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# Detection of Living Anionic Species in Polymerization Reactions Using Hyperpolarized NMR

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Ⓢ *Supporting Information*

**ABSTRACT:** Intermediates during the anionic polymerization of styrene were observed using hyperpolarized NMR. Dissolution dynamic nuclear polarization (DNP) of monomers provides a sufficient signal-to-noise ratio for detection of $^{13}$C NMR signals in real time as the reaction progresses. Because of its large chemical shift dispersion, $^{13}$C is well-suited to distinguish and characterize the chemical species that arise during the reaction. At the same time, incorporation of hyperpolarized small-molecule monomers is a unique way to generate polymers that exhibit a transient signal enhancement at the active site. This strategy is applicable despite the decay of the hyperpolarization of the polymer due to rapid spin−lattice relaxation. Real-time measurements on polymerization reactions provide both mechanistic and kinetic information without the need for stable isotope labeling of the molecules of interest. These capabilities are orthogonal to currently established methods that separate synthesis and analysis into two steps, making dissolution DNP an attractive method to study polymerization reactions.

NMR spectroscopy has long played a pivotal role in the study of reaction mechanisms in the field of polymer chemistry because this technique reveals molecular structures and interactions with atomic resolution.[1] In the vast majority of cases, it is applied as a steady-state method for analyzing products at the end of the reaction, and thus, sophisticated synthetic strategies such as selective incorporation of stable isotopes are often needed to obtain mechanistic information.[2] A more direct and potentially more powerful approach would be to monitor species that arise as the reaction occurs. Dissolution dynamic nuclear polarization (DNP),[3] a hyperpolarization (HP) technique that can enhance NMR signals by several orders of magnitude, facilitates such real-time observations.[4]

Dissolution DNP is a two-step process in which a frozen aliquot of the analyte is hyperpolarized and then injected into an NMR spectrometer for analysis. Sensitivity is sufficient to enable $^{13}$C NMR spectroscopy at natural isotope abundance even at millimolar to submillimolar analyte concentrations. The large chemical shift range of $^{13}$C further facilitates resolution of the resonances of interest. Dissolution DNP has typically been applied to small molecules containing nuclei with spin−lattice relaxation times of at least several seconds to avoid prohibitive relaxation losses during sample injection. Under certain conditions, it is possible to obtain HP spectra of macromolecules, such as proteins that are biosynthetically labeled with $^{2}$H to counteract spin relaxation.[5] However, for a polymer without specific isotope enrichment, most of the observable signal would likely decay before initiation of the NMR measurement. HP signals from polymers can nevertheless be observed if the polymerization is carried out in situ in the NMR instrument starting from hyperpolarized monomers.[6] Since HP is continuously incorporated at the site of monomer addition, the active site of the growing polymer chain can be selectively enhanced. Here, we used this unique feature to detect intermediates as they arise during the synthesis of polystyrene (PS) by anionic polymerization of hyperpolarized styrene monomers.

PS can be synthesized by several different routes, including radical, anionic, cationic, and metallocene-catalyzed (Ziegler−Natta) polymerizations.[7] Radical polymerization of styrene was recently studied in miniemulsions using HP $^{129}$Xe NMR spectroscopy[8] by monitoring the reaction progress through changes in the $^{129}$Xe chemical shift. In the present work, where we aimed to observe the hyperpolarized products directly, we chose anionic polymerization of styrene as a model reaction. Rich insights into the mechanism and kinetics of this reaction are available[9] from extensive studies conducted since the seminal work of Szwarc and co-workers in 1956.[10] These data provide an ideal background for comparison. The absence of a radical site in the living species ensures that it can be observed without reductions in the NMR signal due to paramagnetic relaxation. At the same time, the reaction requires rigorous conditions that are suitably challenging for the DNP NMR protocol.

Styrene was polymerized in dioxane using sodium naphthalenide ($NaC_{10}H_8$) as an initiator.[10,11] The generation of a bifunctional initiator takes place via single-electron transfer from $NaC_{10}H_8$ to a styrene monomer followed by dimerization of two of the resulting styryl radical anions (Scheme 1). Initiation and propagation of styrene monomers then proceeds bidirectionally to generate telechelic polymer species.

For the DNP experiment, an aliquot of styrene monomers was hyperpolarized in the solid state at 1.4 K, rapidly dissolved in dioxane heated to ~200 °C under pressure, and mixed with a solution of $NaC_{10}H_8$ in tetrahydrofuran (THF) in the NMR spectrometer.[12] The sample injection was driven using He and $N_2$. The reaction progress was monitored for a duration of 13 s through a series of small-flip-angle excitations [Figure 1a; for methods, see the Supporting Information (SI)]. The most intense resonances observed were from styrene monomer, with signal enhancements of >4000-fold relative to a conventional

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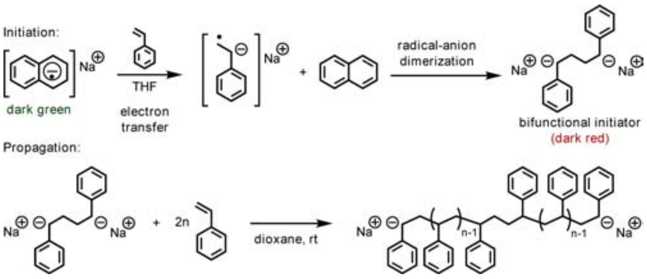
**Scheme 1. Living Anionic Polymerization of Styrene**



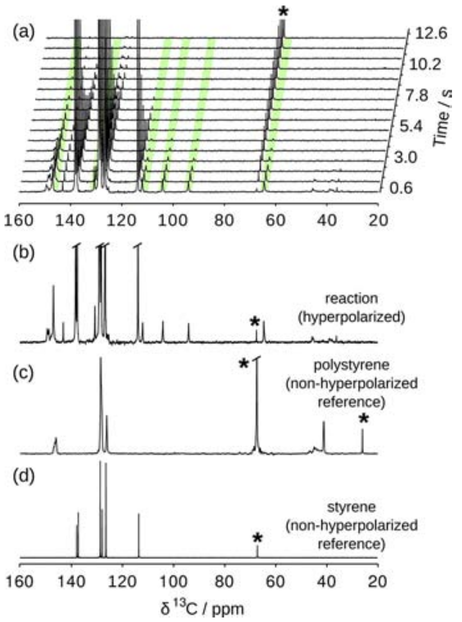


**Figure 1.** (a) Series of $^{13}$C NMR spectra recorded from a single sample of hyperpolarized styrene mixed with $NaC_{10}H_8$. (b) HP $^{13}$C NMR spectrum for the reaction between styrene and $NaC_{10}H_8$. (c, d) Non-HP $^{13}$C NMR spectra of (c) synthesized PS and (d) styrene monomer. The * labels designate dioxane and THF resonances. The dioxane resonance in the PS spectrum was suppressed using a selective 90° pulse and randomized pulsed field gradients.

single-scan NMR spectrum. However, the spectra also contained several smaller signals that were not detected in the reference $^{13}$C NMR spectra of the final PS product or the reactant styrene (Figure 1b–d). These peaks (highlighted in green in Figure 1a) therefore apparently belong to reaction intermediates present only while the reaction proceeds. Here, the characteristic chemical shifts indicated that these resonances stemmed from the dianionic polystyryl intermediate, but in general the identities peaks can be difficult to determine from one-dimensional spectra alone.

To identify such intermediates, peak splittings in an undecoupled $^{13}$C spectrum can be useful, since they can be directly obtained from a sequence of 1D spectra acquired from a hyperpolarized sample. Figure 2a shows individual peaks from proton-decoupled and proton-coupled (i.e., undecoupled) $^{13}$C spectra of the ongoing reaction (also see Figure S1). The group of doublet signals observed at 90–140 ppm (see the SI) arise from the $^{13}$C nuclei in the phenyl ring that are bonded to a single proton (C3–C5). The group of singlet signals observed near 150 ppm are from the substituted aromatic carbon C1 without a directly bonded proton.

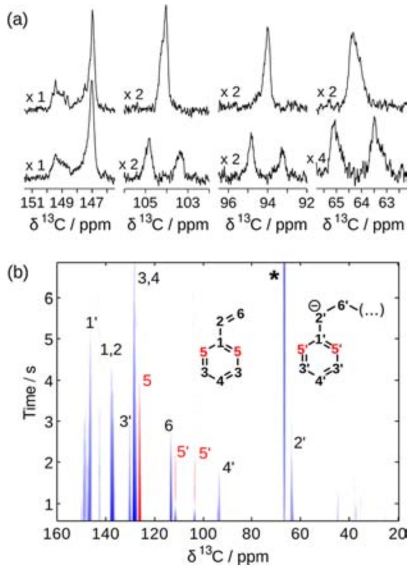


**Figure 2.** (a) Expanded views of $^1$H-decoupled (top) and undecoupled (bottom) $^{13}$C spectra of the reaction of hyperpolarized styrene. Scaling factors are indicated. (b) HP correlation experiment with selective inversion of the C5 resonance at the beginning of the reaction. Positive and negative signals are represented in blue and red, respectively. The * designates dioxane and THF resonances.

Although important information can be extracted from chemical shifts and coupling constants, this usually requires a certain amount of prior knowledge about the molecules under study. An inherent limitation of 1D spectroscopy is the absence of direct correlations between different atoms, which in conventional NMR would most readily be solved by acquiring multidimensional spectra. Here, using HP NMR of the dynamic system, we exploited a different type of correlation that acts over time. The Zeeman population difference giving rise to the signals in a time series of spectra is generated by DNP at the beginning of the experiment. Therefore, a correlation between two chemical species that are transformed into each other can be established by selective manipulation of the spin state of one of those species.[13,14] In Figures 2b and S2, the resonance of the ortho carbons (C5) in styrene was selectively inverted. In the subsequent reaction, negative signals (shown in red) were observed for the peaks at 112 and 104 ppm, which could therefore be unambiguously assigned to C5′ in the polystyryl anion. All of the other (noninverted) spins in the reactant and intermediate yielded positive signals (shown in blue). Two peaks were observed for C5′ because the partial double-bond character between C2 and C1 hinders free rotation of the phenyl ring.[15] The resulting partial sp$^2$-hybridized character of the *α* carbon (C2) is also manifested in the scalar coupling constant ($J_{CH}$) of 152 Hz.[16]

Close inspection of Figure 2b reveals that the C5′ peaks also showed positive signals for a short time at the beginning of the polymerization because the reaction started during sample injection before the selective inversion pulse could be applied. In this reaction, the initiation step is much faster than the propagation step.[17] The signal change from positive to negative therefore confirmed that the product signals observed during the course of the reaction were due to fresh additions of inverted monomers to the living intermediate and not simply due to the initial dimer.

To provide direct verification of the origin of the other peaks in the intermediate, the HP $^{13}$C correlation NMR experiments were repeated by selectively inverting other spins of styrene (see the SI). Inverted peaks were detected at 146.9, 64.5, 130.7, and 94.0 ppm for C1′−C4′. Selective inversion of C6 did not yield an observable inverted signal, likely because of increased spin relaxation in the PS backbone. The measured chemical shifts of the active site in the growing polystyryl chain were in good agreement with the values for a monoanionic polystyryl molecule determined by conventional NMR analysis under equilibrium conditions.[15] A difference of 5.2 ppm was observed at the $\alpha$-carbon (C2′) peak, likely because of the effect of the countercation ($\delta_{Na} > \delta_{Li}$).[15]

The spectra in Figures 1 and 2 also contained peaks from minor species that could be analyzed to gain more information about the reaction conditions and possible side reactions. The sharp singlet signal at 143 ppm and peaks at 128.7, 36.1, and 31.6 ppm were also observed for synthesized 1,4-diphenylbutane (Figure S3) and in the reaction mixture could belong to styrene oligomers quenched by residual water. Additional peaks were also observed near 150 ppm (Figure S4). From their chemical shifts, these peaks may appear to be related to the C1 peak, but they did not show inversion in the experiment of Figure S2.

A benefit of the real-time DNP-NMR measurement is the capability to determine the reaction mechanism and kinetics simultaneously from a single hyperpolarized sample. However, to extract kinetic information, the process of spin relaxation must be considered along with the reaction, since both give rise to changes in signal intensity. The DNP experiments start with a large initial polarization that decays toward the thermal equilibrium value. The latter is negligible, so the hyperpolarized styrene monomers are the only source of observable signals. The living anionic polymerization discussed here is a second-order reaction, and its propagation rate is $v = k_p C_{P^-} \times C_M = k_p I_0 C_M$, where $C_{P^-}$ and $C_M$ are the concentrations of the propagating polystyryl anion and styrene monomer, respectively. We assumed that the propagation rate constant $k_p$ is independent of the length of the polymer chain. Since there is no termination step, $C_{P^-}$ is constant and equal to the initiator concentration ($I_0$). A pseudo-first-order reaction rate constant $k'$ was defined as $k' = k_p I_0$. When the kinetics and spin relaxation rate ($r_M$) are taken into account (see the SI), the time evolution of the styrene monomer signal intensity ($S_M$) is given by

$$S_M(t) = S_M(0)e^{-(k'+r_M)t} \qquad (1)$$

As the living PS chain possesses negative charges at the ends, the chemical shifts of the anionic terminal carbons are different from those of the interior backbone structure. The signal intensity of the anionic chain end ($S_{P^-}$) can be calculated using a model in which fresh polarization is added through monomer addition and polarization is lost through both spin relaxation and the transition of a given moiety to the interior of the polymer:

$$\frac{d}{dt}S_{P^-}(t) = -r_P S_{P^-}(t) + k' S_{M_0} e^{-(k'+r_M)t} - \frac{k' C_0 e^{-k't}}{I_0} S_{P^-}(t) \qquad (2)$$

where $C_0$ is the initial concentration of styrene and $r_P$ is the spin relaxation rate of the anionic chain end, which is assumed to be independent of the length of polymer chain.

The unknown reaction and relaxation rates were obtained by fitting these models to time-resolved DNP NMR data sets (e.g., Figure 1a). To obtain these data, a series of fixed small-flip-angle pulses were applied to acquire NMR spectra at equal time intervals. To account for the depletion of polarization by these pulses, eq 1 and the numerical solution of eq 2 were multiplied by the factor $e^{-\lambda t}$ prior to calculation of the root-mean-square difference (rmsd). In the exponential, $\lambda = -\ln[\cos(\alpha)]/\Delta t$ depends on the flip angle ($\alpha$) and the time interval between NMR acquisitions ($\Delta t$).

Values of $k'$ were obtained by fitting eq 1 to the thus-normalized styrene monomer signal intensities (Figure 3a). This required knowledge of the relaxation rates $r_M$, which were determined from a DNP experiment in the absence of a reaction (i.e., no added $NaC_{10}H_8$). Values of $k_p$ were then calculated from $k'$ and $I_0$,[18] which was determined from the chain-length distribution obtained by MALDI-TOF mass spectrometry of the reaction product (Figure S5).[19] The average value of $k_p$ based on three independent data sets was 5.6 ± 0.6 $M^{-1}$ $s^{-1}$ (Table 1), which is in excellent agreement with literature values [3.4−6.5 $M^{-1}$ $s^{-1}$, measured under similar conditions but without the 5% (v/v) THF present in the DNP experiments].[9a]

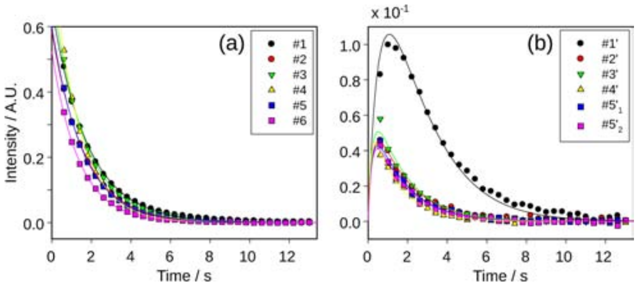


**Figure 3.** (a) Fit of the relative signal intensity of styrene with eq 1 using $S_M(0)$ and $r_M$ as parameters. (b) Fit of the signal intensities of living polystyryl ends obtained by minimizing the rmsd between the experimental data and the numerical solution of eq 2 using $r_P$ as a parameter and $S_{P^-}(0) = 0$ as the boundary condition.

**Table 1. Determination of $k_p$**

| reaction | $k'$ ($s^{-1}$)[a] | DP[b] | $I_0$ (mM)[c] | $k_p$ ($M^{-1}$ $s^{-1}$) |
|---|---|---|---|---|
| 1 | 0.45 ± 0.03 | 6.3 | 92 | 4.9 |
| 2 | 0.30 ± 0.02 | 13.6 | 54 | 5.6 |
| 3 | 0.40 ± 0.03 | 10.8 | 65 | 6.2 |

[a] From eq 1. Values are averages for the six different C atoms of styrene. For the individual values, see Table S1. [b] Degree of polymerization, determined from the MALDI mass spectrum of the reaction product. [c] Determined from DP and known monomer concentration.

Although the reaction kinetics can be determined unambiguously from the monomer signals, we also tested the proposed model for kinetics and spin relaxation in the styrene polymerization reaction by fitting the signal intensities of the living-end intermediate (Figures 3a and S6). This was done by adjusting the single parameter $r_P$ to minimize the rmsd between the experimental data and the numerical solution of eq 2, which was calculated for each iteration of $r_P$ using a variable-step Runge−Kutta method with given values of $k'$, $r_M$, and $C_0$. The initial condition was chosen as $S_{P^-}(0) = 0$, assuming that the initial dimer carries no signal because of rapid relaxation in its precursors, the styryl radicals.

Figure 3b shows signal intensities of the living intermediate and the corresponding numerical fits, and the $r_P$ values obtained from the three independent data sets are given in Table S2. Despite the use of only one fit parameter, the curves agree remarkably well with the experimental data. Small differences, in particular at the beginning of the reaction, may be attributed to a certain amount of remaining signal from the initial styrene dimers, which cannot be modeled reliably with the available data. The NMR signal loss due to the presence of a short-lived radical should depend on the distance from the observed site to the radical. In the future, it would be interesting to determine whether such distance information could be extracted from data measured for a radical polymerization.

The $r_P$ values for all of the nonoverlapping C atoms in the anionic chain ends obtained from the HP data agreed to within 12% with reference rates obtained from a PS standard (Polymer Laboratories, Church Stretton, U.K.; $M_n$ = 1360 g/mol), the measurement of which, however, was not selective for chain ends. Since $r_P$ from the fit was obtained by analysis of the kinetic parameters, the coincidence of the relaxation rates supports the overall validity of this method for the analysis of the DNP data. Furthermore, errors due to sample injection, mixing, and turbulence[14,20] appeared to be minimal under the present conditions.

In summary, we have applied a dissolution DNP NMR method to examine the living anionic polymerization of styrene. Experiments based on HP $^{13}$C NMR spectroscopy allow the reaction mechanism and kinetics to be studied simultaneously as the reaction progresses. Continuous inclusion of hyperpolarized monomers generates selective HP of the active living site, providing a sensitivity sufficient to capture the living species without signal averaging or isotope labeling. In addition, the correlation experiment with selective inversion of a spin of interest allows chemical shifts of the reaction intermediate to be identified unambiguously. The living anionic polymerization reaction studied here is sensitive to water and air. Nevertheless, the DNP NMR technique in combination with rapid sample injection driven by inert gases allowed for the successful study of the reaction. Systematic modifications to allow for loading of the active initiator and dried solvents while excluding air may further improve the results. On this premise, the method presented here is attractive for fundamental studies of polymerization reactions, as alternative techniques would involve cumbersome isotope labeling and synthesis strategies. Having verified the overall DNP NMR approach by studying well-known intermediates involved in the living anionic polymerization of styrene, we are currently applying this technique to investigate less-studied polymerization systems.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Methods and additional data. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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