Dynamic Nuclear Polarization (DNP) 101:

A New Era for Materials

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ABSTRACT

The design of new materials requires a deep understanding of the intricacies underpinning their structure-property relationships. These relationships are modified through synthesis and processing to create materials with new properties and characteristics to achieve a wide range of applications. With the entirety of the periodic table at one's fingertips, understanding the unique microstructure of each of these materials is often challenging. One technique that is expanding the robust ability of solid-state nuclear magnetic resonance (NMR) spectroscopy to delve into these details is dynamic nuclear polarization (DNP). The advent and continual progress in DNP development has allowed researchers to tackle new problems where traditional NMR approaches would have been impractical. This methods/protocols article serves as a general overview of high-field DNP, a polarization technique that boosts the sensitivity of NMR spectroscopy. Some of the nuances of the technique, as well as a few hurdles it aims to overcome in materials science, are discussed. The advances made from utilizing DNP continue to propel the materials field forward, whether it is the need to understand the surface/core features of nanoparticles, catalytic sites on heterogeneous catalytic supports, the complex interfaces in battery materials, or drug-loading of carbonaceous nanofibrils. High-field DNP continues to deliver remarkable results and insights, emerging as an indispensable method for materials science structure determination.

OVERVIEW

Over the past few decades, many advancements in characterization of materials have taken place. One of the most robust analytical characterization methods available to explore atomic- and molecular-level structure and dynamics in solids is nuclear magnetic resonance (NMR) spectroscopy. NMR spectroscopy's widespread use arises from its ability to characterize solids in a non-destructive and isotope-specific manner. It provides local- (< 4 Å) and medium-range structure (< 10 Å) information while offering qualitative and quantitative detail across the nanoscale through to bulk micron-sized materials.

The *Achilles Heel*, if you will, of the technique is its inherent insensitivity brought about by the small magnetic moment of nuclear spins, ultimately leading to poor and ineffective Boltzmann polarization. One rapidly emerging technique to boost NMR sensitivity is dynamic nuclear polarization (DNP). Although DNP dates back to the 1950s,[1,2] a number of critical technological developments to transition this technique to high fields were essential.[3,4] Commercialization of the instrumentation about a decade ago[5] was able to propel this technology to the point that academic researchers could use it; DNP has become the go-to method to address some of the most challenging structural questions facing materials science and biomolecular solids research.[3,4,6,7] Below, we introduce DNP and highlight a sampling of recent applications and advancements using this technique, and hence this methods/protocol article is entitled *Dynamic Nuclear Polarization (DNP) 101: A New Era for Materials*.

WHAT IS DNP?

Dynamic nuclear polarization is a high polarization NMR method that enables substantial gains in overall sensitivity, allowing one to detect NMR signals of challenging- (or once thought impossible) to-detect nuclei. The boost comes about from the interplay between unpaired electrons and nearby nuclei in the material of interest. Overall, sensitivity gains vary depending on many factors such as material composition, crystallite size, magnetic field strength, sample temperature, polarizing agent, sample size, glassing agent, etc.

When one combines DNP with traditional solid-state NMR experiments, enhancements (ε) of 10 to 200 are commonly seen, resulting in substantial savings in acquisition time. This boosting of NMR sensitivity is game-changing, whereby an easily achievable ε value of 20 provides a 400-fold reduction in acquisition time - a one-year experiment would take one day! DNP thus enables smaller sample sizes,

the ability to study more challenging NMR nuclei, accessing surfaces of materials, and other critical features. As a practical example, it permits ^{13}C-^{13}C INADEQUATE type experiments to be used for investigating small quantities of carbonaceous materials without isotopic enrichment. From the leading DNP development researchers, enhancements to signal intensities of several hundreds have been reported, and new frontiers have emerged in the field.[3,4,6-8]

How Does It Work?

Electron spin polarization is orders of magnitude higher than that of nuclear spins at a given magnetic field strength and temperature. By introducing a source of unpaired electrons, one can induce DNP by transferring spin-polarization from electrons to the neighboring nuclei. Depending on the experimental conditions, various spin polarization mechanisms (solid effect, cross effect, Overhauser, thermal mixing) may be responsible for the observed enhancement and can be further impacted by the choice of endogenous or exogenous radical introduced.[3,8] The most common route to achieve high field DNP in solids is to introduce a small amount of organic biradical as a polarizing agent (≤ 10 mM biradical) dispersed within a solvent that readily forms a glass upon freezing. The glassing-radical matrix can be intimately mixed forming a solid-like paste or dispersed in molecular systems acting as a cryoprotectant. This approach is optimal for creating substantial polarization gains in ^{1}H's, which can then be transferred to other NMR active nuclei such as ^{13}C, ^{15}N, ^{29}Si, etc. using a cross-polarization approach. This is often referred to as indirect DNP ($e^- \rightarrow {}^{1}H \rightarrow {}^{n}X$ with the theoretical maximum ε of 658 ($\gamma_{e^-}/\gamma_{^1H}$)). For example, Kovalenko and co-workers resolved bulk and surface atoms in a variety of quantum dot (QD) systems, demonstrating direct evidence for their core-shell structure. The authors used the well-studied CdSe system to probe the structure in detail not seen before, relying on the ability for DNP to distinguish the QD core from the surface.[9] This indirect DNP method used a biradical species to polarize protons in the sample under microwave irradiation. A typical cross-polarization experiment was performed using the DNP-enhanced polarization of ^{1}H to enhance the nucleus of interest (**Figure 1**). Nanoparticles can be extremely difficult to characterize by solid-state NMR due to a host of complications related to surfaces, sample amounts, and unreceptive NMR active nuclei such as ^{13}C, ^{29}Si, ^{67}Zn, ^{77}Se, etc.[10] More impressive still, DNP allowed for the first time 2D NMR spectroscopy of these QDs, enabling the QD surface and capping ligands to be resolved in unprecedented detail. Overall, they saw enhancements up to 80-fold and reduced experimental time up to 6400 times, making this experiment impractical without DNP (saving months or even years of experiment time). This method

was shown to be readily applicable to a variety of QD systems, including CdTe, PbTe, InP and $CsPbBr_3$ QDs.

Indirect DNP may be impractical with particularly complex chemical systems, not only due to the challenging nuclei present, but by the nature of the material itself. An alternative is to polarize low-gamma nuclei using direct DNP ($e^- \rightarrow {}^nX$, $\varepsilon > 700$ (γ_{e^-}/γ_X)) without the need for a cross-polarization step.[11] Direct DNP is a less conventional approach due to the challenges associated with radical selection, nuclear spin-lattice relaxation, abundance, and effective spin-diffusion, although it has been useful for various solids. One example making use of direct DNP looked at hydride-terminated silicon nanoparticles.[12,13] After seeing modest enhancements using the indirect DNP approach (using an organic biradical, glassing agent, cross-polarization, etc.), it was hypothesized that the reactive hydride surface negatively impacted the DNP enhancements by reacting with and quenching the radicals.[13] Instead, the authors used a direct DNP method to take advantage of the intrinsic radicals naturally present on the surface of silicon nanoparticles as dangling bonds. Using the endogenous dangling bonds as the electron source, direct transfer from $e^- \rightarrow {}^{29}Si$ was achieved and was shown to produce higher enhancements than the indirect method, $e^- \rightarrow {}^1H \rightarrow {}^{29}Si$. With as low as 0.70 mM endogenous radical concentration, enhancements up to 6-fold were observed, leading to a ~36-fold reduction of experimental time (**Figure 2**).[13] By tuning the surface chemistry or other material properties, these enhancements may be improved further. For similarly reactive materials, this strategy may come in handy during characterization.

Another impressive achievement made possible by DNP methods is the ability to study single-site catalysts.[14,15] NMR continues to be a powerful tool in defining the structure of active sites of heterogeneous catalysts, although it can be extremely challenging due to sensitivity as the concentration of the catalytic sites is extremely low when compared to bulk material, in addition to issues already posed by insensitive nuclei.[16] DNP has aided extensively in this area and continues to knock down barriers.[3,6] For example, Perras *et al.* showed that by using direct DNP methods it is possible to study unprotonated ^{17}O in single-site catalysts.[17] This result is extremely important, as ^{17}O comes with its own set of problems, namely being a quadrupolar nucleus (nuclear spin, I = 5/2) with only 0.04% abundance, and the fact that cross polarization applied within the indirect DNP approach can create challenges when studying quadrupolar nuclei.[18–20] With only a small enrichment of ^{17}O and direct DNP, the authors were able to show total enhancements up to 57-fold. The enhancements were significant

enough to distinguish the metal-coordinating oxygen sites of the single-site catalysts on mesoporous silica supports (**Figure 3**). Alternatively, detection of ^{17}O at natural abundance in battery and phosphor materials has been made possible by capitalizing on the unpaired electrons introduced from Mn(II) dopants.[21,22] The paramagnetic metal ions were used as endogenous polarizing agents, replacing the organic biradicals, allowing DNP experiments to be performed using unmodified powdered products of these materials.[21] Distinct ^{17}O chemical environments could be discerned from NMR spectra acquired in a matter of days - an impossible feat for an analogous solid-state NMR experiment dependent upon natural abundance ^{17}O. These new structural insights gained from the implementation of DNP technologies will assuredly lead to better understanding and design of future materials.

WHAT ARE THE ESSENTIAL BASICS OF DNP INFRASTRUCTURE?

To perform DNP, a few critical pieces of instrumentation are essential (**Figure 4**). Presently, one needs (i) a solid-state NMR spectrometer equipped with a wide-bore magnet; (ii) a device that generates high-frequency and high-power microwaves (typically a gyrotron, but extended interaction klystrons (EIKs) have also been used); (iii) a cryogenic magic-angle spinning probe with a microwave transfer line (couples the microwaves to the probe, enabling them to be launched onto the sample) and (iv) a N_2 cooling cabinet equipped with a high-pressure nitrogen gas supply. Note that research and development of DNP is quite active, and variations that address this parameter will arise in the near future.

DID YOU KNOW?

- *High field DNP instruments range from 211 MHz (^1H) / 140 GHz (e^-)[23] to 900 MHz / 592 GHz[24,25] – Higher fields are on the horizon*
- *Average of 500,000 liters of N_2 gas are consumed in 24 hours of continuous operation*
- *Samples are typically packed into sapphire or zirconia sample holders called rotors*
- *Probe and sample are generally cooled to between 80 and 120 K, while the sample rotates 5 to 35 kHz*
- *ca. 40 high-field DNP instruments are operational world-wide, and this number is actively growing*

WHAT ARE SOME LIMITATIONS TO HIGH-FIELD DNP?

Although substantial gains in sensitivity provide new avenues of scientific exploration, some limitations need to be mentioned. One is related to the inability to study samples at room temperature. Currently, cryogenic temperatures must be used to slow down electron relaxation to allow for efficient polarization transfer to neighboring nuclei but in most cases, this requirement does not impede measurements. However, these low temperatures can impact a few properties, including molecular dynamics, nuclear relaxation properties, and may induce phase changes in some materials. Other complications may arise with sample compatibility, reactivity, and recovery, and thus additional considerations need to be taken when compared to room temperature solid-state NMR spectroscopy. One also needs to ensure an adequate supply of cryogens for active cooling and dry nitrogen gas for sample spinning, which increases the cost and complexity of experimentation. It is essential to note that cryogen-free systems will be the next innovation in spectrometer design and are already being pursued. Are these truly limitations? The low temperatures required may, in fact, prove to be useful and should not necessarily be counted as a negative when considering the DNP technique. For example, although low temperatures may increase spectral complexity, they may reveal once-hidden information not available at room temperature due to fast dynamics or exchange.

DNP 2040

As this field is rapidly advancing, extensive developments will assist in overcoming current limitations and lead to amazing outcomes for the scientific community. A small sampling of activities currently being explored include: Ultralow temperature experiments using closed cycle He cooling,[26] which will provide further gains in sensitivity and reduce operating costs. NMR spectroscopy is advancing rapidly into ultrahigh field magnets (≥ 1 GHz, ^{1}H), and DNP will need to follow suit through gyrotron technology development targeting 1 THz to enable production of DNP systems in the 1000 MHz / 658 GHz to 1500 MHz / 988 GHz range. Improving radical design is of utmost importance to continue the ground-breaking strides at higher fields as we have rapidly expanded beyond 9.4 T (400 MHz/ 263 GHz) over the past few years. A promising development in radical design for use in DNP experiments at high magnetic fields[27] is the subgroup of bisnitroxides referred to as TinyPols.[28] The best performing polarizing agent of this series achieved ^{1}H enhancements of 90 and 32 at 18.8 T and 21.1 T, respectively. These improvements outperform the conventional bisnitroxide polarizing agent, AMUPol, by a factor of ~2 and are so far the largest enhancements reported for a water-soluble radicals at these field

strengths. When a TinyPol derivative was combined with a functionalized mesoporous silica material for a 2D ^{1}H-^{13}C HETCOR experiment at 18.8 T, a proton enhancement of 45 was achieved and a complete assignment of all cross peaks could be accomplished for the organic ligand at natural abundance (**Figure 5**). This feature will be particularly critical for solids composed of quadrupolar nuclei or containing large biological molecules, which is of increasing importance for the vast area of materials science with biological applications. Likewise, we are often far from the theoretical maximum with respect to improving radical design, microwave power, and sample penetration, and methods to increase transfer efficiencies leave much room for development and further advances. Practical approaches to diminish or eliminate the necessity for sample cooling would be a significant leap, although several challenges remain, some of which may not be overcome through technological advancement due to the intrinsic physics on which DNP relies. Another potential innovation is the reduction of the footprint and expense associated with the technique, which would enable existing narrow-bore NMR instruments to be converted to DNP instruments, such as providing an EIK source for lower magnetic fields.[24] The DNP NMR technique can mitigate costly isotopic enrichment, although a balanced approach needs to be considered, as labeling may improve results, enabling further access to more challenging questions or extraction of the most critical structural details with strategic experimental design (2D and 3D). Recently, De Paëpe and co-workers were able to distinguish between grafted and adsorbed active pharmaceutical ingredients (APIs) on the surface on cellulose nanofibrils using DNP NMR spectroscopy.[29] The sensitivity gains observed with this technique allowed for the investigation of an API at natural abundance and confirmed that only 1% of an API was covalently bound to the surface of these nanofibrils (**Figure 6**). Additional organic compounds and by-products could be detected on the surface, and these results were compared to other techniques like elemental analysis and conductometric titrations that can lead to an overestimation of the loading dose of APIs on biomaterials.[29] These examples are only a few of the many areas being targeted to improve characterization of a diverse swath of materials. As the method develops, it surely will be applied to novel applications that have yet to be considered. DNP enables remarkable new insights into solids and can now be considered a new complement to the arsenal of techniques available to materials scientists.

Associated Content

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All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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FIGURES

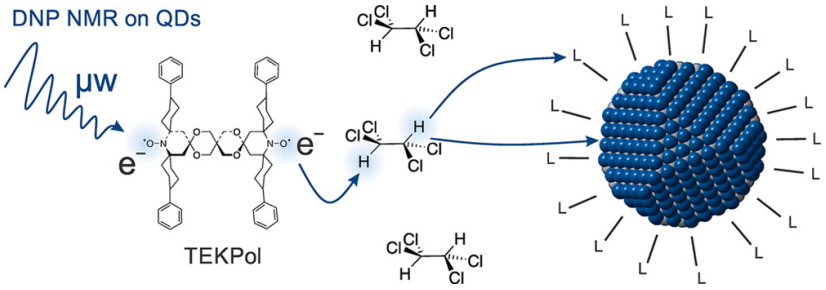

Figure 1. Schematic of indirect DNP mechanism ($e^- \rightarrow {}^1H \rightarrow {}^nX$) applied to the study of CdSe quantum dots (X = ^{13}C, ^{77}Se and ^{113}Cd). Microwaves induce polarization of the biradical TEKPol and induce ^1H polarization of the surrounding solvent molecules. As the solvent is in contact and surrounding the particles this can be transferred to the surface and sub-surface of the QD for structural analysis. Reprinted with permission from Ref. 9. Copyright 2015 American Chemical Society.

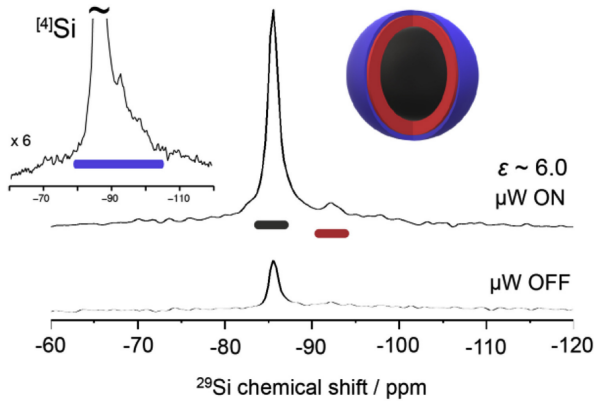

Figure 2. Solvent-free direct DNP mechanism ($e^- \rightarrow {}^{29}Si$) applied to the study of silicon nanocrystals. The microwaves polarize endogenous radicals present within the nanocrystals and polarize ^{29}Si directly to boost sensitivity of the whole particle (surface and core) as shown in the upper (μw on) spectrum. Note "μw on" represents a DNP NMR spectrum and "μw off" represents a solid-state NMR spectrum under otherwise identical conditions (*i.e.,* no microwaves to induce polarization). Reprinted from *Solid State Nucl.*, *100,* Ha *et al*., Endogenous dynamic nuclear polarization NMR of hydride-terminated silicon nanoparticles, 77-84. Copyright (2019), with permission from Elsevier.

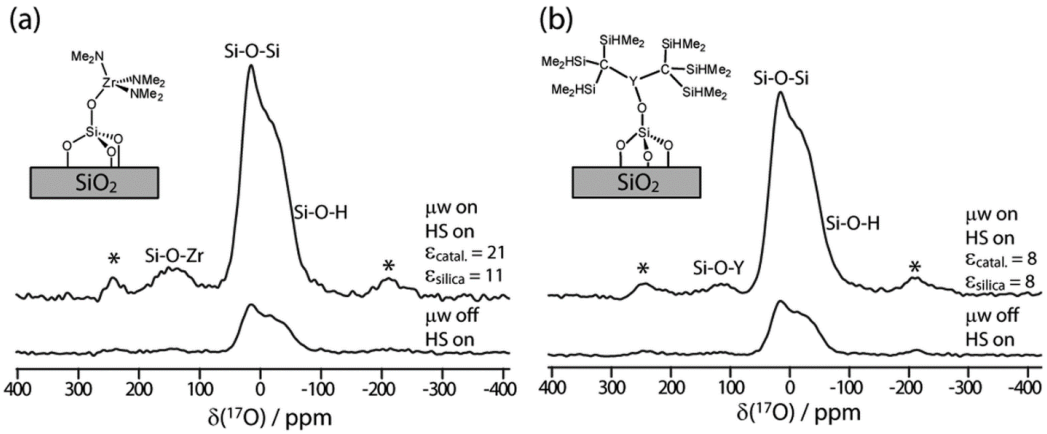

Figure 3. Solid-state ^{17}O DNP NMR spectra for (a) Zr- and (b) Y-based heterogenous catalysts on mesoporous silica, with (μw on) and without (μw off) microwave irradiation. Under DNP enhancement, the Si-O-metal sites appear between 100 and 200 ppm in the spectra. Reprinted with permission from Ref. 17. Copyright 2018 Royal Society of Chemistry.

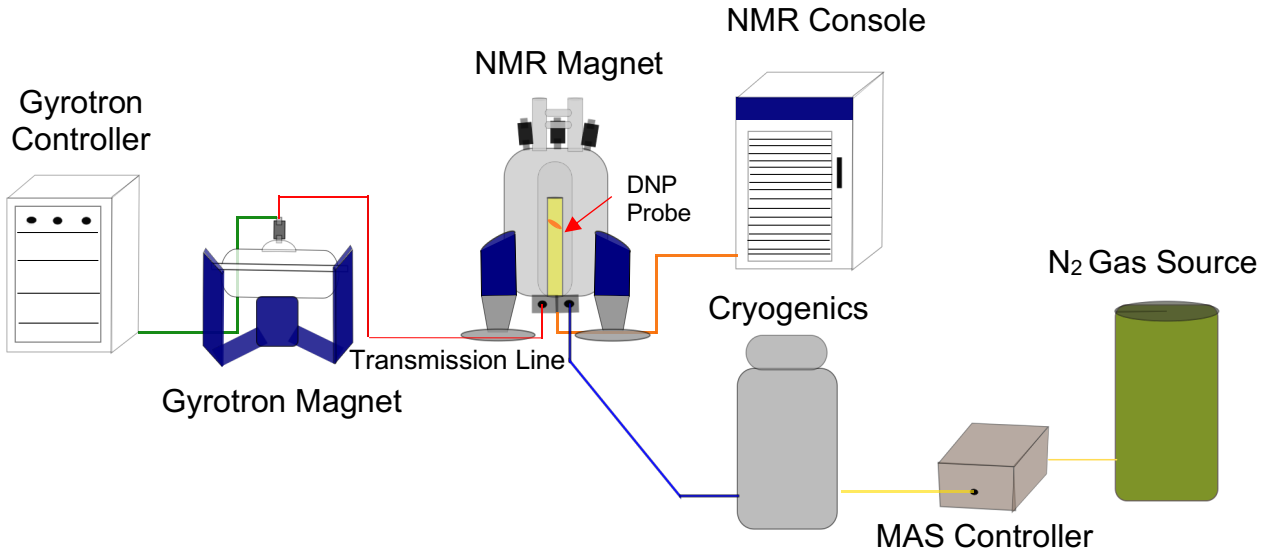

Figure 4: Schematic of a modern commercial DNP NMR spectrometer. Essential components include the microwave source (gyrotron tube (dark grey) inside a superconducting magnet denoted as the Gyrotron Magnet), a controller for microwave output (a Gyrotron controller), a wide-bore NMR magnet and spectrometer (NMR magnet and NMR console) and a DNP NMR probe. Note that a transmission line (red) is needed to connect the microwave output (from the Gyrotron) to the DNP NMR probe that is located inside the NMR magnet. Cryogens and dry nitrogen gas are needed to cool the DNP probe and sample to temperatures between 80 and 120 K. Furthermore, a N_2 gas source and magic angle spinning (MAS) controller are used to rotate and control the spinning speed of the sample at the magic angle to perform MAS DNP NMR experiments.

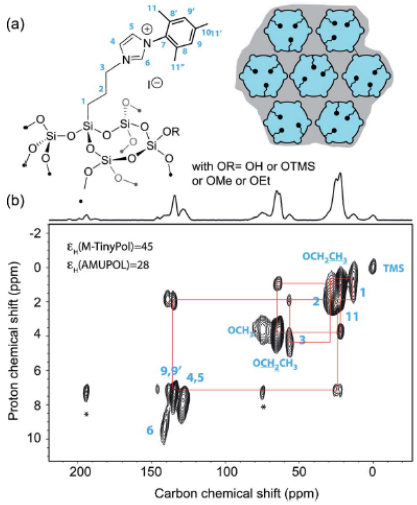

Figure 5. Two-dimensional DNP ^{1}H-^{13}C Heteronuclear Correlation (HETCOR) experiment of functionalized mesoporous silica support obtained at 18.8 T with an MAS frequency of 12.5 kHz. (a) Imidazolium attached to silica material and schematic representation of 6 nm pores filled with either 10 mM AMUpol or a TinyPol polarizing solution (blue). (b) The 2D DNP ^{1}H-^{13}C HETCOR spectrum using an aqueous solution of a TinyPol derivative as the DNP polarizing agent is able to provide clear assignments for the ligands attached to the silica material. Proton (^{1}H) enhancements of 25 and 45 were achieved using AMUpol or TinyPol as the polarizing agent, respectively. Reprinted with permission from Ref. 28. Copyright 2020 Royal Society of Chemistry.

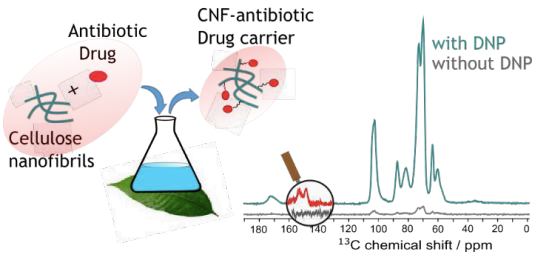

Figure 6. Schematic of an active pharmaceutical ingredient (red) grafted/adsorbed onto cellulose nanofibrils (green) and the previously unobservable signals detected using DNP NMR spectroscopy. Reprinted with permission from Ref. 29. Copyright 2020 Royal Society of Chemistry.

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