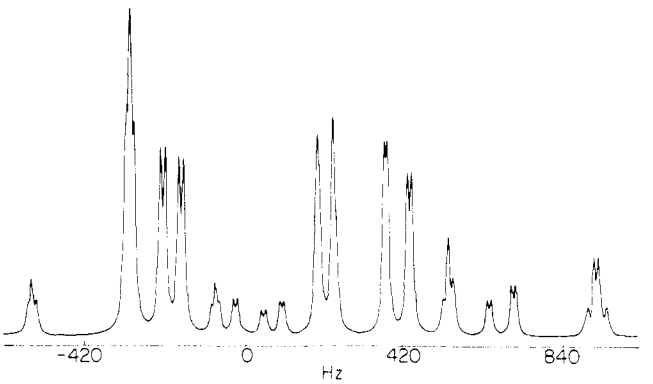


Figure 4. Computer simulation of ^{19}F NMR heteronuclear ^1H "noise decoupled" spectrum for comparison with experimentally obtained spectrum in Figure 3A. The line frequencies were derived empirically from observed spectra. The relative intensities of the multiplets were derived from the ABCD trials for the alternating sequence and by trial and error adjustment of the fractions of alternating and nonalternating sequences.

assignments they made do not explain the spectra completely. However, the following general assumptions, consistent with their assignments, do explain satisfactorily the spectra of the TFE-rich copolymers and are the basis for the estimates of triad probabilities and the nonalternating sequence determination.

The ^{19}F NMR resonances of the alternating triad (n = 1) all fall within the region of δ −108 to −120, except for the doublet at δ −122. The $-C(CH_3)HCF_2-$ and $-CF_2CH_2-$ resonances for all sequences with $n \geq 2$ also fall between δ −108 and −120. The $-C(CH_3)HCF_2CF_2-$ and $-CF_2-CF_2CH_2-$ resonances for all sequences with n = 2 fall very near δ −121 and −125, respectively, or vice versa. The central CF_2 resonances for $n > 3$ fall near δ −123.

Therefore, the relative concentrations of TFE-centered triads containing 1, 2, and 3 or more TFE units were determined by integrating four regions of the spectrum and using the following relationships.

$$\text{area}(-108 \text{ to } -120 \text{ ppm}) + k\ \text{area}(-109.5 \text{ ppm}) = 2N_1 + 2N_2 + 2N_3$$

$$\text{area}(-121 \text{ ppm}) + \text{area}(-125 \text{ ppm}) = 2(N_2 + N_3)$$

$$\text{area}(-123 \text{ ppm}) - k\ \text{area}(-109.5 \text{ ppm}) = 2(N_3)$$

$$N_1 + 2N_2 + 3N_3 = 1.0$$

where N_1, N_2, and N_3 are the proportions of TFE sequences 1, 2, and 3 in length and k is a factor to correct for overlap of the δ −122 doublet for the alternating triad with nonalternating triad resonances. The relative areas must, of course, be normalized to the total CF_2 content, and the last relation normalizes the TFE content.

The factor k = 1.63 is the ratio of the intensities of the δ −122 doublet and the δ −109.5 multiplet of the alternating triad; the latter is well resolved and free from interference. The factor was calculated from computer trials. The intensity ratio of the high field vs. low field multiplet was 2.15 for the meso dyad and 1.11 for racemic dyad. The meso and racemic dyads occur with equal probability, so k is the average. The ratios depend only on the chemical shift differences and the magnitude of the largest J coupling for each half of the ABCD pattern, and vary less than 1% for any reasonable combination of the smaller couplings.

Integration of the ^{19}F NMR spectra and the solution of the simultaneous equations for alternating (n = 1) and nonalternating ($n > 2$) TFE structure gave the results plotted in Figure 2. The precision of the TFE sequence analysis is

about 10% relative. The fifth sample (62.0 mol % propylene) had no detectable nonalternating TFE structure, and therefore is not included in the plot.

The symmetry of the curves for percent nonalternating propylene and TFE sequences confirms the consistency of the analyses of both the ^1H and ^{19}F NMR spectra. Trial calculations of monomer reactivity ratios were made, based on the known monomer feed ratios, copolymer compositions, and percent nonalternating sequences. Quantitatively reliable estimates of reactivity ratios were not possible, because the observed percent nonalternating sequences could not be produced by Bernoulli trial statistics. The data available were insufficient for fitting higher order models.

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Investigation of the Conformations of Four Tetrapeptides by Nuclear Magnetic Resonance and Circular Dichroism Spectroscopy, and Conformational Energy Calculations[1]

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ABSTRACT: Proton nuclear magnetic resonance and circular dichroism studies were carried out on aqueous solutions of the tetrapeptide Asp-Lys-Thr-Gly (which appears as a bend at residues 35–38 of α-chymotrypsin) and its sequence variants Gly-Thr-Asp-Lys, Asp-Lys-Gly-Thr, and Lys-Thr-Gly-Asp; the N and C termini of all four tetrapeptides were blocked with CH_3CO and $NHCH_3$ groups, respectively. The spectroscopic data suggest that bend conformations may exist, to some extent, among the distributions of conformations in the first, third, and fourth, but not in the second, tetrapeptide. This result is consistent with empirical probabilities for the prediction of bend conformations in proteins. Conformational energy calculations on these four tetrapeptides support the indications from the experimental data. It thus appears that, because of short-range interactions, the tendency toward bend formation exists in short peptides, provided that both the composition and amino acid sequence are energetically favorable for bend formation.

In a previous paper,[3] a mechanism for the folding of proteins (involving the formation of β turns, or chain reversals in specific tetrapeptide sequences) was proposed. Subsequently, the conformational energies of several tetrapeptides were minimized[4] to determine the energetic factors responsible for bend and nonbend structures; similar calculations have been carried out on the central dipeptides of numerous tetrapeptides.[5,6] In order to examine the tendencies of specific tetrapeptide sequences to adopt a chain-reversing conformation, we have begun a combined experimental and computational investigation of several isolated tetrapeptides.[7] In this paper, we consider the sequence Asp-Lys-Thr-Gly, which appears as a bend conformation at residues 35–38 in α-chymotrypsin.[8]

Since the tendency toward bend formation depends on both the composition and sequence of the tetrapeptide,[3] we have examined four of the 24 possible sequence permutations of these four amino acid residues, viz., Gly-Thr-Asp-Lys, Asp-Lys-Thr-Gly, Asp-Lys-Gly-Thr, and Lys-Thr-Gly-Asp. The theoretical relative probabilities of occurrence of bends[3] in these four tetrapeptides are 1, 23, 41, and 41, respectively, and hence they are designated as low-probability (L), chymotrypsin-native (N), and high-probability (H_1 and H_2) bends, respectively. In order that these isolated tetrapeptides simulate similar-size segments of polypeptide chains, we have prepared them with blocked end groups, using CH_3CO and $NHCH_3$ at the N and C termini, respectively. Nuclear magnetic resonance and circular dichroism measurements, and conformational energy calculations,[9,10] were carried out on these four tetrapeptides to determine whether a detectable fraction of the population of conformations of each one can exist as a chain reversal and, if so, whether this tendency differs among L, N, H_1, and H_2.

I. Experimental and Computational Procedures

Materials. All solvents used were spectral grade and were used as purchased, except as indicated below. Isobutyl chloroformate, TFA,[11] and $BF_3O(Et)_2$ were purchased from Eastman, and THF and DMF were purchased from J. T. Baker. TFA was distilled over P_2O_5 before use, and $BF_3O(Et)_2$ was distilled as described by Zweifel and Brown.[12] Monomethylamine was purchased from Matheson Co., and *N*-methylmorpholine was purchased from Aldrich Chem. Co.

α-BOC (ϵ-Z) lysine was prepared by the procedure of Ali et al.,[13] and BOC glycine was prepared as described by Schnabel.[14] BOC threonine was prepared by the method of Hofmann et al.,[15] BOC