

Stretched Poly(dimethylsiloxane) Gels as NMR Alignment Media for Apolar and Weakly Polar Organic Solvents: An Ideal Tool for Measuring RDCs at Low Molecular Concentrations

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Residual dipolar couplings (RDCs) in biomolecular NMR have proven the wealth of additional structural information that can be gained from partial alignment of solutes in aqueous solution.¹ Just recently, several groups showed that RDCs can also provide important structural insight into small organic molecules.^{2,3} Nevertheless, there is still need for improvement of the alignment media especially for organic solvents if the full potential of the method shall be utilized. Besides liquid crystalline phases³ and self-aligning solvents,⁴ it has been shown that stretched polystyrene gels allow scalable alignment in some organic solvents.⁵ The approach of aligning molecules by dissolving them into a mechanically constrained polymer gel is called "strain-induced alignment in a gel" (SAG)⁶ and is a further development of techniques used in material science to obtain information about the polymer itself.⁷ Polymer gels such as polystyrene are well suited for partially orienting NMR samples, but residual polymer signals limit their use especially at low solute concentrations. In this communication, we show that cross-linked poly(dimethylsiloxane) (PDMS) forms a superb alignment medium for molecules in weakly polar organic solvents.

PDMS is frequently used as a model polymer for stretched or compressed elastomers,⁸ and it is known that mechanically constrained PDMS gels induce some degree of anisotropy.⁹ We therefore were confident that it can also be used to align organic molecules dissolved in the gel.

The synthesis of cross-linked PDMS can be achieved in many ways. To ensure a homogeneous, impurity-free polymer network, the following procedure was chosen: Trimethylsiloxy-terminated PDMS was purchased from ABCR GmbH & Co. KG (Karlsruhe, Germany) with two polymer chain lengths (PDMS-T61, $M_n \approx 320\,000\text{ g mol}^{-1}$; PDMS-T63, $M_n \approx 450\,000\text{ g mol}^{-1}$) and was used as received. The highly viscous liquids were filled into plastic tubes of 3.6 mm inner diameter. After cross-linking of PDMS by irradiation with 10 MeV β -rays generated by an industrial electron accelerator, the tubes were removed and the colorless clear material was cut into sticks of 12 mm length. Without any further purification, the sticks were then put into standard 5 mm NMR tubes with $\sim 700\ \mu\text{L}$ of solvent. Dichloromethane (DCM), chloroform, tetrahydrofuran (THF), *n*-hexane, and benzene (Bz) could be used as swelling agents. We added 35 μL of chloroform- d_1 to all samples to be able to compare deuterium quadrupolar splittings. The gels were allowed to equilibrate at room temperature for a total of 12 days. Evaporated solvent was replaced during that time whenever necessary.

The quadrupolar splittings $\Delta\nu_Q$ in the ^2H spectra of CDCl_3 that had developed during equilibration in the various samples are summarized in Table 1 and Figure 1A, respectively. Depending on the solvent and the strength of β -irradiation, the samples showed

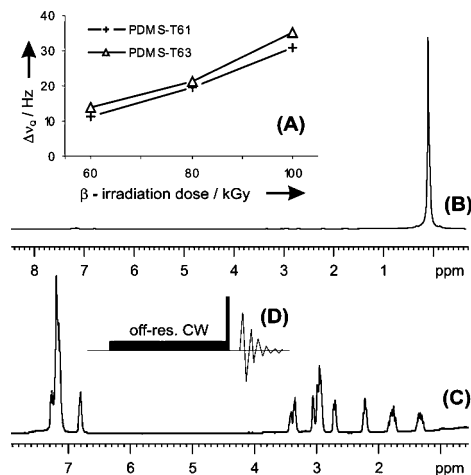


Figure 1. NMR spectroscopic properties of PDMS gels: (A) Quadrupolar splitting $\Delta\nu_Q$ in the deuterium signal of CDCl_3 with respect to the β -irradiation dose. (B) ^1H spectrum of spiroindene **1** (12 mM in PDMS/ CDCl_3) acquired with a standard one-dimensional NMR experiment. (C) acquired with off-resonance presaturation of the PDMS signal using the sequence shown in (D). The spectra were acquired on a 250 MHz spectrometer equipped with a standard dual probehead (^1H , ^{13}C).

Table 1. Quadrupolar Splitting $\Delta\nu_Q$ (in Hz) of the ^2H Signal of CDCl_3 for PDMS Samples Swollen in Various Organic Solvents^a

	hexane	DCM	CDCl_3	THF	benzene
PDMS-T61	44.3	8.0	11.3	6.1	4.5
PDMS-T63	46.7	9.8	14.1	7.1	5.0

^a PDMS was cross-linked with 60 kGy of β -irradiation.

$\Delta\nu_Q$ of 4.5–46.7 Hz. Consistent with previously published data,^{5a} longer polymer chains and increased cross-linking due to higher β -irradiation led to stronger anisotropies (Figure 1A). A very strong quadrupolar CDCl_3 splitting was observed for *n*-hexane, the most apolar solvent used in our study.

The ^1H spectrum of a PDMS/ CDCl_3 sample is shown in Figure 1B. A single, relatively sharp signal at 0.1 ppm is visible. Such a signal can effectively be suppressed by slight modifications to methods originally developed to suppress the water signal in aqueous samples. One elegant method is to apply off-resonant CW-irradiation for saturating the PDMS signal in combination with a sweep width that uses the good cutoff properties of today's digital filters (cf. Figure 1D). In this way, practically artifact-free spectra up to a downfield limit of ~ 0.6 ppm can be obtained in this alignment medium. As an example for the achievable quality, a spectrum of ~ 12 mM spiroindene **1** aligned in PDMS/ CDCl_3 is given in Figure 1C.

Spiroindene **1** is a topologically interesting synthetic compound with three stereocenters at C1, C1a, and C6a. Due to the presence

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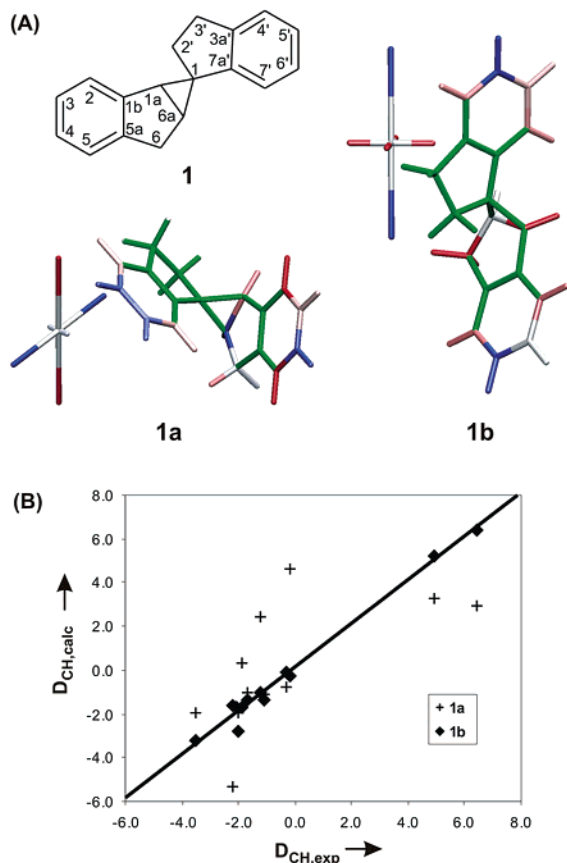


Figure 2. Top: Structures of the two possible diastereomers of **1**. The RDCs determined in a PDMS/ $CDCl_3$ gel are color coded to the structures (red, negative RDCs; blue, positive RDCs; green, no RDCs or RDCs not used in analysis). The axis systems to the left of each structure represent the corresponding alignment tensors. Bottom: Correspondence of experimental vs back-calculated RDC values for structures **1a** and **1b**.

of the cyclopropane ring, the number of possible diastereomers is reduced to the structures **1a** and **1b** shown in Figure 2. Both the X-ray structure¹⁰ and a detailed NMR study (unpublished results) proved that this spiroindene is formed as the **1b** alternative.

We used **1** to test whether the analysis of RDCs obtained from alignment in a PDMS/ $CDCl_3$ gel enables the distinction of the two diastereomers. Approximately 2.1 mg of **1** was added to the top of an equilibrated PDMS/ $CDCl_3$ gel, and after 2 days to allow diffusion of **1** into the gel, RDCs were determined from standard coupled HSQC experiments. After removal of partially overlapped NMR signals, altogether 12 out of 16 possible experimental D_{CH} -couplings were fitted onto the molecular structures of both **1a** and **1b** using the computer program PALES.¹¹ The correlation of measured vs back-calculated RDCs is shown in Figure 2.

For **1b**, the positive RDCs along C_4-H_4 and C_5-H_5 , respectively, are well aligned with the strongest alignment eigenvector A_{zz} (blue), which is parallel to the strained polymer chains. Negative RDCs are found perpendicular to that axis. For **1a** the alignment of positive and negative RDCs with the eigenvectors of the alignment tensor is far less evident. In addition, the comparison of experimental and back-calculated RDC values shows a significantly better correspondence for structure **1b** (Figure 2B). Hence, the two diastereomers can be unambiguously distinguished by alignment in PDMS gels.

Using a simple rod model implemented in PALES, the RDCs for a given molecular structure can be predicted on the basis of

pure steric interactions.¹¹ The analysis of our data resulted in a good correlation of experimental and predicted RDC values ($R^2 = 0.966$) for **1b**. These findings suggest that the intermolecular interactions leading to alignment of spiroindene **1** in PDMS gels are dominantly of steric nature.

In summary, we conclude that stretched PDMS gels can be used as alignment media in NMR spectroscopy with several advantages compared to other media known so far. The induced anisotropy can be scaled by changing the size or consistency of the polymer; the interactions of the molecule with the polymer chains are mainly of steric origin and therefore might enable the prediction of alignment tensors; furthermore, spectra can be obtained without impurities from the alignment medium by simple suppression of the only PDMS signal at ~ 0.1 ppm. Clean spectra are otherwise only possible by uniform deuteration of the alignment medium (cf. refs 4 and 12). Disadvantages of PDMS as presented here are the need for β -irradiation (which is commercially available) and the strong adhesion of PDMS to glassware. Chemically cross-linked PDMS¹³ might be an alternative if chemical reactants can be removed sufficiently. However, the disadvantages could probably be overcome best if the production of PDMS-gels were commercialized.

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Supporting Information Available: Swelling properties in various solvents, temperature dependence of $\Delta\nu_Q$, example 2H spectra, RDCs, alignment tensor information, and steric pictures of **1a** and **1b** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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