Triplet dynamic nuclear polarization of pyruvate via supramolecular chemistry†

T. Hamachi,[*1] K. Nishimura,[*1] K. Sakamoto,[*1] Y. Kawashima,[*1] H. Kouno,[*1] S. Sato,[*3] G. Watanabe,[*3,*4,*5] K. Tateishi,[*6,*7] T. Uesaka,[*6,*7] and N. Yanai[*1,*2,*8]

Nuclear magnetic resonance (NMR) is an important non-destructive technique for analyzing chemical structures, and magnetic resonance imaging (MRI) is an essential medical procedure. Their sensitivity is directly proportional to nuclear spin polarization. Dynamic nuclear polarization (DNP) enhances this polarization by transferring the high polarization of electron spin in polarizing agents. Dissolution-DNP technique rapidly dissolves hyperpolarized solid-state samples and has been applied to *in vivo* metabolite imaging. In particular, [1-^{13}C] pyruvate is the most important molecular probe for high-sensitivity MRI; its metabolic kinetics are used in the diagnosis of various diseases, including cancer.[1)] However, conventional DNP requires severe conditions, such as a high magnetic field (∼7 T) and cryogenic temperatures near 1 K.

Here, we report on the hyperpolarization of [1-^{13}C, d_3] sodium pyruvate (NaPyr) using triplet-DNP (DNP via photoexcited triplet electron spins)[2)] under milder conditions, specifically at 100 K and 0.64 T. The challenge involved molecularly dispersing hydrophobic polarizing agent, 4,4'-(pentacene-6,13-diyl) dibenzoate (NaPDBA), and sodium pyruvate into the solvent. To address this, we used supramolecular chemistry to increase the solubility and dispersibility of the agent. The NaPDBA aggregation was prevented by supramolecular complexation with β-cyclodextrin (βCD) with a saturated concentration of 1.5 M NaPyr in DNP juice (H_2O/D_2O/glycerol-d_8 = 1/3/6, v/v/v) (Fig. 1). The structure of the NaPDBA-βCD inclusion complex was investigated with NMR and molecular dynamics (MD) simulations. All the measurements agreed with the mono-dispersion of the NaPDBA-βCD inclusion complex in DNP juice.

Triplet-DNP was applied with the following procedure. NaPDBA was photoexcited with a 527 nm pulsed laser to produce the polarized electron spins. Then, 17.3 GHz microwaves were irradiated to transfer the polarization from electron spins to ^{1}H spins of water in DNP juice containing 1 mM NaPDBA, 5 mM

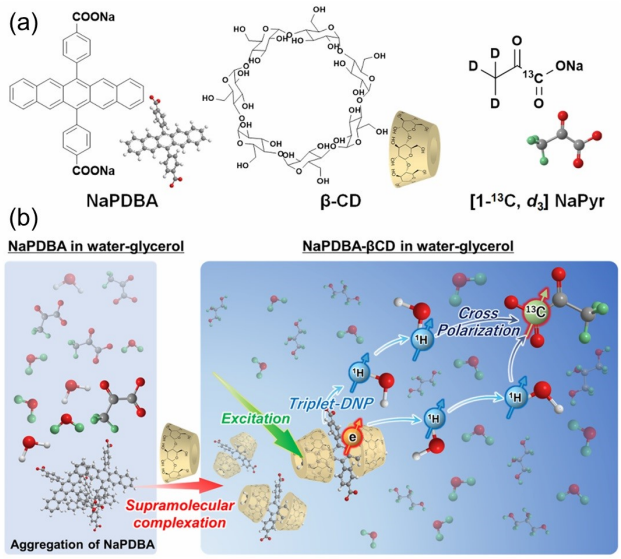

Fig. 1. (a) Molecular structures of NaPDBA, βCD, and [1-^{13}C, d_3] NaPyr. (b) Polarization transfer from photoexcited triplet electron spins to ^{13}C spins in [1-^{13}C, d_3] NaPyr via ^{1}H spins in water.

βCD, and 1.5 M [1-^{13}C, d_3] NaPyr at 100 K and 0.64 T. After repeating the procedure for 2 min, the ^{1}H spin polarization was transferred intermolecularly to ^{13}C spins in [1-^{13}C, d_3] NaPyr with a ramped amplitude cross-polarization (RAMP-CP) sequence (Fig. 2(a)). The enhancement was clear from the fact that no ^{13}C NMR peak was observed via RAMP-CP when using ^{1}H spins at thermal equilibrium (Fig. 2(b)). ^{13}C-methanol was used as a reference, and an enhancement factor of 122 was estimated.

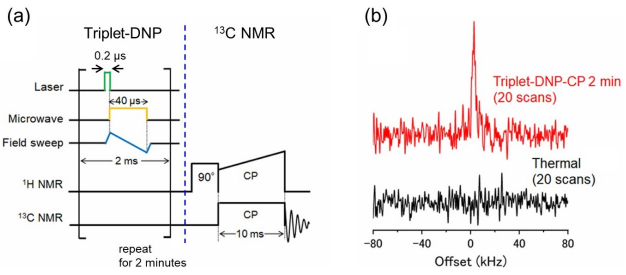

Fig. 2. (a) Sequence of triplet-DNP and ramped-amplitude cross-polarization (RAMP-CP). (b) ^{13}C-NMR spectra of [1-^{13}C, d_3] NaPyr after 2-min triplet-DNP and RAMP-CP (red) and after RAMP-CP with thermal ^{1}H spins (black). The signals were accumulated 20 times.

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*1 Department of Applied Chemistry, Kyushu University
*2 Center for Molecular Systems (CMS), Kyushu University
*3 Department of Physics, Kitasato University
*4 Kanagawa Institute of Industrial Science and Technology (KISTEC)
*5 Department of Data Science, Kitasato University
*6 Cluster for Pioneering Research, RIKEN
*7 RIKEN Nishina Center
*8 PRESTO, FOREST, JST

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Hyperpolarized MRI with triplet-DNP will be possible using supramolecular complexation to hyperpolarize NaPyr. This provides an important step toward the widespread use of ultra-sensitive MRI for cancer diagnosis.

References

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