



Tailored Polarizing Hybrid Solids with Nitroxide Radicals Localized in Mesostructured Silica Walls

Daniel Silverio, Henri A van Kalkeren, Ta-Chung Ong, Mathieu Baudin, Maxim Yulikov, Laurent Veyre, Pierrick Berruyer, Sachin Chaudhari, David Gajan, David Baudouin, et al.

► To cite this version:

Daniel Silverio, Henri A van Kalkeren, Ta-Chung Ong, Mathieu Baudin, Maxim Yulikov, et al.. Tailored Polarizing Hybrid Solids with Nitroxide Radicals Localized in Mesostructured Silica Walls. *Helvetica Chimica Acta*, 2017, 100 (6), pp.e1700101. 10.1002/hlca.201700101 . hal-01838479

HAL Id: hal-01838479

<https://hal.science/hal-01838479>

Submitted on 13 Jul 2018

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Tailored Polarizing Hybrid Solids with Nitroxide Radicals Localized in Mesostructured Silica Walls.

Daniel L. Silverio, Henri A. van Kalkeren, Ta-Chung Ong, Mathieu Baudin, Maxim Yulikov, Laurent Veyre, Pierrick Berruyer, Sachin Chaudhari, David Gajan, David Baudouin, Matthieu Cavaillès, Basile Vuichoud, Aurélien Bornet, Gunnar Jeschke, Geoffrey Bodenhausen, Anne Lesage, Lyndon Emsley, Sami Jannin, Chloé Thieuleux,* and Christophe Copéret*

Abstract: Hyperpolarization by dynamic nuclear polarization relies on the microwave irradiation of paramagnetic radicals dispersed in molecular glasses to enhance the nuclear magnetic resonance (NMR) signals of target molecules. However, magnetic or chemical interactions between the radicals and the target molecules can lead to attenuation of the NMR signal through paramagnetic quenching and/or radical decomposition. Here we describe polarizing materials incorporating nitroxide radicals *within the walls* of the solids to minimize interactions between the radicals and the solute. These materials can hyperpolarize pure pyruvic acid, a particularly important substrate of clinical interest, while nitroxide radicals cannot be used, even when incorporated in the pores of silica, because of reactions between pyruvic acid and the radicals. The properties of these materials can be engineered by tuning the composition of the wall by introducing organic functionalities.

Introduction

Dynamic nuclear polarization (DNP) provides a way to dramatically enhance NMR signals, and as a result has opened new frontiers in the characterization of a broad range of molecules (e.g., biomolecules, metabolites, surface species, complex materials, etc.).^[1] In a DNP experiment, the Boltzmann polarization of electron spins of unpaired electrons (e.g., stable radicals such as nitroxides or trityls) is partially transferred to the nuclear spins of the target molecules.^[2] This polarization transfer

leads to NMR signal enhancement (ϵ) and thereby a reduction of the acquisition time. Proton polarization can propagate throughout the entire frozen sample via spin diffusion, and cross polarization (CP) from protons can be used to obtain sensitivity-enhanced NMR signals of heteronuclei (e.g., ^{13}C , ^{29}Si , etc.).

DNP is increasingly used to enhance the sensitivity of solid-state NMR spectra at cryogenic temperatures (100 K) under magic angle spinning (MAS-DNP) conditions,^[2b] or for hyperpolarizing metabolites at 1.2 K that are rapidly dissolved and transferred to solution NMR spectrometers or MRI scanners (dissolution-DNP).^[3] Biologically relevant hyperpolarized analytes or metabolites can be administered to cell cultures or living animals to reveal metabolic activity allowing, ^[3b, 3d, 4] *inter alia*, a reliable diagnosis of prostate cancer.^[5] However, this kind of DNP experiment suffers from several limitations. Notably, the radicals must be soluble in a solvent that forms a glass at cryogenic temperature to ensure their homogeneous distribution. The radicals should not be in close contact with the analyte, as this can lead to signal quenching or, worse, reactions with the analyte.^[2, 6] In dissolution DNP (d-DNP) experiments, rapid removal of the radicals from the hyperpolarized solution is desirable both for the sake of biocompatibility and to avoid rapid nuclear relaxation leading to losses of signal enhancement.^[7]

Some attempts to alleviate these problems have recently been made by sequestering the radicals in micelles^[8] or cryptands,^[9] hiding the substrate in pores that are too small for the radical to enter,^[10] or shielding the radicals in dendritic structures.^[11] However, while they can be efficient when applicable, none of these solutions are general, and all have drawbacks.

Mesostructured silica materials^[12] have emerged as an alternative strategy to alleviate these limitations. For instance, the use of mesoporous silica materials containing radicals that are regularly distributed at their pore surface obviates the use of a glassing agent to polarize an analyte in pure water because the porous structure prevents solvent crystallization and aggregation of radicals (Figure 1).^[13] Another example is the use of mesoporous silica in MAS DNP to avoid segregation between radicals and colloids upon cooling.^[14] However, in both systems the radical remains in close contact with the analyte and in the second case the approach requires the use of a solvent in which the radical is soluble. Recent work has also shown that radicals could be introduced within the silica matrix via a sol-gel process using a bis-silylated organic moiety that can generate radicals, thus providing a polarizing matrix for MAS DNP, though the localization of the radicals in the silica matrix and their shielding from the analyte were not investigated.^[15]

[*] Dr. D. L. Silverio, Dr. T. C. Ong, Dr. M. Yulikov, Prof. G. Jeschke, Prof. C. Copéret
Dept. of Chemistry and Applied Biosciences, ETH Zürich
Vladimir-Prelog-Weg 1–5, 8093 Zürich (Switzerland)
E-mail: ccoperet@ethz.ch

[*] Dr. H. A. van Kalkeren, Dr. D. Baudouin, Dr. M. Cavaillès, L. Veyre, Dr. C. Thieuleux
Université de Lyon, Institut de Chimie de Lyon, UMR C2P2 CNRS, Université de Lyon 1-ESPE Lyon
43 Bd du 11 Novembre 1918, 69616 Villeurbanne (France)

P. Berruyer, Dr. S. Chaudhari, Dr. D. Gajan, Dr. A. Lesage, Dr. S. Jannin
Université de Lyon, Institut des Sciences Analytiques
CRMN CNRS-ENS Lyon-UCBL, 69100 Villeurbanne (France)

Dr. M. Baudin, Dr. S. Jannin, B. Vuichoud, A. Bornet, Prof. G. Bodenhausen, Prof. L. Emsley
Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne (EPFL), 1015 Lausanne (Switzerland)

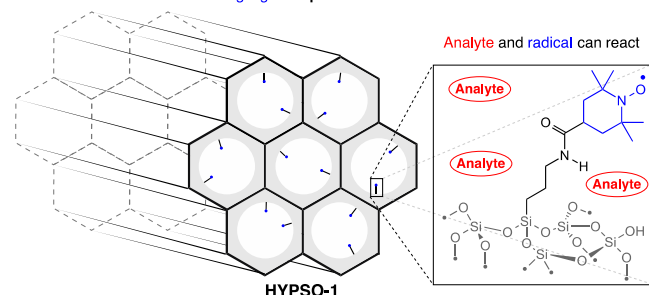
Dr. M. Baudin, Prof. G. Bodenhausen
Département de Chimie, Ecole Normale Supérieure, PSL Research University, UPMC Univ Paris 06, CNRS, Laboratoire des Biomolécules (LBM), 24 rue Lhomond, 75005 Paris (France)

Dr. M. Baudin, Prof. G. Bodenhausen
Sorbonne Universités, UPMC Univ Paris 06, Ecole Normale Supérieure, CNRS, Laboratoire des Biomolécules (LBM), Paris (France)

Supporting information for this article is given via a link at the end of the document.

We reasoned that hybrid mesostructured materials containing radicals embedded in the silica walls (Figure 1 bottom

I. Previous disclosure- Polarizing Agent in pore of material



II. This report- Polarizing agent in wall of material

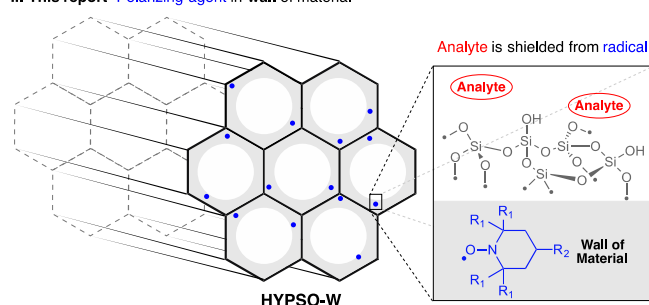


Figure 1. Comparison of materials with radicals in the pores, **HYP SO-1**, with materials with radicals in the walls, **HYP SO-W**.

and Figure 2a) [12, 16] could provide a powerful approach to isolate the radical from the analyte, avoiding possible reactions and signal bleaching, while still removing the restriction to specific solvents or diluting the analyte in a co-solvent mixture. We report here the development of a HYP SO material containing radicals in the walls of the material (**HYP SO-W**) through a template approach and demonstrate its efficiency for MAS-DNP and d-DNP experiments. In particular, we show how engineering the wall structure and its composition by introducing organic functionalities significantly improve the polarization properties.

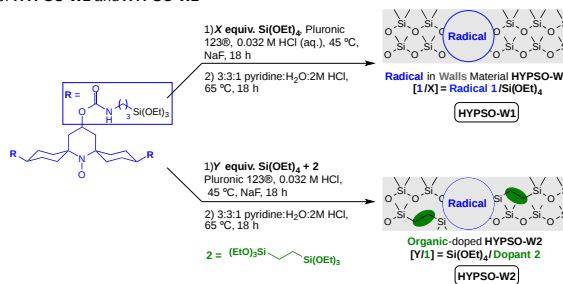
First, using **1**, a tris-silylated precursor containing a nitroxide radical (see ESI), and various amount (X) of $\text{Si}(\text{OEt})_4$, the corresponding HYP SO material (**HYP SO-W1** [$1/X$]) was prepared by a sol-gel process using Pluronic 123® (P123) and NaF as structure-directing agent and catalyst, respectively.^[17] Optimal removal of P123 was achieved by washing with pyridine·HCl.^[18] Using these protocols, a broad range of radical concentrations from 0.022 to 0.11 mmol/g (as determined by EPR; 49 to 58% yield) could be introduced into the silica matrix. We also synthesized materials **HYP SO-W2** that contain bis(triethoxysilyl)ethane **2** (Figure 2a, bottom), as an organic dopant to help polarization transfer via ^1H - ^1H spin diffusion from the radicals to the pores.^[21] **HYP SO-W2** [$Y/1$] materials were all synthesized with the same 1/200 ratio of **1** to Si, but with varying content of the organic dopant **2** as defined by $[Y/1] = [\text{Si}(\text{OEt})_4/2]$.

All materials **HYP SO-W1** and **HYP SO-W2**

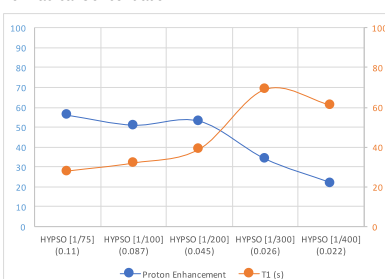
have large pore volumes (0.7 to 1.2 cm^3/g), high surface areas (673 to 1066 m^2/g), narrow pore size distributions (5 to 9 nm) and large wall thicknesses (3 to 6 nm). These properties allow them to enclose the radical **1** (molecular diameter of ca. 2 nm) and to polarize a large volume of analyte. The SA-XRD diffraction patterns complemented by Transmission Electron Microscopy (TEM) are consistent with an ordered hexagonal structure of the porous network for all materials except **HYP SO-W2** [2/1], where the pattern is more indicative of a “wormlike” structure. The radical distribution was evaluated by EPR: decreasing the radical concentration leads to a narrowing of the EPR linewidth (13.1 G for **HYP SO-W1** [1/75] to 12.3 G for **HYP SO-W1** [1/400]) and an increase in the mean electron inversion recovery time ($\langle T_{1e} \rangle$) from 32 μs for **HYP SO-W1** [1/75] to 210 μs for **HYP SO-W1** [1/400]. Both trends agree with an increasing average radical-radical distance with decreasing concentration.^[13a, 22] For **HYP SO-W2**, $\langle T_{1e} \rangle$ and line width are essentially unaffected by varying the concentration of bis-siloxyethane **2** (see ESI).

The ^1H enhancement (ϵ) of the solvent peak in MAS-DNP for materials impregnated with a 4:1 mixture of $\text{D}_2\text{O}:\text{H}_2\text{O}$ did not change significantly with decreasing radical concentration from 0.11 to 0.045 mmol/g, staying at ca. 50-55 (Figure 2b), in contrast to 25 for **HYP SO-1** under the same conditions. Going to an even lower concentration, the enhancement drops but still remains at reasonable levels, i.e., $\epsilon = 34$ for **HYP SO-W1** [1/300] and 22 for **HYP SO-W1** [1/400]. Since the enhancements observed with **HYP SO-W1** [1/75] to [1/200] are approximately the same, we chose **HYP SO-W1** [1/200] as the optimal material, since lower concentrations of radicals should lead to a lower quenching factors.^[23] Compared with **HYP SO-W1** [1/200] (Figure 2c), all **HYP SO-W2** materials afforded approximately the same levels of enhancement, with **HYP SO-W2** [25/1] giving

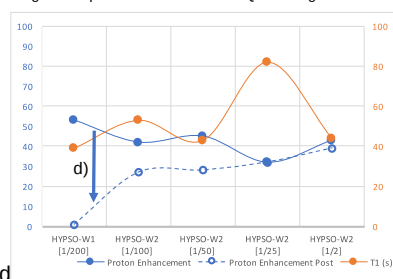
a) Synthesis of **HYP SO-W1** and **HYP SO-W2**



b) Proton Enhancement and T_1 in **HYP SO-W1**: Effect of Radical Concentration



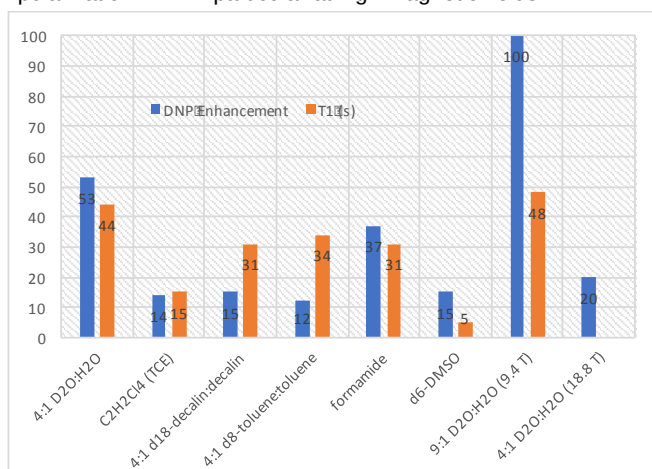
c) Proton Enhancement and T_1 in **HYP SO-W2**: Effect of Organic Dopant Concentration and Quenching



in the walls. MAS DNP performance (Proton enhancement (blue circles) and T_1 (orange circle) of b) **HYP SO-W1**, c) **HYP SO-W2** and d) **HYP SO-W2** and **HYP SO-W1** after treatment with ascorbic acid. All enhancements are determined at 600 MHz proton frequency (14.1 T) and ~100 K with 10 kHz MAS using 4:1 $\text{D}_2\text{O}:\text{H}_2\text{O}$ as a solvent. T_1 determined by a saturation recovery experiment. See ESI for details.

somewhat lower enhancements due to its lower concentration in radicals (See ESI for details).

Notably **HYPISO-W1 [1/200]** yields effective MAS-DNP enhancements in solvents in which traditional polarizing agents like TEKPol^[24] and AMUPol^[25] are poorly soluble, as well as solvents that are poor at forming glasses (Figure 3), properties that, as mentioned above, are generally detrimental for DNP. Examination of the enhancement afforded by **HYPISO-W1 [1/200]** for a mixture of D₂O:H₂O at different magnetic fields reveals an enhancement $\epsilon = 100$ at 9.4 T (400 MHz proton frequency). An enhancement $\epsilon = 20$ is obtained at 18.8 T (800 MHz proton frequency, entries 7 and 8), an expected decrease with increasing field strength for DNP processes dominated by the cross effect.^[2a, 26] Overall, this material is nearly twice as effective as state-of-the-art radical-containing materials for polarization^[13, 15] in particular at high magnetic fields.^[26]



To probe how well the radicals in the **HYPISO-W** materials are shielded from the analytes, we first treated **HYPISO-W1 [1/200]** with a solution of ascorbic acid (known to reduce even sterically hindered nitroxide radicals),^[27] and determined the resulting radical loading by EPR (Figure S1a). The ascorbic acid treatment resulted in only a 36% decrease of radical content.

Figure 3. MAS-DNP enhancement (ϵ) in various solvents and at various magnetic field strengths with **HYPISO-W1 [1/200]**. Enhancements determined at given magnetic field at ~ 100 K. T_1 determined by saturation recovery. At 9.4 T, D₂O : H₂O = 4:1 gave a lower ¹H enhancement of 71 in this case, although there was no difference in enhancement between these two solvent ratios at 14.1 T.

For comparison, this treatment was applied to **HYPISO-1**, a material with comparable physical features but with the radical localized at the pore surface, resulting in complete destruction of the radicals according to EPR (Figure S1b). However, both ascorbic acid-treated materials gave essentially no enhancement in the DNP experiment (Figure S1a). The poor enhancement in **HYPISO-W1** treated with ascorbic acid indicates that the remaining radicals are probably too deeply embedded to contribute to the polarization of the molecules present in the pores.

We therefore examined the polarization properties of **HYPISO-W1** and the organic doped **HYPISO-W2** materials (Figure 2d – opened circles). First, the decrease in radical content upon reaction with ascorbic acid is lower for **HYPISO-W2**

than for **HYPISO-W1 [1/200]** (decrease of 22% vs. 36%). Second, and more importantly, these treated **HYPISO-W2 [100/1]** materials still afford a ¹H enhancement of 27 at 600 MHz, a mere 36% decrease with respect to its untreated form. When increasing the ratio of 2/Si(OEt)₄ to 1/25, no loss of enhancement is observed after treatment. Overall the introduction of organic functionalities in the wall clearly helps to protect the radicals and to transfer the polarization from the radicals to the solvent molecules in the pores.

With these promising results, the **HYPISO-W** materials were also tested in dissolution DNP using pyruvic acid as a prototypical metabolite,^[3b, 3d, 4, 28] which is known to reduce nitroxide radicals, so that previous nitroxide-containing materials failed to give rise to any polarization in d-DNP.

Dissolution-DNP experiments were carried out in a polarizer^[29] operating at 1.2 K and 6.7 T equipped for cross polarization at low temperatures.^[30] The optimal material is **HYPISO-W2 [25/1]**, which affords a polarization $P(^1\text{H}) = 39.5\%$ for neat pyruvic acid with $\tau_{\text{DNP}}(^1\text{H}) = 20$ minutes, resulting in $P(^{13}\text{C}) \sim 17\%$ in about 60 minutes after ascorbic acid treatment. By comparison, a trityl-containing material, compatible with neat pyruvic acid, requires a much longer polarization time of 105 minutes.^[13b] The corresponding **HYPISO-W1 [1/200]**, which lacks the ethyl fragments in its walls, affords a polarization of only $P(^1\text{H}) = 22.4\%$ with $\tau_{\text{DNP}}(^1\text{H}) = 13$ minutes. While ethyl groups are not mandatory to polarize the frozen solutions in the pores, their presence is very beneficial as it significantly boosts the polarization rates and improves the overall maximum polarization attained.

In conclusion, the introduction of electron polarization sources in the walls of mesostructured materials, dubbed **HYPISO-W** yield the highest enhancements in MAS-DNP for HYPISO materials, and are amenable to performing DNP in a wide variety of solvents. Importantly, **HYPISO-W** materials enable polarization of substrates in solution that would otherwise react with the nitroxides in conventional DNP formulations, e.g. neat pyruvic acid, combining the fast polarization buildup of nitroxide radicals and the stability of embedded nitroxide radicals. One critical aspect is the engineering of the structure of the material via incorporation of organic functionalities in the wall allowing more effective polarization transfer to the analyte.

Acknowledgements

We acknowledge the SNF for the 600 MHz DNP spectrometer (206021_150710). This work was supported by the Swiss National Science Foundation (SNF), ETH Zürich, the Ecole Polytechnique Fédérale de Lausanne, Bruker BioSpin Switzerland AG, ERC Advanced Grant No. 320860 and EQUIPEX contract ANR-10-EQPX-47-01, and the ERC Advanced Grant "Dilute para-water". Mr. Wei-Chih Liao, Mr. Tigran Margossian, Ms. Laura Piveteau, and Dr. Martin Schwarzwälder are acknowledged for many useful discussions.

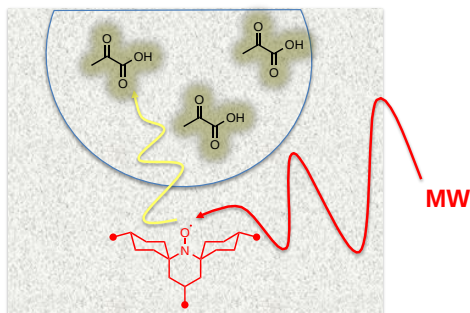
Author Contributions: D.L.S., C.C., C.T., S.J., T.C.O., and L.E. prepared the manuscript. D.L.S. developed and synthesized the HYPISO materials. H.A.v.K. developed the synthesis of radical **1**. T.C.O., D.L.S., P.B., S.C., D.G., A.L., L.E. developed and carried out the MAS-DNP experiments. M. B., D.B., M.C., carried

out the d-DNP experiments. D.L.S., M.Y., L.V., and G.J. characterized the materials. S.J. and A.B. developed the d-DNP spectrometers. A.L. C.C., C.T., D.B., G.B., H.A.v.K., L.E. and S.J. conceived the project.

Keywords: magic angle spinning dynamic nuclear polarization • mesostructured silica • dissolution dynamic nuclear polarization • hybrid organic-inorganic materials

- [1] a) B. A. Barnes, G. De Paëpe, A. P. C. van der Wel, K. N. Hu, C. G. Joo, S. V. Bajaj, L. M. Mak-Jurkauskas, R. J. Sirigiri, J. Herzfeld, J. R. Temkin, G. R. Griffin, *Appl. Magn. Reson.* **2008**, *34*, 237–263; b) M. Lelli, D. Gajan, A. Lesage, M. A. Caporini, V. Vitzthum, P. Miéville, F. Héroguel, F. Rascón, A. Roussey, C. Thieuleux, M. Boualleg, L. Veyre, G. Bodenhausen, C. Copéret, L. Emsley, *J. Am. Chem. Soc.* **2011**, *133*, 2104–2107.
- [2] a) T. Maly, G. T. Debelouchina, V. S. Bajaj, K.-N. Hu, C.-G. Joo, M. L. Mak-Jurkauskas, J. R. Sirigiri, P. C. A. van der Wel, J. Herzfeld, R. J. Temkin, R. G. Griffin, *J. Chem. Phys.* **2008**, *128*, 052211; b) Q. Z. Ni, E. Daviso, T. V. Can, E. Markhasin, S. K. Jawa, T. M. Swager, R. J. Temkin, J. Herzfeld, R. G. Griffin, *Acc. Chem. Res.* **2013**, *46*, 1933–1941.
- [3] a) J. H. Ardenkjaer-Larsen, B. Fridlund, A. Gram, G. Hansson, L. Hansson, M. H. Lerche, R. Servin, M. Thaning, K. Golman, *Proc. Natl. Acad. Sci. U. S. A.* **2003**, *100*, 10158–10163; b) R. E. Hurd, Y.-F. Yen, A. Chen, J. H. Ardenkjaer-Larsen, *J. Magn. Reson. Im.* **2012**, *36*, 1314–1328; c) A. J. Rossini, A. Zagdoun, M. Lelli, A. Lesage, C. Copéret, L. Emsley, *Acc. Chem. Res.* **2013**, *46*, 1942–1951; d) J. H. Ardenkjaer-Larsen, *J. Magn. Reson.* **2016**, *264*, 3–12.
- [4] F. A. Gallagher, M. I. Kettunen, K. M. Brindle, *Prog. Nucl. Magn. Reson. Spectrosc.* **2009**, *55*, 285–295.
- [5] a) S. J. Nelson, J. Kurhanewicz, D. B. Vigneron, P. E. Z. Larson, A. L. Harzstark, M. Ferrone, M. van Criekinge, J. W. Chang, R. Bok, I. Park, G. Reed, L. Carvajal, E. J. Small, P. Munster, V. K. Weinberg, J. H. Ardenkjaer-Larsen, A. P. Chen, R. E. Hurd, L.-I. Odegardstuen, F. J. Robb, J. Tropp, J. A. Murray, *Sci. Transl. Med.* **2013**, *5*, 198ra108; b) S. J. Nelson, J. Kurhanewicz, D. B. Vigneron, P. E. Z. Larson, A. L. Harzstark, M. Ferrone, M. van Criekinge, J. W. Chang, R. Bok, I. Park, G. Reed, L. Carvajal, E. J. Small, P. Munster, V. K. Weinberg, J. H. Ardenkjaer-Larsen, A. P. Chen, R. E. Hurd, L.-I. Odegardstuen, F. J. Robb, J. Tropp, J. A. Murray, *Sci. Transl. Med.* **2013**, *5*, 198ra108.
- [6] T.-C. Ong, M. L. Mak-Jurkauskas, J. J. Walsh, V. K. Michaelis, B. Corzilius, A. A. Smith, A. M. Clausen, J. C. Cheetham, T. M. Swager, R. G. Griffin, *J. Phys. Chem. B* **2013**, *117*, 3040–3046.
- [7] a) P. Miéville, S. Jannin, G. Bodenhausen, *J. Magn. Reson.* **2011**, *210*, 137–140; b) P. Miéville, P. Ahuja, R. Sarkar, S. Jannin, P. R. Vasos, S. Gerber-Lemaire, M. Mishkovsky, A. Comment, R. Gruetter, O. Ouari, P. Tordo, G. Bodenhausen, *Angew. Chem. Int. Ed.* **2010**, *49*, 6182–6185.
- [8] a) K. G. Valentine, G. Mathies, S. Bédard, N. V. Nucci, I. Dodevski, M. A. Stetz, T. V. Can, R. G. Griffin, A. J. Wand, *J. Am. Chem. Soc.* **2014**, *136*, 2800–2807; b) M. Lelli, A. J. Rossini, G. Casano, O. Ouari, P. Tordo, A. Lesage, L. Emsley, *Chem. Commun.* **2014**, *50*, 10198–10201.
- [9] J. Mao, D. Akhmetzyanov, O. Ouari, V. Denysenkov, B. Corzilius, J. Plackmeyer, P. Tordo, T. F. Prisner, C. Glaubitz, *J. Am. Chem. Soc.* **2013**, *135*, 19275–19281.
- [10] E. Pump, J. Viger-Gravel, E. Abou-Hamad, M. K. Samantaray, B. Hamzaoui, A. Gurinov, D. H. Anjum, D. Gajan, A. Lesage, A. Bendjeriou-Sedjerari, L. Emsley, J.-M. Basset, *Chem. Sci.* **2017**, DOI:10.1039/C1036SC02379G.
- [11] W.-C. Liao, T.-C. Ong, D. Gajan, F. Bernada, C. Sauvee, M. Yulikov, M. Pucino, R. Schowner, M. Schwarzwälder, M. R. Buchmeiser, G. Jeschke, P. Tordo, O. Ouari, A. Lesage, L. Emsley, C. Coperet, *Chem. Sci.* **2016**, DOI: 10.1039/C1036SC03139K.
- [12] a) R. J. P. Corriu, A. Mehdi, C. Reye, *J. Mater. Chem.* **2005**, *15*, 4285–4294; b) F. Hoffmann, M. Cornelius, J. Morell, M. Fröba, *Angew. Chem. Int. Ed.* **2006**, *45*, 3216–3251.
- [13] a) D. Gajan, M. Schwarzwälder, M. P. Conley, W. R. Grüning, A. J. Rossini, A. Zagdoun, M. Lelli, M. Yulikov, G. Jeschke, C. Sauvee, O. Ouari, P. Tordo, L. Veyre, A. Lesage, C. Thieuleux, L. Emsley, C. Copéret, *J. Am. Chem. Soc.* **2013**, *135*, 15459–15466; b) D. Gajan, A. Bornet, B. Vuichoud, J. Milani, R. Melzi, H. A. van Kalkeren, L. Veyre, C. Thieuleux, M. P. Conley, W. R. Grüning, M. Schwarzwälder, A. Lesage, C. Copéret, G. Bodenhausen, L. Emsley, S. Jannin, *Proc. Natl. Acad. Sci. U. S. A.* **2014**, *111*, 14693–14697; c) D. Baudouin, H. A. van Kalkeren, A. Bornet, B. Vuichoud, L. Veyre, M. Cavailles, M. Schwarzwälder, W. C. Liao, D. Gajan, G. Bodenhausen, L. Emsley, A. Lesage, S. Jannin, C. Coperet, C. Thieuleux, *Chem. Sci.* **2016**, DOI: 10.1039/C1036SC02055K; d) W. R. Grüning, H. Bieringer, M. Schwarzwälder, D. Gajan, A. Bornet, B. Vuichoud, J. Milani, D. Baudouin, L. Veyre, A. Lesage, S. Jannin, G. Bodenhausen, C. Thieuleux, C. Copéret, *Helv. Chim. Acta* **2016**, DOI: 10.1002/hlca.201600122.
- [14] L. Piveteau, T.-C. Ong, A. J. Rossini, L. Emsley, C. Copéret, M. V. Kovalenko, *J. Am. Chem. Soc.* **2015**, *137*, 13964–13971.
- [15] E. Besson, F. Ziarelli, E. Bloch, G. Gerbaud, S. Queyroy, S. Viel, S. Gastaldi, *Chem. Commun.* **2016**, *52*, 5531–5533.
- [16] a) G. Dubois, R. J. P. Corriu, C. Reye, S. Brandes, F. Denat, R. Guillard, *Chem. Commun.* **1999**, 2283–2284; b) O. Olkhoviyk, M. Jaroniec, *J. Am. Chem. Soc.* **2005**, *127*, 60–61.
- [17] a) P. Schmidt-Winkel, P. Yang, D. I. Margolese, B. F. Chmelka, G. D. Stucky, *Adv. Mater.* **1999**, *11*, 303–307; b) R. J. P. Corriu, A. Mehdi, C. Reye, C. Thieuleux, *Chem. Commun.* **2002**, 1382–1383.
- [18] A. Boullanger, J. Alauzun, A. Mehdi, C. Reye, R. J. P. Corriu, *New J. Chem.* **2010**, *34*, 738–743.
- [19] D. Zhao, J. Feng, Q. Huo, N. Melosh, G. H. Fredrickson, B. F. Chmelka, G. D. Stucky, *Science* **1998**, *279*, 548–552.
- [20] Y. Ma, C. Loynes, P. Price, V. Chechik, *Org. Biomol. Chem.* **2011**, *9*, 5573–5578.
- [21] a) P. C. A. van der Wel, K.-N. Hu, J. Lewandowski, R. G. Griffin, *J. Am. Chem. Soc.* **2006**, *128*, 10840–10846; b) A. J. Rossini, A. Zagdoun, F. Hegner, M. Schwarzwälder, D. Gajan, C. Copéret, A. Lesage, L. Emsley, *J. Am. Chem. Soc.* **2012**, *134*, 16899–16908.
- [22] K.-N. Hu, H.-h. Yu, T. M. Swager, R. G. Griffin, *J. Am. Chem. Soc.* **2004**, *126*, 10844–10845.
- [23] A. J. Rossini, A. Zagdoun, M. Lelli, D. Gajan, F. Rascon, M. Rosay, W. E. Maas, C. Coperet, A. Lesage, L. Emsley, *Chem. Sci.* **2012**, *3*, 108–115.
- [24] A. Zagdoun, G. Casano, O. Ouari, M. Schwarzwälder, A. J. Rossini, F. Aussenac, M. Yulikov, G. Jeschke, C. Copéret, A. Lesage, P. Tordo, L. Emsley, *J. Am. Chem. Soc.* **2013**, *135*, 12790–12797.
- [25] C. Sauvee, M. Rosay, G. Casano, F. Aussenac, R. T. Weber, O. Ouari, P. Tordo, *Angew. Chem. Int. Ed.* **2013**, *52*, 10858–10861.
- [26] G. Mathies, M. A. Caporini, V. K. Michaelis, Y. Liu, K.-N. Hu, D. Mance, J. L. Zweier, M. Rosay, M. Baldus, R. G. Griffin, *Angew. Chem. Int. Ed.* **2015**, *54*, 11770–11774.
- [27] J. T. Paletta, M. Pink, B. Foley, S. Rajca, A. Rajca, *Org. Lett.* **2012**, *14*, 5322–5325.
- [28] S. E. Day, M. I. Kettunen, F. A. Gallagher, D. E. Hu, M. Lerche, J. Wolber, K. Golman, J. H. Ardenkjaer-Larsen, K. M. Brindle, *Nat. Med.* **2007**, *13*, 1382–1387.
- [29] A. Comment, B. van den Brandt, K. Uffmann, F. Kurdzesau, S. Jannin, J. A. Konter, P. Hautle, W. T. Wenckebach, R. Gruetter, J. J. van der Klink, *Concepts Magn. Reson. B* **2007**, *31B*, 255–269.
- [30] a) S. Jannin, A. Bornet, S. Colombo, G. Bodenhausen, *Chem. Phys. Lett.* **2011**, *517*, 234–236; b) S. Jannin, A. Bornet, R. Melzi, G. Bodenhausen, *Chem. Phys. Lett.* **2012**, *549*, 99–102; c) A. Bornet, R. Melzi, A. J. Perez Linde, P. Hautle, B. van den Brandt, S. Jannin, G. Bodenhausen, *J. Phys. Chem. Lett.* **2013**, *4*, 111–114.

Walls can talk. Hybrid materials containing nitroxide radicals embedded in the walls can polarize analytes efficiently while being protected by inorganic silica, thus leading to efficient polarization matrices for solid state and dissolution DNP.



D. L. Silverio, H. A. van Kalker, T.-C. Ong, M. Baudin, M. Yulikov, L. Veyre, P. Berruyer, S. Chaudhari, D. Gajan, D. Baudouin, M. Cavaillès, B. Vuichoud, A. Bornet, G. Jeschke, G. Bodenhausen, A. Lesage, L. Emsley, S. Jannin, C. Thieuleux, and C. Copéret**

Page No. – Page No.

Tailored Polarizing Hybrid Solids with Nitroxide Radicals Localized in Mesoporous Silica Walls