Application of $\{^2H\}^{13}C$ INEPT NMR to the Study of Polymer Reactivity

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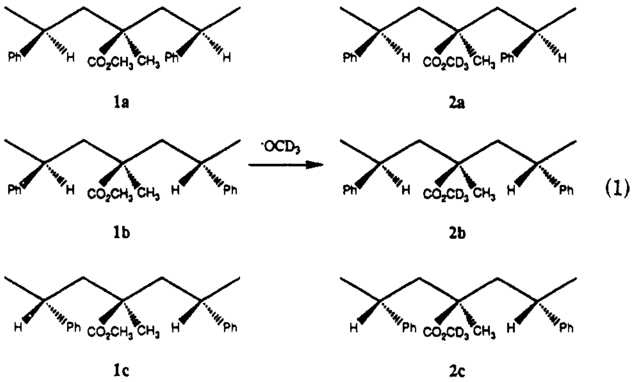
In this paper we describe the utility of $\{^2H\}^{13}C$ INEPT[1,2] NMR experiments for following the transesterification reaction of poly[styrene-*alt*-(methyl methacrylate)] with methoxide-d_3 as shown in eq 1. The ester groups in this polymer reside in three different stereochemical environments (**1a–c**) and have different reactivities in hydrolysis and transesterification reactions.[3,4] These can be studied by monitoring changes in the ^1H and ^{13}C resonances of methoxy groups in **1a–c** during reactions between the copolymer and a methoxy-d_3 ion. Previous ^1H NMR studies[4] employing this approach lacked sensitivity because of the difficulty of measuring small changes in the intensities of large signals at early stages in the reaction. This difficulty was surmounted by investigating the exchange of methoxide ion with polymer containing methoxy-d_3 groups, but at considerable expense and inconvenience. An analogous approach employing conventional ^{13}C NMR would require the use of a ^{13}C-enriched methoxide ion or of a copolymer with ^{13}C-enriched methoxy groups and has not been attempted. However, the $\{^2H\}^{13}C$ INEPT NMR technique enables the study to be done using a methoxy-d_3 ion and an unlabeled polymer. Furthermore, it enables the early stages of the reaction to be studied with considerable precision, and it avoids interference from methylene carbon resonances that would be encountered in a conventional ^{13}C NMR study.



(1)

Isotopic labeling experiments are commonly used to elucidate mechanistic and structural features in chemical sciences. ^{13}C and ^2H are two isotopes which have been especially useful, because they usually have a minimal effect on the structure and reactivity of organic molecules.[5] Although ^2H is usually easier than ^{13}C to incorporate into a structure, it suffers from several disadvantages. ^2H has a nuclear spin $I = 1$; consequently, efficient quadrupolar relaxation produces broad resonances. These broad peaks combined with a narrow frequency range over which the resonances are found (almost $^1/_7$ that of ^1H at the same field strength) greatly reduce chemical shift dispersion, making it difficult to study all but the simplest of molecules using standard NMR techniques. While ^{13}C signals are usually sharper and dispersed over a much larger frequency range, it is more costly and difficult to incorporate ^{13}C into organic structures.

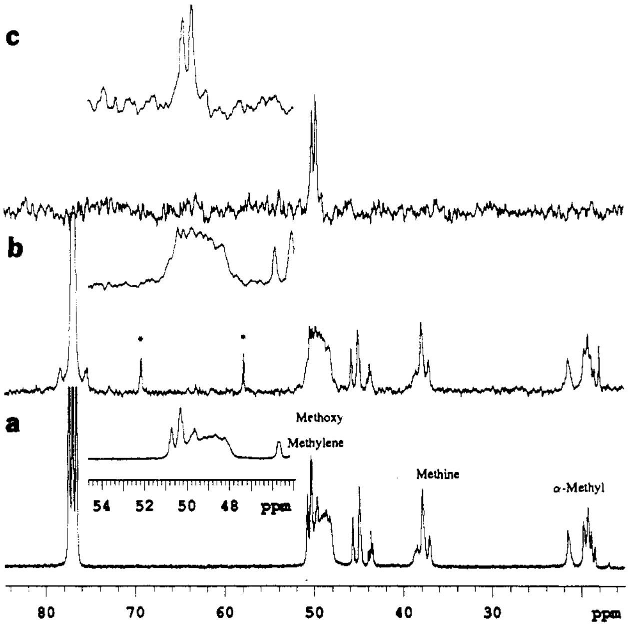


Figure 1. NMR spectra of poly[styrene-*alt*-(methyl methacrylate)] (MW ca. 250 000) in $CHCl_3$ (4% w/v) isolated from an aliquot of the reaction mixture after transesterification for 48 h with $NaOCD_3$ in benzene. The bottom spectrum (a) shows the ^{13}C spectrum of unreacted starting material in $CDCl_3$; three signals from methoxy carbons are detected in the 45–55 ppm region. The inset shows an expansion of the methoxy and methylene region. The middle spectrum (b) shows the ^{13}C spectrum (obtained with continuous ^1H WALTZ modulated decoupling) of a sample isolated from an aliquot of the reaction mixture after exchange with CD_3O^- for 48 h. The top spectrum (c) shows the $\{^2H\}^{13}C$ INEPT spectrum (with continuous ^1H decoupling and ^2H decoupling during the acquisition time) of the same sample used to obtain the ^{13}C spectrum in b. Only the resonances from the $-OCD_3$ groups which have displaced $-OCH_3$ groups are seen; signals from the overlapping methylene resonances no longer interfere; even the solvent ($CHCl_3$ which is present in large excess) signal at 77 ppm is suppressed. The spectrum was acquired with a 0.1-s relaxation delay, a 25-ms polarization transfer delay, a 6-ms refocusing delay, a 0.115-s acquisition time, an 8896-Hz spectral window, and 11 000 transients. The 90° pulse widths were 17.5, 90, and 13.0 μs on ^1H, ^2H, and ^{13}C channels, respectively. The data were collected over 45 min in the unlocked mode. The signals marked with asterisks are from 18-crown-6 and ethanol.

The potential use of ^2H labeling combined with $\{^2H\}^{13}C$ polarization transfer NMR experiments has been described in the past.[1,2,6] The site of interest on the chemical structure was labeled, and $\{^2H\}^{13}C$ polarization transfer NMR (such as INEPT[7,8] or DEPT[9]) was used to relay the ^2H magnetization to directly bound ^{13}C atoms; the ^{13}C signal could then be observed to give an indication of the label position, taking advantage of the larger ^{13}C chemical shift range. This technique has the additional advantage that only ^{13}C signals from carbon sites with directly bound ^2H are detected, in effect filtering the undesired resonances from the rest of the molecule and simplifying the spectrum. While related methods of filtering NMR spectra[10] based on the presence of interactions with rare isotopes have been used extensively for simplifying complex 2D NMR spectra of biomolecules, reports of applications in polymer chemistry have been rare.

Figure 1a shows portions of the ^{13}C NMR spectrum, obtained with ^1H decoupling, from an aliquot of the

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reaction mixture obtained after 48 h. The inset in Figure 1a, showing the 45–54 ppm region, contains the methoxy and methylene ^{13}C resonances. Figure 1b shows the same region of the $\{^2H\}^{13}C$ INEPT spectrum from the same sample. All but the deuterated methoxy signals have been suppressed. The sample was dissolved in $CHCl_3$ to eliminate possible interference from the resonances of deuterated solvent.

The signals at 49.0, 49.7, and 50.1 ppm in Figure 1b have been assigned to the methoxy resonances of **2a–c**, respectively.[11,12] Despite the statistical distribution (1:2:1) of structures **1a–c** in the initial polymer, at early stages in the reaction almost as many $-OCH_3$ groups in **1c** have been displaced by $-OCD_3$ as in **1b**, and very little of **1a** has reacted. This reflects the relative accessibility of the ester group to the attacking CD_3O^-: in **1c**, both of the flanking phenyl groups are disposed away from the ester functionality, making it accessible; in **1b** the ester group is only partially blocked by one phenyl group, while in **1a** the phenyl groups are disposed toward the same face as the reacting ester group, effectively blocking approach of the reagent.

In order to carry out these experiments, it is necessary to pulse and decouple ^1H, ^2H, and ^{13}C simultaneously. We have built a fourth radio-frequency channel and interfaced it to four spare, software-controlled, logic lines on a VXR-300 NMR spectrometer. This hardware provides the ability to pulse with 90° phase shifting increments and/or use attenuated WALTZ-16 modulated decoupling,[13] independent of the activity on the two transmitter channels provided on the original instrument. The three channels can be used for 300, 5–300, and 5–300 MHz, respectively. The fourth channel is the 46-MHz ^2H lock, which cannot be used when one of the other channels is operating at 46 MHz. The magnetic field on this instrument is stable enough to run unlocked for extended experiments of 12–24 h. The measured drift accounts for less than 1-Hz line broadening in an overnight ^{13}C experiment; this is insignificant with most of our polymer samples which have 5–10-Hz natural line widths. For longer experiments data are collected in 12-h blocks, the individual spectra are shifted in the frequency domain to compensate for field drift, and the resulting spectra are added. The standard $^1H-^{19}F$/broad-band switchable probe supplied with the instrument is employed for these experiments, with the lock channel on the probe used for the additional ^2H pulsing and decoupling.

The application of this methdology to mechanistic and structure problems in polymer chemistry is a fruitful area for future research and will provide a means to obtain answers to many questions which are not readily available from other experimental techniques. Very often minor structural components in a regular polymer are the most crucial for determining that polymer's properties, but the resonances from these components are obscured by numerous signals which are much more intense. Incorporation of labels, combined with selective polarization transfer, will enable detection of resonances from minor structural components without interference from the resonances of the rest of the polymer.

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