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A Magnetic Switch for Spin-Catalyzed Interconversion of Nuclear Spin Isomers

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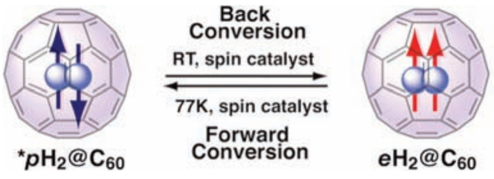
Received December 4, 2009; E-mail: njt3@columbia.edu

Dihydrogen, H_2, exists as two allotropes or nuclear spin isomers: a nuclear singlet state with antiparallel (↿⇂) nuclear spins, termed *para*-hydrogen (pH_2), and a nuclear triplet state with parallel (↿↾) nuclear spins, termed *ortho*-hydrogen (oH_2).[1]

According to the Pauli Principle, singlet pH_2 is required to occupy even rotational states ($J = 0, 2, 4, ...$) and triplet oH_2 odd rotational states ($J = 1, 3, 5, ...$). Since $J = 0$ is the lowest rotational level of H_2, pH_2 is the ground rotational state and oH_2 a rotationally excited state. The energy gap between the $J = 0$ and $J = 1$ rotational states is 120 cm^{-1} (0.343 kcal mol^{-1}). The equilibrium mixture at any given temperature is termed eH_2. At room temperature (RT), triplet oH_2 dominates at equilibrium (eH_2 = 75% oH_2/25% pH_2) because of its higher statistical weight and the small energy gap between the two rotational levels.

The two allotropes of hydrogen, oH_2 and pH_2, may be quantitatively incarcerated into C_{60} to form the endofullerene guest@host complexes[2–4] $oH_2@C_{60}$ and $pH_2@C_{60}$, respectively. We have developed[5] the following procedure for producing samples of pH_2-enriched $H_2@C_{60}$ in which the incarcerated H_2 spin isomers are not in spin equilibrium at RT: (1) adsorbing a sample of $eH_2@C_{60}$ on the external surface of NaY zeolite at RT; (2) cooling the sample to 77 K; (3) immersing the sample in liquid oxygen at 77 K, thereby converting the sample to a 50% oH_2/50% pH_2 mixture (which is eH_2 at 77 K); (4) removing the spin catalyst (O_2) by applying a vacuum; (5) rapidly bringing the sample to RT before the sample can back-convert to equilibrium at RT; and (6) extracting the sample into a solvent at RT. The sample at RT is enriched in pH_2 (nonequilibrium 50% pH_2 rather than the equilibrium 25% pH_2) and is termed $^*pH_2@C_{60}$.

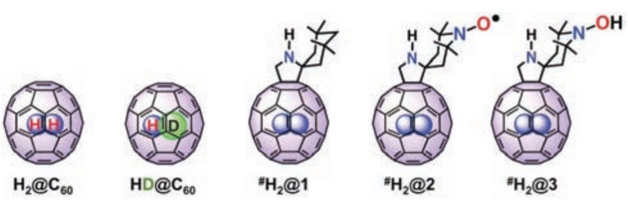
At RT, the back conversion of $^*pH_2@C_{60}$ to $eH_2@C_{60}$ takes days in the absence of an added spin catalyst. The conversion of $^*pH_2@C_{60}$ to $eH_2@C_{60}$ (eq 1) is followed conveniently by ^1H NMR spectroscopy using a sample that contains $HD@C_{60}$, which does not have spin-rotational isomers, as an internal standard.



(1)

At RT, nitroxides serve as paramagnetic spin catalysts for the back conversion of $^*pH_2@C_{60}$ to $eH_2@C_{60}$.[5] We reasoned that if a derivative of $H_2@C_{60}$ could be rapidly switched from a diamagnetic nitroxide precursor to a paramagnetic nitroxide, a "magnetic switch" for forward conversion ($eH_2@C_{60} \rightarrow {}^*pH_2@C_{60}$) at 77 K and back conversion ($^*pH_2@C_{60} \rightarrow eH_2@C_{60}$) at RT would be available. We describe the design and demonstration of such a magnetic switch based on the reversible nitroxide/hydroxylamine system[6] $^{\#}H_2@\mathbf{2}$ and $^{\#}H_2@\mathbf{3}$ (Chart 1).

Chart 1. Structures of $H_2@C_{60}$, $HD@C_{60}$, $H_2@\mathbf{1}$, $H_2@\mathbf{2}$, and $H_2@\mathbf{3}$ (Blue Balls Indicate Incarcerated H_2 or HD; # Indicates That the Sample Is a Mixture of H_2@Host and HD@Host)



We investigated the spin conversion of $^{\#}H_2@\mathbf{1}$, a diamagnetic derivative of $^{\#}H_2@C_{60}$, in order to determine the effect of substitution on the forward and back conversions of the incarcerated spin isomers of H_2. Figure 1a shows the initial and final ^1H NMR spectra of $^{\#}H_2@\mathbf{1}$ that was put through the enrichment procedure described above. The black curve corresponds to the initial sample of $eH_2@\mathbf{1}$. The signal at −4.43 ppm corresponds to the ^1H signal from $oH_2@\mathbf{1}$, and the other three signals correspond to the ^1H signals from $HD@\mathbf{1}$ (the triplet results from the coupling of ^1H with ^2H).[7] The red curve corresponds to the ^1H NMR signals after conversion. Clearly, the proportion of $oH_2@\mathbf{1}$ relative to $HD@\mathbf{1}$ decreased as expected: the signal intensities are consistent with a 50%/50% mixture of $oH_2@\mathbf{1}$/$pH_2@\mathbf{1}$, corresponding to $^*pH_2@\mathbf{1}$. At RT, the back conversion rate of $^*pH_2@\mathbf{1}$ to $eH_2@\mathbf{1}$ without a spin catalyst is similar to that of $^*pH_2@C_{60}$ to $eH_2@C_{60}$ (see Table 1), showing that the substitution by itself does not significantly modify the rate of the back conversion.

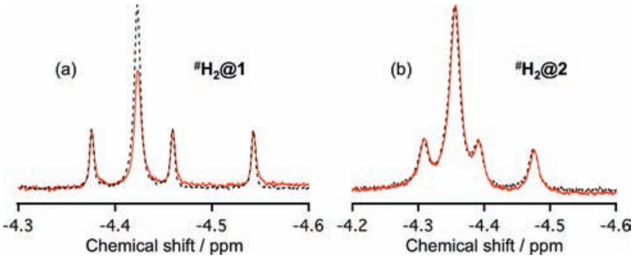


Figure 1. ^1H NMR analysis of the forward conversion of (a) $eH_2@\mathbf{1}$ (black curve) to $^*pH_2@\mathbf{1}$ (red curve) and (b) $eH_2@\mathbf{2}$ (black curve) to $^*pH_2@\mathbf{2}$ (red curve) in $CDCl_3$.

The $H_2@\mathbf{2}$ sample was cooled to 77 K for several hours according to the usual procedure, and then the NMR spectrum was recorded as

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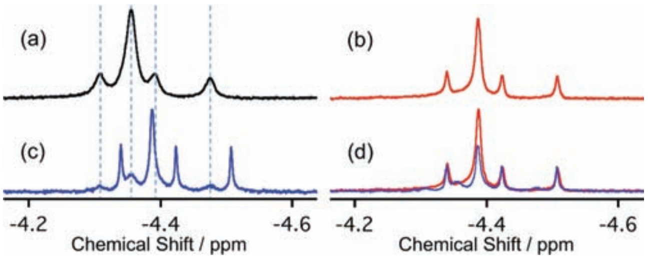
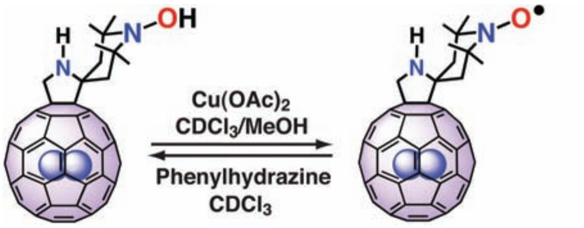


Figure 2. ^{1}H NMR analysis in $CDCl_3$. (a) Initial sample of $^{\#}H_2@\mathbf{2}$. (b) After treatment of $^{\#}H_2@\mathbf{2}$ to produce $^{\#}H_2@\mathbf{3}$. (c) After treatment of $^{\#}H_2@\mathbf{3}$ with liquid O_2 at 77 K and sample workup. (d) Normalized overlap of (b) and (c). Dotted lines indicate the $^{\#}H_2@\mathbf{2}$ signals.

quickly as possible after the sample was warmed to RT. Within the fastest workup possible (90 s), no spin enrichment was observed [in Figure 1b, the final ^{1}H signals (red and black curves) are indistinguishable]. We hypothesize that the paramagnetic nitroxide substituent of $H_2@\mathbf{2}$ is such an effective spin catalyst that at RT it causes a rapid back conversion of $^*pH_2@\mathbf{2}$ produced at 77 K to $eH_2@\mathbf{2}$ during the workup of the sample.

To test the hypothesis that spin enrichment to $^*pH_2@\mathbf{2}$ occurs but is rapidly reversed to $eH_2@\mathbf{2}$ during workup, we synthesized[8] (eq 2) a diamagnetic "masked" nitroxide, $^{\#}H_2@\mathbf{3}$ (Chart 1). In addition, we expected that $^{\#}H_2@\mathbf{2}$ would be regenerated by oxidation of $^{\#}H_2@\mathbf{3}$, creating a reversible *magnetic switch* for interconverting incarcerated nuclear spin isomers.



(2)

The broadened NMR (Figure 2a) and ESR (Figure S1a in the Supporting Information) spectra of the initial sample are consistent with those expected for paramagnetic $eH_2@\mathbf{2}$. Treatment of the sample with phenylhydrazine resulted in the conversion of paramagnetic $eH_2@\mathbf{2}$ to diamagnetic $eH_2@\mathbf{3}$. As expected, the resulting NMR signals were sharpened (Figure 2b) and the ESR signal disappeared (Figure S1b), consistent with essentially quantitative conversion of $eH_2@\mathbf{2}$ into $eH_2@\mathbf{3}$. Treatment of the $eH_2@\mathbf{3}$ with $Cu(OAc)_2$[8] produced the NMR and ESR spectra of $eH_2@\mathbf{2}$, demonstrating the reversible conversion of $eH_2@\mathbf{3}$ back to $eH_2@\mathbf{2}$ in >95% yield.

The hypothesis concerning the lack of a net conversion when $eH_2@\mathbf{2}$ is cycled to 77 K and back to RT (Figure 1b) could be tested next, since $eH_2@\mathbf{3}$ is a "caged" diamagnetic analogue of $eH_2@\mathbf{2}$. The strategy to test the hypothesis was to convert $eH_2@\mathbf{3}$ to $^*pH_2@\mathbf{3}$ at 77 K (analogous to the result for $eH_2@\mathbf{1}$ in Figure 1a), return the sample to RT, "uncage" the nitroxide to produce the paramagnetic $^*pH_2@\mathbf{2}$, and determine the extent of conversion.

The specific execution of the strategy for testing the hypothesis was as follows: First, treatment of $eH_2@\mathbf{3}$ under the forward conversion conditions (NaY/77 K/liquid O_2) was expected to cause conversion of $eH_2@\mathbf{3}$ to a sample of enriched $^*pH_2@\mathbf{3}$ that would be stable to back conversion at room temperature. Treatment of $^*pH_2@\mathbf{3}$ with $Cu(OAc)_2$ at room temperature would generate enriched $^*pH_2@\mathbf{2}$. If the hypothesis of rapid interconversion of the nuclear spin isomers of $^*pH_2@\mathbf{2}$ is correct, then at RT, that portion of the sample that was oxidized to $^*pH_2@\mathbf{2}$ would be rapidly converted to $eH_2@\mathbf{2}$.

The results of applying this strategy are shown in Figure 2. The ^{1}H NMR spectrum of the initial sample of $eH_2@\mathbf{3}$ is shown in Figure 2b.

Table 1. Relative Rates of *para*–*ortho* Conversion and Lifetimes of H_2, $H_2@C_{60}$, $H_2@\mathbf{1}$, and $H_2@\mathbf{2}$ at RT

conversion	relative rate	lifetime (s)
$^*pH_2 \rightarrow eH_2{}^a$	12−18	$3.6{-}5.4 \times 10^4$
$^*pH_2@C_{60} \rightarrow eH_2@C_{60}{}^b$	~1	$\sim 6.5 \times 10^5$
$^*pH_2@\mathbf{1} \rightarrow eH_2@\mathbf{1}^b$	~1	$\sim 6.5 \times 10^5$
$^*pH_2@\mathbf{2} \rightarrow eH_2@\mathbf{2}^b$	>7200	<90

[a] Data from ref 10. [b] In deoxygenated 1,2-dichlorobenzene-d_4.

The intensity of the H_2 signal relative to the integrated HD signal is a measure of the oH_2/pH_2 ratio and corresponds to the expected 75%/25% mixture of oH_2/pH_2 (eH_2 at RT). After the forward conversion procedure, the ^{1}H NMR showed that the sample was a mixture of $H_2@\mathbf{3}$ and $H_2@\mathbf{2}$ (Figure 2c), demonstrating that some degree of oxidation of $H_2@\mathbf{3}$ occurred, presumably during the treatment with O_2 during the workup.[9] Comparison of the ^{1}H NMR signals (Figure 2d) shows that $eH_2@\mathbf{3}$ was indeed enriched in pH_2 while $eH_2@\mathbf{2}$ was not. The results can be interpreted as follows: (1) some (~25%) of the $H_2@\mathbf{3}$ was oxidized to $H_2@\mathbf{2}$ during the procedure; (2) the $H_2@\mathbf{3}$ that survived oxidation was enriched in pH_2; (3) $H_2@\mathbf{2}$ was not enriched in pH_2; and (4) the concentration of $H_2@\mathbf{2}$ in the sample was insufficient to serve as a bimolecular catalyst for the back conversion of $^*pH_2@\mathbf{3}$. These results demonstrate convincingly that the $H_2@\mathbf{3}/H_2@\mathbf{2}$ system can act as a reversible switch that interconverts the incarcerated oH_2/pH_2 nuclear spin isomers.

These results show that the rate of nuclear spin interconversion of encapsulated H_2 can be markedly increased by attaching the paramagnetic catalyst to the cage. Furthermore, comparison of the catalyzed lifetime of $H_2@\mathbf{2}$ (< 90 s) with the uncatalyzed lifetime of ~7.5 days (6.5×10^5 s) for $H_2@\mathbf{1}$ (Table 1) demonstrates that the rate of back conversion may be varied by ~4 orders of magnitude by turning the catalyst on and off.

We are attempting to couple the ability to control the rate of conversion with the generation of nuclear polarization of the oH_2 produced by the interconversion. These results have potential for magnetic resonance imaging applications employing fullerenes containing H_2 as an imaging agent and for the application of the nitroxide and H_2 components of $H_2@\mathbf{2}$ for dynamic nuclear polarization.

Acknowledgment. The authors thank the National Science Foundation for its generous support through Grant CHE 07-17518.

Note Added after ASAP Publication. The structures of the fullerene derivatives were corrected on February 25, 2010.

Supporting Information Available: Synthesis and experimental details, including EPR analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA910282P