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REGULAR ARTICLE

Electric field effects on nuclear spin–spin coupling tensors and chiral discrimination via NMR spectroscopy

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Abstract Nuclear magnetic resonance spectrometers presently available are unable to recognize the two mirror-image forms of a chiral molecule, because in the absence of a chiral solvent, the NMR spectral parameters (chemical shifts and spin–spin coupling constants) are identical for the two enantiomers. This paper discusses how chirality may nevertheless, at least in theory, be recognized in liquid-state NMR spectroscopy by applying strong d.c. electric fields and measuring a pseudoscalar contribution to nuclear spin–spin coupling polarizability. Calculations are reported for medium-size chiral molecules, (2R)-*N*-methyloxaziridine, (R_a)-1,3-dimethylallene, and (2R)-2-methyloxirane. The very small contributions provided by the pseudoscalar of nuclear spin–spin coupling polarizability seem rather difficult to detect via NMR experiments in disordered phase.

Keywords Chiral discrimination · Enantiomeric molecules in disordered phase · Nuclear magnetic resonance spectroscopy · Electric dipole polarizability of nuclear spin-spin coupling

1 Introduction

Nuclear magnetic resonance (NMR) spectroscopy cannot be directly used to determine the absolute configuration of chiral molecules in disordered media, as the chemical shifts and spin–spin coupling constants are exactly the same for the two enantiomers of a chiral molecule, if parity violation contributions [1–3] are neglected. Therefore, NMR spectral parameters are not suitable for chiral discrimination, that is, for the recognition of different enantiomers.

However, recent papers suggest that chirality could actually be observable in NMR spectroscopy through application of an electric field. The effect is in principle detectable via especially designed experimental setups [4–8]. The response properties involved are referred to as electric polarizability of the nuclear magnetic shielding and polarizability of the nuclear spin–spin coupling, [4, 5, 9] that is, third-rank tensors even under time-reversal and odd under parity, having components with the same magnitude but opposite sign for *D* and *L* enantiomers of a chiral species.

In crystal phase, all polarizability components are possibly observable. In liquid and gas phase, a $\overline{\sigma}_I^{(1)}$ pseudoscalar of the nuclear shielding polarizability of nucleus *I* in a molecule is defined via quantum mechanical methods [4].

Dedicated to Professor Pekka Pyykkö on the occasion of his 70th birthday and published as part of the Pyykkö Festschrift Issue.

Contribution to honor the scientific work and life of Prof. Pekka Pyykkö.

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As shown in Sect. 2, for two coupled nuclei I and J, $\overline{\mathcal{K}}^{(1)}_{IJ}$ pseudoscalars can also be defined by spatial averaging [10, 11] of these polarizabilities, much in the same way as the optical rotation pseudoscalar G' [12].

Both pseudoscalars vanish in achiral molecules and have equal but opposite values for the two enantiomers of a chiral molecule in disordered media. However, the small magnitude predicted for the ^{13}C,^{15}N, and ^{17}O pseudoscalars of nuclear magnetic shielding polarizability in some simple systems seems to preclude experimental detection via presently available NMR spectrometers [5–8].

More promising techniques have been suggested by Buckingham and Fischer via measurement of nuclear spin–spin coupling polarizability: a possible application could be to induce zero-quantum transitions by a time-dependent electric field $E_\alpha(t)$ oscillating at $|\omega(I) - \omega(J)|/2\pi$, that is, the difference of the Larmor precession frequencies of two coupled nuclei I and J [5].

The present preliminary investigation is aimed at estimating quantitatively the effect of a static homogeneous electric field on the average nuclear coupling constant in disordered phase for (2R)-2-methyloxirane, (R$_a$)-1,3-dimethylallene, and (2R)-*N*-methyloxaziridine. The paper is organized as follows: electric dipole polarizabilities of nuclear spin–spin coupling are defined in Sect. 2, the Ramsey Hamiltonians [13, 14] are reported in Sect. 3, and a computational procedure is outlined in Sect. 4. Details on calculation are given in Sect. 5, and the results are discussed in Sect. 6 in view of further investigations.

2 Electric dipole polarizability of the nuclear spin–spin coupling

Standard tensor notation is employed throughout this article, e.g., the Einstein convention of implicit summation over two repeated Greek subscripts is in force. The total energy of a molecule in the presence of intramolecular perturbations, i.e., the permanent magnetic dipoles $\mathbf{m}_I = \gamma_I \hbar \mathbf{I}_I$ and $\mathbf{m}_J = \gamma_J \hbar \mathbf{I}_J$, expressed via the magnetogyric ratios γ_I and γ_J and spins $\hbar \mathbf{I}_I$ and $\hbar \mathbf{I}_J$ of two nuclei I and J, and an external time-independent, spatially uniform electric field $\mathbf{E}$, is

$$W = W^{(0)} + m_{I_\alpha}\mathcal{K}^{I_\alpha J_\beta} m_{J_\beta} + m_{I_\alpha}\mathcal{K}^{I_\alpha J_\beta}_{\gamma} m_{J_\beta} E_\gamma + \cdots, \tag{1}$$

where

$$\mathcal{K}^{I_\alpha J_\beta} = \left.\frac{\partial^2 W}{\partial m_{I_\alpha}\partial m_{J_\beta}}\right|_{\mathbf{m}_I,\mathbf{m}_J,\mathbf{E}\to\mathbf{0}} \tag{2}$$

is the reduced nuclear spin–spin coupling, represented by a second-rank tensor. The polarizability of nuclear spin–spin coupling is a third-rank tensor, obtained as the third derivative of the energy, Eq. 1,

$$\mathcal{K}^{I_\alpha J_\beta}_{\gamma} = \left.\frac{\partial^3 W}{\partial m_{I_\alpha}\partial m_{J_\beta}\partial E_\gamma}\right|_{\mathbf{m}_I,\mathbf{m}_J,\mathbf{E}\to\mathbf{0}}. \tag{3}$$

Three response properties are defined via the coupling tensor, Eq. 2 and the polarizability, Eq. 3. The magnetic field induced at the I-th nucleus is

$$\mathcal{B}^n_{I_\alpha} = -\frac{\partial W}{\partial m_{I_\alpha}} = -\mathcal{K}^{I_\alpha J_\beta} m_{J_\beta} - \mathcal{K}^{I_\alpha J_\beta}_{\gamma} m_{J_\beta} E_\gamma + \cdots, \tag{4}$$

the electric dipole moment induced in the electron cloud is

$$\mathcal{M}_\gamma = -\frac{\partial W}{\partial E_\gamma} = -\mathcal{K}^{I_\alpha J_\beta}_{\gamma} m_{I_\alpha} m_{J_\beta} + \cdots, \tag{5}$$

and the electric-field-induced contribution to the spin–spin coupling is, to first order in E_α,

$$\mathcal{K}^{I_\alpha J_\beta (1)} = \mathcal{K}^{I_\alpha J_\beta}_{\gamma} E_\gamma. \tag{6}$$

In non-ordered media, it is convenient to introduce the average coupling constant $\mathcal{K}_{IJ} = (1/3)\mathcal{K}^{I_\alpha J_\alpha}$, and a pseudoscalar

$$\overline{\mathcal{K}}^{(1)}_{IJ} = \frac{1}{6}\epsilon_{\alpha\beta\gamma}\mathcal{K}^{I_\alpha J_\beta}_{\gamma}, \tag{7}$$

where $\varepsilon_{\alpha\beta\gamma}$ is the skew-symmetric Levi–Civita tensor. Therefore, $\mathcal{K}^{I_\alpha J_\beta}_{\gamma}$ has a chirally sensitive isotropic part $\epsilon_{\alpha\beta\gamma}\overline{\mathcal{K}}^{(1)}_{IJ}$. For an isotropic medium, one obtains

$$\boldsymbol{\mathcal{B}}^n_I = -\mathcal{K}_{IJ}\mathbf{m}_J - \overline{\mathcal{K}}^{(1)}_{IJ}\,\mathbf{m}_J \times \mathbf{E}, \tag{8}$$

$$\boldsymbol{\mathcal{M}} = -\overline{\mathcal{K}}^{(1)}_{IJ}\,\mathbf{m}_I \times \mathbf{m}_J, \tag{9}$$

for the magnetic field induced at nucleus I and the electric dipole induced in the electrons, respectively.

Equations 7–9 are strictly valid only for freely tumbling non-dipolar molecules in the presence of weak electric fields. Alignment with $\mathbf{E}$ occurring for chiral systems which possess an intrinsic electric dipole moment $\boldsymbol{\mathcal{M}}^{(0)}$ would require a different theoretical approach pursued in future investigations.

3 The Ramsey Hamiltonian

The notation adopted in Refs. [15–17] is used. For a molecule with n electrons and N nuclei, charge, mass, position, canonical, and angular momentum of the i-th electron are indicated by $-e, m_e, \mathbf{r}_i, \hat{\mathbf{p}}_i, \hat{\mathbf{l}}_i = \mathbf{r}_i \times \hat{\mathbf{p}}_i, i = 1, 2\ldots n$. Analogous quantities for nucleus I are $Z_I e, M_I, \mathbf{R}_I$, etc. N' nuclei are endowed with an intrinsic magnetic dipole $\mathbf{m}_I = \gamma_I \hbar \mathbf{I}_I$. The distance of electron i from nucleus I is $\mathbf{r}_{iI} \equiv \mathbf{r}_i - \mathbf{R}_I$, $\hat{\sigma}_{i\alpha}$ is a Pauli matrix, and $\mu_B = e\hbar/2m_e$ is the Bohr magneton. Capital letters are used for collective electronic operators, e.g., $\hat{\mathbf{R}} = \sum_{i=1}^{n} \mathbf{r}_i$, $\hat{\mathbf{P}} = \sum_{i=1}^{n} \hat{\mathbf{p}}_i$. SI units [18] are employed.

The non-relativistic Ramsey Hamiltonian accounts for the diamagnetic nuclear spin-electron orbit, paramagnetic nuclear spin-electron orbit, spin-dipolar, and Fermi contact terms [13, 14],

$$\hat{H}_{\mathrm{DSO}} = \left(\frac{\mu_0}{4\pi}\right)^2 \frac{e^2}{2m_e} \sum_{I,J\neq I}^{N'} m_{I_\alpha} \hat{\mathcal{U}}^n_{I_\alpha J_\beta} m_{J_\beta}, \tag{10}$$

$$\hat{H}_{\mathrm{PSO}} = -\sum_{I=1}^{N'} m_{I_\alpha} \hat{B}^n_{I_\alpha} = \frac{\mu_0}{4\pi} \frac{e}{m_e} \sum_{I=1}^{N'} m_{I_\alpha} \hat{M}^n_{I_\alpha}, \tag{11}$$

$$\hat{H}_{\mathrm{SD}} = \frac{\mu_0}{4\pi} \mu_B \sum_{I}^{N'} m_{I_\alpha} \hat{\mathcal{T}}^n_{I_\alpha}, \tag{12}$$

$$\hat{H}_{\mathrm{FC}} = \frac{2}{3} \mu_0 \mu_B \sum_{I=1}^{N'} m_{I_\alpha} \hat{\mathcal{F}}^n_{I_\alpha}, \tag{13}$$

where we have introduced the operators

$$\hat{\mathcal{U}}^n_{I_\alpha J_\beta} = \sum_{i=1}^{n} r_{iI}^{-3} r_{iJ}^{-3} \left(r_{iI_\gamma} r_{iJ_\gamma} \delta_{\alpha\beta} - r_{iJ_\alpha} r_{iI_\beta}\right), \tag{14}$$

$$\hat{\mathbf{M}}^n_I = \sum_{i=1}^{n} \frac{\mathbf{r}_{iI}}{r_{iI}^3} \times \hat{\mathbf{p}}_i, \tag{15}$$

$$\hat{\mathcal{T}}^n_{I_\alpha} = \sum_{i=1}^{n} \left[\left(3 r_{iI\alpha} r_{iI\beta} - r_{iI}^2 \delta_{\alpha\beta}\right) r_{iI}^{-5}\right] \hat{\sigma}_{i\beta}, \tag{16}$$

$$\hat{\mathcal{F}}^n_{I_\alpha} = \sum_{i=1}^{n} \delta(\mathbf{r}_{iI}) \hat{\sigma}_{i\alpha} \tag{17}$$

and where the operator for the magnetic field acting on the I-th nucleus by the orbital motion of n electrons is written as

$$\hat{\mathbf{B}}^n_I = -\frac{\mu_0}{4\pi} \frac{e}{m_e} \hat{\mathbf{M}}^n_I. \tag{18}$$

It is important to recall that recently Pyykkö published a short paper entitled "*Perspective on Norman Ramseys theories of NMR chemical shifts and nuclear spin–spin couplings*", where a concise and interesting assessment of the early development of the theory of high-resolution NMR parameters is given [14].

Within the Rayleigh–Schrödinger perturbation theory, the expressions for the contributions to the energy of a molecule in the reference electronic state $|a> \equiv \Psi_a^{(0)}$ through third order are

$$W_a^{(1)} = \left\langle a \middle| \hat{H}^{(1)} \middle| a \right\rangle, \tag{19}$$

$$W_a^{(2)} = \left\langle a \middle| \hat{H}^{(2)} \middle| a \right\rangle - \frac{1}{\hbar} \sum_{i\neq a} \omega_{ia}^{-1} \left\langle a \middle| \hat{H}^{(1)} \middle| i \right\rangle \left\langle i \middle| \hat{H}^{(1)} \middle| a \right\rangle, \tag{20}$$

$$\begin{aligned} W_a^{(3)} = {} & \frac{1}{\hbar^2} \sum_{i\neq a} \sum_{j\neq a} \omega_{ia}^{-1} \omega_{ja}^{-1} \left\langle a \middle| \hat{H}^{(1)} \middle| i \right\rangle \left\langle i \middle| \overline{\hat{H}^{(1)}} \middle| j \right\rangle \left\langle j \middle| \hat{H}^{(1)} \middle| a \right\rangle \\ & - \frac{2}{\hbar} \sum_{i\neq a} \omega_{ia}^{-1} \Re\left\{ \left\langle a \middle| \hat{H}^{(1)} \middle| i \right\rangle \left\langle i \middle| \hat{H}^{(2)} \middle| a \right\rangle \right\}, \end{aligned} \tag{21}$$

defining overlined fluctuation operators, e.g.,

$$\overline{\hat{H}^{(1)}} \equiv \hat{H}^{(1)} - \left\langle a \middle| \hat{H}^{(1)} \middle| a \right\rangle. \tag{22}$$

In the present paper, $\hat{H}^{(0)}$ is the Born–Oppenheimer unperturbed electronic Hamiltonian of a molecule, so that

$$\hat{H}^{(0)} |j\rangle = W_j^{(0)} |j\rangle$$

and

$$\omega_{ia} = \left(W_i^{(0)} - W_a^{(0)}\right)/\hbar,$$

the first-order perturbed Hamiltonian $\hat{H}^{(1)}$ corresponds to those in Eqs. 11–13, and the second-order Hamiltonian corresponds to Eq. 10. Molecular response properties can be described introducing the following general definitions for the propagators [19–21]

$$\{\hat{A}, \hat{B}\}_{-1} = \frac{2}{\hbar} \sum_{i\neq a} \omega_{ia}^{-1} \Re\{\langle a|\hat{A}|i\rangle \langle i|\hat{B}|a\rangle\} \equiv -\langle\langle A; B\rangle\rangle_{\omega=0}, \tag{23}$$

$$\begin{aligned} \{\hat{A}, \hat{B}, \hat{C}\}_{-2} = {} & \mathbf{S}(\hat{A}, \hat{B}, \hat{C}) \\ & \times \left(\frac{1}{\hbar^2} \sum_{j\neq a} \sum_{k\neq a} \omega_{ja}^{-1} \omega_{ka}^{-1} \langle a|\hat{A}|j\rangle \left\langle j \middle| \overline{\hat{B}} \middle| k \right\rangle \langle k|\hat{C}|a\rangle \right) \\ & \equiv \langle\langle A; B, C\rangle\rangle_{\omega,\omega'=0}. \end{aligned} \tag{24}$$

The symbol $\mathbf{S}(\ldots)$ implies a summation of the six terms arising on permuting the operators within brackets.

4 Computational scheme

The present paper is aimed at developing a computational procedure for calculating all components of nuclear spin–spin coupling polarizabilities, with particular emphasis on the $\overline{\mathcal{K}}_{IJ}^{(1)}$ pseudoscalar, Eq. 7, allowing for the relationships (Eqs. 19–24) within the framework of the Ramsey theory [13].

For computational purposes, it is expedient to rewrite the total electronic Hamiltonian for a molecule in the presence of an external electric field **E** and nuclear intrinsic magnetic dipoles, see Eqs. 10–13, in the form

$$\hat{H} = \hat{H}^{(0)} + \hat{H}^{E_\alpha} E_\alpha + \hat{H}^{m_{I_\alpha}} m_{I_\alpha}, \tag{25}$$

where first-order reduced Hamiltonians are specified by polar

$$\hat{H}^{E_\alpha} = e\hat{R}_\alpha, \tag{26}$$

and axial vector components

$$\hat{H}^{m_{I_\alpha}} = \hat{H}_\alpha^{(1a)} + \hat{H}_\alpha^{(1b)} + \hat{H}_\alpha^{(2)} + \hat{H}_\alpha^{(3)}, \tag{27}$$

so that the operators for the magnetic field of the electrons at the *I*-th nucleus are

$$\hat{\mathcal{B}}^n_{I_\alpha} = -\frac{\partial \hat{H}}{\partial m_{I_\alpha}} = \hat{\mathcal{B}}^{(1a)n}_{I_\alpha} + \hat{\mathcal{B}}^{(1b)n}_{I_\alpha} + \hat{\mathcal{B}}^{(2)n}_{I_\alpha} + \hat{\mathcal{B}}^{(3)n}_{I_\alpha}. \tag{28}$$

Employing relationships (14)–(17) and the established nomenclature of Ramsey [13] and Pyykkö [14], the perturbing first-order Hamiltonians in Eq. 27 are specified by the operators

$$\hat{H}_\alpha^{(1a)} = \left(\frac{\mu_0}{4\pi}\right)^2 \frac{e^2}{m_e} \sum_{J \neq I}^{N'} \hat{\mathcal{U}}^n_{I_\alpha J_\beta} m_{J_\beta} \equiv -\hat{\mathcal{B}}^{(1a)n}_{I_\alpha}, \tag{29}$$

$$\hat{H}_\alpha^{(1b)} = -\hat{B}^n_{I_\alpha} \equiv -\hat{\mathcal{B}}^{(1b)n}_{I_\alpha}, \tag{30}$$

$$\hat{H}_\alpha^{(2)} = \frac{\mu_0}{4\pi} \mu_B \hat{\mathcal{T}}^n_{I_\alpha} \equiv -\hat{\mathcal{B}}^{(2)n}_{I_\alpha}, \tag{31}$$

$$\hat{H}_\alpha^{(3)} = \frac{2}{3} \mu_0 \mu_B \hat{\mathcal{F}}^n_{I_\alpha} \equiv -\hat{\mathcal{B}}^{(3)n}_{I_\alpha}, \tag{32}$$

which are related respectively to the diamagnetic nuclear spin- electron orbit, paramagnetic nuclear spin-electron orbit, spin-dipolar, and Fermi contact terms [13].

Allowing for Eqs. 1, 2, 19, 20, 23, and 29–32, the contributions to the reduced coupling tensors can be recast in the form

$$\mathcal{K}^{(1a)I_\alpha J_\beta} = \left(\frac{\mu_0}{4\pi}\right)^2 \frac{e^2}{m_e} \left\langle a \middle| \hat{\mathcal{U}}^n_{I_\alpha J_\beta} \middle| a \right\rangle, \tag{33}$$

$$\mathcal{K}^{(1b)I_\alpha J_\beta} = -\left(\frac{\mu_0}{4\pi}\right)^2 \left(\frac{e}{m_e}\right)^2 \left\{ \hat{M}^n_{I_\alpha}, \hat{M}^n_{J_\beta} \right\}_{-1}, \tag{34}$$

$$\mathcal{K}^{(2)I_\alpha J_\beta} = -\left(\frac{\mu_0}{4\pi}\right)^2 \mu_B^2 \left\{ \hat{\mathcal{T}}^n_{I_\alpha}, \hat{\mathcal{T}}^n_{J_\beta} \right\}_{-1}, \tag{35}$$

$$\mathcal{K}^{(3)I_\alpha J_\beta} = -\left(\frac{2\mu_0\mu_B}{3}\right)^2 \left\{ \hat{\mathcal{F}}^n_{I_\alpha}, \hat{\mathcal{F}}^n_{J_\beta} \right\}_{-1}, \tag{36}$$

$$\mathcal{K}^{(4)I_\alpha J_\beta} = -\frac{\mu_0^2 \mu_B^2}{6\pi} \left(\left\{ \hat{\mathcal{T}}^n_{I_\alpha}, \hat{\mathcal{F}}^n_{J_\beta} \right\}_{-1} + \left\{ \hat{\mathcal{F}}^n_{I_\alpha}, \hat{\mathcal{T}}^n_{J_\beta} \right\}_{-1} \right). \tag{37}$$

From Eqs. 3, 21, and 24, the contribution of the DSO, PSO, SD, Fermi, and Fermi/spin-dipolar cross terms to the polarizability are, respectively,

$$\mathcal{K}_\gamma^{(1a)I_\alpha J_\beta} = -\left(\frac{\mu_0}{4\pi}\right)^2 \frac{e^3}{m_e} \left\{ \hat{\mathcal{U}}^n_{I_\alpha J_\beta}, \hat{R}_\gamma \right\}_{-1} \tag{38}$$

$$\mathcal{K}_\gamma^{(1b)I_\alpha J_\beta} = \left(\frac{\mu_0}{4\pi}\right)^2 \frac{e^3}{m_e^2} \left\{ \hat{M}^n_{I_\alpha}, \hat{M}^n_{J_\beta}, \hat{R}_\gamma \right\}_{-2}, \tag{39}$$

$$\mathcal{K}_\gamma^{(2)I_\alpha J_\beta} = \left(\frac{\mu_0}{4\pi}\right)^2 \mu_B^2 e \left\{ \hat{T}^n_{I_\alpha}, \hat{T}^n_{J_\beta}, \hat{R}_\gamma \right\}_{-2}, \tag{40}$$

$$\mathcal{K}_\gamma^{(3)I_\alpha J_\beta} = \left(\frac{2\mu_0\mu_B}{3}\right)^2 e \left\{ \hat{F}^n_{I_\alpha}, \hat{F}^n_{J_\beta}, \hat{R}_\gamma \right\}_{-2}, \tag{41}$$

$$\mathcal{K}_\gamma^{(4)I_\alpha J_\beta} = \frac{\mu_0^2 \mu_B^2 e}{6\pi} \left(\left\{ \hat{\mathcal{T}}^n_{I_\alpha}, \hat{\mathcal{F}}^n_{J_\beta}, \hat{R}_\gamma \right\}_{-2} + \left\{ \hat{\mathcal{F}}^n_{I_\alpha}, \hat{\mathcal{T}}^n_{J_\beta}, \hat{R}_\gamma \right\}_{-2} \right). \tag{42}$$

The Fermi contribution is isotropic and the Fermi/spin-dipolar cross contribution is symmetric in the indices α and β, as it is evident from Eqs. 36 and 37. Whereas spin–spin coupling polarizability tensor components can be defined for all the Ramsey mechanisms, only the terms Eqs. 38, 39, and 40 contribute to the pseudoscalar $\overline{\mathcal{K}}^{(1)}_{IJ}$ defined via Eq. 7.

The reduced coupling constants are related to the $J^{I_\alpha J_\beta}$ tensor and to the average value $J^{IJ} = (1/3) J^{I_\alpha J_\alpha}$ commonly expressed in hertz by

$$\mathcal{K}^{I_\alpha J_\beta} = 4\pi^2 \frac{J^{I_\alpha J_\beta}}{h\gamma_I \gamma_J}. \tag{43}$$

Analogous relationships hold for the coupling polarizability

$$\mathcal{K}_\gamma^{I_\alpha J_\beta} = 4\pi^2 \frac{J_\gamma^{I_\alpha J_\beta}}{h\gamma_I \gamma_J}, \tag{44}$$

and for the $\overline{\mathcal{K}}^{(1)}_{IJ}$ pseudoscalar Eq. 7,

$$\overline{\mathcal{K}}^{(1)}_{IJ} = 4\pi^2 \frac{\overline{\mathcal{J}}^{(1)}_{IJ}}{h\gamma_I \gamma_J}. \tag{45}$$

5 Details of calculation

The B3LYP [22–25], KT3 [26, 27] and PBE [28] functionals of density functional theory (DFT) implemented in the DALTON code [29] were used in the calculations on three molecules, (R$_a$)-1,3-dimethylallene, (2R)-2-methyloxirane, and (2R)-*N*-methyloxaziridine, whose nuclear magnetic shielding polarizabilities had previously been estimated theoretically [6].

Molecular geometries were optimized at the B3LYP/6-31G** level of theory by the GAUSSIAN03 code [30]. Response tensors were calculated using four basis sets of

Gaussian functions: B1 ≡ 6-31G** available in GAUSSIAN03; [30] B2, from Sadlej; [31] B3 ≡ aug-cc-pVTZ from Dunning and Woon [32, 33]. The uncontracted (13s/8p//10s) substratum of the B4 basis set taken from the van Duijneveldt compilation [34] for C,O,N//H was augmented with two s functions and four 3d functions on the heavier atoms, and three 2p functions on H, see Supplementary Information Available (SIA) for details useful to reproduce our calculations.

B2 basis sets have been developed for accurate theoretical estimates of electric polarizabilities [31]. Their value for calculating also nuclear magnetic shielding polarizabilities and corresponding pseudoscalars has been recognized in a recent paper [6], proving that a good description of molecular tail regions via diffuse polarization functions is a fundamental requirement. B3 aug-cc-pVTZ basis sets [32, 33] are explicitly meant to account for electron correlation effects. The extended B4 basis sets have also been successfully tested to predict near Hartree–Fock values of nuclear magnetic shielding pseudoscalars [6]. Since we are only interested in the $\overline{\mathcal{J}}_{IJ}^{(1)}$ pseudoscalars that have no contribution from the Fermi contact term, we do not need to employ basis sets optimized for the calculation of the Fermi contact term such as the aug-cc-pVTZ-J, pcJ-n, or ccJ-pVXZ series of basis sets [35–41].

6 Discussion of results, concluding remarks, and outlook

Calculated nuclear spin–spin coupling constants $J^{IJ} = (1/3)J^{I_\alpha J_\alpha}$, expressed in hertz, and pseudoscalars $\overline{\mathcal{J}}_{IJ}^{(1)}$, expressed in hertz a.u., see relationships Eqs. 7, and 43–45, are reported in Tables 1, 2, 3, 4, 5 and 6. Allowing for the CODATA compilation [18], 1 a.u. of electric field $E_h/ea_0 = 5.142\,206\,42(44) \times 10^{11}$ V m^{-1}, the conversion factor from hertz a.u. to SI units is $1.944\,690\,51 \times 10^{-12}$ m V^{-1}.

As recalled in Sect. 4, only Ramsey's DSO, PSO, and SD terms contribute to the $\overline{\mathcal{J}}^{1}_{IJ}$ pseudoscalars. It can be observed from computed values in Tables 1, 2, 3, 4, 5, 6 that (a) the PSO contributions to the $\overline{\mathcal{J}}_{IJ}^{(1)}$ are in general bigger than DSO and SD, (b) contributions from different mechanisms have sometimes different signs.

The dependence of calculated $\overline{\mathcal{J}}_{IJ}^{(1)}$ pseudoscalars on basis set quality was preliminarily tested for (2R)-*N*-methyloxaziridine, using B1–B4 basis sets. The B1 ≡ 6-31G** is insufficiently flexible to evaluate the PSO contributions, as can be seen in Table 1, showing a wrong sign for the pseudoscalar of the C_1–O_1 coupling (−0.47 Hz a.u.) and a calculated value (1.42 Hz a.u.) for the pseudoscalar of the C_1–N_1 coupling smaller than that obtained by basis sets B2–B4. The results from these basis sets (≈ 2.2–2.5 Hz a.u.) are very close to one another and probably close to the limit of the B3LYP level of accuracy. A similar conclusion is obtained for the SD contributions for the C_1–O_1 and C_1–N_1 couplings.

Analogous tests were carried out for the (R_a)-1,3-dimethylallene, and (2R)-2-Methyloxirane molecules using only bigger-size basis sets B2–B4, see Tables 2 and 3, respectively. Calculated $\overline{\mathcal{J}}_{IJ}^{(1)}$ values from B3 and B4 basis sets are fairly stable and arguably close to the limit attainable at the B3LYP level. However, the smaller-sized B2 Sadlej basis set, developed ad hoc for polarizabilities

Table 1 Calculated B3LYP contributions to the $\overline{\mathcal{J}}_{IJ}^{(1)}$ pseudoscalar in (2R)-*N*-methyloxaziridine from four basis sets

Nuclei[a]	Contribution	B1	B2	B3	B4
C_1–C_2	DSO	0.00	0.00	0.00	0.00
	PSO	−0.64	−0.68	−0.87	−0.88
	SD	−0.05	−0.02	−0.02	−0.03
C_1–O_1	DSO	0.00	0.00	0.00	0.00
	PSO	−0.47	0.57	0.69	0.74
	SD	−0.50	−0.40	−0.42	−0.43
C_1–N_1	DSO	0.00	0.0	0.00	0.00
	PSO	1.42	2.18	2.40	2.50
	SD	−0.33	−0.43	−0.46	−0.48

In Hz au. Conversion factor to SI units: $1.944\,690\,51 \times 10^{-12}$ m V^{-1}

[a] See Fig. 1 for the labels of the nuclei

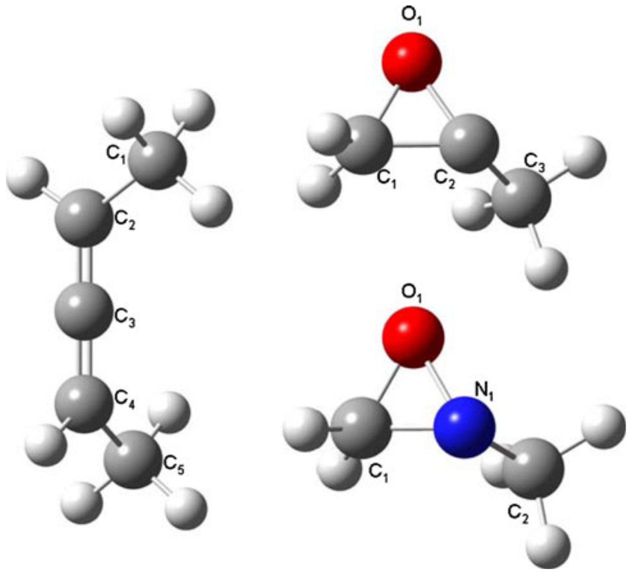

Fig. 1 (R_a)-1,3-dimethylallene, (2R)-2-methyloxirane, and (2R)-*N*-methyloxaziridine

Table 2 Calculated B3LYP contributions to the $\overline{\mathcal{J}}^{(1)}_{IJ}$ pseudoscalar in (R_a)-1,3-dimethylallene from three basis sets

Nuclei[a]	Contribution	B2	B3	B4
C_1–C_3	DSO	0.00	0.00	0.00
	PSO	0.01	0.00	0.00
	SD	0.00	0.00	0.00
C_1–C_5	DSO	0.00	0.00	0.00
	PSO	−0.37	−0.40	−0.42
	SD	0.03	0.03	0.03
C_3–C_5	DSO	0.00	0.00	0.00
	PSO	0.04	0.05	0.05
	SD	−0.02	−0.01	−0.01

In Hz au. See Table 1 for the conversion factor to SI units

[a] See Fig. 1 for the labels of the nuclei

Table 3 Calculated B3LYP contributions to the $\overline{\mathcal{J}}^{(1)}_{IJ}$ pseudoscalar in (2R)-2-Methyloxirane from three basis sets

Nuclei[a]	Contribution	B2	B3	B4
C_1–C_2	DSO	0.00	0.00	0.00
	PSO	−1.62	−1.76	−1.81
	SD	0.21	0.27	0.26
C_1–O_4	DSO	0.00	0.00	0.00
	PSO	1.54	1.67	1.72
	SD	0.23	0.23	0.23
C_1–C_3	DSO	0.00	0.00	0.00
	PSO	−1.07	−1.29	−1.31
	SD	0.10	0.13	0.08

In Hz au. See Table 1 for the conversion factor to SI units

[a] See Fig. 1 for the labels of the nuclei

Table 4 Contributions to the J^{IJ} isotropic nuclear spin–spin coupling constants and to the $\overline{\mathcal{J}}^{(1)}_{IJ}$ pseudoscalars of (2R)-*N*-methyloxaziridine calculated by the B2 basis set via three DFT functionals

Nuclei[a] DFT method	Contribution	J^{IJ}[b] B3LYP	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c] B3LYP	J^{IJ}[b] KT3	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c] KT3	J^{IJ}[b] PBE	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c] PBE
C_1–C_2	DSO	−0.04	0.00	−0.04	0.00	−0.04	0.00
	PSO	−0.20	−0.68	−0.19	−0.51	− 0.20	−0.66
	SD	−0.03	−0.02	−0.02	−0.02	−0.03	−0.02
	FC	−1.89	–	−2.80	–	−2.55	–
C_1–O_1	DSO	−0.10	0.00	−0.10	0.00	−0.10	0.00
	PSO	0.43	0.57	0.35	1.15	0.26	0.91
	SD	0.05	−0.40	0.09	−0.42	0.09	−0.51
	FC	27.26	–	28.13	–	28.00	–
C_1–N_1	DSO	−0.09	0.00	−0.09	0.003	−0.09	0.00
	PSO	0.58	2.18	0.50	1.78	0.48	2.19
	SD	0.27	−0.43	0.28	−0.39	0.29	−0.42
	FC	4.88	–	7.09	–	5.95	–
O_1–N_2	DSO	0.04	0.00	0.04	0.00	0.04	0.00
	PSO	4.97	−4.47	4.33	−4.47	4.63	−4.46
	SD	2.08	−0.68	2.06	−0.95	2.00	−0.75
	FC	−16.04	–	−14.59	–	−16.71	–

[a] See Fig. 1 for the labels of the nuclei

[b] In Hz

[c] In Hz au

Table 5 Contributions to the J^{IJ} isotropic nuclear spin–spin coupling constants and to the $\overline{\mathcal{J}}^{(1)}_{IJ}$ pseudoscalars of (R_a)-1,3-dimethylallene calculated by the B2 basis set via three DFT functionals

Nuclei[a] DFT method	Contribution	J^{IJ}[b] B3LYP	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c] B3LYP	J^{IJ}[b] KT3	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c] KT3	J^{IJ}[b] PBE	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c] PBE
C_1–C_3	DSO	0.17	0.00	0.17	0.00	0.18	0.00
	PSO	−0.85	0.01	−0.85	−0.02	−0.86	−0.02
	SD	0.69	0.00	0.61	0.02	0.62	0.01
	FC	46.61	–	38.62	–	44.44	–
C_3–C_5	DSO	0.18	0.01	0.18	0.01	0.18	0.01
	PSO	−7.76	0.04	−7.00	−0.06	−7.39	0.06
	SD	3.53	−0.02	3.19	−0.02	3.54	−0.02
	FC	118.5	–	106.6	–	115.9	–
C_1–C_5	DSO	−0.04	0.00	−0.04	0.00	−0.04	0.00
	PSO	−0.13	−0.37	−0.14	−0.37	−0.14	−0.37
	SD	0.04	0.03	0.05	0.03	0.07	0.03
	FC	−0.08	–	−0.38	–	−1.83	–
H_6–C_3	DSO	0.82	−0.01	0.82	−0.02	0.83	−0.02
	PSO	0.38	−0.09	0.34	−0.11	0.40	−0.11
	SD	0.14	−0.05	0.20	−0.06	0.22	−0.05
	FC	153.6	–	158.1	–	155.6	–

[a] See Fig. 1 for the labels of the nuclei

[b] In Hz

[c] In Hz au

[31], yields pseudoscalar values of the same magnitude as B3 and B4, and it seems to offer the best compromise between quality of results and computer expense. Its use in further calculations on bigger molecules is recommended.

The sensitivity of calculated $\overline{\mathcal{J}}^{(1)}_{IJ}$ values to the type of DFT functional was studied for the Sadlej basis set [31]. The results are reported in Tables 4, 5 and 6. It can be observed that the SD contributions to the pseudoscalar arrived at via B3LYP, KT3, and PBE functionals are very close to one another. PSO contributions are slightly more affected, as illustrated by the results for the C_1–O_1 coupling in Table 4.

The largest value $\overline{\mathcal{J}}^{(1)}_{IJ} \approx -5.2$ Hz au, obtained by summing DSO and PSO contributions (reported in Table 4) via the B3LYP calculation for the O–N coupling in (2R)-*N*-methyloxaziridine, corresponds to $\approx \pm 1.0 \times 10^{-11}$ Hz m V^{-1} for the *D* and *L* enantiomers. Therefore, a huge static homogeneous electric field, as big as $\approx 1.0 \times 10^{9}$ V m^{-1}, should be applied to observe a change with magnitude $\approx 1.0 \times 10^{-2}$ Hz in the coupling constant between the oxygen and nitrogen nuclei in (2R)-*N*-methyloxaziridine.

Table 6 Contributions to the J^{IJ} isotropic nuclear spin–spin coupling constants (in hertz) and to the $\overline{\mathcal{J}}^{(1)}_{IJ}$ pseudoscalars (in hertz a.u.) of (2R)-2-Methyloxirane calculated by the B2 basis set via three DFT functionals

Nuclei[a]	Contribution	J^{IJ}[b]	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c]	J^{IJ}[b]	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c]	J^{IJ}[b]	$\overline{\mathcal{J}}^{(1)}_{IJ}$[c]
DFT method		B3LYP	B3LYP	KT3	KT3	PBE	PBE
C_1–C_2	DSO	0.22	0.00	0.22	0.00	0.22	0.00
	PSO	−0.68	−1.62	−0.63	−1.46	−0.60	−1.63
	SD	−0.51	0.21	−0.49	0.19	−0.52	0.21
	FC	30.05	–	23.54	–	28.48	–
C_3–C_1	DSO	−0.04	0.00	−0.04	0.00	−0.04	0.00
	PSO	−0.09	− 1.07	−0.09	−1.00	− 0.09	−1.13
	SD	−0.01	0.10	−0.01	0.10	−0.02	0.12
	FC	−0.21	–	−0.51	–	−0.74	–
C_2–C_3	DSO	0.22	0.00	0.22	0.00	0.22	0.00
	PSO	−0.97	−0.04	−0.98	−0.01	−1.00	−0.05
	SD	0.81	−0.11	0.72	−0.03	0.76	0.12
	FC	45.78	–	36.61	–	42.87	–
C_1–C_4	DSO	−0.09	0.00	−0.09	0.00	-0.09	0.00
	PSO	−0.72	1.54	−0.74	1.68	−0.81	1.63
	SD	−0.29	0.23	− 0.27	0.16	− 0.26	0.19
	FC	29.39	–	30.29	–	30.61	–
H_1–C_2	DSO	1.09	0.00	1.09	0.00	1.11	0.00
	PSO	−0.34	0.04	−0.39	0.04	−0.35	0.05
	SD	0.07	0.01	0.11	−0.01	0.15	−0.01
	FC	163.7	–	167.9	–	165.0	–
H_1–C_3	DSO	0.68	0.00	0.67	0.00	0.69	0.00
	PSO	0.78	−0.03	0.69	−0.03	0.80	−0.03
	SD	−0.02	0.00	0.01	0.00	0.03	0.00
	FC	120.9	–	120.28	–	121.1	–

[a] See Fig. 1 for the labels of the nuclei

[b] In Hz

[c] In Hz au

Such an experiment is far beyond the present capabilities of a laboratory for the molecules considered. On the other hand, application of very strong electric fields would align polar molecules, which makes inappropriate the procedure based on the isotropic average Eqs. 7 and 45.

Although the effect may possibly be detected in other chiral systems with ad hoc characteristics, e.g., bigger-size, low-lying states, large amplitude of excited states (observe in relationships Eqs. 20 and 21 the ω_{ja} in the denominator), the present study suggests that the static $\overline{\mathcal{J}}^{(1)}_{IJ}$ pseudoscalar is not suitable for routine chiral discrimination via NMR spectroscopy in non-ordered phase.

It was found that calculated pseudoscalars are generally smaller, and sometimes much smaller, than the six individual components of the coupling polarizability tensor from which they have been obtained by contraction with the Levi–Civita antisymmetric tensor, according to the definition, Eq. 7. The terms of this sum have different sign, typically three positive and three negative, so that partial cancelation takes place. For instance, the components of the PSO contribution to the N–O coupling polarizability in (2R)-*N*-methyloxaziridine from the B3LYP calculation, in Hz a.u., are $xyz = 6.125$, $xzy = 27.466$, $yzx = 13.121$, $yxz = 0.889$, $zxy = 17.973$, $zyx = 35.711$, and then the PSO contribution to the pseudoscalar is $(1/6)(xyz - xzy + yzx - yxz + zxy - zyx) = -4.475$.

This behavior resembles that usually observed in the calculation of the optical rotatory power tensor (characterized by small trace and big diagonal components of different sign) [42]. A similar case is that of the pseudoscalar of nuclear shielding polarizability [6].

Therefore, chiral discrimination may preferably be attempted by NMR spectroscopy in ordered (crystal) and partially ordered (liquid crystal) phase, by measuring the electric-field-induced change of individual components of nuclear coupling polarizability. Candidates characterized by big $\mathcal{K}^{I_\alpha J_\beta}_{\gamma}$ components are presently being sought.

An alternative means of observing chiral effects in NMR for a probe in the presence of a.c. electric fields oscillating at $|\omega(I) - \omega(J)|/2\pi$, i.e., the difference of the Larmor frequencies of the coupled nuclei I and J, suggested by Buckingham [4], will be investigated in a future study.

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