Microstructural Characterization of Poly(methyl methacrylate) Using Proton-Detected Heteronuclear Shift-Correlated NMR Spectroscopy

Proton-detected heteronuclear multiple-bond correlation (HMBC)[1-3] is an extremely effective NMR method for making resonance assignments and determining molecular structures from long-range (two- and three-bond) ^1H–^{13}C connectivities. The increased sensitivity, which these "reverse-detected" NMR techniques provide over conventional ^{13}C-detected experiments,[4-6] has stimulated a renewed interest in shift-correlation experiments of peptides,[7-9] proteins,[10-13] nucleic acids,[14,15] and natural products.[16-18] We report here the first application of ^1H-detected heteronuclear shift-correlated NMR to the microstructural characterization of synthetic polymers and demonstrate its utility in making configurational or stereosequence assignments. The HMBC NMR experiment provides a direct method for obtaining absolute ^1H and ^{13}C stereochemical information, which, in turn, can be used for assigning tacticity in high molecular weight polymer systems.

Recently, heteronuclear shift-correlation (HSC) NMR techniques[19,20] have proven useful for investigating microstructure of synthetic polymers. Polymer chain configuration and branching studies of poly(vinylbutyral),[21] polyolefins,[22,23] and poly(vinyl chloride)[24] nicely demonstrate how one-bond ^1H–^{13}C connectivities can reveal details of polymer microstructure. While previous NMR studies[25] also illustrate the importance that long-range connectivity information plays in configurational analysis, little success has been reported for synthetic polymers using long-range versions of HSC techniques.[26] The inefficacy in this area is due to properties possessed by high molecular weight polymer systems (e.g., short T_2* relaxation times, low solubility, and high viscosity), which contribute to poor NMR sensitivity and limit signal-to-noise ratios in long-range ^{13}C-detected HSC experiments. Improvements in sensitivity have been obtained by using heteronuclear relay NMR techniques or by incorporating ^{13}C labels into the polymer, as has been recently demonstrated for poly(methyl [*carbonyl*-^{13}C]methacrylate).[27] An unexplored alternative to the heteronuclear relay experiment or to isotopic enrichment is to improve the sensitivity of the heteronuclear experiment through detection of the more sensitive ^1H nuclei. We demonstrate in the present paper that this approach, using the HMBC experiment, provides sufficient sensitivity to allow conformational characterization of high molecular weight polymers. As an illustration, we present an application to atactic poly(methyl methacrylate) (pmma), an extensively studied and well-characterized polymer system.

The HMBC experiment is a modification of the one-bond heteronuclear multiple-quantum (HMQC)[28,29] experiment and exploits the effects that two- and three-bond ^1H–^{13}C scalar couplings have on the evolution of heteronuclear multiple-quantum coherence. The pulse sequence used was[1]

^1H: 90_x–Δ_1 $-t_1/2-180_x-t_1/2-$ –acq(t_2)

^{13}C: 90_φ–Δ_2–90_ψ 90_x

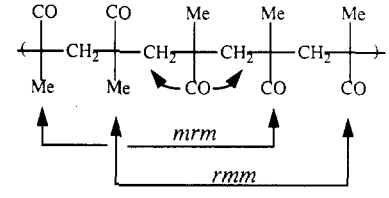
where $\Delta_1 = {}^1/_2{}^nJ_{CH}$ and $\Delta_2 = {}^1/_2{}^nJ_{CH}$ (J_{CH} = one-bond and ${}^nJ_{CH}$ = two- or three-bond long-range ^1H–^{13}C coupling constants). The phase cycling used is as follows: $\varphi = x, x, x, x, -x, -x, -x, -x$; $\psi = x, y, -x, -y$; acq = $x, x, -x, -x$. Spectra were recorded at 500-MHz ^1H frequency on a Varian VXR-500 NMR spectrometer equipped with a reverse-detection 5-mm NMR probe containing a coaxial heteronuclear decoupling coupling coil outside the ^1H observation coil. The data were collected at 30 °C for a nonspinning 52-mg sample of atactic pmma (Pressure Chemical Co.; lot no. 5-12; M_p(GPC) = 840 000; $\bar{M}_w/\bar{M}_n$ = 1.12; P_m (measured by ^1H NMR) = 0.25) dissolved in 0.7 mL of CD_5Cl.

The HMBC NMR spectrum of pmma is presented in Figure 1 and shows groups of long-range ^1H–^{13}C correlations for the molecule. Three different threshold levels are shown to display both high and low intensity correlations. While Figure 1 does not provide sufficient detail to distinguish individual resonances, it does demonstrate the extensive number of long-range ^1H–^{13}C correlations that are observed for pmma.

To illustrate the detail that can be obtained in the current experiment, two regions of the HMBC NMR spectrum have been expanded and are displayed in Figure 2. Numerous multiple-bond proton and carbon connectivities are resolved at this level. The individual methylene proton and carbonyl carbon correlations (top) are very similar to those reported in the previous ^{13}C-labeled study.[27] In addition to these correlations, however, the sensitivity of the HMBC experiments permits detection of many other long-range correlations in the molecule, which were not seen in the ^{13}C-detected experiments. For example, cross peaks between methylene protons and quaternary carbons (bottom) are also detected. Thus, the improved sensitivity that results from detection of protons in the HMBC experiment[4-7] can eliminate the need for isotopic enrichment of polymers *and* provide additional long-range connectivity information. A detailed analysis of the more than 50 long-range correlations detected in Figure 1 will be presented elsewhere.

As in the ^{13}C-detected HSC experiment,[27] the HMBC technique enables stereochemical assignments for subunit interactions in the pmma sample to be made. Two such pentad–tetrad interactions are illustrated below for a heterotactic segment of pmma (methoxy groups omitted for clarity), where r and m represent the racemic and meso symmetry relationships, respectively, between two adjacent monomeric units. Stereospecific assignments for these interactions in the methylene proton and carbonyl carbon region in Figure 2 have been made on the basis of earlier ^1H and ^{13}C NMR studies[30-33] and are consistent with those previously reported for ^{13}C-labeled pmma using the ^{13}C-detected HSC experiment.[27] As in this earlier study, some signals in this region (e.g., (b)) overlap with adjacent resonances, limiting higher level (i.e., hexad and heptad) heterotactic assignment.

pentad (*mrmm*)



By providing new long-range correlations, the HMBC NMR technique permits new stereochemical assignments for pmma to be made. For example, tacticity assignments for correlations between methylene protons and quaternary carbons are displayed in Figure 2. In some cases, assignments are aided by the observation of geminal methylene proton homonuclear coupling, which results in a skewing of the doublet cross peaks for asymmetrical pentad–tetrad interactions.[3] Because of the magnetic equivalence of the methylene protons, cross peaks between

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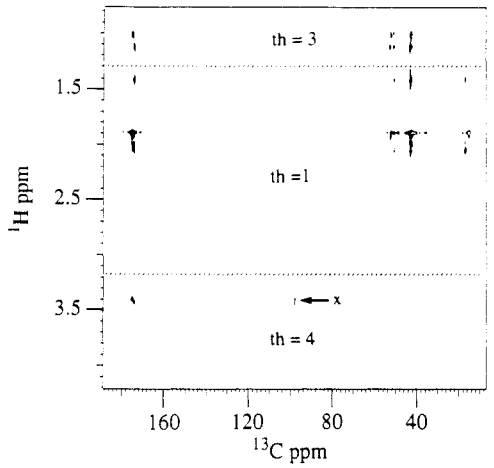

Figure 1. Absolute value contour plot of the long-range ^{1}H–^{13}C correlation spectrum of atactic poly(methyl methacrylate) recorded by using HMBC sequence[1] (Δ_1 = 3.6 ms and Δ_2 = 100 ms). Three linear threshold levels (th = 1, 3, and 4) are presented for different regions of the spectrum to display all contour levels. The initial data matrix (t_1,t_2) consisting of 2048 × 2048 real data points was collected over a total acquisition time of 37 h (t_1 acquisition time = 89.5 ms; t_2 acquisition time = 595 ms; recycle delay = 1.0 s). Prior to Fourier transformation, the data were zero-filled (8K × 8K) and multiplied by phase-shifted sinebell weighting functions in both t_1 and t_2. All chemical shifts are internally referenced to the solvent, and the peak labeled x is a zero frequency artifact.

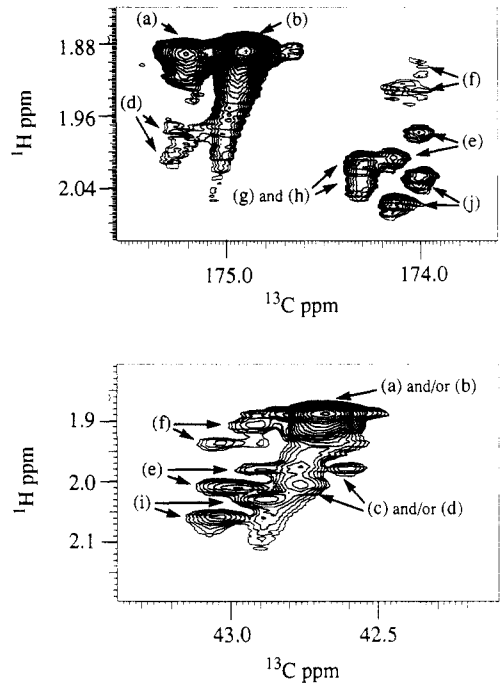

Figure 2. Expanded regions of Figure 1 showing long-range ^{1}H–^{13}C correlations between methylene protons and carbonyl carbons (top) and methylene protons and quaternary carbons (bottom). The carbon–proton pentad–tetrad assignments are labeled as follows: (a) mrrr ↔ rrr; (b) rrrr ↔ rrr; (c) mrrm ↔ mrr; (d) mrrr ↔ mrr; (e) mmrr ↔ mrr; (f) rmrr ↔ mrr; (g) mmrm ↔ mrm; (h) rmrm ↔ mrm; and (i) rmrr ↔ rmr, where r and m represent racemic and meso diads, respectively.

pentads correlating with rrr and mrm tetrads are unsplit. This and other complementary regions of the spectrum (not shown) not only include new correlations and stereochemical assignments but also assist in checking data interpretation for self-consistency.

To achieve adequate ^{13}C digital resolution, a large number of t_1 increments (2048) were collected for the spectrum displayed in Figure 1. Due to the improved sensitivity of the ^{1}H-detection technique relative to the ^{13}C-detection technique,[4-6] this does not impose severe time restraints upon data collection because the number of transients per t_1 increment can be greatly reduced while still providing adequate sensitivity. In fact, significant *reductions* in total experimental time can be expected for the HMBC method if comparable data sets (i.e., similar sweep widths and digital resolution) are collected. For example, long-range correlations similar to those in Figure 2 are still observed for a narrowed ^{13}C sweep width (10 ppm) after only a few hours of data acquisition.

Due to the time dependence of long-range ^{1}H–^{13}C correlation intensities on $^nJ_{CH}$ and homonuclear proton coupling,[3,4] quantitative analysis of configurational sequences in the HMBC experiment is difficult. For a particular set of acquisition parameters, these effects may contribute (along with relaxation processes) to the absence of expected peaks in the spectrum. In practice, two or more experiments collected under different acquisition conditions may be necessary to ensure observation of all detectable signals. The high sensitivity of the HMBC experiment makes this strategy practical, especially if one takes advantage of selective pulses,[35,36] reduced sweep widths, and foldover of NMR signals.[37]

In conclusion, the ^{1}H-detected HMBC NMR experiment provides an effective method for microstructural characterization of synthetic polymers. Detection and assignment of long-range ^{1}H–^{13}C correlations assist in mapping out molecular connectivity and determining configurational sequences and polymer tacticity. The strength of the technique lies in its improved sensitivity over conventional heteroatom-detected HSC experiments and its ability to detect long-range correlations without isotopic enrichment. We have successfully applied this ^{1}H-detected HSC NMR technique, as well as the HMQC technique, to a number of other polymer and copolymer systems and anticipate these methods will play an important part in exploratory polymer research.

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