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Rapid Determination of Polymer Stereoregularity Using Band-Selective 2D HSQC

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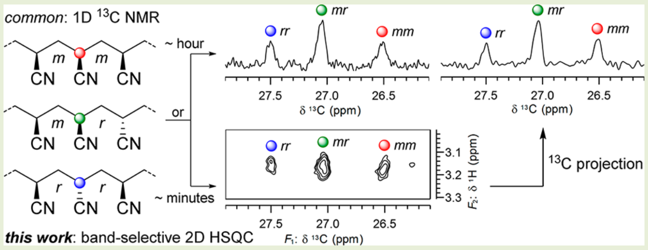
Supporting Information

ABSTRACT: We report the use of band-selective 2D HSQC NMR spectroscopy to rapidly determine the stereoregularity of polymers usually analyzed by 1D ^{13}C NMR spectroscopy. This approach reduced the time required to characterize the triad stereosequences of polyacrylonitrile from about an hour to a few minutes, and can be performed with sufficient ^{13}C resolution to resolve higher-order stereosequences, such as the pentads of polypropylene.



The ordered stereochemistry, or tacticity, of a polymer's main-chain can have a tremendous impact on its physical and mechanical properties.[1] For example, isotactic polypropylene (iPP) is semicrystalline and one of the world's most-produced plastics, while atactic polypropylene (aPP) is waxy and amorphous, with limited commercial applications. Since the discovery of heterogeneous titanium catalysts for the preparation of iPP in the 1950s,[2] the synthesis of many different types of polymers with well-defined stereochemistry has been actively pursued in both industrial and academic laboratories.[3]

One-dimensional (1D) ^{13}C nuclear magnetic resonance spectroscopy (NMR) is one of the most commonly utilized techniques for analyzing polymer tacticity because carbon is ubiquitous in many polymers and ^{13}C has large chemical shift dispersion.[4] Chemical shifts in polymers are often sensitive to the relative stereochemistry of nearby stereocenters resulting in separate resonances for different stereosequences (Figure 1).[5] If the position of each stereosequence in the NMR spectrum has been assigned, both the type of tacticity and degree of stereoregularity can be obtained from the relative areas of resonances. Unfortunately, ^{13}C NMR typically requires long experiment times and large amounts of polymer sample to give spectra with sufficient signal-to-noise ratios (SNRs) to detect minor stereosequences. Acquiring ^{13}C NMR spectra for quantification exacerbates this problem because accurate integration requires higher SNRs, long relaxation delays, and that the experiment be performed without Nuclear Overhauser Effect (NOE) enhancement.[4]

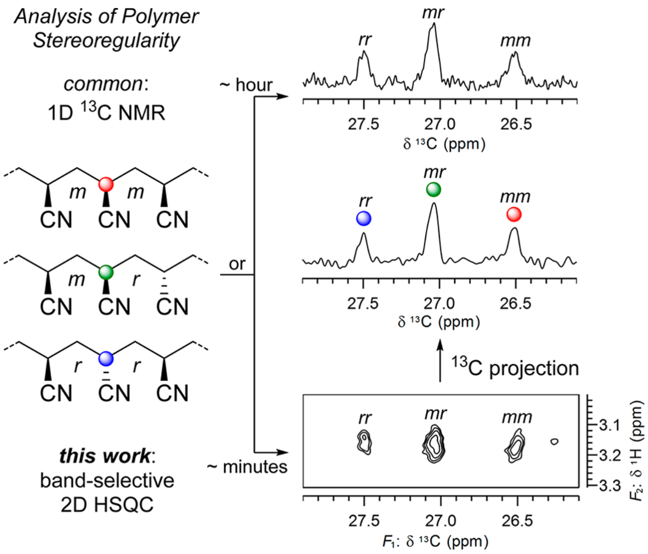


Figure 1. Analysis of polymer stereoregularity: 1D ^{13}C NMR spectroscopy versus band-selective 2D HSQC (bsHSQC) for triad stereosequences of atactic polyacrylonitrile (aPAN).

Herein we describe a dramatic reduction in the time required to determine the tacticity of two polymers usually characterized by 1D ^{13}C NMR using a band-selective variant of the two-dimensional (2D) ^{1}H/^{13}C HSQC (bsHSQC) experiment. Band-selective HSQC combines the improved sensitivity of ^{1}H detection with the capability to approach natural linewidth resolution in the ^{13}C dimension. We found that bsHSQC can easily resolve the triad stereosequences of atactic polyacrylonitrile (aPAN) in minutes (Figures 1 and 2) and can be performed with sufficient resolution in the indirect ^{13}C dimension to resolve the pentad stereosequences of aPP (Figure 3). Two-dimensional NMR has commonly been employed to assign polymer stereosequences using *J*-resolved,[6] homonuclear correlated (COSY, TOCSY),[7] and ^{13}C-detected heteronuclear correlated (HETCOR, INADEQUATE)[8] spectroscopy. More recently, ^{1}H-detected heteronuclear correlated spectroscopy (HSQC, HMQC, HMBC) has been used to assign the stereochemical configuration of a number of

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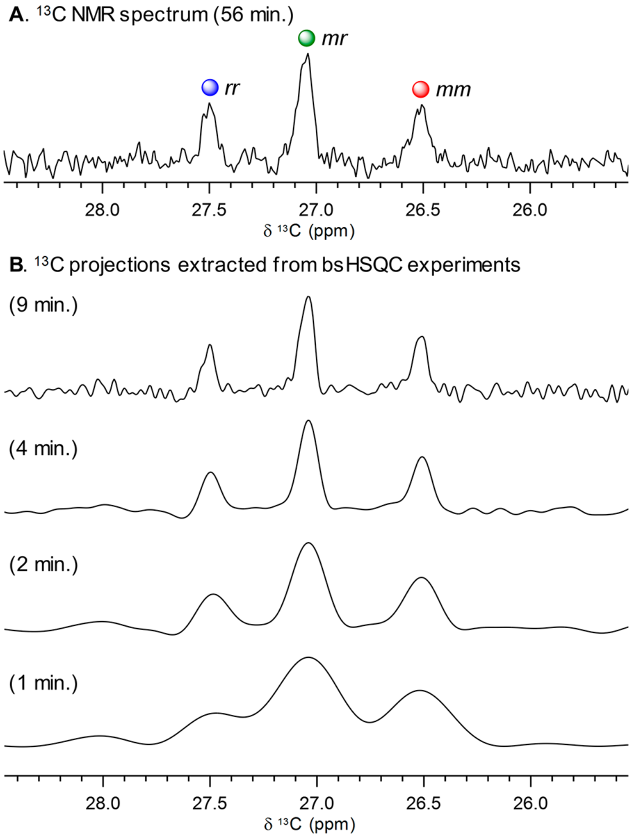

Figure 2. NMR spectra of methine carbon region of aPAN at 80 °C in DMSO-d_6 acquired on a 500 MHz spectrometer with a dual H/X probe head. (A) Direct-observed ^{13}C NMR spectrum (1.2 s acquisition time, 1.0 s relaxation delay, 1500 transients, 56 min total experiment time); (B) ^{13}C projections extracted from the indirect dimension of bsHSQC experiments by summing F_1 slices between δ ^{1}H 3.09 and 3.24 ppm after about 1, 2, 4, and 9 min (25, 50, 100, and 200 complex indirect data points, respectively).

polymers.[9] To the best of our knowledge, there have been no reports describing the use of indirect ^{13}C detection for rapid analysis of the degree of stereoregularity of polymers.

For 1D NMR, the entire time-domain signal is normally collected, which ensures that the resolution is only limited by the relaxation properties of the nuclei and results in natural-linewidth limited spectra. Figure 1 (top right) shows the methine region of a routine 1D ^{13}C NMR spectrum of aPAN which displays natural linewidth resolution. The triads (*mm*, *mr*, and *rr*) are well resolved and present in about a 1:2:1 ratio.[10] In 2D NMR, the linewidths are typically determined by experimental parameters (acquisition time, number of data points, and spectral width) instead of relaxation properties, resulting in spectra with acquisition-time limited resolution. This is especially true for the indirect dimension, where the time-domain data is collected one increment at a time. For example, in an HSQC experiment run with software default parameters (^{13}C spectral width from −10 to 190 ppm and 128 complex indirect data points), the methine region of aPAN appears as a single, broad resonance making it impossible to resolve the triad stereosequences.[11]

One way to improve resolution in the ^{13}C dimension is to increase the number of t_1 increments collected. However, this leads to a directly proportional increase in total experiment time. Because the resulting improvement in resolution is distributed over the whole ^{13}C domain, most of the additional experiment time is wasted on improving the resolution of areas of the spectrum that do not contain useful chemical information. Another approach to improve resolution is to reduce the spectral width in the indirect dimension to only include a narrow band centered on the chemical shift range of interest. This approach requires the use of bsHSQC to avoid aliasing correlations from outside the chosen ^{13}C spectral width.[12] Band selection is achieved by incorporating a double pulsed-field-gradient spin echo (DPFGSE) comprised of frequency-selective, shaped, radio frequency (RF) inversion pulses surrounded by pairs of pulsed field gradients of the same polarity.

We used bsHSQC to narrow the ^{13}C spectral width to an 8 ppm window around the chemical shifts of interest in aPAN (26−28 ppm) allowing us to resolve its triad stereosequences in minutes. Figure 1 (bottom right) shows the 2D bsHSQC spectrum of the methine region of aPAN with the indirect ^{13}C dimension (F_1) plotted on the horizontal axis. A ^{13}C projection (Figure 1, middle right) was extracted from the indirect dimension of the 2D experiment by summing F_1 slices between δ ^{1}H 3.09 and 3.24 ppm to generate a more familiar 1D representation and allow direct comparison with the 1D ^{13}C NMR spectrum. Resolution nearly identical to the 1D ^{13}C NMR could be attained in approximately 9 min (200 indirect complex data points). The relative integrations of resonances corresponding to the triad stereosequences from the 2D experiment were very similar to those obtained by 1D ^{13}C NMR (Table 1).[11] HSQC is inherently not quantitative across a range of chemical environments because it does not account for the degree of substitution, variable relaxation times, differences in $^1J_{\text{C−H}}$ coupling constants, or off-resonance effects. Quantitative HSQC pulse sequences have been developed to account for some of these factors, but they are not band-selective, suffer from poor sensitivity, and often require internal standards.[13] However, HSQC gives good quantification for stereosequences because they differ only in the relative stereochemistry of nearby stereocenters. The degree of substitution is identical, relaxation rates and $^1J_{\text{C−H}}$ couplings are expected to be very similar, and off-resonance effects are negligible since all peaks are within a small chemical shift window. Therefore, these factors affect all cross peaks to the same extent, preserving *relative* quantification of stereosequences regardless of experimental parameters such as relaxation delay.

Table 1. Integration of Methine Triads for aPAN[a]

Spectrum	*rr* ●	*mr* ●	*mm* ●
^{13}C NMR	0.23	0.48	0.29
^{13}C Projection	0.20	0.51	0.29
2D bsHSQC	0.20	0.51	0.29

[a] Relative integrations from spectra shown in Figure 1. Total area set equal to one. See Supporting Information for details.

Figure 2 compares the resolution obtained by 1D ^{13}C NMR (Figure 2A) and ^{13}C projections (Figure 2B) extracted from bsHSQC experiments acquired for about 1, 2, 4, and 9 min. After 1 min of data collection, the triad stereosequences were apparent but not resolved. In 2 min, the triads are baseline resolved allowing the quantification of changes in the relative abundance of stereosequences. Resolution approached natural

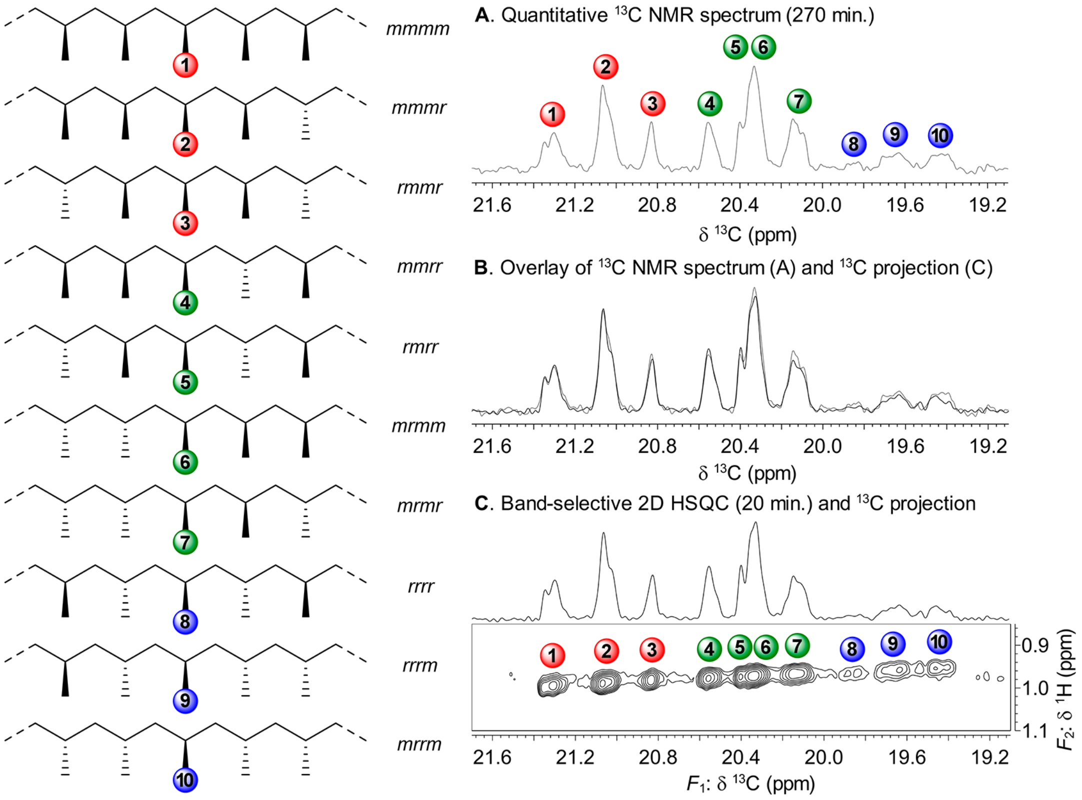

Figure 3. Pentad stereosequences and NMR spectra of methyl carbon region of atactic polypropylene (aPP) at 135 °C in TCE-d_2 acquired on a 500 MHz spectrometer with a dual H/X probe head. (A) Quantitative direct-observed ^{13}C NMR spectrum (1.2 s acquisition time, 30 s relaxation delay, 512 transients, 270 min total experiment time); (B) Overlay of spectrum A and the ^{13}C projection extracted from spectrum C; (C) Band-selective 2D HSQC experiment (20 min total experiment time). The indirect dimension (F_1) is displayed on the horizontal axis. The ^{13}C projection was extracted from the indirect dimension of the 2D experiment by summing the F_1 slices between δ ^{1}H 0.92 and 1.03 ppm.

linewidth after approximately 4 min and was essentially identical to the 1D ^{13}C NMR spectrum after 9 min.

Having demonstrated the utility of bsHSQC for quickly resolving the triad stereosequences of aPAN, we decided to investigate whether the technique could resolve higher-order stereosequences. The methyl region of a high-resolution ^{13}C NMR spectrum of atactic polypropylene (aPP) exhibits ten peaks, each of which represents a stereosequence corresponding to a pentad (Figure 3A).[14] The stereosequences are distinctly resolved, although in this sample some of the pentads (*rrrr*, *rrrm*, and *mrrm*) are barely discernible from the noise despite a highly concentrated sample and long experiment time.[11] We analyzed the same sample of aPP using bsHSQC, narrowing the ^{13}C spectral width to 6 ppm (750 Hz) around the methyl region (19−22 ppm) and acquiring 180 complex data points in the indirect dimension. Figure 3C shows the 2D spectrum with the indirect ^{13}C dimension (F_1) plotted on the horizontal axis and a ^{13}C projection extracted by summing the F_1 slices between δ ^{1}H 0.92 and 1.03 ppm. The ^{13}C projection derived from the band-selective HSQC experiment is essentially indistinguishable from the 1D ^{13}C NMR spectrum and has a slightly better SNR (Figure 3B). Small differences between the spectra are within the noise level of the 1D spectrum. In this instance, bsHSQC allowed us to extract a natural-linewidth limited 1D ^{13}C NMR spectrum of the methyl region of aPP 13× faster than was possible by direct observation.

In conclusion, we have described the use of bsHSQC as a tool for rapidly screening the tacticity of polymers. Band-selective HSQC quickly enables high resolution in the indirect ^{13}C dimension by narrowing the spectral width to the chemical shift range encompassing the stereosequences of interest. The technique accelerates the resolution of triad stereosequences, allowing stereochemical analysis of polymers such as aPAN in minutes. Furthermore, the method can be performed with sufficient resolution to resolve higher-order stereosequences, such as the pentads of aPP. We believe this type of application of bsHSQC may be useful for speeding up the discovery of catalysts for stereoregular polymerization, batch-to-batch quality control in industrial polymer production, and anytime there is a need for fast acquisition of a high-resolution ^{13}C NMR spectrum of a narrow chemical shift window. Future work will focus on the application of bsHSQC for analyzing tacticity in a wide variety of polymers and quantitative comparison of results obtained from routine 1D ^{13}C, quantitative 1D ^{13}C, and bsHSQC NMR experiments.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsmacrolett.5b00866.

Details of NMR experiments, copies of spectra, and experimental procedure for the preparation of aPP (PDF).

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Notes

The authors declare no competing financial interest.

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(5) A polymer segment containing two successive stereocenters is referred to as a dyad. Isotactic dyads (substituents on the same side of the chain) are assigned the letter *m* (meso). Syndiotactic dyads (substituents alternating between the two sides) are assigned the letter *r* (racemo). Segments of chain containing three stereocenters are called triads, which result from the succession of two dyads, and are indicated by the letters *mm*, *mr* (indistinguishable from *rm* in vinyl polymers), and *rr*.

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