Surface Enhanced NMR Spectroscopy by Dynamic Nuclear Polarization

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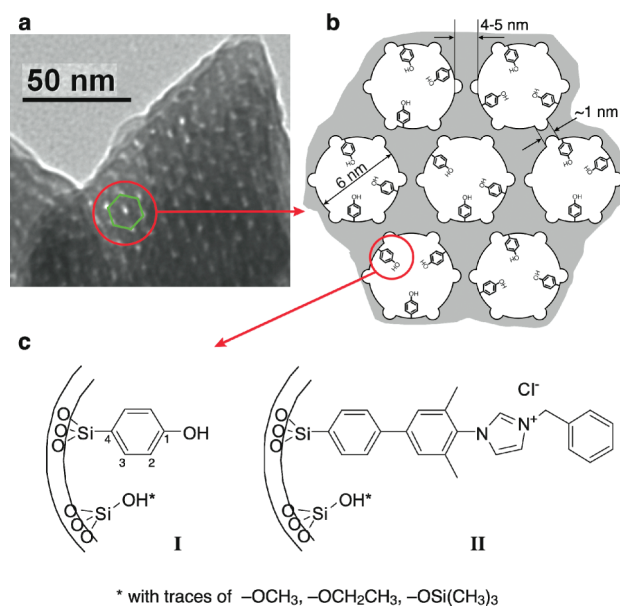
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Abstract: It is shown that surface NMR spectra can be greatly enhanced using dynamic nuclear polarization. Polarization is transferred from the protons of the solvent to the rare nuclei (here carbon-13 at natural isotopic abundance) at the surface, yielding at least a 50-fold signal enhancement for surface species covalently incorporated into a silica framework.

Solid-state NMR spectroscopy is a powerful technique for characterizing inorganic and hybrid materials that offers the possibility to directly investigate both the bulk (silica and/or alumina) and surface functionalities (e.g., adsorbates, grafted molecules, organic fragments, etc.). In applications such as sensing and catalysis, having a precise understanding of the structure of surface species is critical, since one of the most powerful ways to develop systems with improved properties is through the determination of structure−activity relationships. However, the sensitivity of NMR methods poses a major limit for surfaces. Even when highly porous nanoparticles are used, the concentration of NMR-active nuclei often remains low (typically below 1 mmol/g for ^{1}H and 0.01 mmol/g for ^{13}C in natural abundance), requiring many hours or even days to accumulate simple one-dimensional spectra with reasonable signal-to-noise ratios.[1] This often prevents the acquisition of multidimensional correlation spectra, thus severely limiting the characterizing power of solid-state NMR techniques. NMR sensitivity is thus one of the key barriers to further progress in many areas of surface chemistry.

In this communication, we show how dynamic nuclear polarization (DNP) can yield up to a 50-fold increase in the NMR sensitivity of molecular organic functionalities of hybrid silica materials.

In the past few years, DNP has made great progress, and the technique, which was originally developed for low magnetic fields,[2] has been shown to be applicable in high magnetic fields and notably to frozen solutions.[3] Griffin and co-workers[4] have demonstrated signal enhancement factors (ε) of up to ∼400 in cross-polarization magic-angle-spinning (CP MAS) ^{13}C and ^{15}N spectra of frozen solutions of proteins in a D_2O/H_2O/glycerol mixture at temperatures below 90 K using stable radicals such as TEMPO[5] or TOTAPOL[6] as the source of polarization. Saturation of the EPR transitions of the radicals leads to polarization enhancement of nearby protons,

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Figure 1. (a) Transmission electronic microscopy image of the nanoporous silica material. (b) Schematic representation of the pore [mesopores (6 nm diameter) are shown as circles and micropores (<1 nm diameter) as small half-circles] and channel network with phenol functionalities. The shaded gray area represents the silica bulk. (c) Different covalently incorporated aromatic substrates.

and subsequent spin diffusion leads to uniformly enhanced polarization of most of the protons in the sample. This polarization can then be transferred to other nuclei (such as ^{13}C or ^{15}N, or even ^{14}N,[7] by cross-polarization). As an alternative, direct DNP enhancement of low-γ nuclei (^{2}H, ^{13}C, etc.) without the involvment of magnetization transfer through ^{1}H nuclei is also possible.[8]

The nature of the polarizing agent, the composition of the solvent mixture, and the capacity of the solvent to form a homogeneous glass at low temperature appear to be critical ingredients in a successful DNP experiment. It is not immediately obvious how to adapt such experiments to surface species, since the sample is by nature heterogeneous and the native sample usually has no solvent.

We have found experimental conditions under which it is possible to achieve DNP enhancements for surface species. To demonstrate the approach, we used organic−inorganic mesostructured materials obtained by a sol−gel process using a templating route.[9,10] Figure 1 shows a schematic view of this framework silica, in which the pore network possesses regular channels with diameters of ∼60 Å and the surface is functionalized with phenol (**I**) or imidazolium

(**II**) units [see the Supporting Information (SI) for details of the syntheses of these two materials].

The sample preparation is key to obtaining DNP enhancements in these materials. Here we carefully wetted the dry samples by incipient wetness impregnation with a solution of the organic radical species before filling the rotor with the wet solid. Notably, the sample volume did not increase significantly in this process, and after wetting it had the aspect of a translucent slush.

Figure 2 shows the DNP enhancements obtained in this way for the surface substrate **I** shown in Figure 1 using the pulse sequence in Figure 2a. Figure 2b shows the carbon-13 CP MAS spectrum obtained using the TEMPO radical (dissolved in a 90:10 D_2O/H_2O solution) as the polarization agent. Notably, with this solvent combination, ∼90% of the surface SiOH groups were replaced by SiOD. Spectra were obtained with and without microwave irradiation. With 30 mM TEMPO, a direct enhancement of $\varepsilon_H = 18$ was observed in the proton spectrum of the solvent (see the SI). The observed ^{13}C enhancement, $\varepsilon_C \geq 17$, demonstrates that the polarization can be efficiently transferred from the ^1H spins of the solvent to those of the surface organic functionality. The ^{13}C spectra of Figure 2b were obtained using only 2048 scans in less than 35 min. Experiments done with variable polarization-buildup times indicated that the optimal signal-to-noise ratio per unit time is obtained when the recycle delay is ∼1 s. Greater polarization per scan is obtained with longer delays, but the increased polarization does not compensate for the longer delay required in determining the optimum signal-to-noise ratio per unit time. Proton T_1 measurements (with microwaves on) clearly indicated a fast-relaxing component with a T_1 value of ∼900 ms that is related to the solvent protons and a second minor component with a much longer T_1 of ∼8 s that is possibly related to ^1H spins in the silica pores that are not in contact with the radical and thus do not benefit from paramagnetic relaxation enhancement[11] (these could be in the micropores, which are too small for TEMPO to enter). This made it possible to combine sizable DNP enhancements with unusually short recycle delays, opening the way to viable multiscan experiments. Notably, we observed DNP enhancements without adding glycerol[4] to the water solution to form a homogeneous glass. It is possible that disordered phases are formed directly upon freezing water in mesoporous materials.[12] This important point will be the subject of further investigations.

Figure 2c shows the ^1H DNP enhancement (ε_H) and the ^{13}C CP MAS peak integral as a function of TEMPO concentration. While ε_H increased with the radical concentration for all concentrations measured here, the ^{13}C spectrum reached a maximum enhancement at ∼30 mM TEMPO. Higher radical concentrations provoked increased paramagnetic relaxation of both the ^1H and ^{13}C spins,[4a,6] reducing the efficiency of CP transfer to the species on the silica surface. Higher radical concentrations also led to broadening in the ^{13}C spectrum.[4a] Broadening was minor at the optimum carbon-13 conditions found here (the 5−8 ppm linewidths observed here are typical for these kinds of materials).

Griffin and co-workers have shown that the biradical TOTAPOL can produce larger DNP enhancements than single radicals because of a more efficient transfer mechanism.[13,6] Indeed, when we used TOTAPOL as the source of polarization instead of TEMPO, we found that merely 25 mM TOTAPOL yielded $\varepsilon_H = 25$. The enhancement was even higher in the ^{13}C CP MAS spectrum, being a factor of 3.2 greater than with 30 mM TEMPO, yielding an estimated ^{13}C enhancement of $\varepsilon_C \geq 56$ (carbon-13 enhancements were estimated as described in the SI). Obtaining a carbon-13 spectrum with the same signal-to-noise ratio without DNP would take at least 70 days!
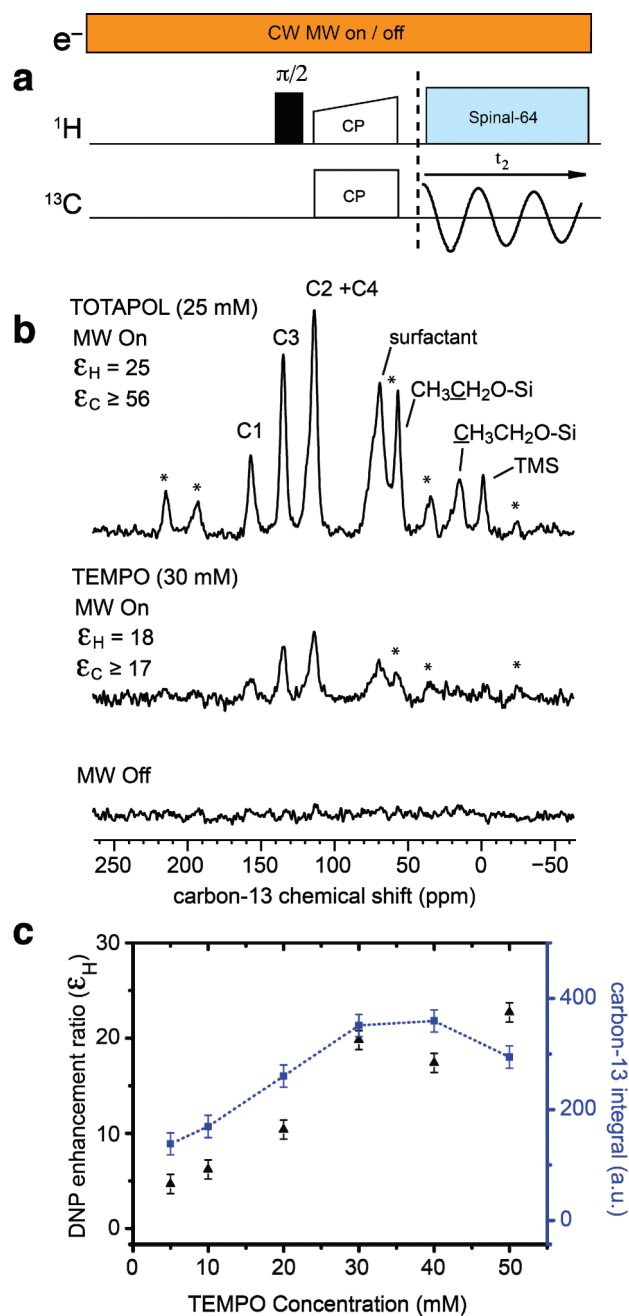
Figure 2. (a) Pulse sequence used for 1D CP MAS NMR spectroscopy. The microwave (MW) irradiation was switched on or off continuously. (b) Carbon-13 CP MAS spectra of **I** with (top and middle) and without (bottom) MW irradiation at 263 GHz to induce DNP. All of the spectra were recorded using 2048 scans with an interval of 1 s between scans. The figures compare the best enhancements observed using TEMPO and TOTAPOL radicals ($T \approx 105$ K, $B_0 = 9.4$ T, $\omega_H/2\pi = 400$ MHz, $\omega_C/2\pi = 100$ MHz, $\omega_{rot}/2\pi = 8.0$ kHz). It should be noted that significant DNP enhancement of the alkyl moiety of the surface ethoxy groups was also observed. (c) Experimental ^1H DNP enhancement (ε_H, black ▲) and integrals of the ^{13}C peak at 115 ppm (blue ■) as a function of the TEMPO concentration.

In order to extend the method to systems that may be sensitive to water, we investigated the use of aprotic solvents. When **I** wetted with a solution of 30 mM TEMPO in 90:10 toluene-d_8/toluene was used, the enhancement was lower than in water but still sizable ($\varepsilon_H \approx \varepsilon_C = 10$). Further experiments would be required to fully optimize the solvent systems, with room for improvement for both aqueous and nonaqueous solvents.
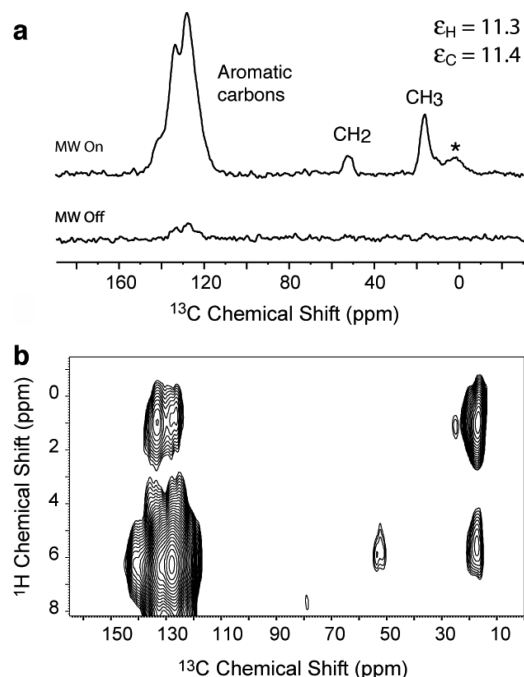
Figure 3. (a) Carbon-13 CP MAS spectra of **II** with (top) and without (bottom) MW irradiation at 263 GHz to induce DNP. All of the spectra were recorded using 2048 scans with an interval of 1.5 s between scans. The sample was wetted with 30 mM TEMPO in 90:10 D_2O/H_2O, $T \approx 105$ K, $B_0 = 9.4$ T, $\omega_H/2\pi = 400$ MHz, $\omega_C/2\pi = 100$ MHz, $\omega_{rot}/2\pi = 12.5$ kHz. The star indicates a spinning sideband. (b) Contour plot of a two-dimensional $^1H-^{13}C$ spectrum of **II** recorded with DNP using MW irradiation at 263 GHz. A total of 72 t_1 increments of 64 μs with 128 scans each were recorded. The overall acquisition times in t_1 and t_2 were 2.3 and 20 ms, respectively. The cross-polarization contact time was 1 ms, and the polarization-buildup interval was 1.5 s. The total experiment time was 3.8 h. SPINAL-64[14] heteronuclear decoupling was applied during t_2 ($\omega_1/2\pi = 80$ kHz, $\tau_c = 6$ μs). During t_1, eDUMBO-1$_{22}$[15] homonuclear decoupling was applied with an rf amplitude of $\omega_1^H/2\pi = 100$ kHz. Quadrature detection was achieved using the States-TPPI scheme[16] by incrementing the phase of the ^1H spin-lock pulse of the CP step. A scaling factor of 0.56 was applied to correct the ^1H chemical shift scale.[15]

The surface sensitivity enhancements obtained using DNP here open the way to the broad use of multidimensional correlation spectroscopy. Clearly, such spectra are required for detailed characterization of surface species, but they are not feasible without DNP in the systems considered here. Figure 3b shows a contour plot of the 2D $^1H-^{13}C$ correlation spectra acquired on the more complex imidazolium species **II** (Figure 1). The DNP enhancement was obtained here using a sample wetted with 30 mM TEMPO in 90:10 D_2O/H_2O (it should be noted that the spectrum was obtained with a sample spinning frequency of $\omega_{rot}/2\pi = 12.5$ kHz, rather than 8 kHz as used in Figure 2, which may explain the slightly lower enhancement factor). This spectrum was acquired using 128 scans for each of 72 t_1 increments, with a 1.5 s polarization-buildup delay, yielding a total experimental time of less than 4 h. It allows the detailed characterization of the material (including the assignment of the methylene resonances at 50 ppm). Acquisition of this kind of spectrum at natural isotopic abundance is inconceivable without polarization enhancement.

In conclusion, we have shown that surface enhanced NMR spectra can be obtained using DNP. Polarization is transferred from the protons of the solvent to the rare nuclei (here carbon-13 at natural isotopic abundance) at the surface, yielding at least a 50-fold signal enhancement. The implications of this new method for a broad range of surface science problems are enormous. This approach is in principle general and could be applied even to the investigation of adsorbed substrates or, by finding appropriate experimental conditions (solvent, radical concentration, etc.), to the investigation of surface catalytic processes.

Supporting Information Available: Sample preparation, experimental methods, and proton NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Blanc, F.; Copéret, C.; Lesage, A.; Emsley, L. *Chem. Soc. Rev.* **2008**, *37*, 518. (b) Avenier, P.; Taoufik, M.; Lesage, A.; Baudouin, A.; Solans-Monfort, X.; De Mallmann, A.; Veyre, L.; Basset, J. M.; Eisenstein, O.; Emsley, L.; Quadrelli, E. A. *Science* **2007**, *317*, 1056.

(2) (a) Carver, T. P.; Slichter, C. P. *Phys. Rev.* **1953**, *92*, 212. (b) Carver, T. P.; Slichter, C. P. *Phys. Rev.* **1956**, *102*, 975. (c) Slichter, C. P. *Phys. Chem. Chem. Phys.* **2010**, *12*, 5741.

(3) (a) Becerra, L. R.; Gerfen, G. J.; Temkin, R. J.; Singel, D. J.; Griffin, R. G. *Phys. Rev. Lett.* **1993**, *71*, 3561. (b) Rosay, M.; Tometich, L.; Pawsey, S.; Bader, R.; Schauwecker, R.; Blank, M.; Borchard, P. M.; Cauffman, S. R.; Felch, K. L.; Weber, R. T.; Temkin, R. J.; Griffin, R. G.; Maas, W. E. *Phys. Chem. Chem. Phys.* **2010**, *12*, 5850.

(4) (a) Barnes, A. B.; De Paëpe, G.; van der Wel, P. C. A.; Hu, K.-N.; Joo, C.-G.; Bajaj, V. S.; Mak-Jurkauskas, M. L.; Sirigiri, J. R.; Herzfeld, J.; Temkin, R. J.; Griffin, R. G. *Appl. Magn. Reson.* **2008**, *34*, 237. (b) Maly, T.; Debelouchina, G. T.; Bajaj, V. S.; Hu, K.-N.; Joo, C.-G.; Mak-Jurkauskas, M. L.; Sirigiri, J. R.; van der Wel, P. C. A.; Herzfeld, J.; Temkin, R. J.; Griffin, R. G. *J. Chem. Phys.* **2008**, *128*, 052211. (c) Debelouchina, G. T.; Bayro, M. J.; van der Wel, P. C. A.; Caporini, M. A.; Barnes, A. B.; Rosay, M.; Maas, W. E.; Griffin, R. G. *Phys. Chem. Chem. Phys.* **2010**, *12*, 5911.

(5) (a) Gerfen, G. J.; Becerra, L. R.; Hall, D. A.; Griffin, R. G.; Temkin, R. J.; Singel, D. J. *J. Chem. Phys.* **1995**, *102*, 9494. (b) Hall, D. A.; Maus, D. C.; Gerfen, G. J.; Inati, S. J.; Becerra, L. R.; Dahlquist, F. W.; Griffin, R. G. *Science* **1997**, *276*, 930.

(6) Song, C.; Hu, K.-N.; Joo, C.-G.; Swager, T. M.; Griffin, R. G. *J. Am. Chem. Soc.* **2006**, *128*, 11385.

(7) Vitzthum, V.; Caporini, M. A.; Bodenhausen, G. *J. Magn. Reson.* **2010**, *205*, 177.

(8) (a) Maly, T.; Miller, A.-F.; Griffin, R. G. *ChemPhysChem* **2010**, *11*, 999. (b) Maly, T.; Andreas, L. B.; Smith, A. A.; Griffin, R. G. *Phys. Chem. Chem. Phys.* **2010**, *12*, 5872.

(9) (a) Burkett, S. L.; Sims, S. D.; Mann, S. *Chem. Commun.* **1996**, 1367. (b) Macquarrie, D. J. *Chem. Commun.* **1996**, 1961. (c) Margolese, D.; Melero, J. A.; Christiansen, S. C.; Chmelka, B. F.; Stucky, G. D. *Chem. Mater.* **2000**, *12*, 2448. (d) Mercier, L.; Pinnavaia, T. J. *Chem. Mater.* **2000**, *12*, 188. (e) Corriu, R. J. P.; Datas, L.; Guari, Y.; Mehdi, A.; Reyé, C.; Thieuleux, C. *Chem. Commun.* **2001**, 763. (f) Maishal, T. K.; Alauzun, J.; Basset, J.-M.; Copéret, C.; Corriu, R. J. P.; Jeanneau, E.; Mehdi, A.; Reyé, C.; Veyre, L.; Thieuleux, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 8654.

(10) (a) Corriu, R. J. P.; Mehdi, A.; Reyé, C. *J. Mater. Chem.* **2005**, *15*, 4285. (b) Hoffmann, F.; Cornelius, M.; Morell, J.; Fröba, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 3216.

(11) van der Wel, P. C. A.; Hu, K.-N.; Lewandowski, J.; Griffin, R. G. *J. Am. Chem. Soc.* **2006**, *128*, 10840.

(12) (a) Hansen, E. W.; Stöcker, M.; Schmidt, R. *J. Phys. Chem.* **1996**, *100*, 2195. (b) Akporiaye, D.; Hansen, E. W.; Schmidt, R.; Stöcker, M. *J. Phys. Chem.* **1994**, *98*, 1926. (c) Hansen, E. W.; Schmidt, R.; Stöcker, M.; Akporiaye, D. *J. Phys. Chem.* **1995**, *99*, 4148.

(13) Hu, K.-N.; Song, C.; Yu, H.-h.; Swager, T. M.; Griffin, R. G. *J. Chem. Phys.* **2008**, *128*, 052302.

(14) Fung, B. M.; Khitrin, A. K.; Ermolaev, K. *J. Magn. Reson.* **2000**, *142*, 97.

(15) Elena, B.; De Paëpe, G.; Emsley, L. *Chem. Phys. Lett.* **2004**, *398*, 532.

(16) Marion, D.; Ikura, M.; Tschudin, R.; Bax, A. *J. Magn. Reson.* **1989**, *85*, 393.

JA104771Z