

producing signal in the range of 170 to 200 Hz. Long range couplings to other spins yield additional splitting.

**[0074]** FIG. 10 shows a zero-field PHIP spectra for several compounds in accordance with an exemplary embodiment of the present invention. In FIG. 10(a) parahydrogen is added to 1-phenyl-1-propyne, labelled with  $^{13}\text{C}$  in the  $\text{CH}_3$  group. In FIG. 10(b), parahydrogen is added to acetylene dimethylcarboxylate with  $^{13}\text{C}$  in natural abundance. In FIG. 10(c) parahydrogen is added to 3-hexyne with  $^{13}\text{C}$  in natural abundance FIG. 10(c). In FIG. 10(a) and FIG. 10(b), the imaginary component is presented; in (c), magnitude is presented.

**[0075]** Observations

**[0076]** The present invention can operate in zero magnetic field. Working in small but finite fields on the order of 1 mG may yield additional information regarding molecular structure, albeit at the expense of additional spectral complexity.<sup>27</sup>

**[0077]** A common objection to low- and zero-field NMR is that spectra become complex as the number of spins increase, as exemplified by comparison of the ethanol- $\alpha$ - $^{13}\text{C}$  spectrum reported in McDermott<sup>4</sup> and the ethylbenzene- $\alpha$ - $^{13}\text{C}$  obtained via the present invention. The increasing complexity of spectra with spin system size is a feature that is also encountered in standard high-field NMR, and has been successfully addressed by application of multi-pulse sequences and multidimensional spectroscopy. The theory of multiple pulse sequences for zero-field NMR has been worked out some time ago<sup>28</sup>, and presumably, many of the techniques developed for high field could be adapted to zero-field.

**[0078]** The present invention achieved linewidths of about 0.1 Hz. For  $^{13}\text{C}$ -H J-coupled systems, the dispersion in signal is about 300 Hz, so roughly 1500 lines can fit in a spectrum without overlapping. This is similar to what may be achieved in a 400 MHz spectrometer if proton chemical shifts ranging over 6 ppm and proton linewidths of about 0.5 Hz are assumed.

**[0079]** The sensitivity of the magnetometer used in the present invention was about 0.15 nG/Hz<sup>1/2</sup> using a vapour cell with a volume of 10 mm<sup>3</sup>. Sensitivities about 2 orders of magnitude better have been achieved in larger vapour cells<sup>29</sup>, which will enable measurements on larger samples with much lower concentration.

**[0080]** The present invention provides NMR without the use of any magnets by using parahydrogen induced polarization and a high sensitivity atomic magnetometer with a micro-fabricated vapour cell. The mechanism by which the symmetry of the singlet states is broken in zero field relies only upon the presence of heteronuclear J-coupling and not chemical shifts, in contrast to many experiments performed in high field. Hydrogen-carbon J-couplings through at least three bonds, and hydrogen-hydrogen couplings through four bonds are observed. It has been observed that polarization is naturally transferred through several bonds to remote parts of the molecule. This can be contrasted with in-situ hydrogenation in high field, where chemical shifts larger than J-couplings prevent efficient polarization transfer without the use of auxiliary RF pulses. Sensitivity is sufficient to perform J-spectroscopy on samples with  $^{13}\text{C}$  in natural abundance with very little signal averaging. The resulting spectra, while exhibiting a large number of lines, can easily be divided into different parts, which can directly be assigned to different isotopomers of the molecule at hand. While the present invention may appear limited to molecules to which hydrogen can be added, recent advances using iridium complex catalysts enable polarization of molecules without hydrogenation<sup>18,19</sup>, sig-

nificantly expanding the scope of applicability of zero-field PHIP. Since the development of zero-field NMR is still at an early stage it is not possible to fully gauge its competitiveness with high field NMR or portable lower resolution versions thereof, but it clearly has potential to become a low cost, portable method for chemical analysis.

#### Example

**[0081]** The invention will be described in greater detail by way of a specific example. The following example is offered for illustrative purposes, and is intended neither to limit nor define the invention in any manner.

**[0082]** Experimental Setup

**[0083]** The zero-field spectrometer of the present invention is similar to that of McDermott<sup>4</sup> and is shown schematically in FIG. 7 (a), including an atomic magnetometer, consisting of a Rb vapour cell and two lasers for optical pumping and probing, operates in the spin-exchange relaxation-free<sup>8</sup> regime. The cell is placed inside a set of magnetic shields (not shown), and residual magnetic fields are zeroed to within  $\approx 1$   $\mu\text{G}$ . The vapour cell has dimensions 5 mm $\square$ 2 mm $\square$ 1 mm, contains  $^{87}\text{Rb}$  and 1300 torr of  $\text{N}_2$  buffer gas mm, and was microfabricated using lithographic patterning and etching techniques.

**[0084]** The cell is heated to 210° C. via an electric heating element wound around an aluminium-nitride spool. The sensitivity of the magnetometer is about 0.15 nG/Hz<sup>1/2</sup> above 120 Hz, and the bandwidth is in excess of 400 Hz. A set of coils can be used to apply sharp,  $\approx 1$  G DC pulses in arbitrary directions to excite NMR coherences, and a separate set of coils (not shown) controls the ambient magnetic field inside the shields. Mixtures of catalyst, solvent, and substrate could be brought into proximity of the atomic magnetometer via a glass sample tube.

**[0085]** The sample was maintained at 80° C. by flowing air through a jacket surrounding the glass tube. In experiments at lower temperature, it was found that there was some nonuniform broadening of spectra, presumably due to the presence of catalyst in solid form. Parahydrogen was bubbled through the solution via 0.8 mm inner-diameter tube for several seconds at a pressure of about 70 PSI and flow rate of about 120 standard cc/min. Bubbling was halted prior to application of excitation pulses and signal acquisition. Data were acquired with sampling rate of 2 kS/s. In acquiring the spectrum of styrene with natural-abundance  $^{13}\text{C}$ , the phase of the excitation pulses was cycled with respect to that of the 60 Hz line frequency in order to reduce the line noise and its harmonics.

**[0086]** Production of Parahydrogen

**[0087]** Parahydrogen was produced at 29 K by flowing hydrogen gas through a bed of iron oxide catalyst in a setup similar to that described in Koptiyug<sup>30</sup> and then stored in an aluminium canister at room temperature and initial pressure of 150 PSI. Conversion of hydrogen to parahydrogen was about 95%, and storage lifetime was in excess of one week.

**[0088]** Sample Preparation

**[0089]** Isotopically labeled styrene was obtained from Cambridge Isotope Labs. Natural-abundance styrene and Wilkinson's catalyst<sup>31</sup> were obtained from Sigma-Aldrich. Styrene hydrogenations were performed with 300  $\mu\text{L}$  styrene and 4 mG Wilkinson's catalyst, Tris(triphenylphosphine)rhodium(I) chloride (CAS #14694-95-2). The 1-phenyl-propyne and dimethyl acetylenedicarboxylate reactions were performed with 100  $\mu\text{L}$  substrate in 300 ml tetrahydrofuran, catalyzed by 1,4-Bis(diphenylphosphino)butane(1,5-cy-