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The Detection and Reactivity of Silanols and Silanes Using Hyperpolarized ^{29}Si Nuclear Magnetic Resonance

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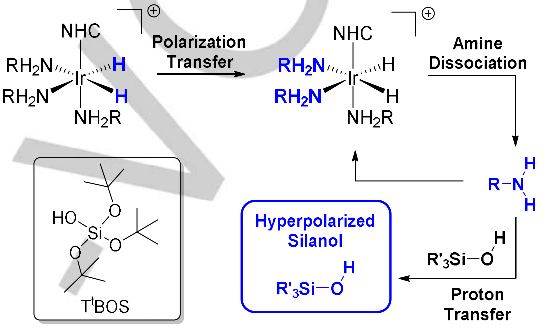
Abstract: Silanols and silanes are key precursors and intermediates for the synthesis of silicon-based materials. While their characterization and quantification using ^{29}Si NMR has received significant attention, it is a technique that is limited by the low natural abundance of ^{29}Si and its low sensitivity. Here, we describe a method using p-H_2 to hyperpolarize ^{29}Si. The observed signal enhancements, approaching 3000-fold at 11.7 T, would take many days of measurement for comparable results under Boltzmann conditions. The resulting signals are exploited to monitor the rapid reaction of tris(*tert*-butoxy)silanol with triflic anhydride in a T_1 corrected process that allows for rapid quantification. These results demonstrate a novel route to quantify dynamic processes and intermediates in the synthesis of silicon materials.

Silicon is one of the most abundant elements known to man. Silicon based materials find use in a wide range of applications, from the synthesis of bulk materials through to roles in molecular transformations. Of it's three naturally occurring isotopes, only ^{29}Si has a non-zero magnetic moment and its nuclear magnetic resonance (NMR) detection is of wide interest. It's wide chemical shift dispersion makes it highly diagnostic for characterization purposes and allows the examination of dynamic processes in solution and the solid state.[1] However, ^{29}Si NMR spectroscopy has limitations that reduce its potential use,[2] primarily due to its low sensitivity that is dependent upon the small population differences that exist between nuclear spin energy levels within a magnetic field. These populations are governed by the Boltzmann distribution and therefore a ^{29}Si NMR signal reflects just 1 in 125 500 of these nuclei at 11.7 T. Its 4.7% natural abundance and typically long T_1 values also hinder detection.[1] Furthermore, as it is found in materials that make up an NMR probe, and an NMR tube, the broad background signal can impede the detection of low concentration species.

Hyperpolarization is a route to overcome this insensitivity and refers to a situation whereby the spin energy level populations are perturbed from Boltzmann equilibrium conditions. These techniques have been utilized in both medical and analytical science and, with respect to ^{29}Si, a number of hyperpolarized magnetic resonance applications using dynamic nuclear polarization (DNP) have been reported.[3] The *para*hydrogen (p-H_2)[4] based method, Signal Amplification of Reversible Exchange (SABRE),[5] has been applied to the polarization of ^{1}H and a number of heteronuclei, including ^{29}Si.[6] However, these studies were limited to *N*-heterocyclic functionalized silanes because of the need to bind the substrate to the transition metal polarization transfer catalyst.

The SABRE-Relay technique,[7] overcomes this barrier and consequently, the scope of p-H_2 based hyperpolarization has been greatly expanded.[8] Now a carrier agent, such as an amine, becomes hyperpolarized through the initial formation of an active polarization transfer catalyst of the type $[Ir(H)_2(NHC)(RNH_2)_3]Cl$ as depicted in Scheme 1. The hyperpolarized carrier amine enhances the target substrate *via* proton transfer. Here, we develop the SABRE-Relay technique for the hyperpolarization of silanols by p-H_2 and direct silane polarization by SABRE.



Scheme 1. SABRE-Relay polarization transfer proceeds through the scalar coupling network between the p-H_2 derived hydride ligands into the carrier amine (RNH_2). Ligand dissociation and proton transfer yields a spin hyperpolarized silanol (R'_3SiOH). Inset: Tris(tert-butoxy)silanol (T^tBOS).

The Stöber process[9] is the method of choice for the synthesis of silica-based materials. It is a sol-gel process[10] that begins with the hydrolysis of a tetra(ortho)silicate to give a mixture of silanols which are subsequently condensed to form the material. The nature of the silanol intermediates determine the physical properties of these materials[11] and therefore methods for their rapid and cost efficient detection and characterization are desirable. Our starting point was to take tris(*tert*-butoxy)silanol (T^tBOS, inset, Scheme 1) as a model substrate to develop the p-H_2 derived hyperpolarization of silanols. A 5 mm NMR tube fitted with a J. Young's tap containing a solution of [IrCl(COD)(IMes)] (**1**, 5 mM), benzylamine-d_7 ($BnNH_2$ -d_7, 50 mM), T^tBOS (50 mM) in CD_2Cl_2 (0.6 mL) was placed under a 3 bar atmosphere of H_2. After 1 h at 298 K, the resulting ^{1}H NMR spectrum showed clean conversion into $[Ir(H)_2(IMes)(BnNH_2\text{-}d_7)_3]Cl$.[7-8] No evidence for T^tBOS binding to this iridium center was observed by NMR or MS methods. After shaking this sample under 3 bar p-H_2 for 10 s at 298 K at 70 G it was rapidly transferred into an 11.7 T spectrometer for interrogation by ^{29}Si NMR. A ^{29}Si signal that was 82 ± 5-fold larger than the corresponding thermally equilibrated control spectrum was detected. The transfer of hyperpolarization from the silanol ^{1}H to the ^{29}Si is likely to occur through both low field thermal mixing[12] and nuclear Overhauser enhancement.[13] Consequently, we sought to improve the ^{29}Si NMR signal gain to enable *in situ* reaction monitoring.

We began by varying the identity of the catalyst's *N*-heterocyclic carbene (NHC) ligand as it has been shown to affect the observed polarization level. The selective ^{2}H labelling of the NHC can result in increased levels of polarization due to reduced spin dilution and longer T_1 relaxation times.[14] Therefore,

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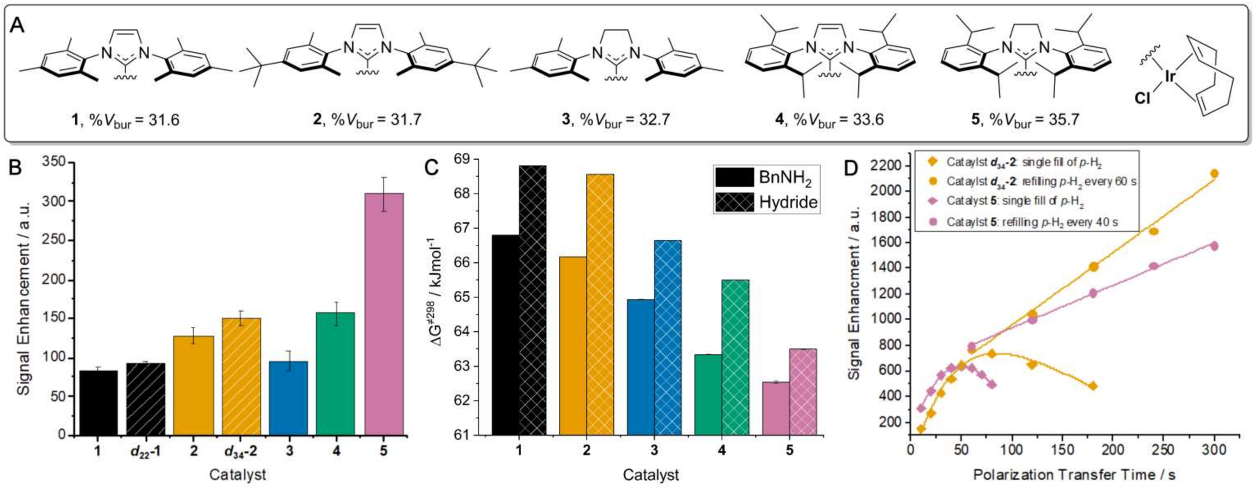

Figure 1. Catalyst effects on the SABRE-Relay polarization of (T^{t}BOS). **A**. Structures of catalysts and their buried volumes (%V_{bur}).[15] **B**. SABRE-Relay Signal Enhancements using [IrCl(COD)(NHC)] (5 mM), BnNH$_2$-d_7 (50 mM), T^{t}BOS (50 mM) in CD$_2$Cl$_2$ (0.6 mL), 3 bar p-H$_2$ for 10 s at 70 G. **C**. $\Delta G^{\neq 298}$ values for BnNH$_2$ (solid) and hydride (hashed) ligand dissociation from the active catalysts of type [Ir(H)$_2$(NHC)(BnNH$_2$)$_3$]Cl. **D**. Polarization transfer time effect on signal enhancement of T^{t}BOS when using ***d*$_{34}$-4** (orange) and **5** (pink) with a single filling of p-H$_2$ (diamonds) or multiple refills (squares).

an analogous SABRE-Relay sample was prepared using ***d*$_{22}$-1**. After SABRE-Relay transfer, an improved silanol signal gain of 92±4-fold was observed (Figure 1B). Modification of the steric and electronic properties of the NHC ligand has also been shown to modulate the ligand dissociation rates and thereby lead to better SABRE enhancement.[15] The rate of equatorial BnNH$_2$ dissociation from [Ir(H)$_2$(IMes)(BnNH$_2$-d_7)$_3$]Cl is 3.33 s^{-1} and therefore slower than predicted to be optimal.[16] Bulky catalyst **2**, furnished with *tert*-butyl groups, increases the signal gain to 128 ± 11-fold whereas its isotopologue, ***d*$_{34}$-2**, gave a 150 ± 9-fold gain. Catalyst **3**, which bares the even more bulky SIMes ligand, also improved the ^{29}Si signal gain when compared to **1**. Continuing with this trend, we were able to further increase the steric effects of the NHC through the use of catalysts **4** (IPr) and **5** (SIPr) which gave signal enhancements of 157 ± 15 and 310 ± 22 respectively. We would expect these signal enhancements to be further improved by the use of the deuterated isotopologues and are currently exploring routes to their synthesis.

In order to rationalize these differences in polarization level, we calculated the $\Delta G^{\neq 298}$ of ligand dissociation for equatorially bound BnNH$_2$ and H$_2$ loss for the active complexes. These values were calculated as described in the supporting information. The barrier to H$_2$ loss is consistently higher than that of BnNH$_2$ dissociation for each catalyst which is consistent with the expected dissociative mechanism (Figure 1C). The catalyst derived from **1**, [Ir(H)$_2$(IMes)(BnNH$_2$)$_3$]Cl, gave $\Delta G^{\neq 298}$ values of 66.79 and 68.81 kJmol^{-1} for BnNH$_2$ and H$_2$ loss respectively. These $\Delta G^{\neq 298}$ values decrease when the steric bulk of the NHC ligand is increased across the series of catalysts **1**-**5**. For catalyst **2**, they are 66.16 and 68.56 kJmol^{-1} respectively. Catalyst **5**, which gave the largest ^{29}Si signal enhancements after 10 s polarization transfer, has the lowest values of $\Delta G^{\neq 298}$ (62.54 and 63.5 kJmol^{-1} for BnH$_2$ and H$_2$ loss respectively). These data confirm that lower barriers to ligand loss promote more effective SABRE-Relay transfer. This effect is likely to be attenuated by relaxation of the NH protons of BnNH$_2$-d_7 in the presence of [Ir(H)$_2$(SIPr)(BnNH$_2$-d$_7$)$_3$]Cl whose T_1 was now just 0.8 s at 11.7 T. Thus, rapid ligand exchange allows for the effective replenishment of the polarized transfer agent, however, if this exchange is too fast, rapid relaxation will limit hyperpolarization build-up whilst depleting the p-H$_2$.

The corresponding hyperpolarized ^{29}Si signal lifetime of T^{t}BOS was 138.4 s as measured by a variable flip angle pulse sequence (see supporting information). As the decay of the created ^{29}Si magnetization is slow, we postulated that the NMR signal gains could be increased if the SABRE-Relay time was extended beyond 10 s. Consequently, an increase in signal gain to 625 ± 34-fold was obtained using **5** when the polarization time was extended to 50 s (Figure 1D). Extending this time further decreased the signal intensity due to the finite amount of p-H$_2$ becoming limiiting during the SABRE-Relay process. Upon repeating this experiment with ***d*$_{34}$-2**, a signal gain of 767 ± 38-fold is reached after 70 s exposure to p-H$_2$. We conclude that while **5** leads to a more rapid buildup of polarization, its higher rate of ligand exchange consumes the p-H$_2$ in the sample. ***d*$_{34}$-2** yields higher signal gains with extended polarization transfer times and the same finite volume of p-H$_2$, as relaxation effects are reduced by slower exchange. In support of this, the NH protons of BnNH$_2$-d_7 in the presence of ***d*$_{34}$-2** were measured to be 3.2 s at 11.7 T.

The polarization times were extended further by evacuating and refilling the NMR tubes containing the SABRE-Relay solutions with p-H$_2$ periodically until 300 s was reached. For **5**, the time between fills was 40 s and for ***d*$_{34}$-2** it was 60 s. For both catalysts, a linear increase in ^{29}Si polarization level was observed over time but ***d*$_{34}$-2** led to the highest signal gain of 2142 ± 180-fold after 300 s. For **5**, the signal gain was 1580 ± 120-fold. This behavior is reflected in the lower magnetization build up slope illustrated in Figure 1D. Increasing the pressure of p-H$_2$ from 3 bar to 5 bar yields a further 10% increase in signal gain to 2313-fold with ***d*$_{34}$-2** due to increased p-H$_2$ availability. An automated polarizer, which introduces a constant flow of p-H$_2$ into the solution, gave a similar linear increase in signal gain; however, the signal gains only reach a maximum of 100-fold (see supporting information). We suggest that this is due to inefficient mixing of p-H$_2$ in solution.

After optimization, we conclude that the best conditions for the polarization T^{t}BOS are ***d*$_{34}$-2** (5 mM), BnNH$_2$-d_7 (50 mM), T^{t}BOS (30 mM) in CD$_2$Cl$_2$ (0.6 mL) and exposure to p-H$_2$ at

5 bar for 300 s at 70 G with refreshing the p-H_2 every 60 s. This yields a total signal gain of 2852 ± 112-fold (2.3%) in the ^{29}Si NMR spectrum (Figure 2). These conditions were then applied to the polarization of a number of other silanols as summarized in Figure 2. As their T_1 relaxation times are shorter than T^{t}BOS's, the maximum signal gains are achieved with shorter total polarization transfer times.

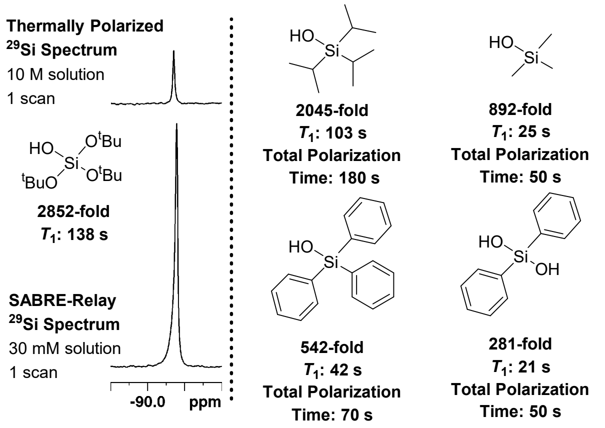

Figure 2. Silanol ^{29}Si NMR response results after hyperpolarisation by SABRE-Relay transfer using ***d*₃₄-2** (5 mM), silanol (30 mM), $BnNH_2$-d_7 (50 mM) in CD_2Cl_2 (0.6 ml) at 5 bar p-H_2.

DNP has previously been used for quantitative reaction rate determination using ^1H and ^{13}C nuclei.[17] The hyperpolarized ^{29}Si NMR signals and long T_1 relaxation time of T^{t}BOS were exploited to monitor a molecular transformation. The nucleophilic substitution of triflic anhydride (Tf_2O) with T^{t}BOS was chosen as it has been reported as a method for functionalization of silica surfaces.[18] A relaxation corrected variable flip angle sequence was used to overcome the loss of magnetization due to T_1 relaxation during the reaction and give an immediate concentration profile as detailed in the supporting information.[19] The SABRE-Relay polarization of T^{t}BOS was conducted using our previously optimized conditions, prior to the introduction of a solution of Tf_2O (10 eq.), pyridine (10 eq.) in CD_2Cl_2 (0.1 mL). Subsequent rapid sample insertion into an 11.7 T magnetic field prior to a ^{29}Si spectrum being acquired every 5 s for a 60 s duration (Figure 3). When Tf_2O is present in excess, we observe conversion of T^{t}BOS (δ_{Si} −90.8), to its triflate derivative (δ_{Si} −102.7). The identity of these signals was unequivocally confirmed by independent synthesis (see supporting information). After an induction period of 10 s, which we attribute to diffusion of the Tf_2O into the NMR detection region, the expected pseudo-first order consumption of the starting silanol and corresponding production of its triflate product is observed. The rate constant for this was determined to be $0.070 \pm 0.001\ s^{-1}$ and is not affected by changing the concentration of the SABRE catalyst which confirms that it does not participate in the nucleophilic reaction. This data would not be possible to collect using ^{29}Si NMR under Boltzmann conditions due to the requirement for signal averaging and long T_1 values; the speed of this reaction means that it would be complete before the first measurement could be made. When the reaction is repeated with substoichiometric quantities of Tf_2O a new peak at δ_{Si} −93.2 is observed which we attribute to the product of dimerization (see supporting information). It is formed by reaction of T^{t}BOS with its triflate intermediate in a two-step process. The same signal is present in the ^{29}Si NMR spectrum when a the reaction was repeated with tris(*tert*-butoxy)silyl chloride, however, the reaction is now too rapid to derive any kinetic data. As the oligomerization of silanols is a key step in the synthesis of silica materials, the result demonstrates that it may be possible to detect and quantify intermediates in the sol-gel process.

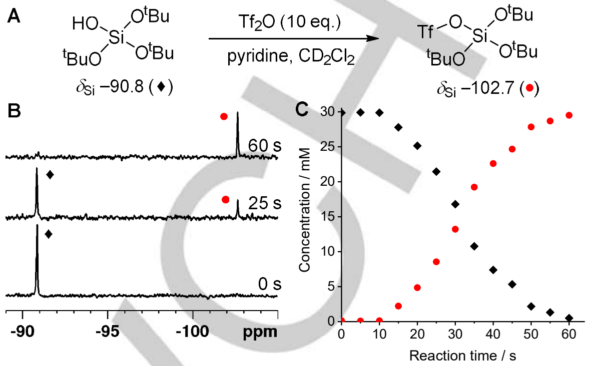

Figure 3. Hyperpolarized nucleophilic substitution of Tf_2O with T^{t}BOS. **A**. Reaction scheme. **B**. SABRE-Relay hyperpolarized ^{29}Si spectra at indicated reaction time points. **C**. Concentration of T^{t}BOS (♦) and the triflate product (●) as a function of reaction time calculated from corresponding T_1 corrected hyperpolarised ^{29}Si NMR spectra.

During the course of our investigation into hyperpolarized ^{29}Si NMR spectroscopy, we also discovered a method to hyperpolarize important silanes *via* SABRE. When a sample containing ***d*₂₂-1** (5 mM), dimethylethoxysilane (50 mM), $BnNH_2$-d_7 (50 mM) in CD_2Cl_2 (0.6 mL) was shaken at 70 G for 10 s, a hyperpolarized signal gain of 206 ± 24-fold is observed in the ^{29}Si NMR spectrum as an antiphase doublet ($J_{Si\text{-}H}$ = 205 Hz, Figure 4B). Antiphase character is typically seen for two inequivalent p-H_2 derived hydride ligands,[4b, 5c, 12] here similar complex polarization is spontaneously created, but now shared between a ^{29}Si and a ^1H nucleus. The T_1 value for this signal was measured to be 38 ± 1.2 s. In the ^1H NMR spectrum, after SABRE polarization, the Si-H proton is 70 ± 5 times larger than a thermally equilibrated reference spectrum. The dominant hydride containing species in the ^1H NMR was $[Ir(H)_2(d_{22}\text{-}IMes)(BnNH_2)_3]Cl$[8a] and no hydride ligands were seen that could be attributed to a silane complex. As SABRE transfer is seen when a 70 G field is employed, it demonstrates the existence of a polarization transfer route involving p-H_2 derived hydride ligands and dihydride-η^2-silane complexes have been exemplified elsewhere.[20] We searched spectroscopically for the presence of such a species at low temperature in our SABRE sample, however, no signals attributable to an intermediate η^2-silane complex could be detected.

After SABRE catalysis at 70 G, a ^1H-^{29}Si INEPT based transfer sequence was utilized at 11.7 T to create the same antiphase signal as that of Figure 4B with an increased signal gain of 772 ± 56 (Figure 4C). The use of alternative co-ligands, such as DMSO-d_6 and CD_3CN, did not increase the signal gains when compared to those with $BnNH_2$-d_7. Additionally, when the sample is placed under a D_2 atmosphere (3 bar) at room temperature for 24 h, a 60% reduction in the Si-H signal was observed in the ^1H NMR spectrum thus indicating that while H/D exchange occurs, it is slow. No Si-H site exchange was observed by EXSY methods on the timescale of relaxation which further suggests that the key intermediate is of an η^2-silane type rather than an oxidative silyl-hydride which would undergo rapid Si-H scrambling.

Changing the silane to pentamethyldisiloxane gave a ^{29}Si signal gain of 252 ± 22 in the ^{1}H-^{29}Si INEPT spectrum. However, a number of other silanes, such as triethoxysilane and triphenylsilane, yielded no SABRE catalysis and therefore highlight the sensitivity of this approach to the silanes steric and electronic properties. Work is now ongoing to further characterize the intermediates involved in this process.in order to broaden scope and applicability.

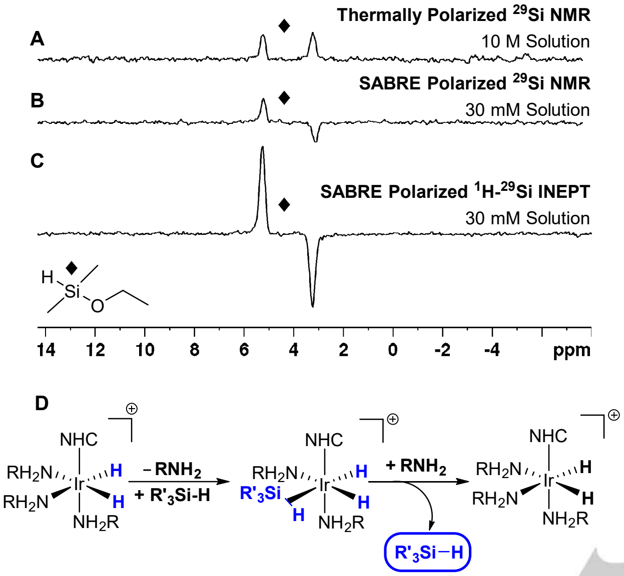

Figure 4. SABRE hyperpolarization of dimethylethoxysilane. **A** Thermally polarized ^{29}Si NMR spectrum of a 10 M solution. **B** ^{29}Si NMR spectrum after SABRE hyperpolarization with [IrCl(COD)(d_{22}-IMes)] (***d*$_{22}$-1**) and 3 bar p-H_2 at 70 G. **C** ^{1}H-^{29}Si INEPT NMR spectrum after SABRE hyperpolarization under analogous conditions. **D**. Proposed route for silane hyperpolarization.

In summary, we have demonstrated the hyperpolarization of silanols and silanes using p-H_2. Development of the SABRE-Relay method[7] gave large ^{29}Si signal gains that approach 3000-fold. The effects of catalyst structure and their influence on ligand exchange processes was determined through calculation of $\Delta G^{\neq 298}$ values and the influence on carrier amine T_1 relaxation rates. The large polarization levels attained and long T_1 values were exploited using a relaxation corrected variable flip angle pulse sequence to measure kinetic data for the reaction of a silanol and Tf_2O through a ^{29}Si NMR response. Finally, silanes have been shown to be amenable to SABRE based polarization transfer when $BnNH_2$-d_7 was used as a co-ligand to give ^{29}Si signal gains 772 ± 56-fold. We propose an iridium dihydride-η^2-silane is the active catalyst in this process,[20] and full rationalization of this SABRE pathway is ongoing. We anticipate that the hyperpolarized methods exemplified here for ^{29}Si will extend more generally to other slow relaxing heteronuclei such that intermediate characterization by NMR is widely supported.

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Keywords: Silicon • NMR • Hyperpolarization • SABRE • Catalysis

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