Low concentration measurements of nuclear spin-induced optical rotation using SABRE hyperpolarization

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Abstract

Nuclear spin-induced optical rotation (NSOR) is a promising phenomenon for molecular structure elucidation due to its sensitivity to electronic structure near atomic nuclei. It is the only experimentally verified nuclear magneto-optic effect, so far observed usually in neat liquids or in concentrated binary mixtures, with the proportion of the minor component at least 10%. We report a method to extend the lower concentration range of NSOR measurements by two orders of magnitude by employing continuous-flow SABRE (signal amplification by reversible exchange) hyperpolarization. This approach significantly increases sensitivity of NSOR and enables its detection in dilute samples, as demonstrated with measurements of NSOR of 90 mmol/l solutions of pyridine and pyrazine. The results are compared with first principles calculations and a good agreement is found. The possibility to measure low concentration solutions significantly extends the pool of samples available for further studies of nuclear magneto-optic effects.

Keywords: NSOR, nuclear spin-induced optical rotation, SABRE, hyperpolarization, nuclear magneto-optic effects, nuclear magnetic resonance, first principles quantum-chemical calculations

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Nuclear magneto-optic effects (NMOEs) is an umbrella term for a family of spectroscopic methods based on observing changes in the polarization state of light beam after its interaction with molecules possessing a non-zero nuclear spin magnetization. Since the perturbations involve electron cloud around the particular nucleus, the NMOEs promise to give new insights into the molecular structure with the resolution given by the local chemical environment, similarly as in nuclear magnetic resonance (NMR). Due to its relation to NMR, NMOEs contain information about detailed structural parameters, such as dipolar, quadrupolar or recently experimentally verified spin-spin couplings[1], or nuclear shielding. Moreover, the electromagnetic field of the light causes perturbations of the electron cloud that are not present in NMR and thus give rise to new observables. This is reflected in NMOEs as an additional aspect of the electronic structure and, for example, provides a selective response from groups involved in the electronic excitation[2, 3].

Out of the five described NMOEs[4, 5, 6, 2, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 1, 3], so far only nuclear spin-induced optical rotation (NSOR) has been observed, for a range of molecules including water[4, 6, 13, 12], organic liquids, such as alcohols[12], hydrocarbons[6, 12], halogenated hydrocarbons[6, 7, 12], organic phosphines and thiols.[7] and for xenon[4]. In general, these experiments share two common features: a) in most cases neat substances (pure liquids) were used as samples and b) they were polarized thermally in a strong magnetic field. Notable exceptions are work of Pagliero et.al [7], which probed binary mixtures of organic liquids with ratios as low as 1:9 and work of Savukov et al.[4], in which spin exchange optical pumping (SEOP) was used for hyperpolarization of Xe.

The choice of the sample of pure - i.e., highly concentrated - liquids is motivated by the rather low signal intensity of NSOR. This feature originates from low nuclear spin magnetization achievable via thermal polarization and limits sensitivity of NSOR in the same way as in the traditional NMR. The signal intensity of NSOR (for a single type of chemically distinct nucleus K) as a function of the incident light frequency $\nu$ can be expressed as

$$\Theta(\nu) = \eta(\nu) c_K l P_K$$

where $\Theta(\nu)$ is the rotation of the plane of polarization of the light in radians, $\eta(\nu)$ is a molecule-specific parameter (molar NSOR), $c_K$ is the concentration of the observed nucleus K, $l$ is the length of the sample traversed by the light beam and $P_K \in [0; 1]$ is the fractional magnetization of the nucleus K along the light beam. As $\eta(\nu)$ is a molecule-specific constant, the signal can be increased by varying only the remaining three parameters: concentration, length of optical path, and spin polarization. Increasing the concentration $c_K$ is the most straightforward approach and justifies the usage of pure substances in the previous studies. However, it is of a limited use, for example when investigating concentration dependence, chemical equilibria, when the sample is prohibitively expensive or simply is not in a liquid form by itself and has low solubility. The optical path $l$ can be varied rather freely, assuming the optical properties of the sample allow it. As an example, the increase of path has been exploited in previous works using multiple passes through a long cell, bringing the total length over 3 meters[12].

A very promising way how to increase the NSOR signal is through the polarization $P$, which is in thermally polarized samples, such as those produced in standard high-field NMR magnets, on the order of about $\sim 10^{-5}$. Since small values of $P$ are a nuisance in standard NMR and MRI as well, the so-called hyperpolarization (HP) techniques have been heavily investigated in recent years. Thanks to these advances, it is now possible to boost the signal by several orders of magnitude to achieve polarization levels of up to tens of percent[22, 23, 24, 25, 26, 27, 28]. The use of hyperpolarization was demonstrated in NSOR for the case of Xe polarized via spin-exchange optical pumping (SEOP)[4]. However, SEOP is limited solely to hyperpolarization of noble gases.

In this work, we demonstrate increase in the NSOR signal by employing the Signal Amplification by Reversible Exchange (SABRE) technique to boost the nuclear polarization. SABRE is a solution-based technique based on a reversible exchange of para-hydrogen gas and the target molecule at a metal catalyst center, which facilitate transfer of spin order from para-hydrogen to the substrate being hyperpolarized. SABRE has been shown to be a powerful method for several nuclei, including $^1$H, $^{13}$C, $^{15}$N, $^{19}$F, $^{31}$P, $^{29}$Si and $^{119}$Sn [29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39,
Figure 1: Sketch of the NSOR system. The laser beam produced by a diode laser (LAS, 520 nm or 690 nm, Thorlabs) is polarized to 45 degrees via linear polarizer (LP) and passes through the sample in a 7 cm long flow-through cell. The resulting beam is analyzed by Wollaston prism (WP) and balanced detector. The spin polarization is produced in a SABRE polarizer\cite{51}, which continuously supplies the fresh sample to the cell. The magnetization precesses along the $B_0(z)$ field, which is modulated with a frequency of 1 Hz to bring it in and out of resonance with continuous spin-locking field $B_1(y)$. The magnetization is thus periodically spin-locked in precession around the $z$-axis in the $xy$-plane or resting along the $B_0$. See SI for details.

Its further advantages compared to the other hyperpolarization techniques is its low costs and relative versatility accommodating for a range of different substrates.

The NSOR was measured in a low-field custom-build system, schematically depicted in Fig. 1. The sample, which is produced in SABRE polarizer\cite{51} interfaced with the optical system, is continuously pumped into a cylindrical glass cell (length 70 mm, inner/outer diameter 10 mm/13 mm) inside a custom-made electromagnet coil system. Thermally polarized sample prepared by placing a container in a superconducting 14.1 T (600 MHz) NMR magnet was measured for reference. Since the sample in SABRE experiment contains salts and organic solvents, it is preferable to isolate the pumping mechanism from the contact with the sample itself. This motivated us to use a peristaltic pump, which, however, has usually rather limited available flow rates. For these reasons we opted for a smaller cell with shorter pathlength (7 cm) compared to previous experiments and compensated for this by longer measurement time.

The spin-polarized sample is subjected to two magnetic fields: an alternating field $B_1$ in the $y$-direction (perpendicular to the axis of the cell) and a static $B_0$ field in the $z$-direction (vertical), which is sum of stray field from the 600 MHz NMR magnet (0.12 mT) and a field generated by the electromagnet (0.37 mT). The $B_0$ field is modulated at the frequency of 1 Hz using a slow ramp, to bring the proton Larmor frequency in and out of the resonance with the $B_1$ field. The signal is thus modulated at frequency of 1 Hz (see Methods section and SI for more details).

The obtained values were compared with the NSOR calculated using BHandHLYP density functional and coupled cluster singles and doubles (CCSD) with three completeness optimized basis sets\cite{52} co0\cite{9}, co2\cite{53,12} and co2-MOR\cite{18}. Theoretical results were corrected for the local effects of the medium on the optical field and for the Faraday rotation arising from the long-range...
The results of measurements are shown in Fig. 2. Three experiments were conducted: a) NSOR of thermally polarized neat pyridine; b) NSOR of pyridine solution in methanol, polarized using SABRE; c) NSOR of solution of pyrazine in methanol, polarized using SABRE. The NSOR signals normalized for concentration, length of optical path, and nuclear polarization and calculated values corrected for the medium effects\cite{8, 9} (see SI for details) are reported in Table 1. The data were obtained by averaging a total of 16000 s measurement.

Figure 2a shows the NSOR signal of thermally polarized neat pyridine ($c_{\text{pyridine}} = 12.4 \text{ mol/l}$) as a function of the $B_0$ modulation. The sharp peak at 1 Hz clearly indicates presence of observable NSOR signal. To affirm that the signal is not caused by any interference, a baseline measurement was performed where the container with the pyridine was lowered below the NMR magnet, placing it in a comparatively negligible magnetic field and thus removing the thermal polarization. Under these circumstances the peak at 1 Hz could no longer be observed, indicating its origin in nuclear magnetization (see SI).

Figure 2b shows the NSOR signal of pyridine ($c_{\text{pyridine}} = 90 \text{ mmol/l}$), in methanol polarized using SABRE. The NSOR signal stemming from the hyperpolarized pyridine can be clearly observed. The intensity is slightly larger compared to the case of thermally polarized pyridine, in line with the increase of nuclear polarization as observed with NMR. It is worth noting that the NSOR intensities are not directly proportional to the increase in NMR signal due to contribution of the Faraday effect, which is considerably larger in pyridine than in methanol.

The results for the third sample, the solution of pyrazine ($c_{\text{pyrazine}} = 86 \text{ mmol/l}$), are shown in Fig. 2c. Note that laser of different wavelength ($\lambda = 690 \text{ nm}$) compared to the above experiments was used due to the optical properties of the solution. The NSOR signal is again clearly visible above the noise level, with the statistical significance safely exceeding 3 standard deviations (see Table 1). This result demonstrates the main benefit of our approach, i.e., the possibility to observe NSOR from molecules that are at standard conditions solid and thus require to be measured in solution.

It might be noticed that the level of noise between different experiments vary. This can be explained by usage of different laser sources and as an effect of different properties of the solution, such as viscosity and the amount of dissolved gasses, which affect the flow and the bubble formation in the liquid during the pumping.

The results for NMR signals and experimental as well as calculated NSOR intensities are
Table 1: Summary of the results and relevant properties of the three measured samples, showing concentration $c$, measured NMR signals in nA, calculated average proton polarization $P_H$, measured optical rotation reported with $\pm 3\sigma$, normalized experimental NSOR and theoretically calculated NSOR using CCSD/co2-MOR, including corrections for bulk properties. NSOR values are reported as average per proton. Further results from calculation using different methods are shown in SI.

| Sample          | $c$ mol-$\text{l}^{-1}$ | NMR current nA | $P_H$ % | $\Theta$ nrad | NSOR (exp) $\mu$rad mol-$\text{l}^{-1}$ cm$^{-1}$ | NSOR (calc) |
|-----------------|-------------------------|----------------|--------|--------------|--------------------------------|-------------|
| pyridine (thermal) | 12.4                    | 475            | 1.56e-3 | 1.53 ± 0.21  | 0.87                                | 1.03        |
| pyridine (SABRE)   | 0.090                   | 718            | 0.324  | 1.72 ± 0.14  | 0.65                                | 0.80        |
| pyrazine (SABRE)   | 0.086                   | 881            | 0.521  | 1.28 ± 0.19  | 0.39                                | 0.47        |

summarized in Table 1 together with key sample properties. NMR intensities of comparable magnitude can be observed in all three samples, despite two or more orders of magnitude difference in their concentrations, confirming presence of hyperpolarized sample. Accordingly, the NSOR signals are of similar intensity.

It can also be seen that the experimentally obtained NSOR signals compare rather well with the ones from quantum chemical calculations. The differences can be attributed to the common features of the first principle calculations of properties of moderately sized molecules in condensed phase, such as approximate wavefunction (or density), basis set effects and absence of rovibrational corrections and explicit solvent-solute interactions. The calculated values were corrected for the average effect of the solvent on the optical field and for the Faraday rotation caused by the magnetization of the sample. It is noteworthy that the latter correction accounts for the difference between NSOR of pyridine in neat liquid and in methanol, as pyridine has about three times larger Verdet constant and thus more significant contribution to the rotation. This effect is reproduced in the calculated results.

The total NSOR signals are on the similar scale, albeit somewhat weaker, compared to protons in other organic molecules reported earlier[12]. The overall weaker signal is in large part due to longer laser wavelength compared to previously used 405 nm, as NSOR signal is decreasing with wavelength[4, 9]. The shift in wavelength is also the cause of most of observed difference in NSOR between pyridine and pyrazine as quantum chemical calculations show that at the same wavelength the signals would be of similar magnitude.

We have presented a new approach to measure nuclear spin-induced optical rotation at low concentrations by employing continuous polarization with SABRE method and demonstrated the utility of the technique on measurements of dilute solutions of pyridine and pyrazine. The approach allows to measure samples at concentrations by at least two orders of magnitude lower compared to neat substances employed in majority of previous studies. Notably, we demonstrated the feasibility of NSOR measurements of solid substances by combination of dissolution and hyperpolarization. Although SABRE is not as general method for hyperpolarization as DNP (dynamic nuclear polarization), the setup can be constructed with only modest financial investments and the preparation of the sample is repeatable, rather fast and can be implemented in continuous mode. The presented methodology opens a way to significantly broaden the range of molecules accessible for NSOR measurements and development of deeper understanding in this new emerging field of spectroscopy.

**Methods**

The laser beam is supplied by a 520 nm or 690 nm laser diode (Thorlabs) and is passed through a linear polarizer, which prepare the light polarized at 45 degrees with respect to the vertical plane. The light beam passes through the sample, acquires optical rotation and is analyzed by Wolaston prism and difference detector. Due to the flow of the liquid and formation of small bubbles, the light intensity is diminished from the initial value by about 30% (50 % in the case
of pyridine/SABRE due to slight absorption by SABRE catalyst). The signal from the optical detector is fed into lock-in amplifier (MFLI, Zurich Instruments) tuned to the frequency of $B_1$. Since the envelope of the measured signal is modulated at the frequency of the $B_0$ field, the signal from the optical detector is Fourier transformed and the NSOR signal appears at the $B_0$ modulation frequency (i.e., 1 Hz). To obtain the degree of nuclear magnetization, a reference NMR signal was measured as a current induced in a solenoid coil wound around the sample cell (140 turns, 4 layers, $R = 8.6 \, \Omega$, $L = 1.139 \, \text{mH}$). The NMR circuit was kept open during the measurement of NSOR to avoid induction of extraneous magnetic field which would give rise to Faraday rotation artefacts. The instrument control and data acquisition was done using custom LabVIEW programs.

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Low concentration measurements of nuclear spin-induced optical rotation using SABRE hyperpolarization

Supplementary Information

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1 Sample preparation

The SABRE polarizer has been described in detail in previous publication[1]. The sample is continuously pumped by peristaltic pump in a closed loop between the measurement cell and polarizing cell, where it is bubbled by para-hydrogen in the field of 6.8 mT to constantly renew the solution and the nuclear polarization. The para-hydrogen gas is produced by a commercial generator (Bruker PHG0090-2), yielding approximately 92% para-H$_2$. The pressure of para-hydrogen was kept constant at 3.5 bar (absolute) by back-pressure regulator. The samples for SABRE were degassed prior to measurement using two pump-freeze cycles with liquid nitrogen to increase relaxation times. Deuterated methanol was used to avoid production and detection of hyperpolarized solvent[2, 3, 4, 5, 1], which would complicate the signal interpretation since the low-field setup does not allow to easily separate NSOR signal from chemically distinct hydrogen centers. Moreover, it also helps to further increase relaxation time compared to non-deuterated methanol. The relaxation times in SABRE experiments were 13 seconds, compared to 3.3 seconds in pure pyridine.

The sample for measurement of pyridine has been prepared by dissolving 135.6 mg of SABRE catalyst precursor [Ir(COD)(IMes)]Cl in 75 ml of deuterated methanol (Sigma Aldrich) and adding 544 µl of pyridine (Sigma Aldrich). The fresh sample was yellow and turned paler upon activation with bubbling hydrogen.

The pyrazine sample was prepared by dissolving 140.4 mg of SABRE catalyst and 515.4 mg of pyrazine (Sigma Aldrich) in 75 ml of deuterated methanol (Sigma Aldrich). The freshly prepared sample was yellow-orange and upon activation turned darker, about the color of strong rooibos tea. Due to this change in color, the laser used in this experiment was not 520 nm as in the case of pyridine, but was changed to 690 nm. The need to take into account the color of the catalyst presents a certain restrictions on the substrate/catalyst/laser wavelength combinations.

A reference measurement of neat pyridine was done with pure thermally polarized pyridine using a PTFE container positioned in maximum $B_0$ field inside 600 MHz NMR magnet and continuously pumped to the cell. The optical and magnet setup was otherwise identical to the experiments using SABRE.

The SABRE catalyst was prepared according to previous protocols[1].

2 NSOR signal measurement and processing

The optical rotation is measured using a beam oriented at 45 degrees with respect to horizontal plane. After splitting the beam into two orthogonal components corresponding to horizontal and vertical polarization, the difference in optical rotation from the diagonal plane can be calculated from light intensities polarized in horizontal ($I_h$) and vertical ($I_v$) plane

$$\Theta(t) = \frac{1}{2} \frac{I_h(t) - I_v(t)}{I_h(t) + I_v(t)}$$

All of the quantities are measured over time. Since the signal is beating at the frequency of 1 Hz as the spins are periodically flipped from the z-axis to precess around the z-axis in the $xy$-plane, the $\Theta(t)$ is Fourier transformed to obtain its representation in frequency domain.

$$\Theta(f) = A_w A_c \cdot F[\Theta(t)]$$

The factor $A_w$ stands for a correction of the wave-shape. Although the form of the $B_0$ field modulation is known, the magnetization is spin-locked into $xy$-plane only when the $B_0$ field reaches value close enough for the spin-locking field to engage and rotate the magnetization to the $xy$-plane. Thus, the form of $B_0$ and the envelope of NMR/NSOR beats do not have the same wave-shape (see Fig. S1). For this reason the reference NMR signal has been used to calibrate the amplitude of the Fourier coefficient of the signal envelope at 1 Hz. By comparing the amplitude obtained by simple averaging of 1 second-long blocks of the NMR signal in time domain with the amplitude of
Figure 1: Due to the less efficient spin-locking far from resonance the envelope of demodulated NMR/NSOR signal has different profile than the $B_0$ modulation. The coefficient $A_w = 2.27$ describes the ratio of the full signal amplitude (peak-to-peak between on resonance vs. off resonance) to the amplitude obtained from Fourier transform, and was obtained experimentally from NMR measurements by comparing peak-to-peak currents and signal at 1 Hz after Fourier transform.

its Fourier image in frequency domain at 1 Hz it is possible to calculate the correction factor for the NMR and NSOR Fourier coefficient at 1 Hz and obtain the correct amplitude for weaker NSOR signal. The coefficient was determined to be $A_w = 2.27$, which means that a wave of this shape, frequency 1 Hz and peak-to-peak amplitude of 1 V would produce intensity at 1 Hz $0.44 = 1/2.27$ in the frequency domain.

The cell geometry also needs to be taken into consideration. In previous studies using flow systems the cell length was considerably larger than in our case, such as 50 cm[6, 7] or 22.5 cm[8]. This means that in the present case the outer edges of the cell represent a relatively significant portion of the cell. Moreover, because of the single pass geometry, the laser beam samples only one particular trajectory through the cell and does not necessarily intersect the path yielding the same average nuclear polarization obtained from measurement of the bulk. For this reason we introduce a factor, $A_P = 1.7$, which has been determined as ratio of NSOR of methanol from the literature[8] and that measured in our cell. This factor scales the obtained values and account for both the flow in the cell and beam path geometry.

The Fourier transform was performed on 4000 seconds long blocks and eq. 2 was applied. From there the normalized NSOR signal has been calculated using the eq. 1 in main text with $l = 7$ cm, spin polarization $P_K$ determined from NMR, and corresponding concentrations $c_K$.

3 Nuclear polarization calculation from NMR

Macroscopic magnetization, $M$, along the external magnetic field, $B_0$ (in the z direction), arising from the magnetic moments of individual protons (spin = 1/2) is

$$M = \frac{\Delta n \mu_H}{V_s},$$  

(3)

where the magnetic moment $\mu_H = 1.410 \times 10^{-26}$ J/T, $V_s$ is the active volume of the sample cell and $\Delta n = (n_\alpha - n_\beta)$ is the population difference between the two energy levels. The magnetic flux density arising from this magnetization is

$$B_m = \mu_0 M,$$  

(4)

where $\mu_0 = 4\pi \times 10^{-7}$ H/m is the vacuum permeability. Due to the spin-lock field, $B_1$ applied on frequency $\nu_0 = \frac{B_1}{2\pi}$ along y-axis, the magnetization rotates with this frequency in the $xy-$plane.
Figure 2: Plots of measured NSOR signals for thermally polarized pyridine (top) and SABRE polarized pyrazine (bottom) showing also the baseline measurements (right side). The baseline measurements were taken in exactly the same way, except a) the container taken out of the 600 MHz magnet in the case of thermal polarization; b) the system was not supplied with para-hydrogen in the case of SABRE.
According to the Faraday’s law of induction, the magnetic flux, \( \phi_B(t) = \int B_m(t) \cdot dA \), will induce a voltage, \( U_{\text{ind}} \), into the solenoid coil wound along the \( x \)-axis around the sample cell

\[
U_{\text{ind}} = -N_s \frac{d\phi_B(t)}{dt}
\]

which will lead to peak-to-peak voltage

\[
U_{\text{pp}} = \frac{4\pi\nu_0\mu_0\mu_H N_s A_s \Delta n}{V_s}
\]

where \( N_s \) = number of the loops in the solenoid, \( A_s = \frac{1}{4} \pi d^2 \) is the cross-sectional area of the solenoid (\( d \) = diameter). The solenoid had four layers of 140 loops per layer. The efficiency of the coil was tested to scale linearly with the number of layers by measuring the induced current while reducing layers one by one, i.e. in our experiments \( N_s = N_{\text{loop}} \times N_{\text{layer}} = 560 \). The induced peak-to-peak current is now

\[
I_{\text{pp}} = \frac{U_{\text{pp}}}{Z_s}
\]

where \( Z_s = \sqrt{(2\pi\nu_0 L)^2 + R^2} \) is the impedance of the solenoid. From the measured currents, \( I_{\text{rms}} = I_{\text{pp}}/(2\sqrt{2}) \), we can now calculate the polarization level as

\[
P = \frac{\Delta n}{n} = \frac{2\sqrt{2}I_{\text{rms}}Z_s V_s}{4\pi\nu_0\mu_0\mu_H N_s A_s n}
\]

where \( n = n_{\alpha} + n_{\beta} = cN_A V_s n_{\text{mol}} \) (\( c = \) concentration, \( N_A = \) Avogadro’s number and \( n_{\text{mol}} = \) number of contributing spins in a molecule) is the total number of active spins i.e. number of pyridine/pyrazine molecules in the studied sample volume times 5 protons per each pyridine molecule or 4 protons per each pyrazine molecule. In the thermally polarized pyridine, all protons make equal contribution to the magnetization (apart from slight deviations due to different relaxation times of the protons), but in SABRE this is not typically the case as different protons gain different amount of polarization in the process. As we have no exact knowledge about the individual contributions, calculation of the polarization level gives an average value for the protons. According to calculations, the NSOR is comparable for all protons in pyridine/pyrazine, so this assumption does not have effect on the obtained results. For fully polarized sample \( P = 1 \), and for spin-1/2 nuclei this corresponds to the average spin component along \( z \)-axis \( I_{K,z} = 1/2 \).

4 Quantum chemical calculations

The measured NSOR molecular parameters of pyridine and pyrazine have been compared with the theoretical calculations of NSOR using DALTON[9] program package. The molecular geometries were optimized at B3LYP/def-TZVP level in Turbomole 7.2[10]. NSOR parameters were calculated using BHandHLYP density functional and coupled clusters singles and doubles (CCSD) with completeness optimized basis sets[11] co0[12], co2[13, 8] and co2-MOR[14]. The co2 basis set was optimized for related molecular property of laser induced NMR shifts, the other ones for magnetic optical rotation properties. It should be noted that co2 sets were constructed using molecules containing only hydrogen and carbon, while co0 was calibrated using HF molecule and thus covers wider range of atoms up until fluorine. The results were corrected for the effects of medium on the local optical field[12] by multiplication with

\[
\frac{1}{n} \left( f_c + \frac{f_{\alpha} f_{\alpha}}{1 - \alpha f_{\alpha}} \right)
\]

5
where $n$ is index of refraction of the medium and $\alpha$ the molecular polarizability. The first factor in eq. 9 $f_c = \frac{3\epsilon_r(\omega)}{2\epsilon_r(\omega)+1}$ accounts for the modification of the local optical field by the cavity the molecule occupies in the solution. The second factor with $f_r = \frac{1}{2\pi\epsilon_0 a^3} \left( \frac{\epsilon_r(\omega)}{2\epsilon_r(\omega)+1} \right)$ takes into account the reaction field of the molecule\[12\]. In here $\epsilon_r(\omega)$ is relative permittivity, $\epsilon_0$ is permittivity of vacuum and $a$ is the radius of the molecular cavity, calculated as $a = \left( \frac{3}{4\pi N} \right)^{1/3}$, where $N$ is the number density.

Since the magnetized sample also induces Faraday rotation in the bulk medium, the results were corrected by adding a corresponding contribution to the calculated value.

$$\Theta_{FOR} = \frac{1}{3} N \mu_0 N l V_{K,z}$$

where $N$ is the concentration of the polarized nuclei, $l$ is the length of the cell, $\mu_0$ is vacuum permeability, $\mu_N$ is the nuclear magnetic moment - product of reduced Planck constant $\hbar$ and gyromagnetic ratio $\gamma_K$, $V$ is the Verdet constant of the medium and $I_{K,z}$ the average spin polarization in the direction of the light beam $z$. Note that the magnetic field is generated in the case of SABRE experiments by the spins from pyridine or pyrazine, for which the concentration and polarization must be calculated, but the affected medium - and thus the corresponding Verdet constant - is methanol. Verdet constants used were $V_{\text{MeOH}}(520\text{ nm}) = 3.49\text{ rad/T/m}$, $V_{\text{MeOH}}(690\text{ nm}) = 1.93\text{ rad/T/m}$ [15] and $V_{\text{pyridine}}(520\text{ nm}) = 9.78\text{ rad/T/m}$. Value of Verdet constant for pyridine was measured in our system calibrated by measurements of methanol and water.

The results are summarized in Table 1. As can be seen, the basis sets co2-MOR and co0 compare quite well, despite the co0 being almost twice as large as co2-MOR. The very close agreement between experiment and calculations with co2 basis set is most likely fortuitous and a result of error cancellation since our model includes several approximations. Nevertheless, the values are reproduced with all models to within about 20% accuracy.
|                              | pyridine (neat) | pyridine (MeOH) | pyrazine (MeOH) |
|------------------------------|-----------------|-----------------|-----------------|
| Experiment                   | 0.87            | 0.65            | 0.39            |
| Faraday rotation contribution| 0.35            | 0.12            | 0.07            |
| $f_c/n$                      | 0.815           | 0.879           | 0.782           |
| $f_R/n$                      | 0.130           | 0.065           | 0.119           |
| Total medium correction      | 0.945           | 0.945           | 0.900           |
| BHandHLYP/co0               | 0.69            | 0.69            | 0.43            |
| Medium corrected             | 0.65            | 0.65            | 0.39            |
| Total                        | 1.00            | 0.78            | 0.46            |
| Total                        | 0.87            | 0.65            | 0.37            |
| BHandHLYP/co2               | 0.55            | 0.55            | 0.33            |
| Medium corrected             | 0.52            | 0.52            | 0.30            |
| Total                        | 0.87            | 0.65            | 0.37            |
| BHandHLYP/co2-MOR           | 0.69            | 0.69            | 0.43            |
| Medium corrected             | 0.65            | 0.65            | 0.39            |
| Total                        | 1.00            | 0.78            | 0.46            |
| CCSD/co2                    | 0.57            | 0.57            | 0.34            |
| Medium corrected             | 0.53            | 0.53            | 0.31            |
| Total                        | 0.88            | 0.66            | 0.38            |
| CCSD/co2-MOR                | 0.72            | 0.72            | 0.45            |
| Medium corrected             | 0.68            | 0.68            | 0.41            |
| Total                        | 1.03            | 0.80            | 0.47            |

Table 1: Comparison of NSOR values from experiment and calculated from first principles using DFT (BHandHLYP functional) or coupled cluster (CCSD) methods and different basis sets. Correction factors for medium effects as well as additive correction for Faraday effect are listed. Medium corrected values correspond to medium correction only (eq 9) while Total values include the Faraday rotation. All values are in $\mu$rad / cm / mol dm$^3$. CCSD/co0 was not performed as the basis set is rather larger for this calculation.
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