

# Hyperpolarization of Frozen Hydrocarbon Gases by Dynamic Nuclear Polarization at 1.2 K

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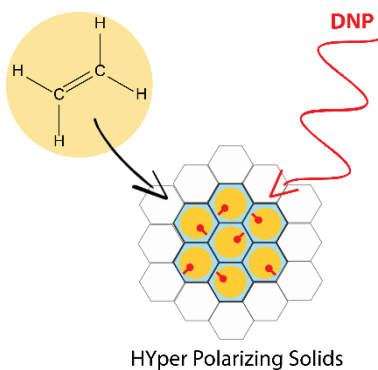
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## ABSTRACT

We report a simple and general method for the hyperpolarization of condensed gases by DNP. The gases are adsorbed in the pores of mesoporous silica matrices known as HYPSOs (HYper Polarizing SOLids) that have paramagnetic polarizing agents covalently bound at the surface of the mesopores. DNP is performed at low temperatures and moderate magnetic fields ( $T = 1.2$  K and  $B_0 = 6.7$  T). Frequency-modulated microwave irradiation is applied close to the electron spin resonance frequency ( $f = 188.3$  GHz), and the electron spin polarization of the polarizing agents of HYPSO is transferred to the nuclear spins of the frozen gas. A proton polarization as high as  $P(^1\text{H}) = 70\%$  can be obtained, which can be subsequently transferred to  $^{13}\text{C}$  in natural abundance by cross-polarization, yielding up to  $P(^{13}\text{C}) = 27\%$  for ethylene.

## TOC GRAPHICS



Optical pumping<sup>1,2</sup> is an established method for hyperpolarizing noble gases such as  $^{129}\text{Xe}$  and  $^3\text{He}$ ,<sup>3, 4</sup> offering polarization levels close to unity, albeit with limited throughputs.<sup>5</sup> Applications range from material science to biomedical research, in particular to lung imaging by MRI.<sup>6, 7</sup> Unfortunately, optical pumping is restricted to a few noble gases, and molecular gases have never been hyperpolarized so far. Molecules with double or triple carbon-carbon bonds can be hydrogenated with parahydrogen by heterogeneous catalysis to produce hyperpolarized gaseous reaction products,<sup>8-10</sup> though with polarization levels well below unity. Dissolution dynamic nuclear polarization (D-DNP)<sup>11</sup> has become a method of choice for the hyperpolarization of a broad range of small molecules in solution. The use of D-DNP to polarize  $^{129}\text{Xe}$ <sup>12-14</sup> and  $^{15}\text{N}_2\text{O}$ <sup>15</sup> has been demonstrated. In this study, we propose a general method to extend the use of D-DNP to virtually any condensed gas.

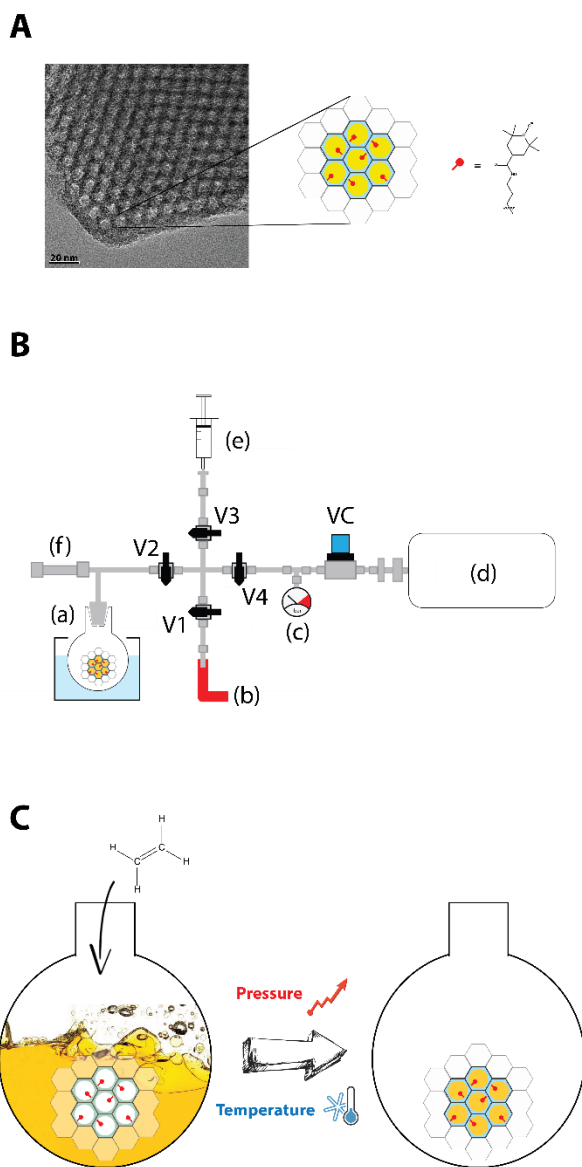
Compared to optical pumping or hydrogenation with parahydrogen, D-DNP requires rather complex instrumentation (low temperature cryostats, superconducting magnets, microwave sources, etc.) D-DNP has found applications to various fields of chemistry such as drug discovery<sup>16-19</sup> and metabolomics.<sup>20, 21</sup> One can detect the presence of tumors in patients by real-time imaging of metabolic conversion rates after intravenous injection of hyperpolarized metabolites such as  $^{13}\text{C}$ -enriched pyruvate.<sup>22</sup> D-DNP usually consists in three steps: (i) preparing a frozen sample containing the molecules of interest that are mixed with paramagnetic polarizing agents (PAs) in solutions that become glassy upon freezing. (ii) Polarizing the sample at low temperatures in moderate fields ( $T = 1.2\text{ K}$  and  $B_0 = 3.35\text{ T}$  in many laboratories; in our case  $B_0 = 6.7\text{ T}$ ) by applying suitable microwave irradiation, (iii) rapidly melting the frozen hyperpolarized sample with superheated water, and transferring the solution to an NMR or MRI machine.

The DNP sample preparation is a critical step, which is traditionally performed as follows: (i) the polarizing agents are homogeneously dissolved in a solution together with a substance to be hyperpolarized, (ii) the solution is subsequently frozen, and (iii) the resulting sample is visually inspected and discarded if it has a "milky" appearance. When a transparent glassy state cannot be achieved, the formation of crystalline domains inevitably leads to the aggregation of the polarizing agents. Such samples are not suitable for DNP. Obtaining a glassy frozen sample often requires the addition of a glassing agent such as glycerol. This is critical to ensure a good DNP efficiency. To achieve hyperpolarization of  $^{129}\text{Xe}$  by D-DNP,<sup>12</sup> the condensed gas was mixed with a co-solvent like isobutanol doped with TEMPO as polarizing agent. This was achieved under relatively high pressure (*ca.* 1 MPa) and at low temperatures (*ca.* 200 K) to ensure that both xenon and isobutanol were in a liquid state and could be homogeneously mixed. The solution was subsequently rapidly frozen by plunging into a liquid nitrogen bath, which resulted in a homogeneous glassy matrix, suitable for DNP. This sample preparation is difficult to reproduce since it may lead to the formation of Xe clusters.<sup>14 15</sup> Furthermore, this method cannot easily be generalized to other gases. Our attempts to use a similar approach for ethylene have failed so far. More specifically, we have successfully mixed liquid ethylene with ethanol and TEMPO, but this mixture did not produce a homogeneous glass upon freezing. The frozen mixture was characterized by a non-uniform color distribution, clearly indicating segregation of the components, and the proton polarization could not be enhanced by DNP.

We therefore propose an alternative route for polarizing condensed gases by using recently developed HYper Polarizing SOLids (HYPSOs).<sup>23, 24</sup> These mesoporous hybrid organo-silica materials contain surface-bound polarizing agents (TEMPO here) that are homogeneously distributed on the surface of the mesopores (see Fig 1A). HYPSOs were initially developed for

polarizing metabolites, since they can easily be filtered out after dissolution, resulting in pure hyperpolarized solutions without contaminants. We show here that HYPsOs can be also used for polarizing gases such as propane, butane and ethylene. In this preliminary study, we simply condensed these gases using first and third generations of HYPsO materials (HYPsO-1<sup>24</sup> and HYPsO-3<sup>25</sup>), and we polarized the frozen impregnated materials using our state-of-the-art DNP polarizer.<sup>26, 27</sup> We have designed and built a simple system for impregnating HYPsOs with controlled amounts of gas (Fig. 1B). Here, 50 mL of a mixture of *n*-butane, isobutane and propane from a gas canister (“butane refill gas” for lighters, sold by Migros) was condensed with 10.2 mg of HYPsO-1. The loading capacity of HYPsO-1 being 1.8 mL/g, only about 8.9 mg of the liquefied gas were expected to enter the pores (Fig. 1C).<sup>24</sup> The sample was then rapidly frozen in our DNP polarizer<sup>26, 27</sup> at 4.2 K, before lowering the temperature to 1.2 K. A similar procedure was applied for 50 mL of ethylene (Carbagas) with 22.5 mg of HYPsO-3<sup>25</sup> precooled in a bath of liquid ethanol at 159 K. The loading capacity of the cubic three-dimensional HYPsO-3 is 0.47 mL/g, hence only 6 mg of liquid ethylene were expected to enter the pores. The samples were polarized at  $B_0 = 6.7$  T and  $T = 1.2$  K<sup>26, 27</sup>, using a saddle-coil probe doubly tuned for  $f(^1\text{H}) = 285.3$  MHz and  $f(^{13}\text{C}) = 71.73$  MHz. The sample was irradiated at 188.29 GHz (negative polarization) with  $P_{\mu\text{w}} = 87.5$  mW using triangular microwave frequency modulation<sup>28</sup> with a frequency  $f_{\text{mod}} = 10$  kHz over a range  $\Delta f_{\text{mod}} = \pm 50$  MHz. The build-up curves of the polarization  $P(^1\text{H})$  were monitored with  $1^\circ$  pulses applied every 5 s. Cross-polarization<sup>29,30</sup> from  $^1\text{H}$  to  $^{13}\text{C}$  was performed with multiple adiabatic contacts as described elsewhere,<sup>31</sup> and the polarization  $P(^{13}\text{C})$  was measured with  $5^\circ$  pulses every 37.5 s for the mixture of *n*-butane, isobutane and propane, and every 75 s for ethylene. After DNP, the initial volume of condensed gas (ca. 50 mL) could be fully recovered by connecting the sample cup to an empty syringe while the sample was still frozen, and

gently warming-up to room temperature. Such an amount of undiluted gas would be sufficient for various applications, for instance to follow a chemical reaction in a batch or a continuous flow reactor. Similar studies dealing with D-DNP of  $^{129}\text{Xe}$  yielded comparable volumes of gas.<sup>12-14</sup>

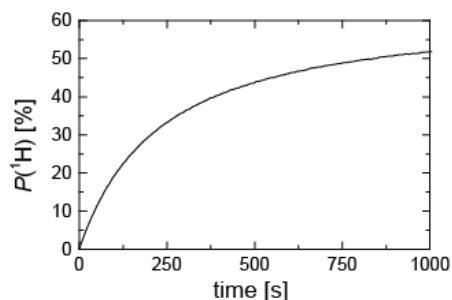


**Figure 1.** (A) Transmission electron microscopy image of mesoporous HYPSO-1 taken with a Philips CM30 TEM operating at 300 kV. In the hexagonal structure, the red dots indicate the polarizing agents derived from TEMPO. (B) System used to impregnate

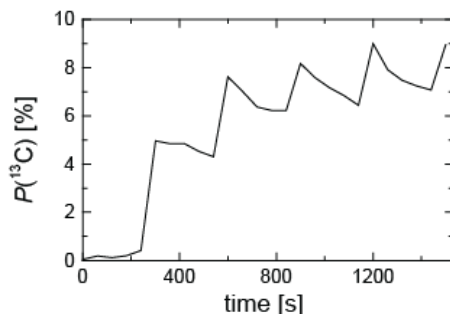
HYPSO materials with condensed gases equipped with (a) a flask containing the HYPSO material which can be cooled to liquid nitrogen temperature. A vacuum is established in the entire system by opening valves V1, V2, V3 and V4 and pumping with a rotary pump connected to (b). A manometer (c) monitors the pressure. With valves V1 and V2 closed, valves V3 and V4 are opened and the control valve VC is opened gently to let a desired volume of gas escape from the gas tank (d) and fill the syringe (e). Finally, V4 is closed and V2 is opened to let the gas adsorb onto the HYPSO powder. An overpressure valve (f) ensures safety. (C) By decreasing the temperature in (a) to 159 K using an ethanol – liquid N<sub>2</sub> bath and increasing the pressure, the gas is forced to enter the pores of HYPSO.

Figure 2 shows the build-up of the proton polarization in a mixture of *n*-butane, isobutane and propane at 1.2 K. A remarkable  $P(^1\text{H}) = 53\%$  could be achieved in 1000 s with a build-up time constant  $\tau_{\text{DNP}}(^1\text{H}) = 228 \pm 4$  s. The build-up of the polarization  $P(^{13}\text{C})$  (Figure 3) was boosted by cross-polarization (CP) every 5 min to transfer the  $^1\text{H}$  polarization to  $^{13}\text{C}$ . For the mixture of *n*-butane, isobutane and propane, an average polarization  $P(^{13}\text{C}) = 9\%$  was achieved after 20 min. For ethylene, the build-up at 1.2 K reaches  $P(^1\text{H}) = 70\%$  with  $\tau_{\text{DNP}}(^1\text{H}) = 1384 \pm 13$  s. Two cross-polarization (CP) contacts were performed (after 10 and 20 min) to transfer the polarization from  $^1\text{H}$  to  $^{13}\text{C}$ , to achieve  $P(^{13}\text{C}) = 27\%$  for ethylene.





**Figure 2.** Build-up of the proton polarization in a mixture of *n*-butane, isobutane and propane adsorbed on HYPISO-1 at 1.2 K to  $P(^1\text{H}) = 53$  % with a time constant  $\tau_{\text{DNP}} = 228 \pm 4$  s.



**Figure 3.** Build-up of natural-abundance  $^{13}\text{C}$  polarization in a mixture of *n*-butane, isobutane and propane adsorbed on HYPISO-1 at 1.2 K with 5 cross-polarization (CP) contacts every 5 min, leading to  $P(^{13}\text{C}) = 9$  %.

This initial study demonstrates that hydrocarbon gases such as propane, butane and ethylene can be condensed in porous HYPISO materials and readily polarized by DNP. With these encouraging results in hand, we are currently trying to develop strategies for collecting the hyperpolarized hydrocarbon gases as a gas, a pure liquid, a solution in a solvent, or a solid, while preserving the hyperpolarization. In this respect, gases represent a greater challenge than liquids since the predominance of the spin-rotation mechanism leads to fairly short  $T_1$  relaxation times.<sup>32-</sup>

<sup>36</sup> There are a number of ways to significantly extend the lifetimes of non-equilibrium spin states in gases, such as increasing the pressure or mixing with a heavier buffer gas.<sup>32,36</sup> By simply liquefying gases one can extend the lifetime of the polarization; the  $T_1(^1\text{H})$  of liquid ethylene at 169 K is ca. 20 s.<sup>37</sup> Pure liquids could be produced by melting the frozen gas (for example with an IR laser).<sup>38</sup> Finally, one can use long-lived spin states.<sup>19, 39-43</sup> In particular, at low magnetic fields, non-equilibrium spin states with the lifetimes as long as 5-6 s have been reported for propane gas,<sup>44,45</sup> 100 s for ethylene-d<sub>2</sub> dissolved in perdeuterated hexane<sup>46</sup> and 1000 s for ethylene gas.<sup>34</sup> As demonstrated earlier,<sup>47</sup> a non-equilibrium spin state corresponding to a singlet order can be directly populated by D-DNP. Typically, for a polarization  $P(^1\text{H}) = 0.7$  that was achieved in this work, for a pair of  $I=1/2$  nuclei the singlet-triplet imbalance (i.e., the difference between the population of the singlet state and the average population of the three triplet states, which is proportional to  $[P(^1\text{H})]^2 = 0.49$ ) is 49% of its maximum possible value, with the latter achieved when the singlet state is fully depleted ( $[P(^1\text{H})]^2 = 1$ ).

The ability to produce hyperpolarized gases with lifetimes as long as 5-1000 s is promising for the development of a number of novel applications. In particular, catalytic transformations such as hydrogenation, oxidative and non-oxidative dehydrogenation, hydroformylation, oxidation, metathesis and other reactions are of primary importance in modern chemical industry.<sup>48</sup> Such reactions can unlock long-lived spin states produced by DNP and make them observable by NMR. In most cases, a much deeper insight into the mechanisms of industrially important processes, including synthesis of various hydrocarbons, production of fuels, polymerization, etc., is needed to achieve any significant progress in improving reaction conversion and selectivity and reducing its environmental impact. This requires detailed mechanistic studies of these reactions and calls for the implementation of novel advanced methods and instrumental techniques. Most

hyperpolarized NMR studies of catalytic processes are currently limited to the use of parahydrogen in the homogeneous catalytic hydrogenation of unsaturated hydrocarbons in solution.<sup>49-52</sup> Yet the vast majority of industrial catalytic processes use heterogeneous rather than homogeneous catalysis. The extension of parahydrogen-based studies to heterogeneous catalysis, while successful,<sup>8-10</sup> faces some major limitations and is still naturally restricted to reactions that involve H<sub>2</sub>. The use of hyperpolarized gases to study chemical reactions is particularly promising in this context and has the potential to significantly advance hyperpolarization-based mechanistic NMR studies of catalysis and other areas of research.

## **Notes**

The authors declare no competing financial interests.

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