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Spontaneous Transfer of *Para*hydrogen Derived Spin Order to Pyridine at Low Magnetic Field

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Abstract: The cationic iridium complex $[Ir(COD)(PCy_3)(py)]BF_4$ (**1**) is shown to react with dihydrogen in the presence of pyridine (py) to form the dihydride complex *fac,cis*-$[Ir(PCy_3)(py)_3(H)_2]BF_4$ (**2**). Complex **2** undergoes rapid exchange of the two bound pyridine ligands which are *trans* to hydride with free pyridine; the activation parameters for this process in methanol are $\Delta H^{\ddagger} = 97.4 \pm 9$ kJ mol^{-1} and $\Delta S^{\ddagger} = 84 \pm 31$ J K^{-1} mol^{-1}. When *para*hydrogen is employed as a source of nuclear spin polarization, spontaneous magnetization transfer proceeds in low magnetic field from the two nascent hydride ligands of **2** to its other NMR active nuclei. Upon interrogation by NMR spectroscopy in a second step, signal enhancements in excess of 100 fold are observed for the ^{1}H, ^{13}C and ^{15}N resonances of free pyridine after ligand exchange. The degree of signal enhancement in the free substrate is increased by employing electronically rich and sterically encumbered phosphine ligands such as PCy_3, PCy_2Ph, or P^iPr_3 and by optimizing the strength of the magnetic field in which polarization transfer occurs.

Introduction

NMR spectroscopy has undoubtedly become the most important tool available to the scientist for the characterization of molecules, as well as the study of their dynamic behavior and reactivity in solution.[2,3] This technique suffers, however, from the limitation that it is inherently insensitive due to the small population difference that exists between the energy levels that it interrogates. Hence, at a magnetic field strength of 9.4 T, the normally observed ^{1}H NMR signal results from an effective contribution of only 1 in every 31 200 molecules present in the sample.

Several "hyperpolarization" techniques have been reported that allow detected NMR signals to be enhanced through the generation of non-Boltzmann spin state populations between these energy levels. For instance, hyperpolarized ^{129}Xe can be generated by optical pumping of this gas in a magnetic field.[4] A related and recently commercialized polarization technique is dynamic nuclear polarization (DNP).[5−7] Here, the NMR active nuclei are polarized at 1.3 K in a glassed solvent matrix while exposed to a magnetic field in conjunction with magnetization transfer from the electron of an added radical which is irradiated by a microwave source. When such samples are rapidly thawed and transferred into an NMR tube, signal enhancements in excess of 10 000 fold have been observed for ^{13}C and fast two-dimensional approaches are now available.[8]

A further chemical "hyperpolarization" method that has been used extensively by our research group and others involves *para*hydrogen induced polarization (PHIP) or more rigorously PASADENA (parahydrogen and synthesis allow dramatically enhanced nuclear alignment).[9,10] There are two forms of H_2, *ortho*hydrogen where the nuclei are described by one of the three possible magnetic states, $|\alpha\beta\rangle + |\beta\alpha\rangle$, $|\alpha\alpha\rangle$ or $|\beta\beta\rangle$ and *para*hydrogen where the nuclei are in the $(|\alpha\beta\rangle - |\beta\alpha\rangle)$ or singlet state. *Para*hydrogen is restricted to having even values of the rotational quantum number J while *ortho*hydrogen must have odd values of J and they hence lie 120 cm^{-1} apart in energy. The selective formation of *para*hydrogen at low temperatures makes use of the fact that interchange between these two forms is formally forbidden, as both the spin and rotational states much change for interconversion. Consequently *para*hydrogen can be prepared in an almost pure form at 20 K by employing a suitable spin exchange catalyst.[11] While *para*hydrogen, the nuclear singlet, is itself NMR silent, reaction products derived from it are often produced with non-Boltzmann nuclear spin state populations and thus exhibit greatly enhanced NMR signals. For example, when the complex $[Ru(dpae)(CO)_2(H)_2]$ (dpea = 1,2-(diphenylarsino)ethane) is generated from the tricarbonyl parent by irradiation, the two hydride ligands exist in a magnetic state that is indistinguishable from that of a pure singlet spin

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state.[12] This results in a 31 200 fold increase in the ^{1}H NMR signal strengths associated with the hydride ligands of this species. Not surprisingly, PHIP has therefore served as a useful tool for the study of catalytic reactions where H_2 is a reactant. Indeed, many low concentration intermediates would otherwise be invisible, and their reactivities have been studied by this approach.[11]

In recent years, PHIP has attracted wider interest because of its potential to generate highly polarized organic molecules via the hydrogenation of unsaturated organic substrates. Golman et al. have exploited this phenomenon for the generation of PHIP enhanced contrast agents for use in magnetic resonance imaging (MRI).[13] While this methodology has been taken up by others, the formal hydrogenation step represents a distinct limitation of the underlying method because a reactive unsaturated analog of the desired material is required.[14] Nonetheless, recent studies employing succinic acid[15] and propane[16] and the development of an automated polarizer[17] continue to expand the horizons of this approach.

In this paper, we detail a new approach to the generation of PHIP sensitized materials. This method relies on bringing both *para*hydrogen and the substrate to be polarized into temporary contact via a suitable transition metal based host. Polarization is shown to be spontaneously transferred from the *para*hydrogen derived hydride ligands in this template to the bound substrate under low magnetic field conditions over the period of a few seconds. This approach is therefore related to that demonstrated for hydrogenation products under ALTADENA conditions.[18] Dissociation of the magnetically labeled substrate then enables the build up of polarization in this chemically unmodified material which is then interrogated in a second step by NMR spectroscopic methods. The magnetic signals that are measured during this process can be several orders of magnitude larger than those which are normally obtained. This process corresponds to the production of non-hydrogenative *para*hydrogen induced polarization (NH-PHIP) or more usefully signal amplification by reversible exchange (SABRE) and is achieved without any chemical modification of the substrate.

It works by taking the nuclear singlet state of parahydrogen, ($-$I1zI2z $-$ I1xI2x $-$ I1yI2y) and transferring this polarization into a reaction product in low field under conditions where the magnetic equivalence of the two metal hydrides, and hence symmetry restrictions for spin-state interconversion, are removed.[19] In the template, the ensuing proton chemical shift differences begin to match the frequencies associated with the field invariant scalar coupling framework. In other words, the resulting spin system, under these conditions, evolves to share the *para*hydrogen spin order across the network of coupled spins that exist within the template according to the difference in chemical shifts between pairs of spins, the size of their scalar couplings and the time spent on the template. Consequently, varying and enhanced spin-state amplitudes result for magnetically active nuclei within the template which upon dissociation produce the magnetically polarized substrate.

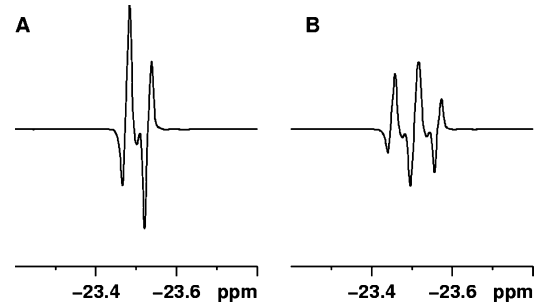

Figure 1. (a) Hydride region of a $^1H^{24}$ NMR spectrum recorded during the reaction of **1** with *p*-H_2 in the presence of ^{15}N-pyridine at 300 K, (b) corresponding ^{1}H NMR spectrum.

We exemplify this polarization transfer process in this paper for pyridine and employ inorganic templates of the type *fac*,*cis*-[Ir(PCy$_3$)(py)$_3$(H)$_2$]BF$_4$ to achieve it. We recently reported results from a related study on analogous aryl phosphine complexes such as *fac*,*cis*-[Ir(PPh$_3$)(py)$_3$(H)$_2$]BF$_4$ and *fac*,*cis*-[Ir(PPh$_3$)$_2$(py)$_2$(H)$_2$]BF$_4$ that established the direct sensitization of the ^{15}N signal of free pyridine could be achieved through ligand exchange in conjunction with a radio frequency based polarization transfer procedure.[20] Some of these results have recently been communicated.[21]

Results and Discussion

Reaction of [Ir(COD)(PCy$_3$)(py)]BF$_4$ (1) with *Para*hydrogen and Pyridine. When a sample of [Ir(COD)(PCy$_3$)(py)]BF$_4$ (**1**), in methanol-d$_4$, reacts with *para*hydrogen in the presence of pyridine at 300 K a nonenhanced doublet is observed in the hydride region of the corresponding ^{1}H NMR spectrum at δ $-$23.52 (d, J_{PH} = 24.3 Hz). Upon repeating this procedure with 100% ^{15}N-labeled pyridine, the hydride signal exhibits an extra splitting of 20.4 Hz and is now strongly polarized through its formation from *para*hydrogen (Figure 1) and the generation of an [AX]$_2$ spin system (neglecting ^{31}P). It is the production of magnetic inequivalence that leads to polarization with the 20.4 Hz splitting corresponding to $|J_{NH}(\text{cis}) + J_{NH}(\text{trans})|$.[22] Additionally, the ^{31}P resonance for **2** exhibits a *trans* ^{15}N splitting of 43.2 Hz under these conditions. When a 20% ^{15}N, 80% ^{14}N mixture of pyridine is employed, polarized hydride resonances for the dihydride complex **2** are seen for the ABX spin system isomer (neglecting ^{31}P, hydride *trans* to ^{15}N) [Ir(PCy$_3$)(^{15}N-py)(^{14}N-py)$_2$(H)$_2$]BF$_4$] and through simulation we estimate that J_{NH}(trans) is of the order of |20.9| Hz while J_{NH}(cis) is approximately |0.5| Hz.[23] The behavior of the δ $-$23.52 signal

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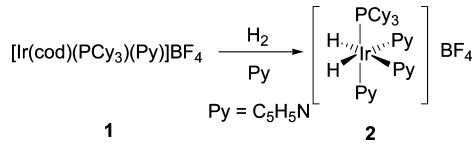
Table 1. NMR Data for **2** in CD_3OD at 300 K[a]

$^1H/\delta$	$^{31}P/\delta$	$^{13}C^b/\delta$	$^{15}N^c/\delta$
−23.52 (d, $^2J_{PH}$ = 24.3 Hz, 2H, Ir−H)[d]	13.1 ($J_P{}^{15}{}_{N(trans)}$ = 43.2 Hz)	155.1 (*trans*-Py, o)	−58.4 (d, $^2J_{N-P}$ = 50.9 Hz, *cis*-Py)
8.93 (d, br, *J* = 4.42 Hz, 4 H, *trans*-Py, ortho)		155.0 (*cis*-Py, o)	−48.3 (s, *trans*-Py)
8.61 (s, br, 2 H, *cis*-Py o)		137.4 (*trans*-Py, p)	
7.99 (t, *J* = 7.2 Hz, 2 H, *trans*-Py, para)		137.4 (*cis*-Py, p)	
7.89 (m, *cis*-Py, p)		126.2 (*trans*-Py, m)	
7.49 (t, *J* = 6.1 Hz, 4 H, *trans*-Py, meta)		125.8 (*cis*-Py, m)	
7.28 (t, *J* = 6.1 Hz, 2 H, *cis*-Py, m)			

[a] δ in ppm, J in Hz. [b] Assigned via $^{13}C-^1H$ HMQC. [c] Relative to ^{15}N-pyridine = 0 ppm, assigned from $^{15}N-^1H$ HMQC experiments using **2** prepared with ^{15}N-Py. [d] Appearance of the hydride resonance is complicated by slow H-D exchange in methanol-d_4 and broadened due to pyridine and hydrogen exchange processes; *trans*-Py = py *trans* to H, *cis*-Py = py *cis* to H.

Scheme 1. Reaction of **1** with H_2 and Pyridine Yields **2**



in the presence of the ^{15}N label is therefore indicative of the formation of *fac*,*cis*-$[Ir(PCy_3)(py)_3(H)_2]BF_4$ (**2**) and NMR data for this material can be found in Table 1. Figure 1 illustrates two NMR spectra which are differentiated according to the presence of ^{31}P decoupling. In the first, only a simplified doublet multiplicity remains since the effect of ^{31}P is removed while in the second, the antiphase doublet appears with a pseudo triplet multiplicity due to *cis*-$^{31}P-H$, and the combination of *cis*- and *trans*-$H-^{15}N$ couplings for a 100% ^{15}N-labeled sample. The chemical changes that take place during reaction of **1** with *para*hydrogen in methanol-d_4 are summarized in Scheme 1.

Single crystals of **2** were grown from methanol solution, and an X-ray diffraction analysis confirmed the formulation of the complex. The structure reveals that the phosphine ligand and the pyridine *trans* to it bend slightly away from the two in-plane pyridine ligands which lie *trans* to the two hydrides such that the P(1)—Ir(1)—N(1) angle is 168.63(6)°. The two in-plane pyridine ligands that are *trans* to hydride also bend away from the bulky PCy_3 ligand, with the angle P(1)—Ir(1)—N(2) being 105.12(5)°. Notably, the pyridine ligands *trans* to hydride have relatively long Ir—N bond distances (Ir(1)—N(2), 2.2101(19) Å; Ir(1)—N(3), 2.216(2) Å) which agrees with the later observation that these pyridine ligands are labile in solution. We note that the analogous distances in $[Ir(PPh_3)_2(py)_2(H)_2]BF_4$ are 2.177(2) Å and 2.196(2) Å and that the corresponding ligand exchange rate is much slower at 0.4 s^{-1} and 335 K.[20]

Spontaneous *Para*hydrogen Polarization Transfer to the ^{1}H Signals of Free Pyridine. The most noticeable features of the NMR spectra of **2** in the presence of excess pyridine are seen when the sample is first observed after the reaction with *para*hydrogen takes place in a magnetic field of 0.5×10^{-4} T (the earth's magnetic field) outside the 9.4 T NMR magnet. This observation is illustrated in Figure 3 which shows two single scan ^1H NMR spectra that only differ in the time of their observation. Trace (a) corresponds to the situation after the sample has been in the magnet for 10 min while trace (b) was obtained immediately after the reaction and its introduction into the spectrometer. In this trace, large signal enhancements are observed for the three proton sites of free pyridine at δ 8.56, 7.88, and 7.46 the first two of which are in emission and the latter absorption. Similar effects are seen regardless of whether the pyridine is specifically ^{15}N-labeled or not.

These enhanced signals persist for a few scans with low tip angle pulses but can be seen optimally only once when a 90° read pulse is employed. This demonstrates that the observed proton polarization at pyridine is not generated by a process that occurs while the sample is in the high magnetic field

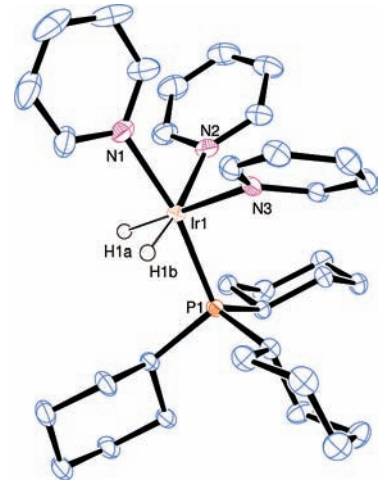


Figure 2. ORTEP diagram of the molecular structure of the cation **2**. Thermal ellipsoids at 50%. Selected bond distances (Å) and angles (deg). Ir(1)—P(1), 2.4249(6); Ir(1)—N(1) to N(3), 2.144(2), 2.2101(19) and 2.216(2) respectively; P(1)—Ir(1)—N(1), 168.63(6); P(1)—Ir(1)—N(2), 105.12(5); P(1)—Ir(1)—N(3), 98.85(5); N(1)—Ir(1)—N(2), 84.61(8); N(1)—Ir(1)—N(3), 85.44(7).

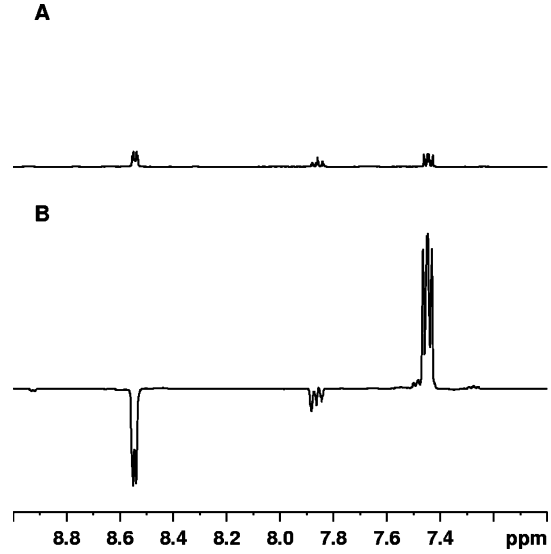


Figure 3. (a) Single scan ^1H NMR spectrum of the aromatic region of a sample of **2** showing resonances for free pyridine that were obtained prior to polarization, (b) ^1H NMR spectrum recorded immediately after polarization in a 0.5×10^{-4} T field revealing the newly enhanced hydrogen atom signals for free pyridine.

environment of the observation magnet but instead is generated during the period when the sample is in the lower 0.5×10^{-4} T field. This effect can be observed again if the sample is removed, shaken to dissolve fresh *para*hydrogen in solution for a period of five seconds, and then reinterrogated.

In addition to the enhanced signals for free pyridine, smaller signals at δ 8.93 and 7.99 corresponding to the *ortho*- and *para*-protons positions of the pyridine ligands in **2** that are *trans* to hydride in **2** also show this effect. It would therefore seem that the transfer of *para*hydrogen induced polarization into the free pyridine proton resonances is mediated by **2** and the prerequisite ligand exchange; repeating this process without the metal complex results in no pyridine signal enhancement.

Mechanism of Polarization Transfer. Evidence that the aforementioned NMR polarization does not build up when such a process occurs within the 9.4 T magnetic field of the spectrometer was indicated first by the fact the polarized magnetization can only be read effectively by a single 90 degree pulse, with a second scan resulting in substantially less visible magnetization. To further confirm this point, a fresh sample was prepared at −78 °C before being shaken to dissolve the *para*hydrogen and immediately transferred into the spectrometer at 330 K. A series of single acquisition ^{1}H NMR spectra were then recorded. In the first of these spectra, no hydride signals were observed nor any polarization seen in the proton signals for pyridine. In the second and subsequent spectra, as the sample had warmed and hence reacted, the hydride signals of **2** are observed to increase in intensity before reaching a steady state. At no point are signal enhancements observed for the free pyridine resonances as described earlier. When this sample was removed, shaken to ensure the solution contains fresh *para*hydrogen, and immediately reintroduced, the resultant ^{1}H NMR spectrum now shows enhanced proton signals for pyridine. Furthermore, when this sample is removed, recooled to −78 °C, and reexamined, no pyridine signal enhancements are seen. These data confirm therefore the need for a low magnetic field step in the life of the sample to facilitate the polarization transfer step and the need for a reaction that is kinetically significant on the NMR time scale.

To rule out the possibility that the ^{1}H NMR signals of pyridine were being enhanced by the iridium catalyzed incorporation of *para*hydrogen through a CH bond activation pathway, a series of control experiments were performed.[25] In the first of these experiments, **1** was reacted with *para*hydrogen and d_5-pyridine in methanol and the formation of $\mathbf{d_{15}}$-**2** was found to take place as expected. Under these conditions, however, the intensity of the enhanced ^{1}H NMR signals that result from the residual ^{1}H label in the d_5-pyridine were very small. We further note that ^{2}H-labeling studies, in conjunction with GC-MS analysis, failed to detect any ^{2}H incorporation into the ^{1}H-pyridine substrate either on the time scale of polarization buildup or over a further 24 h period.

It has been shown by others that when unsaturated substrates are hydrogenated by *para*hydrogen under low magnetic field conditions, spontaneous sharing of the polarization with directly coupled heteronuclei such as ^{13}C that are located within the hydrogenation product results.[14] In the results discussed here, however, the polarized substrate is actually chemically identical to that which is present at the start, and the hydride ligands do not visibly couple to all of the sites within **2** where polarization is observed. Nonetheless, we conclude that the observed

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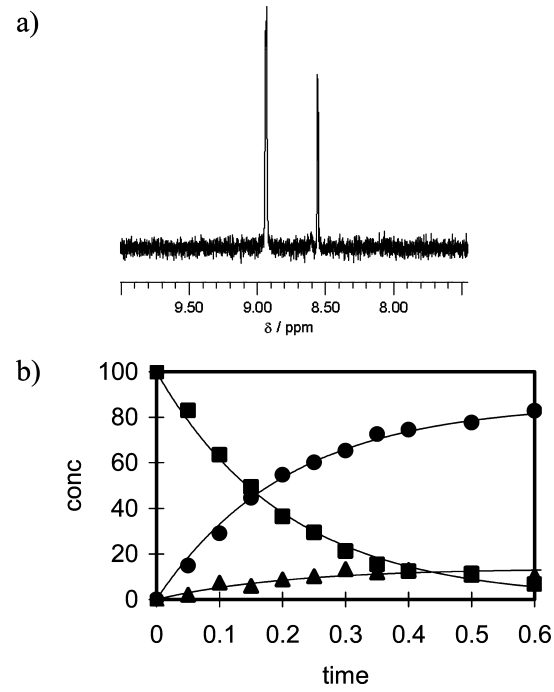

Figure 4. (a) ^{1}H EXSY NMR trace for the situation where the δ 8.91 signal of **2** was selected which reveals exchange into the free pyridine signal at δ 8.56, (b) plot of the change in peak intensities (percentage) for the pyridine *trans* to hydride (■), free pyridine (●), and bound pyridine *trans* to phosphine (▲) at 313 K as a function of the exchange or reaction time.

polarization arises from the spontaneous and sequential transfer of polarization from the *p*arahydrogen derived hydride ligands of **2** in low magnetic field. Exchange of bound and free pyridine would then be necessary to build up a concentration of free pyridine that is polarized.

Pyridine Ligand Exchange by 2. A series of ^{1}H EXSY experiments were recorded in order to establish whether **2** undergoes pyridine exchange on the necessary time scale. When the ligated pyridine signal at δ 8.93, due the pyridine *trans* to hydride, was selected magnetization transfer into the corresponding position of free pyridine at δ 8.56 was observed with limited exchange into the signal for the unique pyridine ligand of **2** at δ 8.61 also being seen. Representative data obtained via these studies are presented in Figure 4 which shows how the location of the magnetization varies with reaction time. The extraction of variable temperature based kinetic data allowed activation parameters of $\Delta H^{\ddagger} = 97.4 \pm 9$ kJ mol^{-1} and $\Delta S^{\ddagger} = 84 \pm 31$ J K^{-1} mol^{-1} to be determined for pyridine dissociation in **2** from the site *trans* to hydride. The associated rate constant is 0.45 s^{-1} at 295 K and hence consistent with the ligand based exchange hypothesis.

Effect of the Ratio of 1 to Pyridine on the Extent of Polarization Transfer in a 0.5×10^{-4} T Magnetic Field. A series of samples were prepared that contained **1** and pyridine (concentration always 103 milli-molar) in methanol-d_4. The ratio of **1** to pyridine was varied from 1:1000 to 1:5, beyond which the catalyst precipitated from solution. These samples were then filled with *para*hydrogen and warmed to 318 K before being shaken for approximately 5 s in the earth's magnetic field. After this point, following a 5 s delay for sample insertion, ^{1}H NMR spectra were recorded to assess the degree of signal enhancement shown by the three pyridine proton sites. These data are illustrated pictorially in Figure 5 and reveal that the degree of

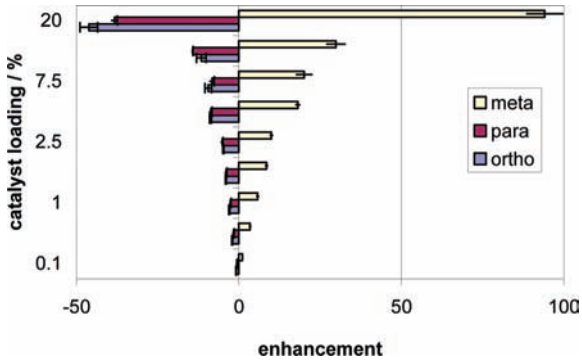

Figure 5. Effect of the ratio of **1** to pyridine on the extent of the ^{1}H NMR spectral signal enhancement for the three proton sites of pyridine when magnetization transfer is completed at 318 K in a 0.5×10^{-4} T magnetic field.

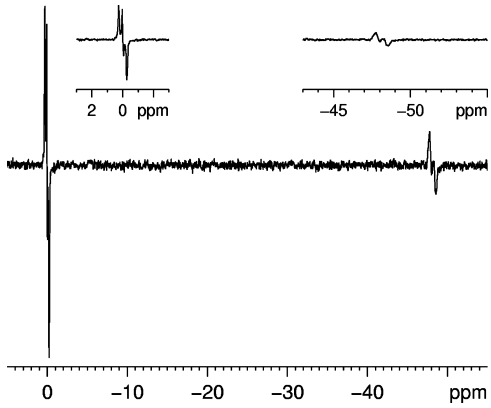

Figure 6. Single scan ^{15}N spectrum of a sample charged with **1** and ^{15}N-pyridine dissolved in CD_3OD the two inset traces correspond to expansions of the two polarized resonances for free pyridine (left) and the pyridine site in **2** which is *trans* to hydride.

enhancement is maximized at the 1:5 loading level where the *ortho* proton signal is 94 times stronger than normal when polarization transfer is undertaken at 318 K. When the same process is repeated for samples where the absolute concentrations of **1** and pyridine are halved, the signal gain is reduced to 66 fold. We therefore conclude that there is a concentration dependence on the efficiency of the enhancement process which would be expected given the bimolecular nature of the H_2 addition step, even if the pyridine dissociation step is dissociative in character in accordance with the larger positive value of $\Delta S^{\ddagger}$.

Spontaneous *Para*hydrogen Spin Order Transfer to the ^{13}C and ^{15}N Signals of Free Pyridine. Since we observe strong polarization for the hydrogen atoms of free pyridine after contact with *para*hydrogen in low magnetic field, we reasoned that a similar process might be occurring at both the ^{13}C and ^{15}N nuclei. A single scan ^{15}N spectrum is illustrated in Figure 6 which confirms this to be the case. Based on S/N arguments we have seen a 128 fold increase in signal strengths available at ^{15}N when compared to that obtained without the polarization step. We discuss below how substantial polarizations are also present at the three ^{13}C sites of free pyridine. In both cases, weakly enhanced signals are seen for the corresponding ^{13}C and ^{15}N nuclei in the pyridine ligands of **2** that are *trans* to hydride. This method therefore leads to the spontaneous transfer of polarization located in *para*hydrogen to magnetically active ligand-based sites that originate in **2**. The ligand exchange

Table 2. Effect of Temperature and Polarization Field on the ^{1}H and ^{13}C Magnetization Observed at the *ortho*, *para* and *meta* Sites of Pyridine

polarization field strength (Tesla)	polarization temperature (K)	pyridine ^{1}H signals relative enhancement level (*ortho*:*para*:*meta*)	pyridine $^{13}C^1$ signals relative amplitudes (*ortho*:*meta*:*para*)
0.5×10^{-4}	298	−144:−47:+220	−
0.5×10^{-4}	353	−84:−5:+182	15:5:−8
0.5×10^{-3} to 1×10^{-2}	298	−0.5:−0.44:3.22	−
0.5×10^{-3} to 1×10^{-2}	353	16.8:7.5:4.4	−6:15:43

studies establish a route to explain how the free pyridine resonances become polarized in turn.

Effect of the Strength of the Polarization Field on the Free Pyridine Magnetization Profile. We prepared a series of samples of **2** and pyridine to test how the magnetization seen through the proton and ^{13}C resonances of free pyridine depends on the strength of the polarization field. The concentration of **2** in solution in these samples was 4.46 mM and a 24 fold excess of pyridine was employed; the results are summarized in Table 2. These experimental results revealed the relative amplitudes of the signals seen for the *ortho*, *para* and *meta* sites of free pyridine were −144:−47:+220 when compared to the corresponding unpolarized signals of 2:1:2; the signal enhancement for the *meta* site is therefore 110.

When the spectrometer was used to record matching ^{13}C spectra, I_zS_z magnetization proved to be created at the three ^{13}C sites of pyridine, as evidenced by the observation of antiphase I_xS_z product terms (where S is ^{1}H and I now ^{13}C) in the corresponding spectra. ^{13}C data were then recorded after leaving a delay of $1/2J_{HC}$ between the 90 degree ^{13}C observation pulse and starting free induction decay storage in order to refocus the magnetization prior to decoupling (Figure 7a). The signals for the three *ortho*, *para* and *meta* ^{13}C sites then exhibited a polarization profile of 15:5:−8 (relative phase); the ^{13}C signal intensity gain for the *ortho* site is, however, greater than 50 fold.

These data also reveal that when the same process is completed in a polarization field of between 0.5×10^{-3} and 1×10^{-2} T the magnetization that is created changes. (The

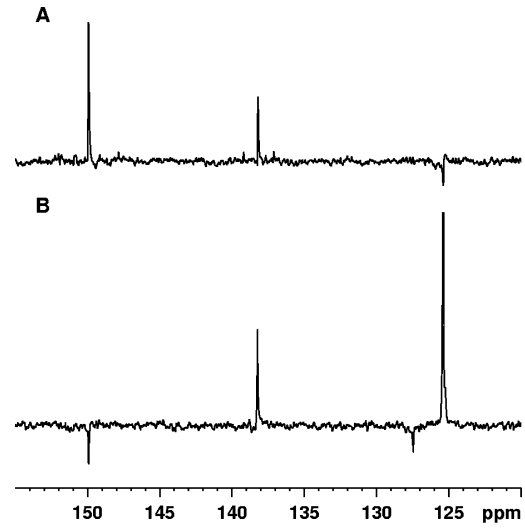

Figure 7. Single scan refocused $^{13}C^1$ NMR spectra of a sample comprising of **2**, *para*hydrogen and 5 μL of pyridine; a) sample polarized in an external 0.5×10^{-4} T field (earths field); b) sample polarized in an external field that varied between 5×10^{-3} T and 1×10^{-2} T (i.e., in the stray field of a 9.4 T magnet).

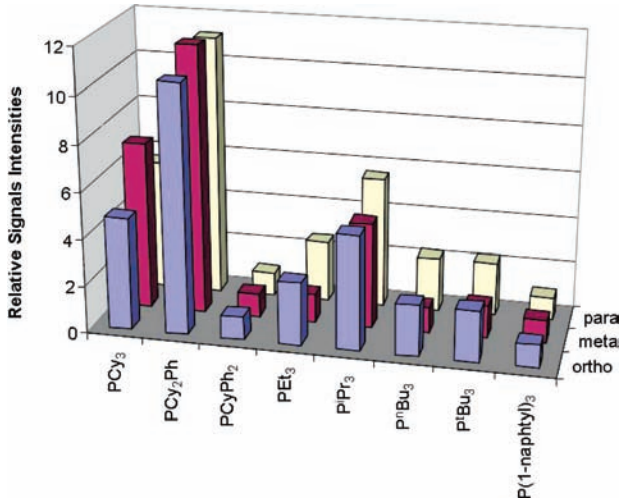

Figure 8. Plot of the relative absolute signals strengths for the three pyridine proton sites (relative to signals for free pyridine at equilibrium). Results represent an average of five measurements, each recorded immediately after shaking the NMR tube in a 0.5×10^{-4} T field (these methanol-d_4 based samples contained $[Ir(COD)(py)_2]BF_4$, one equivalent of PR_3 and pyridine).

indicated variation in polarization field simply reflects the fact that we are shaking the sample in the stray field of the main NMR magnet and consequently the sample experiences a varying magnetic field during this process.) Under these conditions, the ^1H sites magnetization amplitudes is dramatically reduced and hence so is the efficiency of polarization transfer. In contrast, the efficiency of polarization transfer to ^{13}C increases as shown in Figure 7b. We also note, that no magnetization transfer is observed when the polarizing field strength exceeds 1 T. These data therefore confirm that the user must be wary of the effects of both the polarization field and the associated temperature on the strength of the NMR signals that can be observed later. We interpret these effects to relate both to the lifetime of the complex and the interplay between the chemical shift difference of these resonances and the spin−spin couplings that connect them while bound to the template. Such effects are expected and have been rationalized for hydrogenation products previously.[26]

Effect of the Phosphine's Identity on the Iridium Template's Ability to Polarize Pyridine. Others have shown, that related complexes $[Ir(COD)(PR_3)(py)]BF_4$ can be prepared *in situ* by the simple addition of the appropriate phosphine to a solution of $[Ir(COD)(py)_2]BF_4$ (**3**).[25] This complex therefore serves as an ideal precursor for the screening of the phosphines influence on this process by the collection of comparative data. A series of samples, containing equimolar amounts of **3** and a phosphine from the list PCy_3, $PPhCy_2$, PPh_2Cy, PEt_3, P^iPr_3, P^nBu_3, P^tBu_3 and P(1-naphthyl)$_3$ were therefore prepared. Figure 8 reveals how the signal enhancements for the three free pyridine resonances (quoted relative to the intensity of the same sites pyridine signal recorded under equilibrium conditions) change with phosphine for polarization transfer in an external magnetic field of strength 0.5×10^{-4} T. On this basis, we conclude that the identity of the phosphine has a dramatic effect on the efficiency of polarization, presumably as a consequence of changing the ligand exchange rates. We further note that the electron rich and most sterically demanding phosphine PCy_2Ph was the most successful in achieving polarization transfer to the hydrogen atoms in pyridine. It can also be seen from the data, that the single *para*-proton consistently shows the largest signal gain with the resultant intensities for the PCy_2Ph system be close to 1:1:1 and can therefore be integrated.

Experimental Section

NMR measurements were made on a Bruker Avance III series 400 MHz NMR spectrometer (^1H at 400.13 MHz, ^{31}P at 161 MHz, ^{15}N at 40 MHz). NMR samples were made up in 5 mm Young's tapped NMR tubes. Typical samples contained 2 mg of the iridium complex dissolved in CD_3OD (600 μL) with the pyridine being added by microsyringe. Samples were degassed at −78 °C and then pressurized with 3.5 bar p-H_2 before appropriate NMR measurements were recorded. p-H_2 was prepared by cooling the gas to 20 K over activated charcoal as described previously.[27]

X-ray data were obtained for a crystal of **2** at 110 K using a Bruker Smart Apex diffractometer with Mo Kα radiation (ν = 0.71073 Å) in conjunction with a SMART CCD camera. Diffractometer control, data collection and initial unit cell determination was performed using "SMART" (v5.625 Bruker-AXS). Frame integration and unit-cell refinement software was carried out with the "SAINT+" (v6.22, Bruker AXS) package. Absorption corrections were applied by SADABS (v2.03, Sheldrick). The structure was solved via a Patterson map using ShelXS (Sheldrick, 1997) and refined using ShelXL (Sheldrick, 1997). Crystals were grown from a methanol solution of **1** which contained H_2 and pyridine. Syntheses: Tri(cyclohexyl)phosphine was secured from Aldrich, pyridine (Aldrich) and ^{15}N-pyridine (Cambridge Isotopes) were used as supplied and stored under N_2. $[Ir(COD)(PCy_3)py]BF_4$ (**1**) and $[Ir(COD)(py)_2]BF_4$ (**3**) were prepared by literature methods.[28,25] The remaining phosphines were sourced from STREM.

Conclusions

We have illustrated here an alternative method for the generation of non-Boltzmann spin state populations in organic substrates by utilizing *para*hydrogen as a polarization reservoir. Unlike previous approaches, it does not involve a formal hydrogenation reaction. Instead, the substrate and *para*hydrogen are brought into temporary association through a transition metal complex. Spontaneous sharing of spin polarization occurs from the hydride ligands of this template to the substrate over seconds while they are located in a low magnetic field regime. Ligand exchange then results in the free and chemically unmodified substrate achieving a non-Boltzmann spin state population for its NMR active nuclei. This route has been shown to lead to magnetization transfer to ^1H, ^{13}C and ^{15}N nuclei by reference to pyridine with the resultant magnetization profile that is created being critically dependent on the strength of the magnetic field the sample is in during the polarization transfer step. When samples of polarized pyridine were interrogated by NMR spectroscopy, the observed ^1H signal strengths were found to exceed those normally available by up to 110 fold. Such signal improvements are of great significance since the signal-to-noise ratio varies with the square of the number of observations. In the case of one ^{13}C measurement, the 116 fold signal gain requires a 13450 scan average to match the signal-to-noise ratios when normal magnetization is employed. If there is a 15 s delay between measurements, 56 h of spectrometer time would be

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needed to achieve this rather than the 3 s necessary for the polarized measurement.

This simple method of achieving magnetic polarization has clear advantages over earlier approaches with *para*hydrogen since there is no longer a need to incorporate *para*hydrogen derived nuclei into the product. Consequently, the nuclear polarization of materials is now possible where no dehydro-analogues of the substrate are available. Thus, the method presented here has the potential to polarize a range of substrates that are not amenable to polarization by the more traditional hydrogenative route, and we believe there is clear potential for utilization of this approach in both routine high-resolution NMR experiments and medical imaging applications.

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Supporting Information Available: X-ray data, sample preparation and signal enhancement methods. This material is available free of charge via the Internet at http://pubs.acs.org.

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