Expeditious Dissolution Dynamic Nuclear Polarization without Glassing Agents

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Introduction
Dissolution dynamic nuclear polarization (DNP) technique involves hyperpolarization of low-abundance nuclei, such as $^{13}$C or $^{15}$N, by transferring electron polarization from persistent radicals using microwave radiation at very low temperature, followed by rapid dissolution of the hyperpolarized substance with hot solvent and injection of the solution into a sample or organism for data acquisition via NMR or MRSI.\textsuperscript{1} The extent of polarization of the nuclei is dependent on several factors, including the mechanism of polarization transfer, magnetic field strength, microwave power and frequency, temperature and sample composition.\textsuperscript{2,3} We explored an alternative method of sample preparation which removes the need for a toxic glassing agent using isopentane as a cooling bath. This work has been published in *NMR in Biomedicine*, 2016, 11, 6892-6905.

Experimental
Samples were prepared using (1-$^{13}$C)-enriched metabolites (sodium acetate, pyruvate or butyrate) (3.0 M) co-dissolved with 4-oxo-TEMPO or trityl OX063 in solvent ($\text{D}_2\text{O}/\text{H}_2\text{O}$ alone or with perdeuterated glassing agent). Samples were frozen in liquid nitrogen or 2-methylbutane cooled to 130 K, polarized and monitored using small flip angle for every five minutes up to 3 hours at low temperature ($\sim$1.2 K) at 5 T.

Results and Discussion
The solid state polarization of an aqueous solution ($\text{D}_2\text{O}$) of sodium acetate frozen with isopentane is 28 ± 2%, and the polarization of sodium acetate ($\text{D}_2\text{O}/\text{EtOH-D}_6$) frozen in liquid N$_2$ is 26 ± 2%. The polarization buildup time constant is three times faster for the $\text{D}_2\text{O}$/isopentane sample (480±70 s) relative to the glassed sample prepared with liquid N$_2$ (1150 ± 200 s). The use of $\text{D}_2\text{O}$ removing glassing agent in $\text{D}_2\text{O}$/isopentane samples means more concentrated and coupled spin bath with shorter inter-spin distances, enabling stronger dipolar interactions for spin diffusion in the matrix and faster polarization of the sample.

Conclusions
Rapid freezing of sample without glassing agents using isopentane enabled a 1.5–3-fold time savings in polarization buildup time and equal achievable polarization in comparison to the sample with glassing agents frozen in liquid nitrogen for dissolution DNP.

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References
Fig. 1 Schematic diagram of sample set-up for rapid freezing of an aqueous solution to form a vitrified solid.

Fig. 2 Polarization buildup curves at 5 T and ≤1.2 K for 3.0 M sodium acetate and 50 mM 4-oxo-TEMPO dissolved and frozen as indicated.