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Magnetically aligned nanodiscs enable direct measurement of ^{17}O residual quadrupolar coupling for small molecules

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ABSTRACT

The use of ^{17}O in NMR spectroscopy for structural studies has been limited due to its low natural abundance, low gyromagnetic ratio, and quadrupolar relaxation. Previous solution ^{17}O work has primarily focused on studies of liquids where the ^{17}O quadrupolar coupling is averaged to zero by isotropic molecular tumbling, and therefore has ignored the structural information contained in this parameter. Here, we use magnetically aligned polymer nanodiscs as an alignment medium to measure residual quadrupolar couplings (RQCs) for ^{17}O-labelled benzoic acid in the aqueous phase. We show that increasing the magnetic field strength improves spectral sensitivity and resolution and that each satellite peak of the expected pentet pattern resolves clearly at 18.8 T. We observed no significant dependence of the RQC magnitudes on the magnetic field strength. However, changing the orientation of the alignment medium alters the RQC by a consistent factor, suggesting that ^{17}O RQCs measured in this way can provide reliable orientational information for elucidations of molecular structures.

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1. Introduction

Oxygen is an essential component of organic and biological molecular structures, which NMR spectroscopy is uniquely positioned to directly observe. A wealth of work has established the utility of probing molecular structure using ^{17}O NMR spectroscopy [1–3]. However, compared to other commonly used nuclei in NMR spectroscopy of organic molecules (hydrogen, carbon, nitrogen, phosphorus), several factors contribute to the difficulty of studying oxygen nuclei by NMR spectroscopy. First, the only NMR-active oxygen nucleus, ^{17}O, has a natural abundance of only 0.037 % [4]. Second, sensitivity of ^{17}O NMR is limited by its low gyromagnetic ratio (about 1/7th of that of ^{1}H) [1,5]. And third, because ^{17}O has a nuclear spin quantum number of 5/2, it undergoes the nuclear electric quadrupolar interaction [1]. In solution, the quadrupolar interaction leads to very short transverse relaxation times (T_2), providing a fundamental limit to spectral resolution in this phase. T_2 times can be relatively long in the solid-state due to restricted molecular motions, though the quadrupolar interaction still causes substantial line broadening because quadrupolar coupling has an anisotropic dependence. Due to the second-order quadrupolar interaction scaling inversely with the strength of the external magnetic field, high magnetic fields are desirable for NMR spectroscopy of quadrupolar nuclei. Practically, the result of these considerations is that ^{17}O NMR spectroscopy has been largely restricted to studies of isotope-labelled molecules using solid-state NMR experiments conducted under high magnetic fields [1].

Nevertheless, recent improvements to experimental methodologies have demonstrated the feasibility of overcoming each challenge to using ^{17}O NMR spectroscopy to study organic and biological molecules. Advances in total and site-specific ^{17}O-labelling techniques based on water exchange and recombinant protein expression have reduced the experimental burden of ^{17}O incorporation into organic small molecules and proteins [6–8]. Generally applicable sensitivity enhancement techniques, such as dynamic nuclear polarization (DNP) [9], ultrafast and cryogenic magic angle spinning (MAS) [10], and paramagnetic doping [7], offer powerful approaches for improving ^{17}O spectral resolution and sensitivity. And lastly, the quadrupolar interaction can be at least partly avoided by employing methods which simulate isotropic conditions, such as quadrupole-central-transition (QCT) NMR and multiple-quantum MAS. Collectively, such labelling, sensitivity enhancement, and quadrupolar interaction suppression or avoidance strategies have allowed ^{17}O NMR-based studies of inorganic solids at natural abundance [11], of hydrogen bonding networks

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