The Exploration and Analysis of Alternative Orienting Media for use in Residual Dipolar Coupling NMR

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Introduction

Residual dipolar couplings (RDCs) occur when a molecule is in an anisotropic environment.[1-3] The magnitude of these residual dipolar couplings can be used to determine the 3-dimensional structural information of a molecule in solution.[1-5] This information has been used to determine stereochemistry, *cis* or *trans* alkenes configuration, and the structure of proteins.[2-5] Anisotropic environments have been achieved with either liquid crystals or polymers present. Often these compounds are difficult to prepare, incompatible with solvents, and reactive with some molecules.[2] This research focuses on the development of an inert, easy to use anisotropic environment for RDC NMR spectroscopy.

Methods

In this research, several types of orienting media were tested for their quality as an anisotropic environment. These substances were deemed chemically inert and were expected to orient solely mechanically by creating small channels throughout the length of the NMR tube.

Each of these samples were solvated and analyzed using deuterated chloroform ($CDCl_3$). ^{1}H NMR experiments were acquired using Bruker's standard Proton (zg30) NMR pulse sequence with the following parameters: Relaxation delay, 1s; 90° pulse, 12.0 µs; spectral width, 10,000 Hz; number of data points, 32K; and digital resolution, 0.153 Hz/point. ^{2}H NMR experiments were acquired using the locking channel of the NMR, and were corrected using the frequency of deuterium for both the 300 and 500MHz NMRs on which the data was acquired.

The fiberglass was washed in mixed Xylenes purchased from Sigma Aldrich without alteration and sonicated to remove any coating on the fiberglass. Excess xylenes was decanted and the fiberglass was dried *via* evaporation, and bundled or braided as shown in the figures. The wooden dowel was cut to length and soaked and sonicated in chloroform to completely fill the internal cavities with solvent. The compressed gel data was acquired by Will Graham (used with permission) and Sailajah Gukathasan (used with permission).

References

1. Kramer, F.; Deshmukh, M.; Kessler, H.; Glaser, S. *Concepts in Magnetic Resonance* **2004**, *21A*(1), 10–21
2. Thiele, C. M. *European Journal of Organic Chemistry* **2008**, *2008* (34), 5663–5663.
3. Losonczi, J. A.; Andrec, M.; Fischer, M. W.; Prestegard, J. H. *Journal of Magnetic Resonance***1999**, *138* (2), 334–342.
4. Yan, J.; Delaglio, F.; Kaerner, A.; Kline, A. D.; Mo, H.; Shapiro, M. J.; Smitka, T. A.; Stephenson, G. A.; Zartler, E. R. *Journal of the American Chemical Society* **2004**, *126* (15), 5008–5017.
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Results

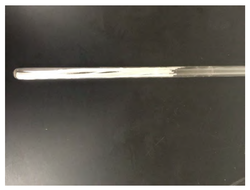
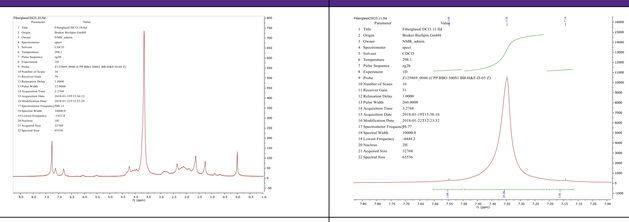
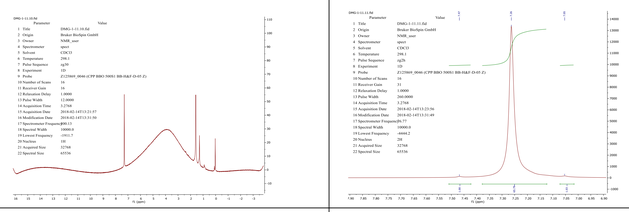
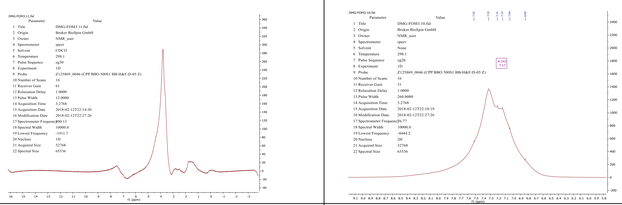
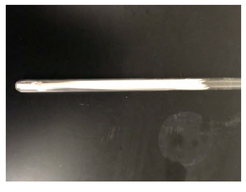
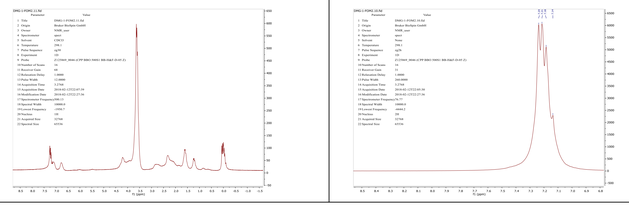
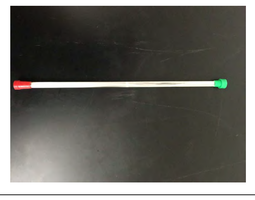
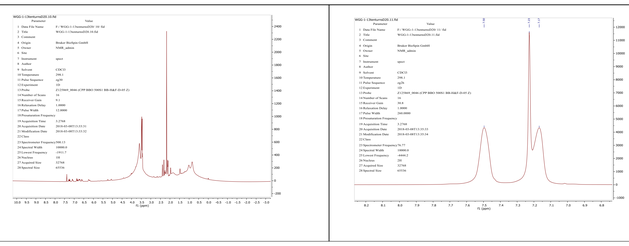
Medium	^{1}H-NMR	^{2}H-Observe
Loose Fiberglass			
Wooden Dowel			
Braided Rope			
Bundled at One end			
Open-ended Tube		This apparatus proved incompatible with the Chloroform solvent.
Compressed Gel (PMMA/ D_2O) 10 turns			

Table 1. Orienting Strength

Media	Solvent	Compressed?	Number of Turns	PPM Coupling	Hz Coupling
PMMA	Chloroform	no	-	*2.031*	*93.53*
PMMA	D_2O	yes	5	0.21	16.12
PMMA	D_2O	yes	6	0.24	18.43
PMMA	D_2O	yes	7	0.26	19.96
PMMA	D_2O	yes	8	0.27	20.73
PMMA	D_2O	yes	9	0.29	22.26
PMMA	D_2O	yes	10	0.33	25.34
PVAC	Acetone	no	-	*1.088*	*50.11*
PVAC	DMSO	no	-	*0.437*	*20.13*
PVAC	DMSO	yes	*	*0.382*	*17.59*
Loose Fiberglass	Chloroform	no	-	0.41	31.48
Wooden Dowel	Chloroform	no	-	0.42	32.24
Braided Fiberglass	Chloroform	no	-	multiple	multiple
Bundled at One End	Chloroform	no	-	0.06, 0.07	4.61,5.37
Open-ended Tube	Chloroform	no	-	**	**

* Unknown number of turns
** Unable to collect data due to apparatus failure
Acquired on the 300MHz NMR instrument

Conclusions

The orienting media tested in this exploration had a variety of outcomes. The compressed gel is used as a control and comparison to show what is currently the standard of orienting media. When compared to the compressed gel, the media that proved to be the least useful was the braided rope and bundled fiberglass. In this case, the media did not orient uniformly throughout the length of the tube leading to multiple solvent environments.

The loose fiberglass media showed considerably better results with a large relative orienting strength as can be seen in Table1. The downside of this medium is that there is very little volume in the anisotropic environment as can be seen by the relative area of the singlet and doublet peaks. The wooden dowel had the most orienting strength for the alternative media, but had the same issues of low isotropic volume as well as issues with the baseline in ^{1}H-NMR spectra cause by issues locking and shimming the sample. Without further optimization to correct these disadvantages, these alternative orienting material are not suitable for this technique.

Future Works

Future testing material could be Teflon tape which is known to be inert. Also other materials that may prove compatible are Zeolites or organo-metallic frameworks which have micro-meter channels. They will need to be tested for their inertness and orienting strength. However, at this time it is not deemed imperative to further characterize or optimize these alternative media.

Acknowledgements

Thank you to Dr. Carroll for assisting me in designing and executing this exploration, and challenging me to design a new orienting media and advance the field of RDC NMR spectroscopy. Thank you to Will Graham and Sailaja Gukathasan for their hard work in characterizing the more traditional media.